This progress report summarises the academic and clinical activities of the Unit during the two last academic years, 2011/12 and 2012/13.

Background summary

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 (initially The Edmond J. Safra Chair), and as Honorary Consultant Neurosurgeon at the National Hospital for Neurology and Neurosurgery (NHNN). From 1st October 2012, the Chair was formally named as The Simon Sainsbury Chair of Functional Neurosurgery in recognition of the support and further funding from the Monument Trust.

The Unit is dedicated to the treatment of patients with Parkinson’s disease and other movement and brain disorders, mainly using Deep Brain Stimulation (DBS), a surgical technique to modulate 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 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 National Hospital for Neurology and Neurosurgery (NHN): in particular the operating theatres, the wards, and the Advanced Neuroimaging Suite with Interventional Surgical MRI.

The Unit occupies the entire 2nd floor, housed in same building as the clinical research teams in the areas of Parkinson’s disease and human movement and balance, and epilepsy, together with the outpatient facilities for patients attending with those neurological conditions, and the Lecture theatre in the basement.

Current Staff

Professor Marwan Hariz, MD, PhD (Simon Sainsbury Chair of Functional Neurosurgery)
Professor Patricia Limousin*, MD, PhD (Consultant Neurologist)
Professor Marjan Jahanshahi, PhD (Consultant Neuropsychologist)
Mr Ludvic Zrinzo*, MD PhD FRCS (Clinical Senior Lecturer and Consultant in Neurosurgery)
Dr Thomas Foltynie, MRCP PhD (Clinical Senior Lecturer and Honorary Consultant Neurologist)
Dr Elina Tripoliti, PhD (Speech Therapist)
Mr Joseph Candelario (Movement Disorder Specialist Nurse)
Ms Catherine Milabo (Movement Disorder Specialist Nurse)
Ms Linda Taib (PA to Professor Hariz and secretary to the Unit)
Ms Debbie Phillips (PA and secretary to Drs Foltynie, Limousin and Zrinzo)
Mrs. Sivagini Puvichandran (secretary to Drs Foltynie, Limousin and Zrinzo)

Fellows and students 2011- 2013

Dr. Francesca Preda (Neurologist, clinical research fellow)
Dr Katerina Aggeli (Neurologist, Visiting Research Associate)
Mr. Ignacio Obeso (Psychology PhD obtained 2013)
Mr Mazda Beigi (Psychology PhD obtained 2013)
Dr. Louise McDonald (Psychology, post-doc)
Ms Mariam Torkamani (Psychologist, research fellow)
Ms Agata Ryterska (Psychology, PhD student)
Dr. Iciar Aviles-Olmos (Neurologist, PhD student)
Dr. Zinovia Kefalopolou (Neurology post-doc clinical research fellow)
Mr Joshua Kahan (Research fellow, PhD student)
Dr James Gratwicke (Research fellow, PhD student)
Mr. Harith Akram (Neurosurgeon, Specialist registrar, PhD student)
Dr. Isabelle Sastre (Neurologist, PhD student)
Dr. André Zacharia (Neurologist, PhD student)
Dr. Rania Kalliolia (Neurologist, clinical research fellow)
Dr. Zuzana Kosutzka (Neurologist, clinical research fellow)
MSc students and other visiting fellows: Wisdom Young, Bobby Sachdev, Erica Tirr, Fahid Rasul, Feyi Taiwo, Hannah Brooke-Ball, Yasir Chowdhury, Dr Adrian Zammit, Ines Pote, Catherine Cheung, Dr Tomas Nicolai, Dr. Michel Lefranc, Dr. Pedro de la Rosa, Dr Pedro Roldan, Isobel Williams, Tomas Nicolai, Josh Pepper.

*We were delighted to record the appointment of Dr Ludvic Zrinzo to the post of Clinical Senior Lecturer from 1st February 2012, and the promotion of Dr Patricia Limousin to a Personal Chair as Professor in Clinical Neurology from 1st October 2013.

Clinical Activity

To date, a total of 442 patients have undergone surgery in the Unit, with over 700 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, cluster headache, and obsessive compulsive disorders. New indications and new brain targets for DBS are being investigated within framework of scientific trials (please see more below). The success rate of the Unit
remains very good, and the safety of the procedures remains excellent without fatality, brain haemorrhage or paralysis occurring in any patient.

Since the summer of 2011, all surgeries for DBS have been performed in the Interventional Surgical MRI (iMRI) suite. This move has facilitated more rapid surgery, avoiding the need for patient transfer between MRI and theatres. Together with important advances in our surgical technique, this has permitted the doubling of the number of patients operated. Two patients may now undergo primary DBS implantation in one day, instead of one patient as was the case in the past (and is still the case in most other other DBS services around the world). In addition to this increase in workflow, clinical demand is such that we have also added an extra theatre day on alternate weeks to allow an additional two to three new patients to undergo surgery each month.

The techniques developed in London have been successfully applied abroad. For example in Malta, where a member of the Unit has established a novel DBS service. This technique, based on image-guided and image-verified surgery, is also now being implemented in other large centres worldwide, in particular in the US.

**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 patients, and to extend this therapy to other functional brain disorders. Additionally, translational research projects with external collaborators are aimed at 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, neurorehabilitation, neuroengineering, and nano-technology.

**The principal research aims are to:**

- Better understand how DBS works and what it affects, through the use of tractography, functional MRI, recording of local field potentials, Magnetoencephalography (MEG) and Transcranial Magnetic Stimulation (TMS).
- Improve the visualisation on imaging and targeting 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.
- Exploration and studies of gender-related aspects in patients with movement disorders.
- 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.
• 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.
• Generation of predictive models utilising multimodal imaging techniques for the assessment of response to deep brain stimulator surgery in corresponding surgical cohorts.
• PROBAND study “Parkinson’s Repository of Biosamples and Networked Datasets”.
• 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 computerised platform improve the care of patients with Parkinson’s disease and dementia at home, to 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

• Multicentre (UK) trial of DBS for Tourette’s syndrome
  This trial, led by UCL and also recruiting in Salford, has successfully recruited, implanted and followed up ten patients, with a further six patients identified and planned for surgery during 2013-2014.
• Efficacy of DBS in cases of severe OCD
  A project with the aim of establishing the potential and efficacy of DBS for people with severe obsessive-compulsive disorder (OCD), is funded through an MRC Experimental Medicine grant award. 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.
• Single-centre UK trial of DBS for the cognitive deficits associated with Parkinson’s disease.
  This trial is exploring the Nucleus Basalis of Meynert as a possible target for DBS, and has opened to recruitment.
• Multicentre (UK) trial of DBS for cognitive deficits associated with Lewy Body Dementia.
  This trial will be run across two NIHR Biomedical Research Centres (UCL and Newcastle).
• 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).

• Exenatide as a treatment for Parkinson’s disease. Pilot trial completed 2012, leading to larger double blind placebo controlled trial due to open to recruitment from Dec 2013.

• Intraduodenal delivery of levodopa in a European multicentre trial was completed in 2013.

• New DBS applications and new brain targets for DBS

• 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

• PPN DBS in Parkinson’s disease and PSP

Grant Awards 2011-2013

Cure Parkinson’s Trust “A Prospective Evaluation of Exendin-4 (Exenatide) in the treatment of Parkinson’s Disease- a pilot study”. Extension study £50,000. (Foltynie)

MRC. “DBS for Obsessive Compulsive Disorder. Efficacy and mechanisms of ventral striatum and subthalamic nucleus targets”. £302,000 (Joyce, Hariz, Foltynie, Limousin, Jahanshahi, Zrinzo)

Brain Research Trust: “Advanced neuroimaging techniques to improve safety and efficacy in patients undergoing Deep Brain Stimulation” £250,000 2013-2016 (Zrinzo, Hariz, Foltynie, Limousin)

European Union- FP7. “Neural Transplantation in the treatment of patients with Parkinson’s disease”. Foltynie: UCL Principal Investigator €316,000. 2010-2016 (Chief Investigator Dr Roger Barker €11.7m)

Michael J Fox Foundation- “A randomised, double blind, placebo controlled, single centre, trial of Exenatide for the treatment of moderate severity Parkinson’s disease”. (Foltynie, Limousin) $1,980,000.


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 (Neurophysiology); University of Cambridge (Transeuro); as well as with the group of Professor Kostas Kostarelos, Chair of Nanomedicine, Centre for Drug Delivery Research, UCL School of Pharmacy. International collaboration includes Swedish Universities of Umea
(neurosurgery for neuropsychiatric illnesses); Lund (cell therapy for PD); and Linköping (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 thalamotomy 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 and PhD students, as well as acting as invited faculty to national and international meetings, conferences and workshops. In the past year, some forty-five invitations were extended to the PIs in the Unit to meetings in the UK and abroad. Additionally, the Unit has continued to have a record number of visitors from abroad: neurologists, neurosurgeons, neuropsychologists, occupational therapists, physicists, specialist nurses, medical students, industry representatives, and school pupils – for observing and learning.

- Prof Limousin & Dr Foltynie lecture on the Queen Square short course in Movement Disorders.
- Dr Zrinzo is Course Director on the ECMT international course for Image-guided DBS surgery
- Prof Hariz, Prof Limousin and Dr Foltynie 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 the UK, Sweden, France, Norway, The Netherlands, and Italy.

**Clinical Worldwide Impact**

The clinical research of the Functional Neurosurgery Unit has led to improvements in the operative technique of Deep Brain Stimulation with clear and demonstrable impact on patient outcomes with respect to efficacy, safety, and adverse event profiles. Since our published data was described by an independent editorial as a new “Benchmark for Functional Neurosurgery”, several centres worldwide are now using the surgical technique developed in the Unit, and that has resulted in an unmatched safety record while allowing an exponential increase in the number of operations and patient referrals. Demands on training and education are also increasing from international colleagues who wish to come and learn in order to disseminate our practice in their centres.

**10th Anniversary Celebration**

A celebration to mark the 10th Anniversary of the establishment of the Chair and Unit was held at Queen Square on 10th October 2012. Presentations by Professors Richard Frackowiak, Roger Lemon, Mike Hanna, and the Provost of UCL, Professor Sir Malcolm Grant, outlined the work of the Unit as a model of teamwork across disciplines, implementing translational research with proven, positive impact on patient care. Professor Hariz gave an overview of the history of the Unit and its achievements.
Guests included the individuals and representatives of the organisations who had supported and funded the Chair and the Unit over the past ten years; in particular, Lyn Rothman of the Parkinson’s Appeal, and Stewart Grimshaw and Trustees of the Monument Trust. In addition, there was senior representation from Parkinson’s UK, Brain Research Trust, Cure Parkinson’s Trust, Dystonia Society and the European Parkinson’s Disease Association, together with several patients who had been among the first to be operated when the Unit was first established.

We were delighted at the announcement during the ceremony that the Chair had been named The Simon Sainsbury Chair of Functional Neurosurgery from 1st October 2012, in recognition of the long-standing support and further new grant funding of £1.25m from the Monument Trust.

Third International Workshop

The third Queen Square International Workshop on Functional Neurosurgery took place on 11th and 12th October 2012. The Meeting was oversubscribed, with significant worldwide participation.

This meeting was quite innovative combining the topics of basic science and imaging with that of Deep Brain Stimulation (DBS) as well as Lesional Surgery for movement disorders, pain, and psychiatry; with the introduction of Ethics as a major issue needing to be adequately addressed as research in this field advances. Talks from leading international figures were punctuated throughout with helpful and insightful comments from two of the world’s leading functional neurosurgery ethicists: Paul Ford from the Cleveland Clinic and Emily Bell from Montreal.

The Meeting’s highlights included updates from Professors Peter Brown and Hagai Bergman regarding the vital interface between Functional Neurosurgery as a clinical service, and the disciplines of neurophysiology that provide research data that will very likely enable continued technological improvements in the technique. Professor Frackowiak spoke on the future of imaging in basal ganglia diseases, and Professor Benabid on brain-machine interface. A talk from Professor Taira from Tokyo used highly entertaining videos to demonstrate the functional impact of thalamotomy on task specific dystonias, including evaluation of hairdressing ability during the neurosurgical procedure!

An update on the growing number of techniques and issues surrounding the use of functional neurosurgery for patients with severe cluster headache, OCD, refractory depression and as a treatment for cognitive impairment, were reviewed in detail and provoked lively interaction from the audience. Professor Coenen from Bonn described the potential use of a novel DBS target - “the medial forebrain bundle” - for the treatment of depression, and presented excellent new data demonstrating the connectivity of the frontal cortices with the brainstem via this structure. In a complementary “double-bill” talk, Professor Lozano gave an excellent and detailed description of his first-hand experience of the use of Fornix DBS for Alzheimer’s disease and CG-25 DBS for depression.

Judging from the avalanche of emails after the meeting from speakers and attendees, the meeting was rated as scientifically highly successful; yet remained intimate, enabling an
interaction between all disciplines involved, as well as between students and fellows and “pioneers” in the field of functional neurosurgery.

Awards, Knowledge Transfer, Public Engagement & Media

Professor Marwan Hariz:
- Board member of the World Society for Stereotactic and Functional Neurosurgery (WSSFN)
- Member of the subcommittee on psychiatric surgery of the WSSFN
- Life-long member of the Swedish Movement Disorders Society
- Member of the Ethical Committee of the International Movement Disorders Society
- Member of the Editorial Board of the Movement Disorders Journal

Mr Ludvic Zrinzo:
- Received the Clinical Neuroscience Dr Tony Pullen Lecturer of the Year Award (UCL) – 2013
- Received the Merit of the Order of Saint John Awarded by the city of San Gwann, Malta, for Services to Medicine – June 2013
- Appointed member of the subcommittee on pedunculopontine nucleus DBS surgery of the ESSFN
  http://www.uclh.nhs.uk/HP/GPNEWS/Pages/DeepbrainstimulationtrialforpatientswithTourette’s.aspx
  http://www.uclh.nhs.uk/News/Pages/NewhopeforTourettespatients.aspx
- “I have been cured, says Tourette's patient who had electrode implants” London Evening Standard, Dec 23, 2011
- “Woman left a virtual recluse by Tourette's syndrome 'cured' by electrodes implanted in brain” Mail, Dec 23, 2011
- “Tourette’s sufferer has symptoms 'switched off' in revolutionary treatment”, The Telegraph, Dec 23, 2011
- “Brain Implant Cures Woman’s Tourette Tics”, Fox News, Dec 23, 2011
- Feature on Radio 5 live, Dec 24, 2011
- “Deep brain surgery brings fresh hope to sufferers” Times of Malta, Dec 24, 2011
- Three page feature in “First”, supplement to Malta Independent newspaper, Jan 2012
- Two page feature in “Wavelength” (Elekta): “DBS - stimulating a more normal life”, Oct 2012
- Appeared in a three-page interview on the “The Malta Independent on Sunday” – Jan 2012
- Featured in a two-page article on the Radio Times
- Appeared with two of the Unit’s patients who featured prominently in an episode of the BBC television series “Keeping Britain Alive” – April 2013
- Appeared as Featured Neurosurgeon in the 2013 Newsletter of the World Society for Stereotactic and Functional Neurosurgery (WSSFN)
- Featured on BBC 2 Newsnight on 10 October, 2013 showing a DBS surgery for tremor.
- Two of Mr Zrinzo’s MSc students received awards for their presentations: Bobby Sachdev was awarded the best oral presentation prize at the 2013 Cambridge
undergraduate Surgical conference – Feb 2013; Erica Tirr was awarded the Conrad Lewin Prize for the best paper presented by a young scientist at the Winter Meeting of the British Association of Clinical Anatomists – Dec 2012.

- Mr Zrinzo’s PhD student, Harith Akram, received an NHS award for technological innovation, with a new design of a patient- and surgeon-friendly stereotactic frame holder

Professor Marjan Jahanshahi:
- Member of the Editorial Board of Parkinson’s Disease
- Member of Executive Committee, British Neuropsychological Society
- Member of Executive Committee, Division of Neuropsychology, British Psychological Society
- Editorial Board ‘Scientifica’
- Editorial Board ‘Timing and Time Perception’
- One of Prof Jahanshahi’s 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).
- Professor Jahanshahi’s student, Mariam Torkamani, was winner of best poster presentation at the 9th Conference of the Neuropsychological Rehabilitation Special Interest Group of the World Federation for NeuroRehabilitation (WFNR) Bergen, Norway, July 2012.

Professor 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:
- TRANSEURO Steering Committee member. 2010 to date
- PRoBaND Core Steering Committee. 2012 to date
- Clinical Advisory Board member Parkinson’s UK. 2011 to date
- Queen Square Clinical Trials Committee. 2011 to date
- Data Monitoring Committee Prosavin gene therapy. 2010-2012
- Movement Disorders short course Committee, NHNN. 2009 to date
- Academic member of the Cure Parkinson’s Trust research committee. 2009 to date

- Diabetes Drug Shows Promise in Parkinson's - Medscape
- Single-Blind Trial: Diabetes Drug Helps Parkinson's, Maybe ...
  www.alzforum.org/new/detail.asp?id=3510
- Parkinson's UK - Small trial shows promise of diabetes drugs for ...
  www.parkinsons.org.uk/.../small-trial-shows-promise-diabetes-drugs-parkinsons
  http://www.bbc.co.uk/iplayer/episode/b038xrjf/Deep_Down_Inside/
http://www.uclh.nhs.uk/HP/GPNEWS/Pages/DeepbrainstimulationtrialforpatientswithTourette’s.aspx
- http://www.uclh.nhs.uk/News/Pages/NewhopeforTourettespatients.aspx
- “I have been cured, says Tourette's patient who had electrode implants” London Evening Standard, Dec 23, 2011
Parkinson’s Movement- Patient/professional educational videos
http://www.youtube.com/watch?v=e_WOG955zY4
http://www.youtube.com/watch?v=8UR53HpJOBk
http://www.cureparkinsons.org.uk/Sites/parkinsons-movement/pages/webinar-4-gut-feelings

Dr Foltynie’s student, Mr Joshua Kahan, was awarded the Association of British Neurologists’ Undergraduate prize for Clinical case presentation “Sodium Oxybate as a treatment for DBS-Resistant, Alcohol Responsive, Post Anoxic Myoclonus”.

Dr Foltynie’s student, Dr Zinovia Kefalopoulou, was awarded the ESSTS prize for oral presentation “DBS for Tourette syndrome”.

PUBLICATIONS


and BDNF Genes on Dyskinesias and Levodopa Use in Parkinson's Disease. Neurodegener Dis. 2013 Sep 5.


Hariz MI, Hariz GM. Hyping deep brain stimulation in psychiatry could lead to its demise. BMJ. 2012 Aug 13;345:e5447

Hariz MI. Neurosurgeons were indeed promoting evidence-based, ethical, and multidisciplinary psychiatric surgery! Stereotact Funct Neurosurg. 2013;91(4):270-1


Holl AK, Wilkinson L, Tabrizi SJ, Painold A, Jahanshahi M. Probabilistic classification learning with corrective feedback is selectively impaired in early Huntington's disease--


Jahanshahi M. Risky choices link the subthalamic nucleus with pathological gambling in Parkinson's disease. Mov Disord. 2013 Jul 10.


Torkamani M, Jahanshahi M. Neuropsychological and neuropsychiatric features of dystonia and the impact of medical and surgical treatment. In Troster A (Ed) Clinical


Zrinzo, L: Pitfalls in precision stereotactic surgery. Surgical neurology international 2012; 3(1), S53–S61

November 2013.