Queen Square Alumnus Association
International Meeting
UCL Institute of Neurology
London
July 8-9
2013
About the Alumnus logo
The front cover image is an adaptation of an 1898 camera lucida drawing of a cerebellar Purkinje cell by Santiago Ramón y Cajal, the father of modern neuroscience. It is one of the earliest drawings of a neuron. This drawing is merged with the University College London logo here. From an artist's perspective, Cajal's rendition of the neuron resembles the roots and the branches of a tree at the same time, somewhat similar to the Bhagavad Gita's (15.1) description of the 'eternal tree of knowledge' that has "its roots in the heavens and the branches emerging from the earth below". The alumni of an educational institution simultaneously forms the branches that grow out of it and also the roots that nourish the tree.

Sunraj Rajan, MSc, MD

Editors
Dr Sunraj Rajan & Mr David Blundred

Coordinator
Mr David Blundred
Teaching and e-Learning Administrator

The editors are grateful to the Queen Square Library, the Medical Illustrations Department and the UCL Creative Media Services for supplying so many of the images included in this booklet. All rights reserved.

© 2013, UCL Institute of Neurology, London
Contents

Welcome
Mr David Blundred Alumnus Association Secretary

Conference Schedule and Venue guide
July 8 - 9, 2013 | See Campus Maps at the end of the booklet

On the shoulders of giants
A timeline of Queen Square and the NHNN

History of Epilepsy at Queen Square
Professor Simon Shorvon, ION

New treatments for epilepsy – the ideas of Hughlings Jackson realised
Professor Matthew Walker, ION

Queen Square and the development of Neurology Services in Kenya and East Africa
Professor James Jowi, Alumni – Kenya

Britain, the “English Malady”, and Neuropathic pain
Professor Jose Ochoa, Alumni – Chile

Recent developments in Peripheral Nerve Disease
Professor Mary Reilly, ION

PhD Highlights – Research of Current Students
Dr Awin Djamshidian-Tehrani, ION

Recent developments in Dementia Research
Professor Nick Fox, ION

Australia and Queen Square
Dr Catherine Storey, Alumni - Australia

The Present and Future of Neurosurgery
Mr George Samandouras, NHNN

Neurosurgery at Queen Square: A historical perspective
Mr Michael Powell, NHNN

Movement Disorders: Beyond the Basal Ganglia
Dr Mark Edwards, ION

The History of Therapy of MS over the last two centuries – hopes, frustrations and triumphs
Professor Jock Murray Alumni - Canada

Clinical and Research developments in MS
Professor Alan Thompson, ION

Uro-Neurology at Queen Square
Professor Clare Fowler, ION

PhD highlights – research of current students
Mr Sundeep Teki, ION

Kinnier Wilson, his 1912 Brain paper & Movement Disorders at Queen Square
Professor Niall Quinn, ION

Learning from mouse models about the human condition
Professor Elizabeth Fisher, ION

Huntington’s disease, past, present and future
Professor Sarah Tabrizi, ION

Neurology in Thailand & links with Queen Square
Professor Surakpin Jirapimolmard, Alumni - Thailand

Recent Advances in Neuro-oncology
Dr Jeremy Race, NHNN

International Teaching in Queen Square: opportunities to contribute and network
Dr Laura Moriarty, ION

Ophthalmology and the National Hospital
Dr Gordon Plant, ION

Queen Square Campus Map

UCL and Bloomsbury Map
Welcome from the Alumnus Secretary

Dear Queen Square Alumnus Association members,

It is a great pleasure to welcome you all to the 2013 Queen Square Alumnus Association meeting. The Queen Square Alumnus Association was established in 1989 in order to foster a collegiate spirit in people who have undertaken part of their training at Queen Square. The Association was started by Miss Pat Harris who worked at Queen Square from the mid-1960s until the late 1980s. Without her there would be no Alumnus Association, and I think it important that we remember her contribution, not only to the organisation but also her role at Queen Square, in which she formed many close associations with people who worked and studied here.

I have been delighted by the response to this meeting and it is nice to welcome Alumni from all over the world, from Australia and New Zealand, to Thailand, India, Iraq, Nigeria, Kenya, many European countries, the USA, Canada, Brazil and Argentina. It speaks volumes for Queen Square’s reach and influence that we have representatives from six continents, with Alumni who were at Queen Square from the 1960s through to the present day.

I would like to take this opportunity to thank all of our speakers for taking part in this event, some of whom have travelled many miles to make it here. The programme represents just some of the diversity of research and clinical practice that is conducted within Queen Square and in the wider world.

We have tried to offer a mixture of historical perspectives along with more recent developments to highlight the incredible work that has been conducted at Queen Square since its formation until the present day. It is also important to recognise the contribution of Queen Squares Alumni, who have enriched the quality of research, teaching, clinical care and the overall experience of working and studying here.

I am indebted to Professor Simon Sharvon and Professor Andrew Lees for their constant support and encouragement for the Alumnus Association, and to Dr Sunil Tantrapawat who remains for me the inspiration and driving force behind the association. I would also like to thank Ms Daniela Warr-Schori and Ms Hannah Stapley for their help and support in arranging the Alumni Dinner and evening reception.

Finally, I would like to highlight for special praise, Dr Suraj Rajan, who along with myself produced this booklet. Suraj was responsible for the layout and design, and has contributed much to this project and others at Queen Square. Suraj’s ability, dedication and sense of humour is a constant source of motivation.

I hope that you all have an enjoyable and stimulating experience at our meeting, and I look forward to many more such events in the future.

Yours faithfully

DAVID BLUNDRED
Monday, 8th July 2013

Lecture Theatre, 33 Queen Square, National Hospital for Neurology & Neurosurgery

8.25 am  Registration
9.00 am  Welcome and History of Epilepsy at Queen Square  Professor Simon Shorvon, ION
9.45 am  New treatments for epilepsy – the ideas of Hughlings Jackson realised  Professor Matthew Walker, ION
10.30 am  Queen Square and the development of Neurology Services in Kenya and East Africa  Professor James Jowi, Alumni – Kenya
11.05 am  Coffee and Danish pastries
11.30 am  Britain, the “English Malady,” and neuropathic pain  Professor Jose Ochoa, Alumni – Chile
12.15 pm  Recent developments in Peripheral Nerve Disease  Professor Mary Reilly, ION
12.55 pm  PhD Highlights— research of current students  Dr Atbin Djamshidian-Tehrani, ION
1.10 pm  LUNCH
2.00 pm  Recent developments in Dementia Research  Professor Nick Fox, ION
2.40 pm  Australia and Queen Square  Dr Catherine Storey, Alumni - Australia
3.25 pm  Break
3.45 pm  The Present and Future of Neurosurgery  Mr George Samandouras, NHNN
4.30 pm  Neurosurgery at Queen Square: A historical perspective  Mr Michael Powell, NHNN
5.10 pm  Movement Disorders: Beyond the Basal Ganglia  Dr Mark Edwards, ION
5.40 pm  Queen Square Library, Archive and Museum tour  (to register contact Mr David Blundred d.blundred@ucl.ac.uk)
6.00 pm  Evening reception  33QS, Basement
7.00 pm  Queen Square Alumnus Association Dinner  Wilkins Terrace Restaurant, UCL
See UCL & Bloomsbury Map at the Back of this booklet
Tuesday, 9th July 2013

Venue: Lecture Theatre, 33 Queen Square, National Hospital for Neurology & Neurosurgery

9.00 am  The History of Therapy of MS over the last two centuries - hopes, frustrations and triumphs  
Professor Jock Murray Alumni - Canada

9.50 am  Clinical and Research developments in MS  
Professor Alan Thompson, ION

10.35 am  Uro-Neurology at Queen Square  
Professor Clare Fowler, ION

11.10 am  Coffee and Danish pastries

11.30 am  Interview with Professor Andrew Lees, ION

11.50 am  PhD highlights – research of current students  
Mr Sundeep Teki, ION

12.10 pm  Kinnier Wilson, his 1912 Brain paper & Movement Disorders at Queen Square  
Professor Niall Quinn, ION

1.00 pm  LUNCH

1.50 pm  Learning from mouse models about the human condition  
Professor Elizabeth Fisher, ION

2.20 pm  Huntington’s disease, past, present and future  
Professor Sarah Tabrizi, ION

2.55 pm  Neurology in Thailand & links with Queen Square  
Professor Suthipun Jitpimolmard, Alumni - Thailand

3.40 pm  Break

4.00 pm  Recent Advances in Neuro-oncology  
Dr Jeremy Rees, NHNN

4.30 pm  International Teaching in Queen Square: Opportunities to contribute and network  
Dr Laura Moriyama, ION

4.55 pm  Ophthalmology and the National Hospital  
Dr Gordon Plant, ION

5.40 pm  Evening Drinks reception  
33QS, Basement
On the shoulders of giants
History of Epilepsy at Queen Square

Perspective

For a period between the founding of the hospital in 1860 and the beginning of the first war in 1914, the National Hospital led developments in epilepsy worldwide. It was the first hospital to establish a neurological ward specifically for the treatment of epilepsy, at the hospital the conceptual basis of epilepsy was changed, a theory of the physiological structure of the nervous system was developed, cortical localisation of epileptic activity was demonstrated and the principle of focal epilepsy established, the first effective drug treatment of epilepsy (bromide) was extensively studied and the first surgical operation for epilepsy carried out.

Physicians famous for their work in epilepsy at the hospital included: CE Brown-Sequard, Sir John Russell Reynolds, Sir Edward Sieveking, John Hughlings Jackson, Sir David Ferrier, Sir Victor Horsley, Sir William Gowers, and William Aldren Turner. Indeed, of the first twenty appointees (1859–1886), seven were elected Fellows of The Royal Society, three were appointed Physicians to The Royal Household, two were presidents or vice presidents of the Royal College of Physicians and five were knighted.

There has been no parallel before or since for this remarkable record. They brought to the hospital a mixture of basic animal experimentation, clinical observation and novel therapies.

After 1914, epilepsy rather fell from the central focus of work at the hospital, although MacDonald Critchley, FMR Walshe, SA Kinnier Wilson and Dennis Williams were renowned for their epilepsy contributions. This talk will cover this period, and focus particularly on the early years.
New treatments for epilepsy – the ideas of Hughlings Jackson realised

Perspective

Epilepsy is the commonest serious neurological disorder affecting approximately 50 million people worldwide, and ~30% of these people are resistant to optimal drug therapy.

Despite a substantial growth in the number of antiepileptic drugs available, the impact on the number of people seizure free has been modest. Moreover, fewer than 10% of the population of people with pharmaco-resistant epilepsy are suitable for curative epilepsy surgery. There are therefore approximately 15 million people with epilepsy for whom our present treatments are inadequate.

Hughlings Jackson proposed an alternative treatment. He suggested that the cells causing the epilepsy could be destroyed with a microbial treatment. Hundred years later, we are starting to use treatments based around modified viruses (viral vectors) carrying specific genes to modify cellular behaviour. Here I will present our work that has led to a completely novel approach for the treatment of epilepsy using a gene therapy to alter the excitability of neurons in the seizure focus.
Queen Square and the development of neurology services in Kenya and East Africa

Alumni highlights

Neurology services in Kenya and the region is still in its infancy, that as it may, Queen Square has played a significant role in its development. There are 11 adult neurologists and seven pediatric neurologists in Kenya, 50% of us have trained at Queen Square or have had an affiliation with Queen Square. Training neurologists at Queen Square for Kenya started in the seventies; the pace has been very slow mainly due to lack of sponsorship.

Kenya has a population of about 40 million. The ratio therefore stands at 1 neurologist to 2.2 million inhabitants. WHO recommends a ratio of 1:100,000; we therefore need at least 200 neurologists. The other professions who work closely with neurologists are: 20 neurosurgeons, 1 clinical neurophysiologist, 2 speech and language therapists. There are no dedicated neuro-pathologists and neurological nurses. We have about 30 Neurophysiology Technologists mainly trained on EEG evaluation. Most of these services are coalesced around urban areas. The workload is insurmountable.

There are neurological clinical services, University teaching activities and excellent research facilities run by neurologists who have either trained at Queen Square or are affiliated to Queen Square and other UK Universities; notably KEMRI-Wellcome Collaborative Programme, Kilifi, Kenya and University of Oxford, Oxford, UK.

We share common problems in provision of neurology services with Uganda, Tanzania, Rwanda and Burundi. Statistics as regards the number of neurologists and services offered in our neighboring countries is being verified. There are four (4) neurologists in Tanzania for a population of about 45 million.

Neurologists in Kenya have finally gotten together to form a dedicated association for neurologists. There are collaborative plans underway with our neighbors to build capacity of neurologists and allied professionals in Kenya and the region. We are grappling with the best mode of capacity building to fill this gap; cognizant of location, duration, cost and quality of training.
Professor José Ochoa

Professor Ochoa, originally from Chile, worked at Queen Square from 1966 until 1974 in various roles including Senior Lecturer in Clinical Neurophysiology, Wellcome Research Fellow & Honorary Consultant in Clinical Neurophysiology. He later took positions in the USA at Dartmouth Medical School, University of Wisconsin Medical School, Good Samaritan Hospital and the Oregon Health Sciences University where he is currently the director of the Oregon Nerve Centre. He has published extensively, and has special interest in neuropathic pain and mechanical and thermal allodynia.

Britain, the English Malady, and Neuropathic Pain

Alumni highlights

The English malady was defined by its Scottish author as: “Nervous Diseases of all kinds, as spleen, vapors, lowness of spirits, hypochondriacal and hysterical distempers”. That was the early 18th century but the malady is neither English nor a relic: it is current and universal. The malady is often expressed in patients misdiagnosed with the nickname CRPS-I, my favorite non-disease of the sensory system.

As defined by George Cheyne, the “nervous” malady is not a specific biological disease. It comprises plain psychiatric syndromes and is predictably contaminated by undiagnosed pathophysiologically-based sensory and motor disorders and also by pseudoneurological displays of “nervous” symptoms without underlying pathology. One common psychosocial by-product of most “nervous maladies”, for which the doctor fails to identify pertinent pathology or pathophysiology, is the patient’s conclusion “the doctor thinks I am crazy or faking”.

Pseudoneurological disorders are “psychogenic”; the clinical display is characteristically atypical and the anatomo-physiological instruments that seem impaired test normal. If a malady is pseudoneurological, it is generated abnormally in the mind of the brain. No surprise: the psyche is neuronal and generates imperfect cartoons of neurological disease.

The unquestionably pseudoneurological clinical display of most CRPS-I cases gets consistently “diagnosed” as CRPS-I for a simple circular reason: it is the pseudoneuropathic pain patient who gets consistently so nicknamed.

However, pseudoneurological malingering is hard to differentiate from conversion-somatization. The taxonomic itinerary of CRPS-I has been pathetic through decades. Until 1994 this seemingly neuropathic pain profile, in absence of pathology, was nicknamed Reflex Sympathetic Dystrophy, assuming that the pain was “sympathetically maintained”. This fallacy was demolished when Verdugo showed that the gold standard diagnostic test, that is the non-placebo-controlled sympathetic ganglion block, was a placebo artifact. Today, in absence of diagnostic tests, pathology or dysfunction, and embarrassed by the 1994 criteria, newfound pain aficionados, without clinical experience, have targeted the dorsal horn as the site of CRPS-I malady, ignoring that their neuropaophysiological gut felt belief is not testable in humans.

Finally, all undiagnosed patients expressing pseudoneurological Distempers are victims of iatrogenic harm, through omission of proper differential diagnosis and commission of unjustified, dangerous and ineffective “therapies”.

UCL Institute of Neurology
Professor Mary Reilly

Professor Mary Reilly came to Queen Square in 1991 firstly as a researcher and then as a clinical registrar with Professor Anita Harding. Professor Reilly is a consultant neurologist at the National Hospital for Neurology and Neurosurgery and conducts research on Peripheral Nerve Diseases and Neuromuscular Diseases. She has over 250 publications and leads one of Europe's largest peripheral nerve clinics which focuses on the genetics and therapeutics of conditions like Charcot-Marie-Tooth disease, the hereditary sensory and autonomic neuropathies and the distal hereditary motor neuropathies.

Inherited peripheral nerve diseases

Recent developments

The inherited peripheral nerve diseases are a large group of disorders which can be divided into those where the neuropathy is the sole or major part of the disease and those in which the neuropathy is part of a more generalised neurological or multisystem disorder. This talk will focus on the former which include Charcot-Marie-Tooth disease (CMT) and the related disorders hereditary neuropathy with liability to pressure palsies (HNPP), the distal hereditary motor neuropathies (HMSN) and the hereditary sensory and autonomic neuropathies (HSAN).

This has had a major impact on the diagnosis of this group of disorders but has also allowed the study of the pathogenesis of these diseases and the consequent development of candidate therapies.

This talk will provide an update on recent developments with an emphasis on recent gene discoveries and the development of therapies.

The clinical classification of CMT dates from the 1980s and is based on upper limb motor conduction velocities where CMT1 refers to CMT with MCVs < 38 m/s and CMT2 MCVs > 38 m/s. This classification is still the cornerstone of diagnosis but there have now been more than 50 causative genes identified.
Research of current students

PhD highlights

A subgroup of Parkinson’s disease (PD) patients treated develops devastating behavioural side effects collectively termed impulsive compulsive behaviours (ICBs). Although it is still unclear why some patients develop these addictive behaviours, identified risk factors are younger onset of PD, higher novelty seeking personality traits and DA therapy. For my PhD I have tested PD patients with and without ICBs on a variety of different neuropsychological tests and found that dopaminergic medication afect cognitive performance in a complex fashion with improvement in some tasks and deterioration in others.

Anti-Parkinson medication improved response inhibition in both PD groups. On other tests such as a working memory task dopaminergic medication had, however, no effect on performance. Finally, all PD patients became more risk prone in their “on” compared to their “off” state, and those patients who developed pathological gambling made the most risky decisions.

PD patients with and without ICBs were also compared to pathological gamblers and illicit substance abusers, who both did not have PD. Results demonstrated that the non-impulsive PD group resembled pathological gamblers, whereas ICB patients performed similarly to illicit substance abusers. These results strengthen the link between ICBs in PD and substance abuse.
Recent developments in dementia research

Research updates

The last few years have seen important research advances and significant developments in our understanding of the dementias. These include advances in genetics, pathology, imaging and biomarkers. Although there are now symptomatic treatments for Alzheimer's disease (AD) disease-modifying treatments—a key goal—remain elusive. Genetic studies have revealed factors that reduce as well as increase risk. Unravelling the effects of these genes may offer new insights into pathogenesis and potential therapeutic avenues for AD and also for other causes of dementia.

There is a growing emphasis on early detection of AD. A remarkable advance has been the ability to image cerebral amyloid in vivo using PET ligands. Most (if not all) AD patients have positive scans but so do almost 25% of “control” individuals subjects over the age of 70 years. These findings fit with increasing evidence for a long preclinical period to AD.

CSF markers have been the other important diagnostic advance—these are now well-validated and show that reduced CSF-Abeta and raised CSF-tau carry strong positive predictive value for AD even at a very early stage.

These developments have contributed to the new criteria for AD which include imaging (MRI and PET) and CSF markers as supportive features for an early clinical diagnosis.

As significant have been advances in non-AD dementias. A long search for the genetic cause of frontotemporal dementia (FTD) with MND has finally yielded a novel and unusual genetic cause (C9orf72) which joins mutations in the Progranulin and the MAPT genes as (equally) important causes of dominantly inherited FTD. The pathological classification of FTD has also been changing rapidly.

Clinical criteria for dementia with Lewy bodies (DLB) continue to be refined and now incorporate supportive imaging features. Disappointing, despite several promising drug-development strategies (at least for AD), a number of recent trials of disease-modifying therapies have reported negative results.

In this context there is increasing interest in trialling treatments earlier and using biomarkers to identify for inclusion individuals at an early (and even preclinical) stage of AD and then to use clinical, psychometric and imaging markers to assess efficacy.

Recent advances have improved our ability to understand the dementias and their pathogenesis and to make earlier and more accurate clinical diagnoses. Treatments that significantly ameliorate the clinical course of these devastating diseases are urgently needed.

Professor Nick Fox

Professor Fox joined the UCL Institute of Neurology in 1997, becoming a Consultant in 2003 and Professor in 2005. With over 380 publications, his research focuses on the early detection, differential diagnosis and monitoring of progression in cognitive disorders and neurodegenerative dementias. He has particular interest in the use of MRI to improve diagnosis and to measure progression as well as treatment efficacy of novel therapies in Alzheimer's disease and related disorders. Besides this he also works with familial dementias and the use of biomarkers and clinical and cognitive measures to assess AD and FTD.

UCL Institute of Neurology
Queen Square – also a cradle of Australian neurology

Alumni highlights

A subgroup of Parkinson's disease (PD) patients treated develops devastating behavioural side effects collectively termed impulsive compulsive behaviours (ICBs). Although it is still unclear why some patients develop these addictive behaviours, identified risk factors are younger onset of PD, higher novelty seeking personality traits and DA therapy. For my PhD I have tested PD patients with and without ICBs on a variety of different neuropsychological tests and found that dopaminergic medication affect cognitive performance in a complex fashion with improvement in some tasks and deterioration in others.

PD patients with and without ICBs were also compared to pathological gamblers and illicit substance abusers, who both did not have PD. Results demonstrated that the non-impulsive PD group resembled pathological gamblers, whereas ICB patients performed similarly to illicit substance abusers. These results strengthen the link between ICBs in PD and substance abuse.

Anti-Parkinson medication improved response inhibition in both PD groups. On other tests such as a working memory task dopaminergic medication had, however, no effect on performance. Finally, all PD patients became more risk prone in their “on” compared to their “off” state, and those patients who developed pathological gambling made the most risky decisions.
Mr George Samandouras

Mr Samandouras is a consultant Neurosurgeon at the National Hospital for Neurology and Neurosurgery. He directs the education and training of neurosurgical trainees and fellows at the National. His clinical interests include brain tumours, minimally invasive surgery and spine surgery. Surgical neurosurgical techniques employed include fluorescence-guided resection, cortical mapping and intraoperative MRI. He has published 3 books and various articles on a range of neurosurgical themes.

The Present and Future of Neurosurgery

Perspective

In 1886 Sir Victor Horsley was appointed to “The National Hospital for the Paralyzed and Epileptic” as the world’s first brain surgeon. Since that time a series of outstanding neurosurgeons served at the subsequently named as “National Hospital for Neurology and Neurosurgery”, including Sir Wylie McKissock, Valentine Logue and Lindsay Simon.

During the last 130 years, Neurosurgery at Queen Square, has been established as the biggest neurosurgical unit in the UK embracing the latest technologies and introducing advanced techniques. During the last decade only the Neurosurgical Department has introduced the UK’s first intraoperative MRI suite, advanced neuronavigation systems, intraoperative neurophysiological monitoring, and Gamma Knife.

With leadership in academic and clinical neurosurgery, introduction and promotion of advanced technologies and radical new programs in education and training, the future of Neurosurgery at Queen Square seems promising.
Neurosurgery at Queen Square

A historical perspective

The specialty of neurosurgery started at Queen Square when Victor Horsley, the outstanding surgical scientist of the late Victorian and Edwardian era, was appointed to Queen Square to perform brain operations in May 1886. Before that time, although brain surgery, almost exclusively for trauma and infections had been done very sporadically, it had never been a formal surgical discipline. His first operation for epilepsy was considered a great success and within one year, Horsley had performed twelve procedures all but one surviving - an astonishing rate for the time. Formal descriptions of technical approaches and anaesthesia quickly followed in literally hundreds of publications. Within two years, he was regularly operating on the spine. Recognising the need for further assistance, he had three colleagues, most notably Sir Charles Ballance, appointed to assist in the burgeoning workload. Although Horsley, by now Sir Victor, died during the first world war, the discipline was firmly established.

Although the role of world trainer fell to his younger rival, Harvey Cushing, he had set the scene and appointments throughout the developed world followed, often either his former trainees or with his recommendation. In the thirties, the National went through the doldrums, the major UK schools being those of the three Cushing’s trainees in Oxford, Manchester and Edinburgh, but our reputation was revived in the post WWII era by Sir Wylie McKissock, Prof Valentine Logue and then their successors, notably Prof Lindsay Symon and his colleagues who remained world leaders, universally recognised for their contributions to surgical science and technique.
Dr. Mark Edwards has been a Consultant Neurologist at the UCL Institute of Neurology and National Hospital for Neurology since 2008. His research is centred on the pathophysiology of movement disorders covering a diverse range of neurological conditions from Parkinson's disease to tremor and dystonia. He is specially interested in the application of electrophysiological and psychophysical techniques in movement disorders. He has 150 publications and was awarded the Clinical Tutor of the Year prize in 2012 for his teaching of MSc/Diploma Clinical Neurology students.

Movement disorders: Beyond the Basal Ganglia

Changing perspective

What do the basal ganglia do? Given that lesions and degeneration of the basal ganglia commonly produce movement disorders it seems sensible that they must play an important role in movement control. However, this “basal ganglia centric” view of movement control and movement disorders is increasingly being challenged. Here I will discuss the ways in which investigation of the pathophysiology of movement disorders coupled with advances in understanding the normal physiology of movement control are leading to a much more integrated, “whole brain” approach to movement disorders.

UCL Institute of Neurology
From Leeches to CCSVI – A history of multiple sclerosis “cures”

Perspective

The earliest writers on multiple sclerosis were discouraging about the results of therapy, but each still applied an array of therapies. Moxon, who published the first cases in the English literature, listed eighteen therapies he used, even though he found the results “most unsatisfactory”. In the 1930’s Brickner listed 159 MS therapies. Russell Brain, in a review of MS, concluded, “The multiplication of the remedies is eloquent of their inefficacy”.

Since then there have been dozens of therapies heralded as “breakthroughs”, most of no value and some harmful. These include various fever therapies, including transfusion of malaria parasites, heavy metals, anticoagulants, histamine desensitization, various sera and vaccines, forced CSF drainage, snake venom, hyperbaric oxygen, numerous diets, oral myelin, and bee stings.

A review of the history of these therapies reveals even skeptical physicians have a strong therapeutic imperative, that patients and physicians tend to see benefit where none exists, to ignore harms when theory drives the approach, and to allow belief to sometimes trump evidence. Finally I will describe the usual profile of a “breakthrough” in MS therapy.

UCL Institute of Neurology
Multiple sclerosis – Clinical & research developments

Perspective

Although many of the key questions underlying multiple sclerosis (MS) remain unanswered, the last three decades have seen major developments in the field. These have impacted on almost all aspects of the condition from diagnosis to treatment and the team at Queen Square has been at the heart of many of these. The complexity of the mechanisms underlying disability is being unravelled through new pathological insights and an immense contribution from MRI. This includes the appreciation of the extensive involvement of the grey matter and at the cellular level the role of microglia and mitochondria.

The challenge remains to identify targets and subsequently effective treatments for the progressive forms of MS, which is the subject of an international initiative in which investigators from Queen Square are playing a major leadership role.

Overall, MS has now become a treatable and manageable condition with a strong emphasis on self-management and the promotion of a healthy lifestyle, major advances which have been strongly facilitated by the emergence of specialist MS nurses. It is no longer a case of ‘diagnose and adios’!

MRI has also made a major contribution to the diagnosis of MS which is now made earlier and with greater certainty. This is particularly relevant given the fact that MS is now a treatable condition. The last two decades have seen a steady increase in the number and range of treatments moving from ‘injectables’ to, more recently, oral medication.
Professor Clare Fowler

Professor Fowler CRE, FRCP, is an Emeritus Professor of Uro-Neurology at UCL and formerly consultant at the National Hospital for Neurology & Neurosurgery. She established a department of Uro-Neurology at the National Hospital in 1987, and her particular clinical interest has been in treatments and methods of improving continence in patients with neurological problems. Professor Fowler has over 265 publications which include edited works and textbooks. A disorder underlieing urinary retention in young women has been eponymously named “Fowler’s syndrome”.

Uro-Neurology at Queen Square

Perspective

Some 25 years ago the Department of Uro-Neurology came about in an effort to create a unit with a special interest in the neurology of the bladder and the care of bladder disorders in patients with neurological disease. Such patients rarely need surgery, but require a neurological approach to their pelvic organ dysfunction in the context of deteriorating disability.

Anti-muscarinic medications had long been available to treat symptoms of an overactive bladder and although these were effective in mild to moderate urinary urgency, often used in combination with clean intermittent self catheterisation. However with disease progression something more was needed and many different approaches were tried in an attempt to discover a second time therapy. Detrusor injections of botulinum toxin emerged as the best option and this is now a licensed treatment which has been shown to restore quality of life to patients with MS.

The advent of functional imaging had a major impact on understanding the neurology of the bladder and focused attention on the importance of brain control. Most of life is spent with the bladder in its storage mode when cortical processing of afferent signals occurs, and the role of bladder afferents is now an important area of research.

Uro-neurology inevitably became the department to refer patients with bowel and sexual dysfunction and the neurology of those organs and how to best manage neurological patients with problems in those areas is now of current interest.
Mr Sundeep Teki

Mr Teki is a PhD scholar at the UCL Institute of Neurology working under the supervision of Professor Tim Griffiths. He has 21 publications and focuses his research on auditory conditions. He won the 2011 Young Investigator Award at the 13th International Rhythm Perception and Production Workshop at the Max Planck Institute of Human Cognitive and Brain Sciences, Germany.

Basal ganglia and the cerebellum in time perception

PhD highlights

How does the brain measure time? In the absence of a dedicated sensory system, how does the brain analyse and perceive time? Recent evidence from both human and animal work implicates a distributed system consisting of diverse regions such as the basal ganglia, supplementary motor area, temporal and prefrontal cortices and the cerebellum.

I will focus on the role of two critical structures of this temporal processing system, which may be considered “core” areas for timing – the cerebellum and the basal ganglia. The cerebellum was proposed to act as a biological clock in the millisecond range by Braitenberg. Further investigation of the inferior olive that provides the sole input to the Purkinje cells provided additional bases for the olivocerebellar system as a key internal timing network that may operate via error-based learning mechanisms.

The role of the basal ganglia in time perception, specifically regular patterns or “beats” received strong support by studies that implicated the striatum in perceptual timing in healthy volunteers as well as in patients with Parkinson’s.

Selected references:
Professor Niall Quinn

Professor Quinn is Emeritus Professor of Clinical Neurology at the UCL Institute of Neurology. He has over 425 publications that span the length and breadth of Movement Disorders. He is especially interested in Wilson’s disease and Parkinsonian Syndromes. He was formerly Clinical Sub-Dean and course Director for the MS/Diploma Clinical Neurology, and continues to lecture at Queen Square and abroad.

Kinnier Wilson, his 1912 Brain paper, and Movement Disorders at Queen Square

Queen Square legacy

Movement Disorders as a sub-specialty did not really formally exist until the mid-1980’s when David Marsden and Stanley Fahn established both the Movement Disorder Society and its journal, Movement Disorders. Nevertheless from the earliest days of Queen Square physicians were describing, analysing and studying movement disorders. Gowers and Jackson wrote about Parkinson’s disease (PD), Gordon Holmes about tremors, Purdon Martin about the basal ganglia and posture, and Macdonald Critchley about tremor and parkinsonism.

The key early leading light in defining extrapyramidal disease, however, was Kinnier Wilson, and his 1912 Brain paper on Progressive Lenticular Degeneration and his textbook Neurology, remain two of the most classic and comprehensive works in the neurological literature. Post-war neurologists at Queen Square somewhat neglected movement disorders until the 1980’s when Bannister was studying autonomic failure in PD, MSA, and PAF, Andrew Lees was appointed to the staff and set up a brain bank, Anita Harding was sorting out cerebellar ataxias and Huntington’s disease, and David Marsden moved back from Denmark Hill in 1987, bringing with him John Rothwell, Brian Day and Marjan Jahanshahi, Philip Thompson and myself, and recruiting Kailash Bhatia, leading to a renaissance of interest.

The likes of Mark Edwards, Patricia Limousin, Marwan Hariz, Ludovic Zrinzo, Tom Foltyne, Nick Wood, Henry Houlden, John Hardy, Tamas Revesz, Janice Holton and most recently Tom Warner and Huw Morris, currently carry the academic movement disorder torch at Queen Square, with strong contributions also from Tony Schapira and Anette Schrag at the UCL Royal Free Campus.

In view of the recent centenary of Wilson’s 1912 Brain paper, I have chosen in my talk to concentrate on this topic.
Learning from mice about the human condition

Mouse model in Down syndrome

Humans and mice have had a well-established relationship for thousands of years and in recent times we have worked with ‘mouse models’ for medical research. But why mice? Partly because they thrive in captivity, and partly because of history in the early years of the last century. We can now manipulate the mouse genome in order to learn what it is to be human and what it is to be a mouse.

Down syndrome is a gene dosage disorder and arises from having three copies of an entire chromosome, and so identifying individual genes that contribute to different features of the disorder is challenging. Our mouse model has been very helpful for starting to dissect the different biological components of Down syndrome and yet again highlights the importance of working with mouse models.
Huntington's disease – past, present and future

Insights from TRACK-HD

Huntington's disease (HD) is a devastating autosomal dominantly inherited neurodegenerative disease for which there is currently no effective disease modifying therapy. Since the first description in 1872, HD has been at the forefront of Mendelian genetics both in clinical practice and research. The history of HD and its importance for modern genetics will be reviewed. This genetic predictability of HD provides an opportunity for early therapeutic intervention many years before overt symptom onset and at a time when reversal or prevention of neural dysfunction may still be possible. As HD is monogenic, fully penetrant, and characterised by a long premanifest phase, it is emerging as a potential model for studying therapeutic intervention in other neurodegenerative conditions such as Alzheimer's or Parkinson's disease where no preclinical diagnostic tests exist. Understanding of HD pathogenesis is evolving, and there are a number of candidate therapeutics with potential disease-modifying effects that are currently being tested. The most promising approaches will be briefly reviewed.

Since 2008 TRACK-HD has chronicled the earliest stages of the neurodegenerative disease processes in premanifest and mild to moderately symptomatic individuals who carry the HD expansion mutation. TRACK-HD was designed to observe natural disease progression in premanifest and early stage HD with the aim of understanding the preclinical and early phases of neurodegeneration, phenotypic correlates of neuronal dysfunction and to establish sensitive and specific clinical and biological markers of disease progression. Both our 24 month and new 36 month time-point data will be presented, including new insights into predictors of HD progression in both premanifest and early stage subjects, and a range of novel clinical measures that now show significant change in the premanifest group over this period. We have also identified baseline predictors of disease progression which may help enrichment for future disease-modifying clinical trials. Finally I will summarise our ongoing research aiming to identify neural compensatory networks that may occur in the premanifest phase of neurodegeneration in HD.
Neurology in Thailand & links with Queen Square

Alumni highlights

The role of Queen Square in the development of Neurology in Thailand has been an important one. Thailand has a population of 66 million people and around 400 Neurologists. After the first Thai doctor (Professor Athasit Vejjojiva) had clinical neurology training at Queen Square, in 1962, the link has remained strong over the last 50 years. At least 30 Thai doctors have completed their training in clinical neurology or research and a few have completed PhD degrees. They returned home to serve Thailand as teachers, clinicians and researchers. They had made a big change to neurology in Thailand.

All of these centres see patients with all kinds of neurological diseases, and conduct research along with clinical practice. The most common Neurological diseases in Thailand are Stroke, Epilepsy, CNS infection, migraine, tension type headache, peripheral neuropathy, and Parkinson’s disease.

The presentation will cover neurological diseases, findings of research, along with links between Queen Square and Thailand and an update on recent developments within Thai Neurology.

In the Thai neurology training system, trainees who wish to specialise in Neurology can either do three years in internal medicine and two years Neurology or apply directly to Neurology training (1 year internal medicine, 2 years Neurology).

There are a range of university hospitals that treat neurological patients including Mahidol University (Sririraj Hospital, Ramathibodi Hospital), Chulalongkorn University, Chang Mai University, Khon Kaen University and Prince of Songkla University. There are a few which are not attached to universities including Prasat Neurological Institute and Rajvithi hospital.
Recent advances in Neuro-oncology

Perspective

Neuro-oncology is the subspecialty of neurology that deals with brain tumours and neurological complications of cancer and its treatment. The neurologist is now a Core Member of the modern Neuroscience Multidisciplinary Team and therefore must be familiar with recent advances in the subject. As the most common primary tumour is glioma, the talk will highlight the major advances in the diagnosis and management of both low-grade (LGG) and high-grade gliomas (HGG). Data from prospective multi-modality imaging in LGG will be presented demonstrating how MRI can be used as a prognostic tool in addition to conventional monitoring. In the field of HGG, it is gratifying to observe that survival for patients with glioblastoma, the most aggressive glioma, has improved from an average of 10 months to 14 months due to improvements in the standard of care and the advent of chemoradiation after maximal surgical resection. Temozolomide, an alkylating agent with simple oral administration and a favourable toxicity profile, is now used in conjunction with and after radiotherapy. In addition, newer surgical techniques, such as fluorescence-guided resection have increased the surgeon’s ability to maximise resection.

New discoveries in basic and translational research are likely to improve this situation further in the next 10 years, although biological agents that target tumour cell signalling pathways have been disappointing in malignant gliomas. Specifically, antiangiogenic therapy with antivascular endothelial growth factor antibodies (bevacizumab) has not shown any clear impact on Overall Survival. We hope that targeting key molecular pathways in gliomas will lead to a prolongation of survival at little cost in terms of Quality of Life.
Dr Laura Silveira Moriyama

Dr Silveira Moriyama joined the UCL Institute of Neurology in 2004 as a PhD scholar and is a Senior Clinical Research Associate at the Department of Molecular Neuroscience and a UCL Clinical Teaching Fellow. She has over 100 publications and specialties in Movement Disorders. She is the current clinical tutor for the Diploma in Clinical Neurology via Distance Learning. She is also a visiting professor at the University of Campinas, Brazil.

International teaching and opportunities for networking

Queen Square global impact

With the growing role of collaborative research and distance learning in academia, international partnerships are becoming paramount for the success of universities worldwide. Dr Laura Silveira-Moriyama, MD, PhD is a Senior Clinical Research Fellow at ION-UCL and a Visiting Professor at the Neurology Department at the Brazilian university UNICAMP (University of Campinas, Brazil). In addition she has developed partnerships with institutions worldwide including Tartu University in Estonia, Colombo Hospital in Sri Lanka, and The Neurology Institute of Mexico. She will talk about the various opportunities to network and contribute to the Queen Square ethos by participating in various collaborative teaching efforts which aim to boost knowledge transfer.
Dr Gordon Plant

Dr Plant joined the National Hospital for Neurology and Neurosurgery in 1986 and has been a Consultant Neurologist since 1991. He specialises in neurological disorders affecting the eyes and holds positions at St Thomas Hospital and Moorfields Eye Hospital along with the National. He has over 212 publications.

Ophthalmology and the National Hospital
A historical perspective

One of the first four appointees at the hospital in 1860 was Laurence a surgeon specialising in Ophthalmology who founded an eye hospital in South London in 1857. There is no evidence that he ever worked at the hospital and he resigned his post in the same year. He had also been a member of David Wire's planning committee.

Did his involvement signify an early appreciation of the association between eye and Neurological diseases or was it his experience in setting up a specialist hospital that qualified him? Whether this is the case or not the importance of ophthalmoscopy to neurology was early established.

Equally significant were the Physicians on the staff of Moorfields Eye Hospital, particularly Hutchinson. I will discuss the roles of the physicians Hughlings Jackson and Gowers in promoting the use of the ophthalmoscope and their links with Moorfields Eye Hospital. I will illustrate Hughlings Jackson's ophthalmoscope, now in the Moorfields museum, and discuss the publication of "Medical Ophthalmoscopy" by Gowers. Finally the careers of Marcus Gunn and Brunell Carter, the two ophthalmic surgeons appointed to the hospital in the 1880's will be described.
UCL and Bloomsbury area map