



Functional Neurosurgery Unit

Department of Clinical & Motor Neurosciences

UCL Queen Square Institute of Neurology

&

National Hospital for Neurology and Neurosurgery

UCLH Foundation Trust

Annual Report:

1st January 2019 to 31st December 2019



*Compiled by Ludvic Zrinzo with the assistance, and on behalf of, all the members
of the Functional Neurosurgery Unit*

January 2020

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1. Background summary

The Functional Neurosurgery Unit (FuN-Unit) is a *multidisciplinary, clinical academic collaboration* within the Department of Clinical & Motor Neurosciences at the UCL Queen Square Institute of Neurology (IoN) and the National Hospital for Neurology and Neurosurgery. First established in October 2002, the Unit has grown in scope and activity and is recognised as an international centre of excellence in the field.

The Unit is dedicated to the multidisciplinary neurosurgical and neurological management of patients with Parkinson's disease, other movement and neuropsychiatric disorders. *Deep Brain Stimulation (DBS)* and *stereotactic ablation* are commonly used surgical techniques to modulate abnormal function in brain circuits. The Unit's mission is to provide and develop the best possible treatments, to provide comprehensive training & education in the field, and to engage in extensive research aimed at understanding, improving and extending the use of DBS, stereotactic ablation and other neurosurgical techniques.

Prof Marwan Hariz, the first Unit Head, appointed in October 2002, retired from UCL in July 2018. Prof Ludvic Zrinzo was subsequently appointed the new Unit Head. Prof Eileen Joyce joined the Unit in 2019, reflecting the importance of neuropsychiatry in movement disorders and our research interest into neurosurgery for mental disorders.

2. Premises

In 2008, the Unit moved to purpose-built facilities in the new Clinical Neuroscience Centre at 33 Queen Square. This £12m building provides integrated clinical & academic research facilities on the east side of Queen Square, in close proximity to inpatient and outpatient facilities at the National Hospital for Neurology & Neurosurgery (NHNN), in particular the wards, operating theatres, & Interventional MRI suite. The Unit occupies the entire 2nd floor, housed in the same building as the clinical research teams in the areas of Parkinson's disease and human movement, and epilepsy, together with outpatient facilities for patients with these neurological conditions, and a Lecture theatre in the basement.

This progress Report summarises the academic and clinical activities of the Unit for the Year 2019 and follows on from previous Annual Reports.

3. Current Staff

Neurosurgery

- Prof Ludvic Zrinzo MD PhD FRCS
Unit Head, Professor in Neurosurgery & Honorary Consultant in Neurosurgery
- Mr Jonathan Hyam MD PhD
Honorary Senior Lecturer & Consultant Neurosurgeon
- Mr Harith Akram MBChB PhD FRCS
Honorary Senior Lecturer & Consultant Neurosurgeon

Neurology

- Prof Patricia Limousin MD PhD
Professor in Clinical Neurology & Honorary Consultant in Neurology
- Prof Tom Foltynie MRCP PhD
Professor in Clinical Neurology & Honorary Consultant Neurologist

Neuropsychiatry

- Prof Eileen Joyce MB BChir PhD MRCP FRCPsych
Professor of Neuropsychiatry & Honorary Consultant Neuropsychiatrist

Specialist Nurses

- Mr Joseph Candelario-Mckeown *Movement Disorder Specialist Nurse*
- Ms Catherine Hartigan, née Milabo *Movement Disorder Specialist Nurse*
- Ms Maricel Salazar *Movement Disorder Specialist Nurse*

Speech and Language Therapy

- Dr Elina Tripoliti PhD *Clinical Specialist Speech Therapist, Hon Sen Lecturer*
- Mr Tim Grover *Clinical Specialist Speech Therapist*

Administrative Support

- Ms Linda Taib *Unit Academic PA; Depart. Admin Assistant*
- Ms Debbie Phillips *NHS Administration Co-ordinator*
- Ms Sivagini Puvichandran *NHS Administration Co-ordinator*
- Ms Inga Izyczek *NHS Administration Co-ordinator*
- Ms Haris Charalambous *NHS Multidisciplinary Team Coordinator*
- Ms Susan Boateng *NHS Multidisciplinary Team Assistant*

PhD Fellows, Post-doc Fellows, *Clinical Fellows and Students*

- Dilan Athauda (*Neurologist, PhD awarded Aug 2018*)
- Viswas Dayal (*Neurologist, PhD student expected completion Feb 2020*)
- Jinendra Ekanayake (*Neurosurgeon, post-doc fellow*)
- Christine Girges PhD (*Clinical Research assistant*)
- Friederike Leimbach (*Neuropsychologist, PhD awarded 2018*)
- Eoin Mulroy (*Clinical Research Fellow*)
- Wafiq Rahman (*MSc Student - Oct 2018- July 2019*)
- Ali Rajabian (*Neurosurgeon, RCS Fellow*)
- Alexis Roquemaurel (*Neurologist, Clinical Fellow*)
- Audrey Schembri (*Physiotherapist MSc student*)
- Suzette Shahmoon (*Neuropsychologist, Part-time PhD Student*)
- Krista Sibley (*Clinical Research Assistant*)
- Zhangjie (Jack) Su, PhD (*Neurosurgeon, Clinical Fellow*)
- Himanshu Tyagi (*Psychiatrist, PhD fellow*)
- Niro Vijjaratnam (*Neurologist, PhD student*)
- Thomas Wirth (*Honorary Clinical Assistant*)
- Andre Zacharia (*Neurologist, Part time PhD student*)

4. Clinical Activities

Since the establishment of the Unit in October 2002, a total of 1013 new patients have undergone stereotactic surgery, with well over 2000 surgical procedures performed. An increasing number of patients who received DBS have required further surgeries for replacement of their depleted, or almost depleted, batteries, sometimes several times.

The Unit is by far the largest provider of DBS surgery in the UK, as reflected in data collected in the last available national audit (*Figure 1*). Activity has steadily increased over the last decade with further growth expected in the years ahead (*Figure 2*). Indications for stereotactic surgery include patients with Parkinson's disease, dystonia, essential tremor, post-traumatic tremor, orthostatic tremor, tremor of multiple sclerosis, cluster headache and other trigeminal cephalalgias, Gilles de la Tourette syndrome, obsessive compulsive disorders, depression, Parkinson's disease dementia and dementia of Lewy Body. New indications and new brain targets for DBS are investigated within a framework of scientific trials (see below). A number of ablative stereotactic procedures

(thalamotomy, pallidotomy, capsulotomy, cingulotomy) have been performed in patients where DBS is not indicated or desirable.

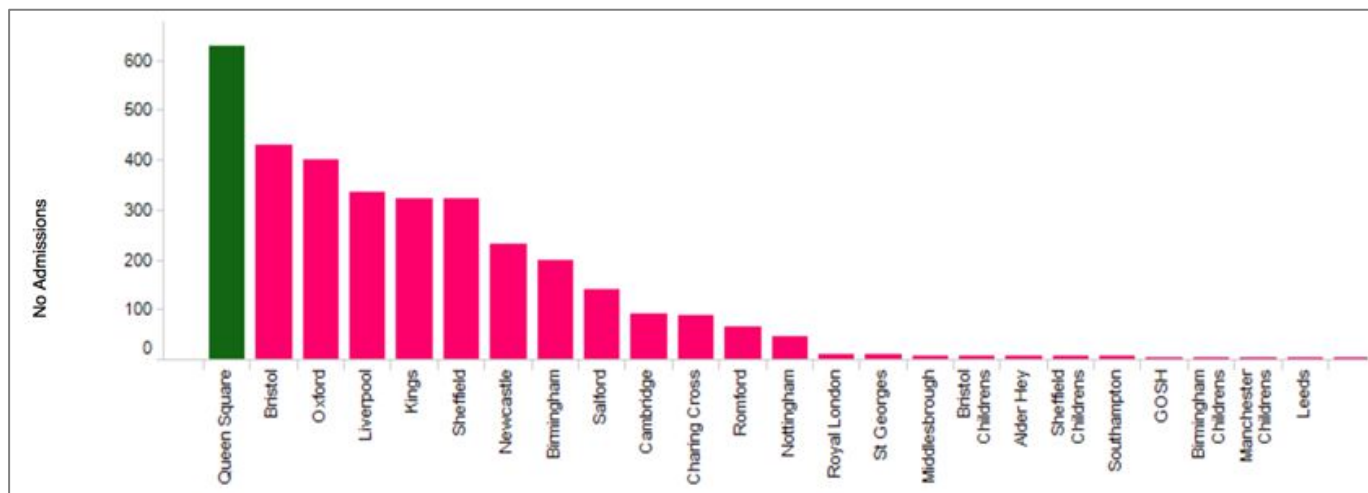


Figure 1: DBS procedures performed in Neurosurgical Units across the UK (data from latest available iNeurosurgery / SBNS National audit).

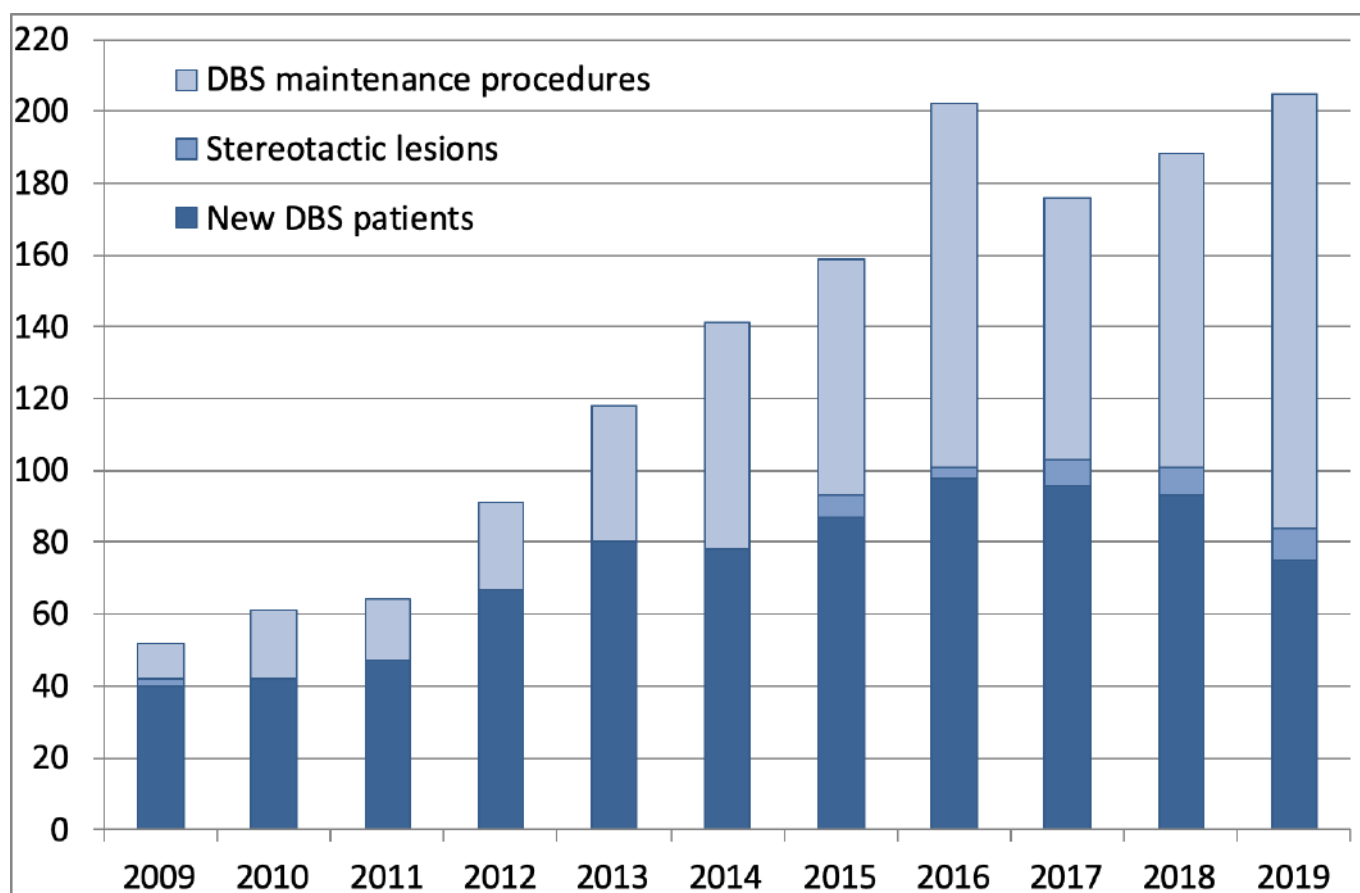


Figure 2: Unit activity at NHNN/Queen Square over the last decade. Despite reduced theatre time due to lack of anaesthetic cover and iMRI BrainLab upgrade, there was no decline in surgical activity during 2019.

The Unit is the **national neurosurgical referral centre for OCD and depression**. This is the result of close collaboration between the Unit and Advanced Interventions Service Team, Dundee University (Prof Keith Matthews, Dr David Christmas), the only nationally commissioned team for psychiatric surgery in the UK. A major MRC-funded project on DBS for OCD had very good results for the treated patients, and the manuscript was published in Biological Psychiatry.

In this 18th year of the Unit, the success rate of the Unit remains high. Surgical safety is truly excellent and unique, without surgical fatality, brain haemorrhage or paralysis occurring in any operated patient. The imaging and surgical techniques developed at Queen Square continue to be successfully applied abroad. This technique, pioneered in the Unit and based on MRI-guided and MRI-verified surgery, is being implemented more and more in other large centres worldwide, in particular in major DBS centres in Europe, Asia and the US.

Since August 2011, all stereotactic DBS and ablative surgeries have been performed in the **Interventional Surgical MRI (iMRI) suite**. This facility has permitted more than 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 DBS services around the world). In addition to this increase in workflow, clinical demand is such that we now have two full theatre days in the iMRI suite every week to allow additional surgeries.

In addition to stereotactic surgery, Unit members have collaborated with other clinicians to provide additional functional neurosurgery services. These include a **service for facial pain** (together with Dr Matharu, Dr Sarah Miller & Prof Joanna Zakrzewska), procedures on the Gasserian ganglion for trigeminal neuralgia and microvascular decompression for facial pain syndromes (trigeminal neuralgia and SUNA) as well **as for hemifacial spasm** (with Dr Tabish Saifee and Dr Pras Korlipara). These services have been developed using a similar framework with multidisciplinary approach to patient and procedure selection involving both neurology and neurosurgery to optimise outcomes.

The Unit has also been active in multicentre trials of stem cell therapy for stroke as well as **gene therapy for Parkinson's disease**.

<https://www.ucl.ac.uk/news/2018/oct/innovative-gene-therapy-trial-parkinsons-disease>

5. Financial Viability

Financial viability is essential for services within the modern NHS and the Unit is a major source of income for NHNN/UCL. The streamlined surgical approach adopted by the Unit allows more procedures to be performed per surgical session, improving on cost efficacy for the NHS and generating significant income for the Trust. Moreover, ancillary services provided to DBS patients generate additional income.

For example, the Unit employs 1-whole-time-equivalent speech and language (S&L) therapist to provide speech evaluation, advice and therapy to patients with Movement Disorders pre and post-operatively as well as perform multidisciplinary research within the field. The S&L clinical work alone generated an income of £268 000 during the year 2018/19, an increase of 24% on the preceding year. The Unit is liaising with hospital management to expand this service given the increasing demand.

6. Research Strategy

The Unit's research strategy is clinical and patient-centred, with the primary objective being to further improve the outcome and the quality of life of patients, and to develop new therapies for 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, national and multinational. Disciplines involved include neurology, neurosurgery, neuroradiology, physics, neuropsychology, neurophysiology, neuropsychiatry, neurogenetics, neurorehabilitation, engineering, mathematics and computer science.

The principal research aims are to:

- Evaluate novel surgical and non-surgical therapies that 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
- Improve the visualisation on imaging and targeting accuracy of existing brain targets by use of high field MRI
- Document the impact of DBS and understand the mechanisms of its effects on cognition, mood and behaviour

- Better understand how DBS works and what it affects, through the use of diffusion MRI, functional MRI, recording of local field potentials, Magnetoencephalography (MEG) and Transcranial Magnetic Stimulation (TMS)
- Improve the delivery of DBS in patients with Parkinson's disease by investigating closed loop stimulation based on physiological feedback from brain targets, and by evaluating new models of electrodes delivering directional electric current
- Develop and validate alternative methods for management of mobility and cognitive problems in PD
- Perform in-depth evaluation of the effects of DBS and stereotactic ablation on quality of life
- Exploration and studies of gender-related aspects in patients with movement disorders
- Explore novel applications of DBS and stereotactic lesional surgery in psychiatry, in particular in depression, obsessive compulsive disorders and anorexia
- Explore MRI-based biofeedback training of patients with Parkinson's disease

7. Ongoing and Planned Projects

- Safety, accuracy and precision of image guided & image-verified stereotactic targeting
- Investigation of the effects of medical and surgical treatments on speech for patients with PD and dystonia
- Investigation of changes in facial expression of patients with PD undergoing surgical and medical treatments" (Tim Grover)
- Long term effects of pharmacological and surgical treatments on speech for patients with Parkinson's Disease
- Gamma knife thalamotomy for Tremor
- Gamma knife radiosurgery for Trigeminal Neuralgia
- Robot-assisted neurosurgery
- Long term effects of Ephedrone abuse on speech- a collaboration with Professor Lees and Dr M. Selikhova
- Speech defects and the potential for their pharmacological treatment in patients with PD, with clues from the songbirds. Collaboration with the

Blizzard Institute, Queen Mary University of London (Professor Priestley) and Professor David Clayton

- Introduction of the “Expiratory Muscle Strength Training device (EMST150)”, a very effective swallowing therapy, (NICE guidelines) - pilot study is underway to evaluate the use of EMST in patients with Parkinson’s and PD plus syndromes (Tripoliti)
- Our S&L service is part of the new UCLH pilot for video clinics, an EPIC initiative to develop a platform to provide therapy through EPIC (Tripoliti)
- Research into using Sound Brenner Pulse watches to improve speech in parkinsonian conditions – the effects were so dramatic in one patient that he kindly donated £650 so that the Unit could purchase further watches (Grover)
- Longitudinal changes in Structural & functional MR connectivity in patients undergoing stereotactic functional neurosurgery
- Electric field simulation in deep brain stimulation; impact on effects and side effects of DBS
- Local Field Potentials and Magnetoencephalography studies on DBS patients
- The use of real-time fMRI and biofeedback in patients with Parkinson’s disease undergoing STN DBS
- Generation of predictive models utilising multimodal imaging techniques for the assessment of response to deep brain stimulation surgery in corresponding surgical cohorts
- PROBAND study “Parkinson’s Repository of Bio samples and Networked Datasets”
- Safety and efficacy of microvascular decompression for SUNA
- Stereotactic Vo-thalamotomy for focal task specific dystonia
- Stereotactic ablation for depression and OCD
- Audit of microvascular decompression for hemifacial spasm
- Imaging neurovascular conflict in patients with cluster and SUNCT headache
- Diffusion MRI studies to inform planning of thalamotomy for tremor
- Multicentre trial of surgery for anorexia nervosa
- Patient expectations and surgical outcome after functional neurosurgery
- Further trials of Exenatide in PD
- Tracking Parkinson’s: The long-term development and analysis of the Parkinson’s repository of biomarkers and networked datasets

- The role of DBS in Tourette syndrome
- Closed-loop stimulation and short pulse width STN DBS: effects on speech and motor outcome
- The nature, incidence and predictors of falls in people with Parkinson's disease after deep brain stimulation - An observational study (Audrey Schembri).
- The use of Artificial intelligence (Kelvin) to objectively rate severity of Parkinson's disease.
- Preliminary phase of stereotactic delivery of gene therapy for Huntington's Disease (with Sarah Tabrizi).

8. Clinical Trials – Current

- A Phase I/II Safety and Dose Evaluation Study of OXB-102 in Patients with Bilateral Idiopathic Parkinson's Disease
- A randomized, double blind, parallel group, placebo-controlled phase 3 trial of Exenatide once weekly over 2 years as a potential disease modifying treatment for moderate severity Parkinson's disease.
- A randomised, parallel group trial of Exenatide for Multiple System Atrophy.
- A Multicentre, Randomized, Double-Blind, Placebo-Controlled Study, with an Active-Treatment Dose-Blinded Period, to Evaluate the Safety, Pharmacokinetics, and Pharmacodynamics of BIIB054 in Subjects with Parkinson's Disease
- A phase II, placebo controlled, double blind, randomised clinical trial to assess the safety and tolerability of 30 mg/kg daily Ursodeoxycholic Acid (UDCA) in patients with Parkinson's disease (PD)
- An open label study to assess the safety and efficacy of neural allo-transplantation with foetal ventral mesencephalic tissue in patients with Parkinson's disease
- Modified target for ventral tegmental area DBS for trigeminal autonomic cephalalgia
- Microvascular decompression in SUNCT

9. Clinical Trials – Completed

- GPi DBS for Tourette Syndrome - trial completed and results published
- NBM DBS for PDD - trial completed and results published

- NBM DBS for DLB - trial completed, manuscript submitted
- Ventral tegmental area DBS for trigeminal autonomic cephalalgia - trial completed and results published
- Efficacy of DBS in patients with severe OCD - trial completed, manuscript published in Biological Psychiatry
- SPGS in cluster headache - manuscript in preparation
- A double-blind, randomized crossover comparison of short pulse width versus conventional pulse width deep brain stimulation (DBS) in Parkinson's disease patients with previously implanted DBS systems - trial completed and results published

10. New Grant Awards

- Parkinson's UK, Trial of Ondansetron as a Parkinson's Hallucinations Treatment. 2019-2023, £973,728.83 (Co-I: Joyce / Foltynie)
- Project ID 1657184 Innovate UK- 2019-2021- KELVIN: Computer Vision Based Biomarkers of Motor Dysfunction in Parkinson's Disease £248,487 (PI Foltynie/ Limousin)
- Project ID 1973191 & 3044120: John Black Charitable Foundation and Van Andel Institute A randomised, open label trial of exenatide as a treatment for Multiple System Atrophy 2019-2022 £220,962.96 + £37,037.04 (PI Foltynie)
- Project ID 3658200 RETROSPECTIVE - A randomized, double blind, parallel group, placebo-controlled trial of Exenatide once weekly over 96 weeks as a potential disease modifying treatment for moderate severity Parkinson's disease: a proof-of-concept imaging sub-study 2019-2023 £192,896.48 (PI Foltynie)
- MRC NIRG (HMR1780), - Brain-Machine-Interface systems based on nerve cell signals (local field potentials) recorded from deep brain structures (the basal ganglia) for neuroprosthetic control and neurofeedback therapy - £16,598.33 (Co-I: Zrinzo)
- European Society for Stereotactic and Functional Neurosurgery (ESSFN) Research award: € 20,000 (PI: Akram)
- Small Acorns grant awarded allowed introduction of the "Expiratory Muscle Strength Training device (EMST150) - (Tripoliti)

11. Open grants

- NIHR Applied Programme Grant, 2014-2020, £2,000, 000. *Building Resilience and Recovery through Enhancing Cognition and quality of Life in the early Psychoses (ECLIPSE)* (Chief Investigator: Joyce)
- Project ID- 509517: NIHR *A randomized, double blind, parallel group, placebo-controlled trial of Exenatide once weekly over years as a potential disease modifying treatment for moderate severity Parkinson's disease.* 5-year award for multicentre phase 3 trial to confirm whether exenatide has PD modifying properties. £1,998,776.24 (PI Foltynie)
- Tracking Parkinson's: *The long-term development and analysis of the Parkinson's repository of biomarkers and networked datasets.* PD Prof Donald Grosset £1,517,866.25 2016-2020 (Foltynie: Co-applicant)
- Medical Research Council: 3 years project supported on Gait and Parkinson's disease. £868 000 (Limousin: Co-applicant)
- Janet Owens Clinical Research Fellowship - This donation will support 2 consecutive PhD fellowships to be supervised by Prof T Foltynie & Prof H Morris. £540 000. Dr Niro Vijiaratnam supported on this fellowship.
- NIHR Biomedical Research Centre: *Developing Precision Medicine for Movement Disorders,* Creation & staffing of a Movement Disorders Centre at UCL IoN £400 000 2017-2020 (Unit PIs co-applicants)
- Safra Foundation: *Enhancing Precision Medicine in Movement Disorders,* £290K, Supports the creation and staffing of a Movement Disorders Centre at UCL IoN 2017-2020 (Unit PIs co-applicants)
- Brain Research Trust: *Application of MRI Connectivity in Stereotactic Functional Neurosurgery* £250 000 (PI: Zrinzo)
- Project ID-530384: John Black Charitable Foundation *Neural Transplantation in the treatment of patients with Parkinson's disease.* This project supports follow up of patients who have undergone foetal cell transplantation for PD £160 000. 2016-2019 (Foltynie)
- Royal College of Surgeons, England: *Neurofeedback in Parkinson's disease;* 2014-2019, £150 000 (Zrinzo)
- Project ID-1674906: Cure Parkinson's Trust: *Differential Risk of Parkinson's disease in Diabetes patients according to diabetes treatments.* The goal is to use large existing epidemiological cohorts to explore the risk of PD among patients with and without type 2 diabetes

and whether this risk is modified according to which diabetes medication is prescribed. £31 860 (Foltynie)

- Project ID-1382294: Michael J Fox Foundation. *Advancing the GLP-1 receptor as a target in Parkinson's disease*. This project is to collect further laboratory data to explore the efficacy and mechanisms of action of exenatide in PD models/ bio-specimens. 2018-2020. £68,190 (Co-I: Foltynie)
- Cure Parkinson's Trust: *Exenatide Post hoc analyses* £45 000 (Foltynie)
- Project ID- 210076: Medical Research Council: *Decoding the effects of neural transplantation in patients with Parkinson's disease: a multimodal imaging study*. This project is to evaluate the long-term PET imaging changes associated with foetal cell transplantation in PD £30,436.22. (Foltynie)
- Rosetrees: *Investigating the mechanism of action of DBS using functional MRI* £15 000 (Foltynie)
- Small Acorns Fund: £4,392: *Impact of Expiratory Muscle Strength Training on swallowing in patients with Movement Disorders*; (Tripoliti)
- NBA/CNMR grant will fund Tim Grover for two-days-a-week for one year to examine reduced facial movement, expression, drooling and speech in PD and the effects of medication, DBS and therapy. Pilot data will assist in preparation of a subsequent NIHR grant application
- MRC: *Randomised Phase II Double-blinded Placebo-controlled Trial of Intravenous Immunoglobulins and rituximab in Patients With Antibody-associated psychosis (SINAPPS2)*; 2017-2021, £2,198,727 (PI: Joyce)
- Brain Research Trust PhD Studentship: *Attentional and inhibitory mechanisms in Tourette's syndrome*; 2015-2019, £340 191 (Joyce Primary supervisor)

12. Collaboration

The Unit collaborates with other research groups on research projects across the IoN, including neuroradiology, neurophysiology, headache and pain, neuropathology, neuropsychiatry, dementia, UCL Centre for Medical Image Computing (CMIC), and the Wellcome Centre for Human Neuroimaging.

External UK collaborations include: University of Cambridge (OCD trial and gene therapy for Parkinson's), Universities of Barts and Queen Mary (speech), University of Dundee (Psychiatry), University of York (speech)

and the University of Oxford (the Wellcome Centre for Integrative Neuroimaging).

International collaboration includes Swedish Universities of Umea, Lund (cell therapy for PD), and Linköping (studies of electrical fields of DBS), University of Malta (DBS studies), Universities of Köln, Maastricht and *Aix-en-Provence* (speech). University of Créteil, Paris (gene therapy)

Specific collaborations by individual members of the unit:

Foltynie:

- OXB102 Gene therapy trial - PI Prof Stephane Palfi (Paris)
- Tracking Parkinson's study- Core Steering Committee, PI Prof Grosset
- Transeuro Transplantation study- Core Steering Committee, PI Prof Barker
- Neural transplantation & PET imaging in patients with PD, PI Prof Piccini
- The UDCA- PD (UP Study)- Trial Steering Committee, PI Prof Bandmann
- Mechanisms of action of Exenatide, PI Dr S Gandhi
- Project: Trial of Ondansetron as a Parkinson's Hallucinations Treatment, PI DR S Reeves

Limousin:

- A Phase IIA Prospective, Single-Centre, Open Label Clinical Trial to Evaluate the Safety, Tolerability and Pharmacodynamic Effects of Ambroxol in Patients with Parkinson's Disease: Ambroxol in Disease Modification for Parkinson's Disease, PI Tony Shapira
- Fondation Paralysie Cerebrale Board member and advisor
- Patric Blomstedt, Umeå, Sweden

Zrinzo:

- OXB102 Gene therapy trial - PI Prof Stephane Palfi (Paris)
- University of Dundee, Psychiatric surgery
- Anorexia Research group (with Edinburgh, Aberdeen, Maudsley)
- University of Malta
- InBrain – development of graphene DBS electrodes

Akram:

- UCL Centre for Medical Image Computing (CMIC)

- University of Oxford, the Wellcome Centre for Integrative Neuroimaging (formerly FMRIB)
- The Wellcome Centre for Human Neuroimaging (formerly the Functional Imaging Laboratory)

Tripoliti:

- Co-chair of the Study group on “Speech impairment in Movement Disorders” of the International Movement Disorders Society
- Member of the MDS Education Team (European section), setting goals for delivery of education in Movement Disorders across Europe.
- Chair of the Focus group on stimulation and speech supported by Boston Scientific
- Lead organizer of multidisciplinary international meeting on “Managing speech post DBS” sponsored by Boston Scientific (May 2019)
- Jan Rusz and Lorraine Ramig: “How to do valid speech recordings in patients with Movement Disorders”

Candelario-Mckeown:

- The current treasurer of Deep Brain Stimulation nurses’ association (DBSNA). Collaborating with other UK centres for in the organization of the annual conference and on-going projects

13. Teaching and Training

All members of the Unit contribute to teaching and training activity on site, including clinical and surgical training, supervising MSc and PhD students, examining PhDs as well as acting as invited faculty to national and international meetings, conferences and workshops. In the past year, numerous 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, and industry representatives for observing and learning.

PIs of the Unit have contributed in teaching on speech therapy, neuropsychology, training in surgery and in DBS inclusion and programming, directing regular ECMT international courses as well as teaching and instructing overseas. Members of the Unit are regular chairs

of Gowers Round and Critchley Round, Faculty on UCL MSc Courses, as well as teach MRES in Translational Neurology and MSc in Clinical Neurology and act as personal tutor for MB BS undergraduates. Unit PIs are co-organisers of the regular meetings of the Queen Square Basal Ganglia Club, as well as acting as examiners of numerous MD and PhD theses in the UK and internationally. Prof Foltynie was on the Organising Committee for the World Parkinson's Congress, Kyoto, Japan.

Events hosted by the Unit during 2019:

- MRI-Guided & MRI-Verified DBS Course on behalf of the ECMT, Nov 11/12 (European Continuing Medical Training, Course Director: LZ)
- Course codirector for the Third MDS Speech meeting in Prague (Tripoliti)
- Multidisciplinary international meeting on “Managing speech post DBS” sponsored by Boston Scientific (May 2019 - Tripoliti)

14. Global 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”, more and more 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 national and international colleagues who wish to come and learn in order to disseminate our practice in their centres. Members of the Unit are invited overseas to train and supervise colleagues using the unique method for DBS developed in the unit.

15. Knowledge Transfer, Public Engagement & Media

All PIs of the Unit serve regularly as referees for international Scientific Journals, grant bodies and universities, and have been examiners of MD and PhD theses, nationally and internationally. Members of the Unit have been invited speakers at numerous events, meetings and conferences worldwide.

Zrinzo:

- Member of the educational subcommittee of the ESSFN
- Member of the ESSFN subcommittee on pedunculo pontine nucleus DBS surgery
- Faculty on the International *Noble Art of Lesioning* Course
- On the Board of the UCL MSc in Clinical Neuroscience Course
- Head of UK research group on ablative neurosurgery for Anorexia
- Member of subcommittee on psychiatric surgery of the World Society
- Clinical Steering Committee for SRT Neurogenetic Therapies Programme at UCL: 2019 to date

Limousin:

- Member of Clinical Neuroscience MSc Course Committee and tutor
- Scientific Board France Parkinson and Fondation Motrice
- Faculty and local training centre for young neurologist DBS training program

Foltynie:

- ABN Advisory Group on Movement Disorders, Member 2015 to date
- Founder member of the UK DBS Network, 2015 to date
- TRANSEURO Steering Committee member, 2010 to date
- PRoBaND Core Steering Committee, 2012 to date
- Queen Square Clinical Trials Committee, 2011 to date
- Movement Disorders short course Committee, NHNN, 2009 to date
- Member Grant Review Board - Weston Brain Institute, 2017 to date
- Clinical Steering Committee for SRT Neurogenetic Therapies Programme at UCL: 2019 to date
- Queen Square Movement Disorders Centre Executive Board member: 2018 to date
- Cambridge Brain Bank (CBB) access advisory committee: 2016- to date

Joyce:

- Royal College of Psychiatrists: Chair (elected), Faculty of Neuropsychiatry, June 2016-2020.
- Royal College of Psychiatrists: Neuroscience Board, July 2018-2021
- Medical Research Council Panels:
 - MRF Emerging Leaders Prize, 2018, 2019

- MRC Clinical Academic Research Partnerships (CARP) 2019
- MRC Therapeutic Target Validation in Mental Health 2019
- British Association for Psychopharmacology: Governance Panel, July 2016-2020
- Foulkes Foundation: Advisory Board: 2012 –present
- Tourette’s Action: Trustee, 2016-present; Research Awards Committee, 2016-present
- Institute of Neurology:
 - Head, Division of Neuropsychiatry & Neuropsychology, from 2005
 - Executive Committee, from 2005
 - MSc in Clinical Neurosciences, Examinations Committee, from 2005
- Institute of Mental Health: Advisory Committee, from 2019
- UCL/UCLH, Biomedical Research Central: Mental Health Theme, Executive Board and neurosurgery theme lead, from 2017

Hyam:

- Specialist adviser to NICE
- London Deanery/UCL Partners Higher Specialist Training Committee for London Neurosurgery
- The Royal Society of Medicine Committee for Clinical Neurosciences since 2016
- PhD Examiner at UCL

Akram:

- The London Deanery: SITE (Surgical In Training Evaluation) assessment for Core Surgical trainees (faculty)
- PhD supervisor (UCL) Machine learning approaches to building predictive models in functional neurosurgery

Tripoliti:

- Sing for Joy choir: Founding member and Trustee. The Choir has been entertaining and improving patients’ lives for the last 16 years
- “Which Way up?” Collaboration with Proudfoot Productions to create a documentary on the abstract painter John McLean - diagnosed with MSA - highlighting the impact of communication problems on daily life
- Course director for the 3rd MDS meeting in Prague with Prof Jan Ruzs.
- Member of the British Laryngological Association
- Clinical Neurosciences MSc Course tutor

Grover

- Article on research using software for analysis of facial movement on Trust Insight magazine

Candelario-Mckeown

- Led and written the Royal College of Nursing (RCN) endorsed 'Standard of practice and proficiency framework for nurse specialist and Allied health professionals' to be launched and to be published this year.

16. Publications

Books / Book chapters

Chen, T, Matharu, M, Zrinzo, L: **Neuromodulation for Trigeminal Autonomic Cephalalgias in Diagnosis and Management of Head and Face Pain, A Practical Approach**; Editors: Suen, James Y., Petersen, Erika (Eds.)

Peer reviewed publications during 2019

Unit PIs contributed to 48 publications (below in alphabetical order):

1. Akram, H., Hariz, M., Zrinzo, L. (2019). **Connectivity derived thalamic segmentation: Separating myth from reality** *NeuroImage: Clinical* 22(Neuroimage Clin. 18 2018), 101758.
2. Apergis-Schoute, A., Tyagi, H., Akram, H., Foltynie, T., Limousin, P., Drummond, L., Fineberg, N., Matthews, K., Jahanshahi, M., Robbins, T., Sahakian, B., Zrinzo, L., Hariz, M., Joyce, E. (2019). **214. Deep Brain Stimulation in OCD: Subthalamic Versus VC/VS Stimulation** *Biological Psychiatry* 85(10), S89.
3. Athauda, D., Gulyani, S., ... Kapogiannis, D., Foltynie, T. (2019). **Utility of Neuronal-Derived Exosomes to Examine Molecular Mechanisms That Affect Motor Function in Patients With Parkinson Disease: A Secondary Analysis of the Exenatide-PD Trial.** *JAMA neurology* 76(4), 420-429.
4. Barbosa, P., Djamshidian, A., O'Sullivan, S., Pablo-Fernandez, E., Korlipara, P., Morris, H., Bhatia, K., Limousin, P., Foltynie, T., Lees, A., Warner, T. (2019). **The long-term outcome of impulsive compulsive behaviours in Parkinson's disease.** *Journal of neurology, neurosurgery, and psychiatry* 90(11), 1288-1289.
5. Barker RA; TRANSEURO consortium. **Designing stem-cell-based dopamine cell replacement trials for Parkinson's disease.** *Nat Med.* 2019 Jul;25(7):1045-1053. doi: 10.1038/s41591-019-0507-2.

6. Barnes, T., Drake, R., Paton, C., ... Joyce, E., Lewis, S., Lingford-Hughes, A., MacCabe, J., Owens, D., Patel, M., Sinclair, J., Stone, J., Talbot, P., Upthegrove, R., Wieck, A., Yung, A. (2019). **Evidence-based guidelines for the pharmacological treatment of schizophrenia: Updated recommendations from the British Association for Psychopharmacology.** *Journal of psychopharmacology (Oxford, England)* 34(1), 269881119889296.
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10. Cappon, D., Beigi, M., Kefalopoulou, Z., Zrinzo, L., Candelario, J., Milabo, C., Akram, H., Dayal, V., Hyam, J., Kass-Iliyya, L., Silverdale, M., Evans, J., Limousin, P., Hariz, M., Joyce, E., Foltynie, T., Jahanshahi, M. (2019). **Globus pallidal deep brain stimulation for Tourette syndrome: Effects on cognitive function** *Parkinsonism & Related Disorders* 69(), 14-18.
11. Coenen, V., Schlaepfer, T., Varkuti, B., Schuurman, P., Reinacher, P., Voges, J., Zrinzo, L., Blomstedt, P., Fenoy, A., Hariz, M. (2019). **Surgical decision making for deep brain stimulation should not be based on aggregated normative data mining** *Brain Stimulation*
12. Dayal, V., Grover, T., Tripoliti, E., Milabo, C., Salazar, M., Candelario-McKeown, J., Athauda, D., Zrinzo, L., Akram, H., Hariz, M., Limousin, P., Foltynie, T. (2019). **Short Versus Conventional Pulse-Width Deep Brain Stimulation in Parkinson's Disease: A Randomized Crossover Comparison** *Movement Disorders* 23(6), 837.
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14. Di Giulio, I., Kalliolia, E., Georgiev, D., Peters, A., Voyce, D., Akram, H., Foltynie, T., Limousin, P., Day, B. (2019). **Chronic Subthalamic Nucleus Stimulation in Parkinson's Disease: Optimal Frequency for Gait Depends on Stimulation Site and Axial Symptoms.** *Frontiers in neurology* 10(), 29.

15. Fischer, P., Pogosyan, A., Green, A., Aziz, T., Hyam, J., Foltynie, T., Limousin, P., Zrinzo, L., Samuel, M., Ashkan, K., Lio, M., Cecco, M., Fornaser, A., Brown, P., Tan, H. (2019). **Beta synchrony in the cortico-basal ganglia network during regulation of force control on and off dopamine** *Neurobiology of Disease* 127; 253-263.
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18. Foltynie, T. (2020). **Seeing through the FOG?** *Movement disorders: official journal of the Movement Disorder Society* 35(1), 3-4.
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20. Grover, T., Georgiev, D., Kalliola, R., Mahlknecht, P., Zacharia, A., Candelario, J., Hyam, J., Zrinzo, L., Hariz, M., Foltynie, T., Limousin, P., Jahanshahi, M., Tripoliti, E. (2019). **Effect of Low versus High Frequency Subthalamic Deep Brain Stimulation on Speech Intelligibility and Verbal Fluency in Parkinson's Disease: A Double-Blind Study** *Journal of Parkinson's Disease* 9(1), 141-151.
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23. Iwaki, H., et al **Penetrance of Parkinson's Disease in LRRK2 p.G2019S Carriers Is Modified by a Polygenic Risk Score** *Movement Disorders* (online)
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26. Joyce, E., Tyagi, H., Apergis-Schoute, A., Akram, H., Foltynie, T., Limousin, P., Drummond, L., Fineberg, N., Matthews, K., Jahanshahi, M., Robbins, T., Sahakian, B., Zrinzo, L., Hariz, M. (2019). **A direct comparison of ventral capsule and anteromedial subthalamic nucleus stimulation in obsessive compulsive disorder: clinical and imaging evidence for dissociable Effects** *Brain Stimulation* 12(2), 404.
27. Kahan, J., Mancini, L., Flandin, G., White, M., Papadaki, A., Thornton, J., Yousry, T., Zrinzo, L., Hariz, M., Limousin, P., Friston, K., Foltynie, T. (2019). **Deep brain stimulation has state-dependent effects on motor connectivity in Parkinson's disease** *Brain* 142(8), 2417-2431.
28. Kim, H., Mason, S., Foltynie, T., Winder-Rhodes, S., Barker, R., Williams-Gray, C. (2019). **Motor complications in Parkinson's disease: 13-year follow-up of the CamPAIGN cohort.** *Movement disorders : official journal of the Movement Disorder Society* 35(1), 185-190.
29. Leimbach, F., Gratwicke, J., Foltynie, T., Limousin, P., Zrinzo, L., Jahanshahi, M. (2019). **The effects of deep brain stimulation of the pedunculopontine nucleus on cognition in Parkinson's disease and Progressive Supranuclear Palsy** *Clinical Parkinsonism & Related Disorders* 1(), 48-51.
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33. Mahlknecht, P., Kaski, D., Georgiev, D., Foltynie, T., Limousin, P. (2019). **Reply: Pathophysiology of gait disorders induced by bilateral globus pallidus interna stimulation in dystonia.** *Brain: a journal of neurology* (online)

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36. Nalls, M et al F. (2019). **Identification of novel risk loci, causal insights, and heritable risk for Parkinson's disease: a meta-analysis of genome-wide association studies.** *The Lancet. Neurology* 18(12), 1091-1102.
37. Nicholson, T., Carson, A., Edwards, M., Goldstein, L., Hallett, M., Mildon, B., Nielsen, G., Nicholson, C., Perez, D., Pick, S., Stone, J., Anderson, D., Asadi-Pooya, A., Aybek, S., Baslet, G., Bloem, B., Brown, R., Chalder, T., Damianova, M., David, A., Epstein, S., Espay, A., Garcin, B., Jankovic, J., Joyce, E., Kanaan, R., Kozłowska, K., LaFaver, K., LaFrance, W., Lang, A., Lehn, A., Lidstone, S., Maurer, C., Morgante, F., Myers, L., Reuber, M., Rommelfanger, K., Schwingenshuh, P., Serranova, T., Shotbolt, P., Stebbins, G., Tijssen, M., Tinazzi, M. (2019). **Outcome Measures for Functional Neurological Disorder: A Review of the Theoretical Complexities** *The Journal of Neuropsychiatry and Clinical Neurosciences* 32(1), online
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population-based Parkinson's disease study *Brain*, Volume 142, Issue 9, September 2019, Pages 2828–2844

42. Tibber, M., Kirkbride, J., Mutsatsa, S., Harrison, I., Barnes, T., Joyce, E., Huddy, V. (2019). **Are socioenvironmental factors associated with psychotic symptoms in people with first-episode psychosis? A cross-sectional study of a West London clinical sample** *BMJ Open* 9(9), e030448.
43. Tyagi, H., Apergis-Schoute, A., Akram, H., Foltynie, T., Limousin, P., Drummond, L., Fineberg, N., Matthews, K., Jahanshahi, M., Robbins, T., Sahakian, B., Zrinzo, L., Hariz, M., Joyce, E. (2019). **A Randomized Trial Directly Comparing Ventral Capsule and Anteromedial Subthalamic Nucleus Stimulation in Obsessive-Compulsive Disorder: Clinical and Imaging Evidence for Dissociable Effects** *Biological Psychiatry* 85(9), 726-734.
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47. Zapparoli, L., Macerollo, A., Joyce, E., Martino, D., Kilner, J. (2019). **Voluntary tic suppression and the normalization of motor cortical beta power in Gilles de la Tourette Syndrome: an EEG study.** *The European journal of neuroscience* 50(12), 3944-3957.
48. Zrinzo, L., Wilson, J., Hariz, M., Joyce, E., Morris, J., Schmidt, U. (2019). **Exploring every ethical avenue. Commentary: The Moral Obligation to Prioritize Research Into Deep Brain Stimulation Over Brain Lesioning Procedures for Severe Enduring Anorexia Nervosa** *Frontiers in Psychiatry* 10(), 326.

Appendix:

Past Faculty:

- Prof Emeritus Marwan Hariz MD PhD (*First Unit Head, Appointed to the first established UK Chair of Functional Neurosurgery Oct 2002, Retired Jul 2018*)
- Prof Emeritus Marjan Jahanshahi PhD (*Professor in Neuropsychology, Appointed Oct 2002, Retired Dec 2017*)

Past PhD Fellows, Post-doc Fellows, Clinical Fellows, and Students:

- Ladan Akbarian-Tefaghi (*MSc student*)
- Harith Akram (*Neurosurgeon, PhD awarded Sep 2018*)
- Salhin Alatrash (*MSc student*)
- Ala'a Al-Moussa (*Neurosurgeon, Clinical Fellow*)
- Saryah Alhejazi (*Neuropsychology MSc student*)
- Caroline Andrews (*Radiographer, MSc student*)
- Iciar Aviles Olmos (*Neurologist, PhD fellow, Spain*)
- Jeffrey Bergman (*MSc student*)
- Artem Bunchuk (*Neuropsychology MSc student*)
- Davide Cappon (*visiting PhD student*)
- Paul Chang (*MRes Translational Neurology (Distinction) Sep 2017*)
- Tsinsue Chen (*Neurosurgeon, Clinical Fellow from Barrow, USA*)
- Cecil Atkinson-Clement (*visiting fellow, University of Aix-en-Provence*)
- Mohamed Draz (*Neurosurgeon, Clinical Fellow*)
- Christopher Hatton (*MSc student*)
- Nik Haliasos (*Neurosurgeon, Clinical Fellow*)
- Jonathan Hyam (*Neurosurgeon, Clinical Fellow*)
- Dejan Georgiev (*Neurologist, Post Doc fellow*)
- Alison Gordon (*MSc student*)
- James Gratwicke (*Neurologist, PhD awarded February 2017*)
- Gilbert Gravino (*MSc student*)
- Samih Hassan (*Neurosurgeon, Clinical Fellow*)
- Etienne Holl (*Neurosurgeon, Clinical Fellow, Austria*)
- Yu-Ting Huang (*Neuropsychologist, PhD student*)

- Joshua Kahan (*PhD student*)
- Rania Kalliolia (*Neurologist, fellow*)
- Zinovia Kefalopolou (*Neurologist, post-doc clinical research fellow, Greece*)
- Zuzana Kosutzka (*Neurologist, clinical research fellow*)
- Michel LeFranc (*Neurosurgeon, Clinical Fellow, France*)
- Friederike Leimbach (*Neuropsychologist, PhD student*)
- Vanessa Lythe (*MSc student*)
- Antonella Macerollo (*Neurologist, PhD awarded 2018*)
- Philipp Mahlknecht (*Neurologist, PhD student*)
- Miguel Malo, (*visiting fellow, University of Zaragoza, Spain*)
- Rayna Mateva (*visiting neuropsychologist, Malta*)
- Jennifer Meeres (*MSc student*)
- Nerys Morton (*MSc student*)
- Tena Nevidal (*MSc student*)
- Tito Petralia (*MSc student*)
- Erika Petersen (*Neurosurgeon, Clinical Fellow, USA*)
- Johanna Philipsson (*Neuropsychologist, PhD student, Sweden*)
- Serge Pinto (*speech and language, France*)
- Vishal Rawji (*Neuropsychologist, PhD student*)
- Sanja Roksar (*Erasmus funded visiting MSc Student*)
- Pedro Roldan (*Neurosurgeon, Clinical Fellow, Spain*)
- Nadia Sari-Sarraf (*Neuropsychology, MSc student*)
- Emma Scelzo (*Neurologist, fellow, Italy*)
- Paul Silberstein (*Neurologist, France*)
- Rasmus Stenmark (*Neurologist, PhD student, Sweden*)
- Stephane Thobois (*Neurologist, France*)
- Erika Tirr (*MSc student*)
- Steve Tisch (*Neurologist, Australia*)
- Elina Tripoliti (*Speech and Language, PhD student*)
- Jonathan Vanhoecke (*MSc student*)
- Jeevagan Vijayabala (*Neurologist, fellow*)
- Saman Vinke (*Neurosurgeon, Clinical Fellow, Nijmegen, Holland*)

- Fiona Wilkes (*Visiting medical student, Australia*)
- Evelina Woin (*MSc student*)
- Katherine Woodall (*MSc student*)
- Chengyuan Wu (*Neurosurgeon, Clinical Fellow, USA*)
- Ludvic Zrinzo (*Neurosurgeon, Clinical Fellow and PhD student*)