

Unit of Functional Neurosurgery

PROGRESS REPORT (14 October 2008)

The Unit of Functional Neurosurgery is based in the Sobell Department of Motor Neuroscience and Movement Disorders at the 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); Professor Hariz was also appointed Honorary Consultant Neurosurgeon at the National Hospital for Neurology and Neurosurgery (NHNN). The Unit of Functional Neurosurgery 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 the technique of Deep Brain Stimulation (DBS), a new technique for correcting abnormal function in brain circuits that control movement.

The mission of the Unit is both to provide first-rate treatment for patients with Parkinson's Disease and other movement disorders, and to lead extensive research aimed at understanding, improving and extending the use of DBS treatment. This research is carried out at the Institute of Neurology.

Clinical Activity in the Unit

By September 2008, a total of 166 patients have been treated with DBS in the Unit, including patients with Parkinson's disease, dystonia, essential tremor, post traumatic tremor, deafferentation pain, and Tourette's syndrome. 38 patients have been part of the MRC PD Surgery Trial. The success rate of the Unit remains very good, and the safety of the procedures has been excellent with neither brain haemorrhage nor paralysis occurring in any patient.

Current Staff of the Unit

Ordinary "permanent" 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)

Additional staff

Dr Irene Martinez-Torres (Honorary Consultant Neurologist, clinical research fellow)

Dr. Diana Ruge (neurologist, research fellow and hon clin assistant)

Ms Freja Hickey (speech therapist and research assistant)

Dr Leonora Wilkinson (Psychologist, Postdoctoral Research Fellow)

Dr Harry Griffin (Psychologist, Post-doctoral Research Fellow)

Mr Ignacio Obeso (Psychologist, PhD student with Prof Jahanshahi)

Mr Mazda Beigi (Psychologist, PhD student with Prof Jahanshahi jointly with Dr Parton at Brunel)

Staff Changes in the Unit

Ms P Forsdick (PA to Professor Hariz) retired in September 2007. She has been replaced by Ms Linda Taib since 1st January 2008

Ms E Borrell (Specialist Movement Disorder Nurse) has taken a year's sabbatical from 1st November 2007, she has been replaced by Mr Joseph Candelario from 1st December 2007

Dr Steve Tisch (Neurologist) has left the unit in December 2007 to take up a post in Sydney

Dr Thomas Foltynie has been appointed Clinical Senior Lecturer and Honorary Consultant neurologist on 1st May 2008

Ms Karen Bayliss was appointed on September First 2008 to the new post of PA and secretary to Mr Zrinzo, Dr. Limousin and Dr Foltynie PDL.

Long-term support for the Unit

Both the Monument Trust and Edmond J Safra Philanthropic Foundation have agreed to extend their financial support for the Unit into the next five-year period of the Unit (2007-2012).

"Meeting of Minds" Art Auction

A very successful art auction "Meeting of Minds" was organised by the Parkinson's Appeal on the 16th October 2007 in support of the Unit. This was hosted by Christie's who auctioned works especially donated to the Appeal by numerous contemporary British artists, including Damien Hirst and Tracey Emin (who attended the auction). With over 500 invited guests in attendance (including HRH Princess Michael of Kent and the UCL Provost, Malcolm Grant), the auction raised £460,000. This is a truly remarkable outcome.

Lyn Rothman, Chair of the Appeal and Fergus Henderson, owner and chef of St John's Restaurant (who is a successful beneficiary of DBS in the Unit) were the key organizers of this highly successful event. Guests were hosted very generously after the Christie's auction at St John's. We are extremely grateful to Lyn Rothman and her organizing committee. The funds raised will be used immediately to provide further neurological staff support for the Unit and its ever-increasing community of treated patients (see below).

DBS Support Group

The DBS support group had a very successful first meeting on the 25th September 2007 organised by Professor Jahanshahi and Ms Ellie Borrell. A full amphitheatre of operated patients and their relatives as well as a few patients at the stage of being assessed for DBS attended some lectures on topics related to the Unit, to DBS, and coping with chronic illness. Afterwards refreshments were served which allowed patients to meet and talk between themselves, as well as have informal discussions with members of the Unit. Patients were very pleased with the event. We will explore the possibility of organizing another one-day event next year. In the interim, to try and facilitate communication between patients; an MSN group page has been created on the web. Membership of the Group is open to any patient who has been operated in the Unit of Functional Neurosurgery. Patients considering the possibility of DBS in the Unit can also be put in contact with patients who have already been treated.

Website

The Parkinson's Appeal website is completely up-to-date. Please visit it at <http://www.parkinsonsappeal.com/>

International Meetings hosted by the Unit

Two international meetings were hosted by the Unit in 2007.

On February 8th and 9th 2007, the Unit hosted its second major international meeting “Functional Neurosurgery for Movement Disorders and Mental Illness” that was attended by over 230 delegates.

On July 2nd and 3rd 2007, Elina Tripoliti, Speech Therapist and PhD student in the Unit organised the first ever workshop on “Speech disorders and deep brain stimulation” attended by 26 international speakers and an audience of over 80 (65 international) with an interest in speech and movement disorders. It is expected that this group will now meet every two years.

Meeting 2008 – Tuesday 1st July 2008

The Fourth International Symposium on Neuroacanthocytosis was held jointly, this year, between Queen Square and Oxford University. During the Symposium, the Unit of Functional Neurosurgery held a forum.

A new home for the Unit: Clinical Neuroscience Centre, 33 Queen Square

In October 2006 work got underway on our new Clinical Neuroscience Centre on the site of 33 Queen Square. The new building is a joint development between the National Hospital and the Institute of Neurology. It will accommodate the Unit and its patients on the east side of Queen Square, in close proximity to hospital wards, imaging facilities, operating theatres and the intensive care unit. The Unit moved to the new Centre in June 2008 and occupies the whole of the second floor

PhD

Dr Steve Tisch was awarded his PhD on the effect of DBS in dystonia, entitled “Neuroplasticity following pallidal stimulation for dystonia” in August 2007. His examiners Dr Bain (Charring Cross Hospital, London) and Professor Krack (Grenoble) approved the Thesis.

COLLABORATIONS

The Unit has a close collaboration with other research groups in the Sobell department and has established collaboration on various research projects with several departments at IoN (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, –all of which have obtained local Swedish ethical committee permissions and are financed–), 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 suthalamotomy patients), as well as links with Industry.

TEACHING AND CONFERENCES

All members of the Unit contribute frequently to teaching activity on site, including supervising MSc students, as well as invited faculty to national and international meetings, conferences and workshops. Additionally, the Unit has regular visitors from abroad, -

neurologists, neurosurgeons and medical students who spend various amount of times observing and learning.

RESEARCH STRATEGY

The research strategy of the Unit of Functional Neurosurgery is **clinical and patient-centred**. Its general and ultimate objective is to improve further the outcome of Functional Neurosurgery and the quality of life of our patients. Our approach is multidisciplinary and involves neurology, neurosurgery, neuropsychology, neurophysiology, neuropsychiatry and neurogenetics.

Our principle research aims are fourfold:

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

Below follow projects that are ongoing or in preparation:

§. Accuracy of image guided functional stereotaxis and accuracy of stereotactic targeting using higher Tesla MRIs as well as interventional MRI

§. Pathophysiology of brain plasticity in Parkinson's and dystonia

- 1) The relationship between candidate genetic polymorphisms, the development of dyskinesias in PD and the response to DBS (measured clinically and using fMRI and rTMS).
- 2) Pathophysiology of speech and brain plasticity in PD and dystonia.

§. Neuropsychology: current research strategies focus on 5 main issues:

- 1) Investigation of cognitive safety of surgical therapy.
- 2) 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.
- 3) Modulatory influence of dopamine on response selection under conflict and learning.
- 4) Application of experimental findings to improve motor function eg investigation of virtual reality glasses as a mobility aid in PD.
- 5) Impact of movement disorders on psychosocial functioning and quality of life of patients, carers and children and how surgical interventions influence these

§. Clinical trials involving new DBS applications and new brain targets for DBS

- 1) Multicentre (UK) study for DBS for Tourette's syndrome,
- 2) European Multicentre study (Queen Square only UK centre) of subgenual cingulum DBS for depression,
- 3) Posteromedial hypothalamic DBS for cluster headache,
- 4) PPN DBS in Parkinson's disease.

§. Clinical trials involving existing therapy

- 1) PD Surg multicentre UK study of surgery versus medical treatments.
- 2) Pallidal DBS in Dystonia
- 3) Pallidal DBS in pediatric populations
- 5) Intraduodenal delivery of levodopa in a European multicentre trial

§. Cell therapies for advanced Parkinson's disease

- 1) Gene therapy (Neurturin), Multicenter European phase II trial, as only UK center,
- 2) Encapsulated cell therapy delivering GDNF collaboration with Lund, Lausanne, Margburg, supported by the MJF
- 3) Collaboration 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

ONGOING AND SUBMITTED GRANTS (2007 onwards)

2008-2009: WELLCOME Equipment Grant Title: 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

2008-2009 (Hariz) SWEDISH PD Society: Studies of PPN DBS in PD: SEK 50.000

2008-2009: (Hariz) Dept of Clinical Neuroscience, University of Umea: Studies of capsulotomy for OCD: SEK 12.000

2007-2010: County Council of Västerbotten, Sweden: Novel applications of DBS in movement disorders and neuropsychiatry SEK 2.610.000 (Prof Hariz Co applicant with Prof Forsgren and Dr Blomstedt)

2007-2009. Neuro-engineering for navigation, intervention and implementation in neurosurgery. Swedish Foundation for Strategic Research (SSF), Swedish Research Council (VR) and Swedish Governmental Agency for Innovation Systems (Vinnova) Co-Applicants: Prof M Hariz and Prof Karen Wardell (Univ of Linköping, Sweden) 2,510,000.SEK

2006-2008 Effective target volume from DBS and RF electrodes for functional neurosurgery – theoretical and experimental analysis. The Swedish Research Council. Co-Applicants: Prof M Hariz and Prof Karin Waardell (Univ of Linköping, Sweden) 1,800,000 SEK

2005-2007. Improving the accuracy and efficiency of surgical implantation of therapeutic DBS electrodes: Intra-operative use of local field potentials to identify the subthalamic nucleus. DANA Foundation Clinical Neuroscience Research Grant: Prof P Brown Co-Applicants: Prof M Hariz and Dr P Magill. \$136,000

2005-2007 (Prof Jahanshahi) Does provision of visual cues through virtual reality glasses improve mobility in Parkinson's disease? A controlled study. Project Grant from the Parkinson's Disease Society. Co-applicants: Dr R Greenlaw, Prof N Quinn £98,193

2005-2007 (Prof Jahanshahi) ParkService – Telematics application service for people with Parkinson's disease. A market validation proposal. European Commission eTen (Trans-European Telecommunications Networks) Co-applicant with OCC, Mestor, ICCS, Promitheas, Parkaid, Grigioni and Scheneckenhaus. €640,000

2006-2008 (Prof Jahanshahi) Career Development Fellowship for Dr Leonora Wilkinson. Parkinson's Disease Society, UK £103,366

2007-2009 (Prof Jahanshahi) Fellowship for Ignacio Obeso, from Fundacion Caja Madrid, 42672 Euros

2008-2010. (Dr Limousin) - Parkinson's disease Society pump priming for Movement disorder speech therapist Clinical Specialist position for 2 years £ 64,953 (year1) £ 68,099 (year 2)

2005-2010 NIH-Medtronic Joint Study "Neural Control of Movement and Posture" £95.000 (Dr Limousin co-applicant, principal applicant Dr Corcos)

2006-2008 Role of cortical plasticity in deep brain stimulation for primary and secondary dystonia. Action Research (Dr Limousin co-applicant, principal applicant Pr Rothwell) £175,000

2005-2010. STN Stimulation – Neural control of movement and posture. Medtronic. Dr Limousin Co-applicant: Prof J Rothwell \$175,000

2006-2009 A therapeutic approach to freezing in Parkinson's disease. MRC project grant. Dr Limousin Co-applicant: Dr B Day £309,588

2005-2008 (Dr Limousin) Impact of Deep Brain Stimulation on speech in patients with Parkinson's disease. Project Grant from the Parkinson's Disease Society £99,698

2006-2008 (Dr Limousin) Quantification of the effect of stimulation parameter adjustment in PD. Rosetrees Trust. £10000

2004-2009. Encapsulated GDNF-producing cells for neuroprotection in Parkinson's disease, Michael J Fox Foundation, \$ 130 214 for this site (Dr Limousin co-applicant, coordinating principal applicant Pr Lindvall)

April 2007-March 2008. (Dr Limousin)European Federation for Neurological Societies Fellowship. 19200 Euros to support research fellow Dr Matinez Torres

2008-2009. (Dr Limousin) Fellowship for Graduated Courses in Universities and Colleges, Fundacion Caja Madrid to support research fellow Dr Matinez Torres. 16800 euros

Dr Limousin contributed to the successful application of UCLH/UCL to become a Biomedical Research Center (2006) and to capital bid of the Biomedical Research Center £ 30.000 toward new stereotactic frame for the Unit of Functional Neurosurgery (2007)

SUBMITTED Grant applications

(Tom Foltynie): Genetic influences on neuroplasticity in Parkinson's disease, dyskinesias, and response to deep brain stimulation. MRC New Investigator Research grant -Support requested £356 640

(Tom Foltynie): The influence of functional genetic polymorphisms on dyskinesia development in Parkinson's disease and response to deep brain stimulation..CLINICAL

RESEARCH & DEVELOPMENT COMMITTEE-Fast track application. Support requested £30405

(Tom Foltynie): Genetic polymorphisms, dyskinesia risk and response to DBS in Parkinson's disease Parkinson's disease society- Innovation Grant -support requested £14 815

PAPERS (PUBLISHED, IN PRESS, or ACCEPTED, January 2007-August 2008)

Androulidakis AG, Kühn AA, Chen CC, Blomstedt P, Kempf F, Kupsch A, Schneider G-H, Doyle L, **Dowsey-Limousin P, Hariz MI**, Brown P: Dopaminergic therapy promotes lateralised motor activity in the subthalamic area in Parkinson's disease. *Brain* 2007; 130: 457-68.

Ashkan K, Blomstedt P, **Zrinzo L, Tisch S**, Yousry T, **Limousin-Dowsey P, Hariz MI**: Variability of the subthalamic nucleus: the case for direct MRI guided targeting. *Br J Neurosurg*, 21:197-200, 2007.

Blomstedt P, Hariz GM, **Hariz MI**, Koskinen LO: Thalamic deep brain stimulation in the treatment of essential tremor: a long-term follow-up. *Br J Neurosurg*. 2007 Oct; 21(5):504-9.

Blomstedt P, **Hariz MI**, Lees A, Silberstein P, **Limousin P**, Yelnik J, Agid Y. Acute severe depression induced by intraoperative stimulation of the substantia nigra: A case report. *Parkinsonism Relat Disord*. 2008;14(3):253-6.

Blomstedt P, Olivecrona M, Sailer A, **Hariz MI**: Dittmar and the History of Stereotaxy or Rats, Rabbits and References. *Neurosurgery* 2007; 60:198-202.

Blomstedt Patric, **Stephen Tisch., Marwan I. Hariz**. Pallidal Deep Brain Stimulation in the Treatment of Meige Syndrome. *Acta Neurol Scand*, 2008, March 7 [Epub].

Brücke C, Kupsch A, Schneider GH, **Hariz MI**, Nuttin B, Kopp U, Kempf F, Trottenberg T, Doyle L, Chen CC, Yarrow K, Brown P, Kühn AA. The subthalamic region is activated during valence-related emotional processing in patients with Parkinson's Disease. *Eur J Neurosci*. 2007 Aug;26(3):767-74

Carmichael DW, Serge Pinto, **Patricia Limousin-Dowsey**, Stephane Thobois, Philip J. Allen, Louis Lemieux, **Marwan I. Hariz**, Tarek Yousry, and John S. Thornton; Corrigendum to "Functional MRI with active, fully implanted, deep brain stimulation systems: Safety and experimental confounds" . *NeuroImage* 37 (2007) 508–517

Chen CC, Litvak V, Gilbertson T, Kühn A, Lu CS, Lee ST, Tsai CH, **Tisch S, Limousin P, Hariz M**, Brown P. Excessive synchronization of basal ganglia neurons at 20 Hz slows movement in Parkinson's disease. *Exp Neurol*. 2007 May; 205(1):214-21.

Doyle Gaynor LM, Kühn AA, Dileone M, Litvak V, Eusebio A, Pogosyan A, Androulidakis AG, **Tisch S, Limousin P**, Insola A, Mazzone P, Di Lazzaro V, Brown P. Suppression of beta oscillations in the subthalamic nucleus following cortical stimulation in humans. *Eur J Neurosci*. 2008 Jul 24.

Eusebio A, Chen CC, Lu CS, Lee ST, Tsai CH, **Limousin P, Hariz M**, Brown P. Effects of low-frequency stimulation of the subthalamic nucleus on movement in Parkinson's disease. *Exp Neurol*. 2008 Jan;209(1):125-30

Filipovic SR, Papathanasiou, I, Whurr R, Rothwell J, **Jahanshahi M** (2008) Differential effect of linguistic and non-linguistic pen-holding tasks on motor cortex excitability, *Exp Brain Res*, Aug 20. [Epub ahead of print]

Fodstad H, **Hariz M**: Electricity in the treatment of nervous system disease. *Acta Neurochir Suppl*. 2007; 97(Pt 1):11-9.

Foltynie T, Cheeran B, Williams-Gray CH, Edwards MJ, Schneider SA, Weinberger D, Rothwell JC, Barker RA, Bhatia KP. BDNF val66met Influences Time To Onset Of Levodopa-Induced Dyskinesia In Parkinson's Disease. Accepted JNNP Sept 2008.

Hariz M, Krack P, Alesch F, Augustinsson LE, Bosch A, Ekberg R, Johansson F, Johnels B, Meyerson B, Nguyen JP, Pinter M, Pollak PR, von Raison F, Rehncrona S, Speelman JD, Sydow O, Benabid AL: Multicentre European study of thalamic stimulation for Parkinsonian tremor; a 6-year follow-up. *J Neurol Neurosurg Psychiatry*. 2007 2008 Jun;79(6):694-9.

Hariz MI: COMMENTS. *Neurosurgery*. 2007;60(Suppl 2):292-293. (Comments on: Pinto S, Le Bas JF, Castana L, Krack P, Pollak P, Benabid AL: C omparison of two techniques to postoperatively localize the electrode contacts used for subthalamic nucleus stimulation. In *Neurosurgery*. 2007 Apr;60(4 Suppl 2):285-294).

Hariz MI, Rehncrona S, Quinn N, Speelman JD, Wensing C, and the multicentre Advanced Parkinson's Disease Deep Brain Stimulation Group: Multicentre study on deep brain stimulation in Parkinson's disease: an independent assessment of reported adverse events at 4 years. *Mov Disord*. 2008 Feb 15;23(3):416-21.

Hariz MI, Yelnik J: Un appel pour une revue critique et vraiment rigoureuse de la littérature. *Mouvements* 2007; 8: 3-4

Hariz MI. Thalamic stimulation does not involve a high rate of suicide. *Mov Disord*. 2008 Jun 25;23(11):1626

Hariz MI: Psychosurgery, deep brain stimulation, and the re-writing of history. *Neurosurgery*, in press

Howell S., **Tripoliti E.**, Pring T., (2007). Delivering the Lee Silverman Voice Treatment (LSVT) by web camera: a pilot study of remote delivery. *International Journal of Language and Communication Disorders*. (accepted).

Jahanshahi M, Alusi SH Pieter S Jones C Aziz TZ Glickman S Stein JF Bain PG (2008) Effect of stereotactic lesional surgery for the treatment of tremor in multiple sclerosis on cognitive function. *Behavioural Neurology*, In Press

Jahanshahi M, Sheikh S. (2007) Long-term neurological illness in parents has a substantial impact on the lives of children. *Br J Neurosci Nursing*, 2, 2-7.

Jones C Malone T Dirnberger G Edwards M **Jahanshahi M** (2008) Basal ganglia, dopamine and temporal processing: Performance on three timing tasks on and off medication in Parkinson's disease. *Brain & Cognition*, Mar 29; [Epub ahead of print]

Kühn AA, Kempf F, Brücke C, Gaynor Doyle L, **Martinez-Torres I**, Pogosyan A, Trottenberg T, Kupsch A, Schneider GH, **Hariz MI**, Vandenberghe W, Nuttin B, Brown P. High-frequency stimulation of the subthalamic nucleus suppresses oscillatory beta activity in patients with Parkinson's disease in parallel with improvement in motor performance. *J Neurosci*. 2008 Jun 11;28(24):6165-73.

Lewis L, Butler A, **Jahanshahi M** (2008) A quantitative and qualitative evaluation of depression in focal, segmental and generalized dystonia. *J Neurology*, In Press

Limousin P, Martinez-Torres I. Deep brain stimulation for Parkinson's disease. *Neurotherapeutics*. 2008 Apr;5(2):309-19. Review.

Mondolo F, **Jahanshahi M**, Granà A, Biasutti E, Cacciatori E, Di Benedetto P (2007) Evaluation of anxiety in Parkinson's disease with some commonly-used rating scales. *Neurol Sci*. Oct;28(5):270-5. Epub 2007 Oct 31.

Osman M, Wilkinson L, Beigi M, Sanchez Castaneda C, **Jahanshahi M** (2008) Patients with Parkinson's disease learn to control complex systems via procedural as well as non-procedural learning. *Neuropsychologia*, 46: 2355–2363.

Page D, Butler A, **Jahanshahi M** (2007) Quality of life in focal, segmental and generalized Dystonia. *Movement Disorders*, 22, 341-347.

Page D, **Jahanshahi M** (2007) Deep Brain Stimulation of the subthalamic nucleus improves set shifting but does not affect dual task performance in Parkinson's disease *IEEE Transactions on Neural Systems and Rehabilitation Engineering*. Special Issue on DBS, Jun;15(2):198-206.

Rahman, S, Griffin H, Quinn, NP, **Jahanshahi, M**, On the nature of fear of falling in Parkinson's disease. *Behavioural Neurology*, In Press

Rahman, S, Griffin HJ, Quinn, NP, **Jahanshahi, M** (2008) Quality of life in Parkinson's disease: the relative importance of the symptoms *Movement Disorders*, Jun 9. [Epub ahead of print]

Rahman, S, Griffin HJ, Quinn, NP, **Jahanshahi, M** (2008) The factors that induce or overcome freezing of gait in Parkinson's disease. *Behavioural Neurology*;19(3):127-36.

Thobois S, Hotton G, Pinto S, **Wilkinson L, Limousin-Dowsey P**, Brooks D, **Jahanshahi M** (2007) Deep brain stimulation of the subthalamic nucleus alters pallidal coupling with prefrontal cortex during response selection under competition. *J Cerebral Blood Flow & Metabolism*, Jun;27(6):1173-84.

Tisch S, Rothwell JC, Bhatia KP, Quinn N, **Zrinzo L, Jahanshahi M**, Ashkan K, **Hariz M, Limousin P**. Pallidal stimulation modifies after-effects of paired associative stimulation on motor cortex excitability in primary generalised dystonia. *Exp Neurol*. 2007 Jul; 206(1):80-5.

Tisch S, Rothwell JC, Limousin P, Hariz MI, Corcos DM. The physiological effects of pallidal deep brain stimulation in dystonia. *IEEE Trans Neural Syst Rehabil Eng.* 2007 Jun; 15(2):166-72. Review.

Tisch S, Rothwell JC, Zrinzo L, Bhatia KP, Hariz M, Limousin P. Cortical evoked potentials from pallidal stimulation in patients with primary generalized dystonia. *Mov Disord.* 2008 Jan 30;23(2):265-73.

Tisch S, Zrinzo L, Limousin P, Bhatia KP, Quinn N, Ashkan K, Hariz M. Effect of electrode contact location on clinical efficacy of pallidal deep brain stimulation in primary generalised dystonia. *J Neurol Neurosurg Psychiatry.* 2007 Dec; 78(12):1314-9.

Tripoliti E, L. Zrinzo, E. Borrell, E. Frost, S. Tisch, I. Martínez-Torres, M. Hariz, P. Limousin (2007) Effects of electrode contact location and voltage amplitude on speech and movement in Parkinson's Disease . *Movement Disorders* (accepted).

Tripoliti E, Limousin P, Tisch S, Borrell E, Hariz M. Speech in Parkinson's Disease following Subthalamic Nucleus Deep Brain Stimulation: preliminary results. *Journal of Medical Speech and Language Pathology*, in press

Wårdell K, Blomstedt P, Richter J, Antonsson J, Eriksson O, Zsigmond P, Bergenheim AT, Hariz M: Intracerebral microvascular measurements during deep brain stimulation implantation using laser Doppler perfusion monitoring. *Stereotact Funct Neurosurg.* 2007; 85(6):279-86.

Wilkinson L, Jahanshahi M (2007) The striatum and probabilistic implicit sequence learning. *Brain Res.* 1137, 117-130.

Wilkinson L, Lagnado, DA, Quallo, M, Jahanshahi M (2008) The effect of feedback on non-motor probabilistic classification learning in Parkinson's Disease. *Neuropsychologia*, 46: 2683-95

Zrinzo L, Zrinzo LV, Hariz M: The pedunclopontine and peripeduncular nuclei: a tale of two structures. *Brain.* 2007 Jun; 130(Pt 6):e73

Zrinzo L, Zrinzo LV, Hariz M: The peripeduncular nucleus: a novel target for deep brain stimulation? *Neuroreport.* 2007 Oct 8; 18(15):1631-2

Zrinzo L, Zrinzo LV, Tisch S, Limousin PD, Yousry TA, Afshar F, Hariz MI. Stereotactic localization of the human pedunclopontine nucleus: atlas-based coordinates and validation of a magnetic resonance imaging protocol for direct localization. *Brain.* 2008 Jun;131(Pt 6):1588-98.

Zrinzo LU, Crocker M, Zrinzo LV, Thomas DGT, Watkins L. Commercial Flight and Patients with Intracranial Mass Lesions: A Caveat. *J Neurosurg*, 2006; 105: 627-630

BOOK CHAPTERS

Foltynie T, Michell A, and Barker RA. Parkinson,s disease. *Book Chapter.*

In Protein Misfolding in Neurodegenerative Diseases. CRC Press 2007. Eds Smith, Simons, Sewell.

Hariz MI. Pallidotomy for Parkinson's Disease. . in Functional Textbook of Stereotactic and Functional Neurosurgery (Eds): Gildenberg, Philip L.; Lozano, Andres M.; Tasker, Ronald, in press.

Hariz MI and Zrinzo L: Globus pallidus stimulation, in Aziz, Bain, In Aziz, Liu, Bain eds Pocket Book on Deep Brain Stimulation - Oxford University Press. In press 2008

Hariz MI, Vayssière N: Stereotactic surgery without microelectrode recording, in Roy Bakay (ed): Movement Disorder Surgery, The Essential, Thieme, New York, 2009

Hariz MI: Functional neurosurgery for dystonias. In: Sindou M (ed): "PRACTICAL HANDBOOK OF NEUROSURGERY" in press.

Hariz MI: Stereotactic CT scanning in Textbook of Stereotactic and Functional Neurosurgery. (Eds): Gildenberg, Philip L.; Lozano, Andres M.; Tasker, Ronald, in press

Jahanshahi M (2007) Parkinson's disease. In A. Baum, C. McManus, S. Newman, J. Weinman and R. West (Eds) Cambridge Handbook of Psychology, Health and Medicine. Second edition, In Press.

Jones C **Jahanshahi M** The substantia nigra, the basal ganglia, dopamine and temporal processing. In Di Giovanni G, Di Matteo, Esposito E. (Editors) Birth, life and death of dopaminergic neurons in the substantia nigra. In Press

Limousin P, Hariz M. part of chapter in "Neurology: A Queen Square Textbook". Blackwell Publishing. In press 2008

Martinez-Torres, P. Limousin. Surgery. In Schapira A (Ed): Parkinsons Disease. Oxford Neurology Library (in press)

Martinez-Torres, S. Tisch, P. Limousin. The Basal Ganglia. In Conn M (Ed): Neuroscience in Medicine, chapter 18. Humana Press (in press)

Tisch S, Limousin P. DBS stimulator programming. In Aziz, Liu, Bain eds Pocket Book on Deep Brain Stimulation - Oxford University Press. In press 2008

Tripoliti E: Electrical Stimulation of deep brain structures and speech. Book chapter in Ben Maassen, Pascal HHM Van Lieshout., (Editors). Speech Motor Control: New development in basic and applied research. Oxford university Press, 2008 In press.

Zrinzo L, Hariz MI. Impedance Recording in Functional Neurosurgery in Textbook of Stereotactic and Functional Neurosurgery. (Eds): Gildenberg PL. Lozano AM. Tasker R, in press

Zrinzo L, Thomas DGT. Stereotactic Approaches to the Brain Stem in Textbook of Stereotactic and Functional Neurosurgery. (Eds): Gildenberg PL. Lozano AM. Tasker R, in press