



QS ION Strategic Plan 2022-27

Identifying Synergies to Maximise Discovery and Translational Neuroscience 2022-2027

Queen Square Institute of Neurology Strategic Plan

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Executive Summary

The overarching vision of the Queen Square Institute of Neurology (QS ION) is to lead translational neuroscience on a global scale by implementing sustainable approaches, thus providing society with deep scientific understanding of how the human nervous system functions across scales, at a molecular, cellular, system and whole organism levels. This progress will drive advances in early diagnosis and in establishing effective therapies for neurological and mental health disorders, thus improving the lives of patients and benefit society.

Background - how we engaged all our community and next steps

The QS ION Director supported by the Institute executive team, launched a clear roadmap in July 2021 to establish a QS ION Scientific strategy and a strategic plan 2022-2027. The aim was for the QS ION strategic plan to align with and be supported by the Faculty of Brain Science strategic vision, and for QS ION to contribute effectively to the UCL strategic planning process by responding collectively to the UCL consultation documents issued by the Provost, in order to deliver a final UCL strategic plan 2022-2027 in summer 2022.

Starting from September 2021, a series of initiatives have been carried out to capture views and direction of travel of all eight QS ION Research Departments and six Divisions, and to discuss the working priorities set by the six QS ION Co-Directors (four newly appointed in Sept 2021). To this end, Departmental meetings led by HoRDs, and town hall meetings led by Deputy Directors were held in September-December 2021, which prioritised staff engagement comprising all ION PIs, early career researchers (ECR), PhD students and Professional and Research Services teams. The Departmental priorities were presented and discussed in the Institute away day in October 2021, whereby selected PIs canvassed the results of the departmental consultation, which was then opened for general discussion. This resulted in a further refinement of the departmental priorities, which have been summarised in **Table 1** and short two-page documents by HoRDs collated in **Appendix 2**. These priorities have been integrated and further aligned with the programmes of work of the QS ION Deputy Directors (**Appendix 1**) and the strategic aims of the Institute's six Divisions (**Appendix 3**) at the QS ION Executive Away day held in December 2021.

This document summarises the results of this process and represents the core elements of the QS ION strategy, outlining the strategic plan for 2022-2027. This document is fully endorsed by all members of the QS ION Executive committee (Director, Deputies, HoRDs, BRC Translational Neuroscience and Dementia theme leads, Heads of Divisions, Institute Manager) and has been reviewed and supported by the Hospital Clinical Director. The intention of this document is to capture all the key considerations from the above process in a single document. The next step is to derive two further more concise documents: 1) the QS ION strategic plan document 2022-2027; and 2) the QS ION collective response document to the Provost's consultation papers, including those relating to *Evolving grand challenges* and *Areas for strategic investment*.

An overarching principle which we believe will enable delivery of our vision and is central to our mission is ***Identifying Synergies to Maximise Discovery and Translational Neuroscience in 2022-2027***.

QS ION Themes and Shared Mission

This series of meetings and general discussion forum provided clear evidence that **discovery science** and **translational science** sit on a continuum in most QS ION Departments and Divisions, allowing seamless connectivity among them. The integrated nature of these activities, merging effectively basic and clinical research, constitutes the backbone of QS ION daily activities and offers solid foundations for future developments, such as the planned QS ION Dual Hub.

In this regard, this consultation process confirmed that the QS ION Dual Hub **is a flexible integrated translational ecosystem combining excellence in clinical research and pathomechanistic discoveries, working towards the identification of novel therapies and predictive biomarkers of neurological diseases**.

Essential for its cohesion and integration, QS ION research culture is highly collaborative and focussed on supporting a growing and diverse community of exceptionally committed ECRs through effective mentoring. We recognise that our research culture is among our best, if not our very best, asset, and we stride for further improving it via boosting equality, diversity and inclusion.

The overall QS ION mission is **to improve the lives of patients with neurological diseases**. This mission is implemented via a series of **general aims** shared across departments:

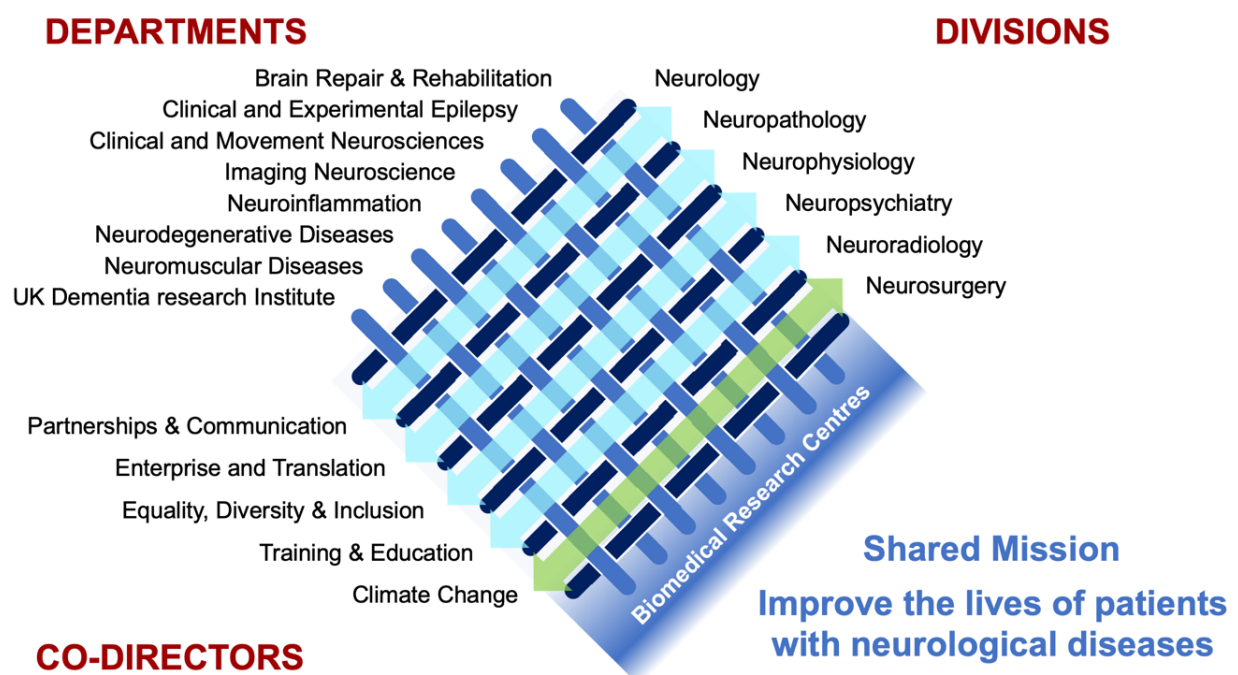
- Enabling bidirectional translational research – from patients to the lab and back.
- Performing deep patient phenotyping and studying patient cohorts.
- Developing personalised and precision therapies through wide collaboration with national and international academic partners, patients, charities, government agencies and funders, public-private partnership initiatives, pharma and biotech.

Among the **shared themes** emerging across departments, some of the prevalent are:

- Understanding the nervous system in health and disease states across biological scales – molecular, cellular, tissue and whole organism in isolation and within a social environment.
- Discovering, developing and implementing new predictive biomarkers and new advanced therapies for neurological disorders.
- Developing therapeutic agents based on targets identified through discovery.

These scientific aims are complemented by important **knowledge- and culture-focussed activities**:

- Educating future basic and clinical scientists at undergraduate, graduate and postgraduate levels through excellence in teaching and academic supervision.
- Providing an outstanding student experience.
- Sharing knowledge and promoting collaboration within and across QS ION departments and divisions, the Faculty of Brain Sciences, UCL Neuroscience, UCL, collaborating Institutions and beyond.
- Create a supportive, open culture harnessing the power of diversity, with zero tolerance of bullying.
- Supporting collaborative working across all sites of the dual hub, Departments, Divisions and BRC for discovery and clinical research.
- Working in a sustainable way, adapting to climate change and its far-reaching consequences.



The fabric of QS ION. Scheme exemplifying the matrix structure of QS ION, with Departments, Division and focussed activities of Co-Directors and NIHR BRC contributing to the integrated structure of the QS ION community and its translational mission. There are many crucial partnerships including with UCLH NHNN.

Shared QS ION Scientific Questions

Excellence in basic and clinical science is reflected by the breadth of scientific questions that are currently addressed by QS ION departments:

- Can we understand the genetic architecture of monogenic and polygenic neurological disease causation, resilience and progression?
- Can we effectively exploit pathogenic pathways (e.g., RNA dynamics, mitochondrial homeostasis, protein aggregation) shared among neurological diseases to develop effective advanced therapies?

Table 1: Summary of the main objectives, opportunities and challenges identified by the QS ION Deputy Directors, Head of Research Departments and Heads of Divisions.

Deputy Directors	Objectives	Challenges & Opportunities
1.1 Sustainability and Climate Change	<p>Declare a climate emergency.</p> <p>Lobby for changes to Academic Careers Framework, by including sustainability measures.</p> <p>Include sustainability in teaching curricula.</p> <p>Review all SOPs in 2022 including sensible sustainability measures.</p> <p>Hold at least two virtual conferences on climate change and neurology over the next five years.</p> <p>Place sustainability on an equal footing with other mandatory training and compliance measures.</p>	<p>Adopt each of the Faculty pledges as soon as they are endorsed by the Faculty.</p> <p>Require that each Department have a sustainability representative and a standing item on sustainability activities.</p> <p>Set within each department a carbon travel budget and develop a QS ION sustainable travel policy, as recently instituted by PALS.</p>
1.2 Education	<p>Offer the best neuroscience teaching via the integration of research and education.</p> <p>Attract excellent students who are globally diverse.</p> <p>Improve the quality and timeliness of feedback for master students.</p> <p>Improve support, supervision and social cohesion for PhD students.</p>	<p>Culture change at QS ION: more educational buy-in from academics and researchers, but also more recognition for educational activities.</p> <p>Establish scholarships for students from low and middle-income countries.</p> <p>Establish a new iBSc for medical students.</p> <p>Strengthen support and training for PhD supervisors.</p>
1.3 Equality, Diversity and Inclusion (EDI)	<p>Increase mental health support and improve workplace culture.</p> <p>Foster a diverse and inclusive culture by improving EDI training and supporting positive action initiatives</p> <p>Embed career support initiatives for all staff groups, including ECRs, research services personnel, research assistant and technicians.</p> <p>Publish QS ION EDI annual report</p> <p>Improving reach of mentoring scheme.</p>	<p>Achieve Athena SWAN Gold in 2024.</p> <p>Increase the proportion of women and ethnic minorities in academic posts.</p> <p>Implement positive action recruitment process.</p> <p>Achieve pay gap and workload gap transparency.</p> <p>Identify Mental Health First Aiders and local first point of contact for discussing instances of Bullying and Harassment.</p> <p>Sponsor minimum two ethnic minority staff per year to participate in a CPD programme.</p>
1.4 Enterprise, Translation and Advanced Therapeutics	<p>Create an entrepreneurship culture by encouraging students and ECRs to undertake targeted training.</p> <p>Promote an entrepreneurship culture by providing early and targeted advice to PI in terms of IP and commercialisation.</p>	<p>Establish a Science Translational Advisory Group, supported by a Translational Research Manager (joint appointment with TRO).</p> <p>Establish a Genetic Therapy Accelerator (GTAc), which will provide a forum to exchange</p>

	<p>Raise awareness of enterprise to the whole QS ION community.</p> <p>Nurture relationships with philanthropy focused on advanced therapies.</p> <p>Organise an annual event on “Advanced Therapies in Neurology and Neurosurgery”.</p>	<p>expertise and make equipment available for obtaining early stage batches of reagents.</p> <p>Facilitate interactions with Research Contracts, UCLB, TRO and JRO.</p>
1.5 Partnerships and communications	<p>Strengthen partnership with UCL Neuroscience.</p> <p>Making QS ION a recognised entity within the broader UCL Neuroscience community</p> <p>Improve communication and collaboration across faculty.</p> <p>Build and maintain relationships with priority partners.</p> <p>Strengthen public engagement portfolio by establishing QS ION ambassadors.</p> <p>Engage with a broader audience for fundraising.</p>	<p>This process necessitates a culture change in how QS ION perceives and implements communication.</p> <p>Promote a sense of cohesion across QS ION might be challenging and requires transparent and accessible leadership.</p> <p>Increase the external visibility and reputation of QS ION through a range of media platforms.</p>
Departments	Objectives	Challenges & Opportunities
2.1 Brain Repair and Rehabilitation	<p>Develop better multimodal diagnostic and predictive biomarkers for a range of neurological disorders</p> <p>Develop personalised and effective treatment and prevention for common and disabling neurological diseases via high dimensional modelling</p> <p>Address the key question: can patients with stroke and dementia improve recovery with guided practice delivered remotely by intelligent digital solutions or gold-standard face to face services?</p>	<p>Establish a neuro-oncology research theme, and contribute to a Faculty Research Board for brain cancer.</p> <p>Establish the Quantitative Neuroradiology Innovation and Adoption Centre (QUINIAC).</p> <p>Develop a Centre for Artificial Intelligence in Neurology Data Science Hub.</p> <p>Improve access to expert biostatistics, bioinformatics, data science.</p> <p>Develop a translational neurological laboratory.</p>
2.2 Clinical and Experimental Epilepsy	<p>Identification of new therapeutic targets in epilepsy.</p> <p>Brain rescue via targeted genetic therapy.</p> <p>Understanding epilepsy-triggered neurodegeneration.</p> <p>Develop multimodal 3D image-guided targeted intracranial therapies.</p> <p>EEG phenotyping with source localisation and OPM-MEG data to identify foci and underlying networks.</p>	<p>Validate genetic biomarkers for treatment outcomes for epilepsy.</p> <p>Clinical trials of disease-modifying therapies for epilepsy.</p> <p>Validate imaging biomarkers of pre-symptomatic epilepsy-related neurodegeneration.</p>
2.3 Clinical and Movement Neurosciences	<p>Understand the genetic architecture of parkinsonism and related movement disorders.</p> <p>Establishing the role of protein misfolding and protein dis-homeostasis in the</p>	<p>Establish a Parkinson’s Disease Centre for Translational Research (PCTR).</p>

	<p>neurodegenerative processes causing movement disorders.</p> <p>Develop personalized therapies and novel trial design for movement disorders</p> <p>Promoting optimal recovery after brain injury</p>	<p>Establish a Centre for Neurorecovery Research (CNR).</p>
2.4 Imaging Neuroscience	<p>Acquire, integrate and use multimodal measurements across a wide range of biological scales, to inform advanced models of human brain function.</p> <p>Discover how the brain works in naturalistic environments and study functions that cannot be recreated in more constrained experimental settings</p> <p>Discover the neural circuitry, dynamics, and functions that of human cognitive processing and behaviour <i>in vivo</i>.</p> <p>Develop non-invasive translational tools to allow: (1) Earlier, more accurate diagnosis; (2) Prediction of clinical outcomes; (3) Precision therapies</p>	<p>Diversify funding for core staff and infrastructure.</p> <p>Bolster collaborations and two-way dialogue across QS IoN and broader UCL neuroscience domain</p> <p>Develop stronger links with NHNN clinical teams and the Queen Square Brain Bank</p>
2.5 Neuroinflammation	<p>Clarifying the role of innate immunity and microglia response in the pathogenesis of MS and neurodegenerative diseases, and explore new immunological targets for novel therapies.</p> <p>Exploring oxygenation as therapeutic opportunity in MS.</p> <p>Discovering novel fluid and imaging biomarkers of neuroinflammatory/neurodegenerative diseases, which have clinical application and utility for diagnosis and prognosis.</p> <p>Achieving precision medicine in MS using MRI, routine NHS data, and high-dimensional modelling.</p> <p>Identifying therapies stopping MS progression.</p>	<p>Recruit senior leads in neuroimmunology and neuropathology-MRI correlation and suitable space for the neuroimmunology laboratory.</p> <p>Develop robust pathways of recruitment of patients in the NHS and create a registry system using electronic health records; capitalise on routine NHS data and access them for clinical research.</p>
2.6 Neurodegenerative Disease	<p>Extend Neurogenetic Therapies Programme (NgTP) - including FIH trials.</p> <p>Expand genetic and molecular understanding of neurodegenerative disease (NDD) pathogenesis.</p> <p>Accelerate search for disease modifying therapies for NDD.</p> <p>Improve research, education and support in early onset, atypical and inherited dementias.</p> <p>Optimise drug target identification for specific and common disease mechanisms.</p>	<p>Establish a Neurogenetic Therapies Centre.</p> <p>Develop a Rare Dementia Support Centre.</p> <p>Create greater capacity for early phase trials.</p> <p>Extend biomarker horizon: wider targets, static and dynamic measures.</p> <p>Integration of AI in discovery science.</p>

	<p>Provide insight into common molecular mechanisms underpinning multiple diseases.</p> <p>Take a personalised medicine approach to understand disease.</p>	
2.7 Neuromuscular Diseases	<p>Identifying novel insights and therapeutic targets emerging from the study of RNA dynamics in neuromuscular diseases (NMDs).</p> <p>Testing novel genetic therapeutic strategies in NMDs.</p> <p>Identification of druggable pathogenic pathways to develop effective therapies for NMDs.</p> <p>Developing biomarkers monitoring disease progression to aid diagnosis, improve stratification, and advance clinical trials.</p>	<p>Creating efficient Core Facilities.</p> <p>Securing expertise in genetic therapies as well as gene editing.</p> <p>Establish dedicated Enterprise Support for QS ION.</p> <p>Increased early phase clinical trial capacity and infrastructure.</p>
2.8 UK Dementia Research Institute	<p>Understanding the basis of human heterogeneity at DNA, and single or multi-cell level in the whole brain.</p> <p>Understanding the impact of ageing, and the basis of healthy aging/disease resilience.</p> <p>Understanding the earliest (preclinical and early clinical) stages of a disease.</p> <p>Understanding the relationship of biomarkers to disease processes.</p> <p>Developing therapeutic agents based on targets identified through discovery.</p>	<p>Access to high-quality brain tissue and (cross-species) neuropathological expertise</p> <p>Develop strong clinical links and access to well characterised patient cohorts.</p> <p>Accelerated access to data resources.</p> <p>Expanding strategic partnerships with industry.</p> <p>Acquiring translational science expertise.</p> <p>Gaining access to human neurophysiology core.</p>
Divisions	Objectives	Challenges & Opportunities
3.1 Neurology	<p>Develop plan for a QS clinical trial centre (QSCTC) to help deliver clinical trials, improve communication with research services and JRO and lead CLRN activity for neurology in QS.</p> <p>Work with education unit to develop and modernise Gowers round to be a hybrid in-person and virtual round which can be recorded and curated for use for all QS ION educational activity.</p> <p>Work with NHNN leadership to ensure division input to all NHNN NHS consultant appointments to ensure the QS ION research translational strategy is embedded in NHNN culture and reflected in consultant appointees being research active.</p>	<p>QS ION has unparalleled basic science and pre-clinical science underpinning translation to clinical.</p> <p>QS ION has the opportunity to be the number 1 neuroscience clinical trial centre in the world.</p> <p>QS ION has one of the largest extensively phenotyped patient cohorts in the world making it the ideal place for genetic therapy trials to be undertaken.</p> <p>The major current challenges to clinical trials in QS ION are the lack of a local clinical trial centre and delays in interactions with JRO and research services in grant and trial set up.</p> <p>Consequently, there is an imminent reputational risk for QS ION.</p>

3.2 Neuropathology	<p>Authoring guidelines for the Royal College of Pathologists and other national and international organisations.</p> <p>Obtaining significant research funding across brain tumours, neurodegeneration, neuromuscular and epilepsy.</p> <p>Integrating digital pathology with radiology using machine learning.</p> <p>Developing Nanopore technology for diagnostics.</p>	<p>The Division of Neuropathology is the largest academic Neuropathology department in the UK.</p> <p>The reconfiguration of the QSH in the context of the opening of GIR offers significant opportunities to rethink the synergies between the currently distinct tissue-based diagnostic and research activities.</p>
3.3 Neurophysiology	<p>Successful completion of 1 STP trainee (3 year course) and 1 HSST trainee (5 year course) to establish a stream of physiologists in training.</p> <p>Create a three-month-long teaching program in neurophysiology for trainees and teachers across the UK.</p> <p>Launch of a core facility using the integration of novel fast TMS hardware, innovative software, brain navigation and robotics to provide one system for research and clinical use.</p> <p>Setting up advanced diagnostics of neurodegenerative diseases such as ALS, dementia or dystonia and response to therapy (5 years). Other applications include basic mechanisms of sensorimotor control, measuring target engagement of drugs in clinical trials and allowing automated non-invasive cortical mapping.</p>	<p>Secure dependable support for epilepsy surgery.</p> <p>Recruit engineer for advanced signal processing.</p> <p>Education: relative lack of coverage of basic neurobiology in clinical neurophysiology.</p> <p>Research: establishment of novel translation biomarkers of target engagement of neuroactive drugs or pharmacodynamic assessment of access to different neural compartments. Opportunities would be combinations of functional neurophysiological assessments with neurotransmitter studies using MRS or comparing receptor occupancy of drugs with direct functional readouts.</p>
3.4 Neuropsychiatry	<p>Supporting translational research by integrating neurology, neurosurgery and neuropsychiatry, especially in movement disorders.</p> <p>To obtain NICE approval to introduce CRT in the clinic.</p> <p>To establish immunotherapy for psychosis in the clinic.</p>	<p>This division fall behind other neuropsychiatry centres whereas it used to be the lead UK service.</p> <p>Academic output would increase with more clinical neuropsychiatrists.</p>
3.5 Neuroradiology and Neurophysics	<p>Establish GIR as the world-leading translational and clinical adoption MR facility.</p> <p>Institutionalise the harmonised working relationships between the MR scanner groups.</p> <p>Establish Academic Radiography.</p> <p>Integrate computer scientists in the Division.</p> <p>Further transform the MSc in Advanced Neuroimaging to be the leading UK course.</p> <p>Establish an educational programme with the Division of Neuropathology.</p>	<p>Partnering with all Divisions still a working progress.</p>

	Expand MR Physics courses.	
3.6 Neurosurgery	<p>Build mechanism-based research from the ground up: integrated academic training (IAT) programmes.</p> <p>Nudge the culture: targeted consultant recruitment, specialty research days, and increased collaboration (QS ION, UCL, and beyond).</p> <p>Develop and expand an MRes (Neurosurgery) programme, which has been approved and will launch in 2022.</p> <p>Develop a simulation centre for neurosurgical training.</p> <p>Expand subspecialty research days.</p>	<p>Clinical culture tends towards the anti-academic side of the spectrum.</p> <p>Securing academic salaries for academic neurosurgeons.</p> <p>Continuing to secure IAT positions.</p>

Capabilities and new technologies

Supporting the research activities addressing these important questions requires coordinated support in several areas. Importantly several of them highlighted in ***italic*** are already included in the core technology platforms planned in the new QS ION Dual Hub and other ongoing initiatives including BRC:

- Core translational tool platform (coordinated trials support across ION QS)
- *Increased access to expert biostatistics, bioinformatics, data science, AI and curated databases*
- *Improved IT infrastructure to facilitate complex modelling, networking and data access*
- Improved the UCL-UCLH interface by boosting support from JRO for contracts, study set up, patient registries & stratified cohorts and sharing of biosamples
- *Increased capacity for clinical trials involving drugs, devices and/or behavioural training*
- *Establish a Science Translational Advisory Group*
- *Create a QS ION-dedicated Enterprise support*
- *Establish a Gene Therapy Accelerator and Neurogenetic therapy Centre*
- *Increased capacity for human iPSCs, organoids, advanced imaging, CRISPR-based screening, histology, viral vectors, BSU, in situ transcriptomics, high-throughput screening*
- Develop quantitative 3T and 7T MRI in research (including post-mortem) and clinical practice together with functional analysis at high spatiotemporal resolution (e.g., EEG, MEG, fMRI)
- PET
- Brain Bank expansion
- Panomics

Appendix 1

Summaries of the Programme of Work of the QS ION Deputy Directors

- 1.1 Sustainability and Climate Change
- 1.2 Education
- 1.3 Equality, Diversity and Inclusion
- 1.4 Enterprise, Translation and Advanced Therapeutics
- 1.5 Partnerships and communications

1.1 Sustainability and Climate Change

Climate change is here. Major reviews have documented the enormous risk posed to human health and livelihoods. The COP26 summit produced some progress, but was by most standards a failure: even if all the new pledges are met, there will still be a continuing vast over-production and release of greenhouse gases, making the likely increase in global mean surface temperature between 2.4-2.8C, with worst case projections of 5.5C. The moral initiative has been taken by other bodies, rather than the governments of the most polluting and emitting nations. The UK NHS has pledged to become net zero by 2040; many other health services declared similar intentions at COP26. Global alliances of healthcare professionals have formed, now numbering over 46 million in their membership. UCL has taken its own initiative and intends to be a net zero institution by 2030. It already sources all its electricity from renewable sources.

The QS ION is rated the top neuroscience institute in Europe and second in the world. It is rightly proud of its leadership in translational neuroscience and the benefits its research brings to people with neurological disease. Extensive research, contained within a review on climate change and neurology submitted to the Lancet, demonstrates the significant impact climate change will have on people with neurological diseases.

In this context, the QS ION should consider its role in the global neuroscience and neurological community. It should set the standards and lead the way, and serve as an example to follow. Moreover, there is growing momentum towards more sustainable research practices: the MRC has adopted UCL's Laboratory Efficiency Assessment Framework to reduce the emissions associated with laboratory research in its own institutes, whilst the Wellcome Trust has made climate and health one of its three pillars of future research, intending to commit £1billion to this specific area for research. Further, the Wellcome already requires applicants to agree to sustainable travel proposals in grant applications. Some universities in Europe do not allow air travel to destinations that can be reached by train within particular time intervals (eg 6 hours). It seems likely that grant applications will soon include demonstration of the environmental sustainability of proposed research, and we should be aware that students have been particularly active and vociferous on climate change – will future students examine our sustainability credentials before deciding to study at QS ION?

Many other strategic areas at UCL and within QS ION have robust formalised processes and guidelines, for example related to the student experience or to Equality, Diversity and Inclusion. Sustainability is a more recent domain at UCL, with many aspects still being seen as voluntary and nice-to-have, rather than being embedded in practice or being compulsory. This position is untenable given the existential nature of the threat from climate change, and the moral perspective. The nations most responsible for emissions are not those that will suffer the greatest hardships or the most deaths. Carbon emissions targets could be met by the existing and upcoming projected behaviours of middle and poorest 90% of the global population: the remaining 10% by themselves account for nearly the entire emissions budget for a 1.5C target rise in global temperature. A substantial proportion of QS ION staff fall into this category, and there are some prolific flyers at UCL. Therefore, it is proposed that QS ION adopt strong, formal, aims and targets in the sustainability arena, as part of its moral imperative, and to set standards as a leader in world neuroscience.

The recently-constituted Faculty Sustainability Committee has devised a series of pledges being considered for adoption:

- Pledge 1 – By next academic year (2022-23): Faculty implements Powered by Plants initiative.
- Pledge 2 - By next academic year (2022-23): Faculty develop an implementable plan to reduce energy usage from the baseline year of 2018-19.
- Pledge 3 - By next academic year (2022-23): all Division and Institute Executives and all-staff meetings to include sustainability as a standing item once per term.
- Pledge 4 – By end of 2022-23 academic session: Each Division & Institute achieve gold in Green Impact & LEAF (where relevant).
- Pledge 5 - Sustainability included in each student's curriculum and induction (Faculty Sustainability Committee to work with Faculty Education Committee to achieve).
- Pledge 6 - To begin in 2022-23, the Faculty offers one PhD studentship in sustainability per year.

The strategy proposed for the QS ION is as follows, with detail to be included in local documents:

1. To adopt each of the above pledges as soon as they are adopted by the Faculty. Some have already been implemented (Pledge 1). QS ION should document within 6 months of adoption information on baseline measures underpinning each pledge, against which annual progress can be measured.
2. To require that each Department have a sustainability representative and a standing item on sustainability activities.

3. To require that all SOPs are reviewed over the course of 2022 to determine whether sensible sustainability measures can be adopted, noting that most SOPs were written without sustainability in mind.
4. To place sustainability on an equal footing with other mandatory training and compliance measures.
5. To set each department a carbon travel budget and develop a QS ION sustainable travel policy.
6. To take an active role in promoting the inclusion of sustainability measures and activities to UCL, for example, lobbying for inclusion of sustainability activities within promotion criteria.
7. To hold at least two virtual conferences on climate change and neurology over the next 5 years.

Sustainability and climate change have simply not been on the agenda or at the forefront of considerations, but need to be in a changing world. Whilst the proposed strategy is robust, there are important gains to be made even with simple changes. In QSH, for example, there are at least 45 freezers set to operate at -80°C, and only 9 set to operate at -70°C. Whilst we undertake some research to establish how high the settings could be set (e.g., -50°C?), just moving all these freezers from -80°C to -70°C would save a substantial amount of carbon emissions, with co-benefits of concomitant savings in air conditioning needs and energy costs.

1.2 Education

Background

This is the mission statement for education and improving the student experience at QS ION:

Our mission is to provide the best quality learning experience for undergraduates, postgraduates and doctoral students wishing to pursue a career in neuroscience

Objectives

These are our main aims:

- Offer the best neuroscience teaching via the integration of research and education
- Become the leading destination for students seeking an education in the neurosciences
- In keeping with UCL's tradition of inclusivity, attract hard-working students who are globally diverse

Actions

These are the main action points for the next five years:

Master students & medical students

1. Culture change at QS ION: more educational buy-in from academics and researchers but also more recognition for educational activity regarding promotion and accelerated increments.
2. Main reason students come is to get a taste of research: we need to ensure that enough masters projects are available for students to choose from.
3. Improving the quality and timeliness of feedback: for essays, library projects and dissertation projects
4. Equity, Diversity and Inclusivity: Increase diversity content in key modules; More scholarships for those from low and middle-income countries.
5. New intercalated BSc for medical students: Clinical Neurology and Brain Sciences to start 2023 (~10 UCL medical students).

PhD students

1. Widen the educational and professional development support base: thesis committees and cohorting:
2. Better PhD supervision: Support sessions/ formal training for supervisors (new and old)
3. Improve social cohesion: Brainstorm with current students; have post-docs assigned to each cohort.
4. Better career support: Researcher Development Programmes; alumni sessions from those who have left academia

1.3 Equality, Diversity and Inclusion

Our 2021/22 EDI strategy includes three phases:

- 1) **To listen and learn:** implement mechanisms to collect quantitative and qualitative data on staff and student experiences at the QS ION. Our achievements in 2020/21 include:
 - Secured wide participation in 2021 FBS Staff Survey (56% response rate)
 - Launched the first QS ION Student Survey in 2021
 - Focus Group with students
 - Focus Group with new recruits
- 2) **To act:** develop action points in response to issues identified in our data analysis and implement policies to address inequities. Our achievements in 2020/21 include:
 - Implemented Exit Interviews
 - Implemented reminders for appraisals to include both the line manager and appraisee
 - Improve on the capacity of the existing QS ION Mentoring Scheme
- 3) **To monitor:** develop and implement mechanisms to monitor the efficacy and impact of our actions. To this effect, the QS ION will:
 - Collect feedback from staff and students on an annual basis
 - Publish annual EDI reports

Progress in 2020/2021:

- **New EDI Governance at the ION, with increased participation and representation.**
 - 2020: appointment of EDI Project Manager and EDI Deputy Director
 - 2020: Athena SWAN Committee comprised of 26 members (58%F:42%M; 19% BAME)
 - 2021: Athena SWAN Committee (renamed EDI Committee) comprised of:
 - Two governance layers: Operation layer (= 9 Action Groups) and Executive Layer
 - 57 members (60% F:40% M; 26% BAME)
 - Creation of 3 representative roles with captive seat at the Executive Layer: Student, ECR and PSS representative
 - 2022: Appointment of two new Athena SWAN Leads
- **Ensure Departmental engagement with EDI issues**

All of QS ION Research Departments have set a departmental EDI committee and/or nominated a departmental EDI representative. At least one representative from each department sits in the ION EDI Committee to facilitate flow of information between the central organ and the local organ.
- **Increase representation from ION in Faculty-wide equality organs/committees.**
 - FBS Disability Equality group: 2 QS ION members
 - FBS Religion and Faith Equality group: 2 QS ION member
 - FBS Gender Equality group: 3 QS ION members
 - FBS LGBTQ+ Equality Group: 2 QS ION members
- **The ION has signed the ALBA Declaration and has made one of its priorities writing a code of conduct for the Institute**
- **Increase opportunities to students of underrepresented backgrounds.** QS ION James Samuel Risien Russell scholarships implemented in 2021, offering 2 placements that year.
- **Increase career development awareness and outcomes.**

EDI Committee has provided support to 2021 ECR and Senior Promotion Workshop.
Recorded impact from 2021 FBS staff survey: Improved awareness of promotion process and criteria (2019: 44%; 2021: 61%)
- **Increase continuous personal development opportunities.**
 - Launch of **Leadership training for Research Assistants and Technicians at the ION.**
 - Minoritized groups (women, ethnic minorities, and people with disabilities) tend to be highly represented in technical and research contracts up to Grade 7.
 - 2021 Staff Survey results show only 33.3% of Technical Staff feel that they have the same career development support as academic staff.
 - **FBS Professional Services & Technical Staff Mentoring Scheme.**

38 participants in mentoring scheme across FBS (r42% of total participants in scheme).
- **Improving our staff and students' understanding of EDI related issues and increasing the visibility of our EDI work**
 - 2021: 'Whiteness and White Fragility'. QS ION participants = 81 (36% of total participants)
 - 2021: inaugural QS ION EDI Seminar Series to discuss Intersectionality with Baroness Oona King. Over 190 people joined the event on the day.
Recorded impact: increase from 45% to 70% in the number of attendees reporting to be moderately to highly confident with EDI issues after the event.
- **Improving the reach of our Mentoring Scheme.**

Identified gaps and priority areas for the Mentoring Programme:

- Underrepresentation of men as mentees
- Underrepresentation of staff from ethnic minority backgrounds as mentors
- Underrepresentation of staff with reported disabilities as mentors
- Programme needs to increase its reach to support female clinical researchers
- Need to increase programme capacity by increasing recruitment and training of new mentors

Actions to address the aforementioned challenges:

- Increase visibility and reputation of the programme
- In 2021, the QS ION has launched the Mentoring Excellence Award
- Nomination of a new Lead for the Mentoring Programme
- Nomination of Deputy Leads for non-Clinical and Clinical Scientists
- Preparing bespoke training material for mentors and mentees

Strategic priorities for 2022:

- **Raise profile of EDI agenda within QS ION and RDs agendas**
 - EDI standing item in departmental meetings and at Executive/HoRD Committees
 - EDI Town Halls
 - Publish an annual QS ION EDI report
- **Capture staff and student experience through qualitative and quantitative data sources**
 - 1- Annual analysis of demographic data for staff and students
 - 2- Data collection and analysis on the intersectionality between race and gender in our staff and student progression pipeline to identify potential problems
 - 3- Promote qualitative data collection through FBS Staff Survey and QS ION Student Survey
 - 4- Establish focus groups to understand underrepresentation in our staff and student population.
Specific areas to explore:
 - Underrepresentation of female clinical researchers in senior contracts
 - Underrepresentation of staff with reported disabilities
 - Underrepresentation of men in PSS roles
- **Support positive action initiatives**
 - Support QS ION James Samuel Risien Russell scholarships and increase offerings in this space.
 - Institute support for the In2Research Programme
- **Improve the experiences of students at the QS ION**

The most salient points that emerged from the 2021 Student Survey were:

 - mental health issues aggravated by sense of isolation and COVID restrictions
 - lack of community sense and lack of peer support
 - lack of awareness of mentoring scheme

The EDI committee will work together with the Education Team to address some of these issues.
Some of the actions we are developing include:

 - support PhD student Away Day in 2022
 - support ECR Symposium in 2022
 - support the establishment of a PhD committee
- **Ensure better outcomes in terms of mental health and bullying and harassment reporting, for both staff and students**
 - Increase visibility of available support
 - Work with departments to identify Mental Health First Aiders
 - Work with departments to nominate a local first point of contact
- **Ensure that priority will be given to BAME staff members to access a career development programme**
- **Promote successful local initiatives at Institute level**
- **Improve EDI training compliance in the Institute**
- **Improve representation of student and ECR rep in the departmental committees**
- **Continued support for ION Athena SWAN work**
- **Continue our work in developing career support initiatives for all staff groups**

Strategic priorities for the next five years:

- **Submit AS Gold application in 2024**
- **Implement bold recruitment strategies/positive action recruitment process (in alignment with Faculty), to increase the proportion of women and ethnic minorities in academic posts**
- **Work towards pay gap and workload transparency**

1.4 Enterprise, Translation and Advanced Therapeutics

1. Enterprise (very loosely = value creation)

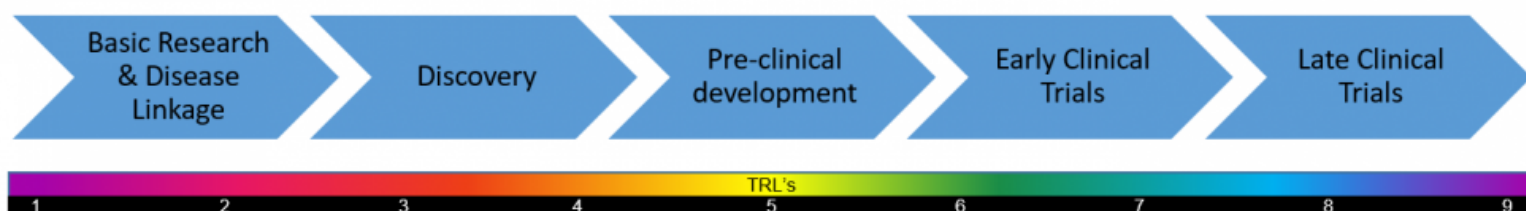
Background

- QS ION may not be maximising opportunities to engage with industry, venture capital, private equity and other commercial entities. There are relatively few revenue-generating licences and spinouts when compared to the QS ION's profile in mechanistic research, experimental epilepsy and industry-sponsored trials.
- Researchers may not always appreciate the relative risks and benefits of conventional disclosure (publication) versus patenting
- Culture barriers ('only academic careers count')
- How does one evaluate the potential commercial or societal value of an invention?
- Researchers may be confused whether to turn to UCLB, UCLC or the OVPA. For UCLB, it is not always clear how to put together an invention disclosure (how to pitch the idea, how to estimate the size of the potential market, competition from existing alternatives or technologies in development)
- After the patent has been filed, what next?

Proposals:

- Education: encourage research students to attend SPERO Entrepreneurship training workshops, understand alternative careers, join London Venture Crawl, intern at VCs; encourage ECRs to attend UCL Venture Insight Series
- Research Departments: Termly meeting for RD enterprise reps – invite UCLB, UCLC, UCL Enterprise & Innovation, UCL Technology Fund, external (e.g., Apollo Fund, LifeArc, Industry, VC)
- Researchers: Provide light touch advice about how to evaluate the potential of an invention and where to go with IP.
-

2. Translation



Background:

- Every researcher has to find their own way from bench to bedside, often with a poor understanding of the translational path and how to navigate TRO/JRO
- Mechanisms for negotiating and approving research contracts other than standard grants are often inefficient
- Few applications for DPFS grants

Proposals:

- Encourage students and ECRs to undertake ACCELERATE training offered by TINs
- Science Translational Advisory Group, supported by Translational Research Manager (joint appointment with TRO). Main roles:
 - Identify research projects with translational potential

- Identify funding opportunities (TAS/TIN pilot data grants, UCLH BRC, NBA, MRC, LifeArc, Industry partnerships, NIHR Invention 4 Innovation, charities)
- Facilitate communication with stakeholders across UCL and linked Trusts and increase visibility of translational research at QS ION
- Help assemble teams able to deliver translational projects on time and on budget
- Facilitate interactions with Research Contracts, UCLB, TRO, JRO
- Help match researchers with clinicians and patient groups
- Raise awareness at UCL Neuroscience Symposium
- Liaise with ARUK UCL DDI and other UCL Departments
- Coordinate collaborative bids for capital equipment
- MRC (NATA) / Wellcome

3. Advanced therapies

Background:

- Total addressable market for genome medicines estimated at \$5 trillion (<https://www.goldmansachs.com/insights/pages/genome-revolution.html>). Other parts of UCL lead in developing new cell, gene and RNA therapies, but QS ION is arguably lagging behind.
- Confusing regulatory landscape, fragmentation of expertise, high entry cost for some advanced therapies, difficulty of securing funding to advance expensive therapeutic modalities towards the clinic (the notorious 'valley of death').
- Scientific challenges include delivery/safety/dosage/efficacy and GMP manufacture
- Need to engage with neurosurgery, MHRA, contract research/manufacturing

Proposals:

- Genetic Therapy Accelerator (GTAc): provide a forum to exchange expertise and make equipment available for early stage batches of reagents (RNA, AAV)
- Develop and nurture relationships with philanthropy focused on advanced therapies (Rausing)
- Annual symposium "Advanced Therapies in Neurology and Neurosurgery"

Cell and Gene Therapy



Uses DNA, RNA, Cells

Reprograms the body to directly fight disease



One-time Treatment

Effect of treatment may be permanent after a single administration



Potentially Curative

Potential to transform medicine, halting the progress of a disease or alleviating the underlying cause of a disease

1.5 Partnerships and communications

Vision and Mission

The QS ION is at a critical transition period as we emerge from COVID and prepare for the move to Grays Inn Road and the dual hub working model. A strong communications and partnerships strategy will be vital to maintaining the ethos of QS ION, ensuring a cohesive community of staff and students underpinned by a transparent and accessible leadership. It is now more crucial than ever to define our brand and mission, aligning all staff and students with an institutional identity and ambition of being the number one translational neuroscience centre in the world. The challenge of bringing together staff and students from disparate locations and specialities is not specific to QS ION, but is present across UCL, where the Neuroscience community is exceptional but fragmented geographically as well as organisationally (i.e., across multiple faculties). Finally, increasing the visibility and legibility of UCL's impact on society is a priority for the whole university, and external recognition of our achievements will increase our visibility and facilitate the development of successful partnerships. Thus, to develop a strong partnerships and communications strategy there are three levels to our vision and mission:

1. **Internal communications within QS ION:** Our vision is to foster a sense of cohesion and community across all sites of QS ION, with all institute members valued for their contributions to the QS ION mission. This will be underpinned by a transparent and accessible leadership, valuing information dissemination and ensuring people feel heard and have the opportunity to communicate directly with the leadership team.
2. **UCL QS ION as a centre within the broader UCL Neuroscience community:** As UCL Neuroscience domain develops its strategy for the next 5 years, we will be proactive members of UCL Neuroscience, promoting integration across sites and a sense of community, aligning with the Provost's priority of "defragmentation" of UCL. We will contribute to the success of UCL Neuroscience by fostering meaningful partnerships to make us greater than the sum of our parts
3. **External engagement and profile of UCL QS ION:** We will increase the external visibility and reputation of QS ION through a range of platforms, integrating with the broader faculty communications strategy and ensuring our outputs are strategically tailored alongside key events such as funding announcements.

Priority actions

1. *Internal (QS ION)*
 - Developing a clear UCL QS ION identity through strong internal communications so that all staff and students feel included as valuable partners in the QS ION vision as we prepare to transfer to the dual hub model.
 - Promoting visible and transparent leadership of QS ION, via all staff "Town Hall" style meetings, providing accessible and frequent communications on our progress and achievements thus promoting a positive research culture. These can be led around a theme (i.e., each of the Director/Deputy Director roles), tailored to specific groups (students, ECRs, Professional Services) or around special topics (REF, Open access policies).
 - Creating further opportunities for colleagues to meet, network and socialise on an informal basis, promoting a sense of community
 - Identifying priority areas from the QS ION staff survey data and other forums where internal communications and staff engagement could be enhanced and develop an achievable action plan to address these. An example of such an area would be the lack of opportunities for informal networking identified at the recent PI away day.
 - Work alongside the Deputy Directors to support internal communications around their strategies as required.
 - Developing a streamlined process for publicising papers and other achievements.
2. *Internal (Within UCL)*
 - Working closely with the UCL Neuroscience Domain and faculty leadership to promote and facilitate integration across the UCL Neuroscience community. This which will be driven by

requirements identified in the recent Neuroscience staff consultation, ensuring this is for the benefit of the grassroots of that community

- Ensuring that QS ION is well represented in the activities of UCL Neuroscience e.g., ensuring representation of translational neuroscience the Neuroscience Symposium.
- Working with the cross-faculty group on barriers to collaboration in Neuroscience to develop a strategy to overcome these
- Maintaining strong relationships with key strategic partners to the QS ION vision, such as BRCs, UK DRI etc, ensuring these help to drive forward progress in translation
- To be a committed and strong ambassador for the QS ION, working closely with OVPA and the Deputy Director of Strategy, and supporting the VP Advancement and VP External Engagement portfolios by showcasing the strengths of QS ION to prospective donors and facilitating donor stewardship

3. *External*

- Increase the external visibility of QS ION, promoting our research excellence and other achievements via our webpages, social media and other outputs
- Build a network of “IoN ambassadors” who can drive our followings on social media, through takeovers and providing content around specific themes e.g. disease awareness weeks, LGBTQ+ in science week etc
- Strategic and proactive communications, streamlined across the institute: for example; recent outputs highlighting the work of the MND Centre to coincide with government announcements on increased funding, which has resulted in a draft framework for designing webpage and social media output
- Working alongside each of the Deputy Directors to ensure achievements in their respective areas are highlighted and support all aspects of the QS ION strategic vision
- Supporting partner fundraising organisations such as the National Brain Appeal to empower and enthuse them as they fundraise to support research at QS ION
- Seek opportunities to increase the presence of ION representatives in external forums such as All Party Parliamentary Groups and Wellcome Trust Health Exchange
- Integrating and supporting the VP London and the UCL London Strategy, engaging our community with the work of QS ION
- Engaging with and leveraging a broader fundraising network of smaller donors via online outputs

Appendix 2

Summaries of the Strategic Priorities of QS ION Research Departments

- 2.1 Department of Brain Repair and Rehabilitation (BRR)
- 2.2 Department of and Experimental Epilepsy (DCEE)
- 2.3 Department of Clinical and Movement Neurosciences (DCMN)
- 2.4 Department of Imaging Neuroscience (DIMG-N)
- 2.5 Department of Neuroinflammation (DNI)
- 2.6 Department of Neurodegenerative Disease (DND)
- 2.7 Department of Neuromuscular Disease (DNMD)
- 2.8 UK Dementia Research Institute at UCL (DRI)

2.1 Department of Brain Repair and Rehabilitation

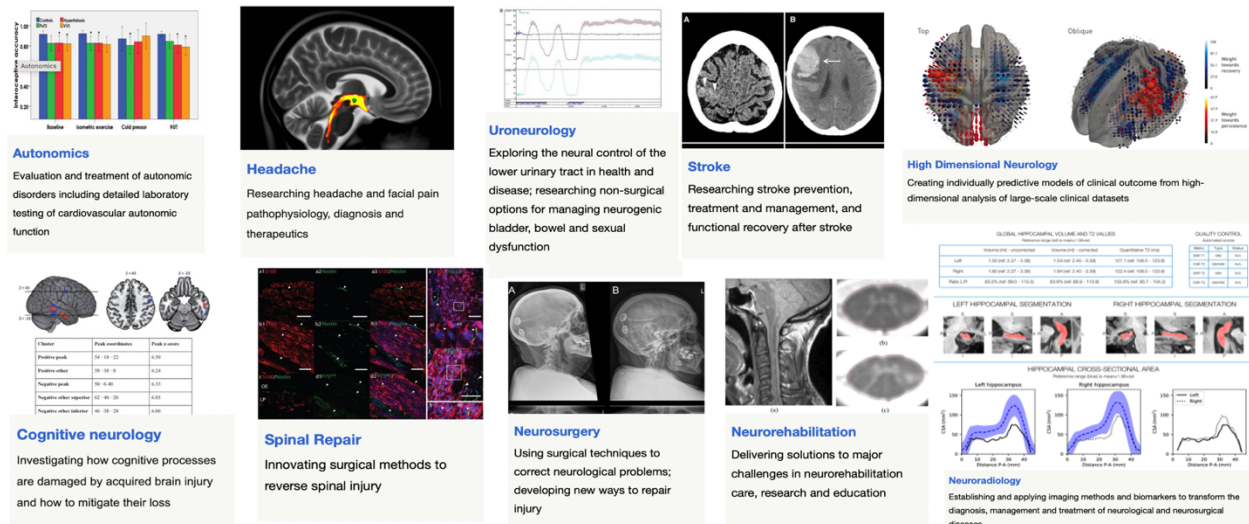
The research vision for department of Brain Repair & Rehabilitation (BRR) is **to discover, develop and implement novel diagnostics and therapies for common and disabling neurological disorders**.

Our unique departmental strength is our diversity, combined with **integration of themes**, which allows BRR to bring together world-class investigators from different but inter-linked groups with shared goals: to advance translational scientific knowledge **to improve the lives of patients with neurological diseases**, and to **educate through teaching and academic supervision**. The uniquely broad scope and collaborative approach makes our research program more than the sum of its component parts.

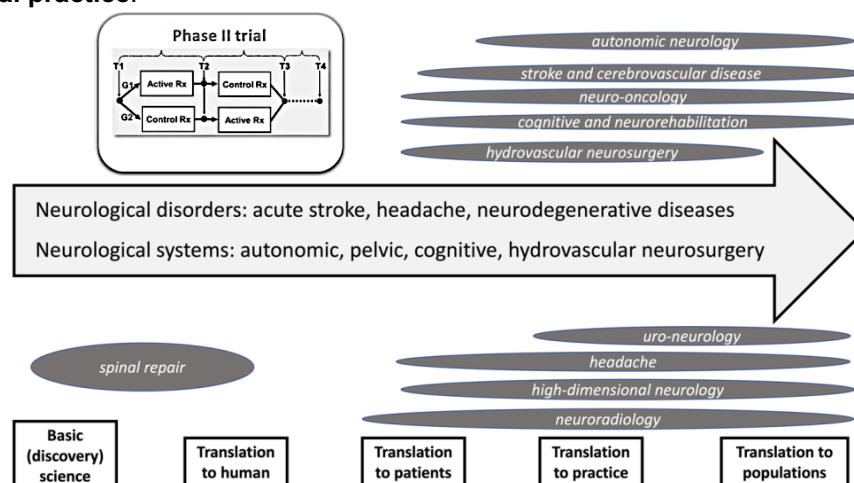
Here, we **describe our most important scientific questions, and the resources required to achieve them**.

About our department

BRR includes 32 principal investigators working collaboratively across the following research themes: autonomics; headache; neuro-oncology; uroneurology; stroke; high-dimensional neurology; cognitive neurology; spinal repair; neurosurgery (hydrovascular); neurorehabilitation; and neuroradiology (see below).



Our members work along the translational pipeline (see below) from basic through to clinical neuroscience and randomised controlled trials. We have a high proportion of clinical scientists, aligned with the BRC Neurological Diseases theme strategy and committed to enterprise and clinical partnerships in the NHS, allowing us to rapidly implement and test new diagnostic and therapeutic approaches in clinical trials and real-world clinical practice:



What are our most important research questions, now and over the next 5 years?

Translational questions

- Can we: (1) develop better **multimodal diagnostic and predictive biomarkers** (derived from clinical or neurophysiological measurements, genomics, and quantitative neuroimaging) for disorders ranging from hyperacute stroke and neurosurgical emergencies, through to headache, brain tumours, neuromuscular

diseases, epilepsy, MS and neurodegenerative diseases; (2) use the two spinouts from the department (**Gold Standard Phantoms** and **Queen Square Analytics**) to help hasten translation into clinical practice; and (3) transform neuro-radiological practice, through the new **QUINIAC** initiative, by translating the latest technological innovations to provide more accurate, timely and personalised diagnoses improving patient outcomes?

- Can we develop **personalised and effective treatment and prevention for neurological diseases** (including common conditions with high disease burden such as stroke, brain tumours, and headache disorders)? (*we hypothesise that high-dimensional modelling will reduce sample sizes and increase efficiency*)
- Can patients with common acquired and degenerative brain diseases (including stroke, brain tumours, and dementias) **improve recovery (including cognition) with better neuropsychological measurements and guided practice** delivered remotely by intelligent digital solutions or gold-standard face to face services?

Discovery questions

- **How do viral infections (including COVID-19), vascular inflammation, and immune factors (including COVID-19 vaccination) influence the CNS**, including links to cerebrovascular disease and stroke?
- **What cause cerebral small vessel disease** (the commonest known brain disorder)? (we will investigate genomic and environmental exposures and ultimately disease mechanisms in experimental models)
- Can basic experimental neuroscience discoveries (including the use of olfactory ensheathing cells) **improve recovery after spinal cord injury**?

What are the near-term and future capacities, capabilities and new technologies required to deliver your discovery and translational research questions?

Capacities

- Establish a **neuro-oncology research theme** in BRR, and contribute to a **Faculty Research Board for brain cancer**
- Establish the **Quantitative Neuroradiology Innovation and Adoption Centre (QUINIAC)**, a UCL Brain Sciences (IoN), UCL Engineering (CMIC), UCLH Neuroradiology and UCLH Digital Health partnership, accelerating the translation and adoption of innovative imaging biomarkers and AI, into UCLH imaging services, and then across the wider NHS and international health systems.
- Develop a **Centre for Artificial Intelligence in Neurology**, based in BRR, to allow widely accessible expertise across the department and ION; increase critical mass in AI to allow integration into research and clinical pathways, enabled by the UCL/H BRC and NHNN
- Establish a **Data Science Hub** to improve co-ordination of secure data management streams to facilitate the above Centre and collaboration with data-rich partners in ION, UCL and worldwide
- **Improve integration of research into clinical services** at NHNN by facilitating more consultant time and improving support structures for research activity by active NHS clinicians
- **Develop a BRR / ION translational neurology Clinical Trials Centre** and network
- **Develop a translational research communication strategy** to facilitate BRR, ION and BRC collaboration

Capabilities and new technologies

- **Increase access to expert biostatistics, bioinformatics, data science**
- Increased basic lab resources to develop a **translational neurological laboratory** (initially cerebrovascular disease, growing to include pain, etc.) in partnership with the spinal repair group
- **Joint development of world-leading computing power with key enterprise partners** to improve IT infrastructure to facilitate complex models
- **Develop and clinically adopt quantitative MRI at 3T and 7T, and phenotyping of cognition and behaviour** in research and routine clinical practice
- **Improve implementation of remote delivery** of neurotherapeutics to treat large populations at scale

Other key goals

- **Strategic senior staff appointments** (Associate Professor, Professor) to facilitate our research aims in stroke and brain tumours
- **Support early career researchers** with grant writing workshops, journal clubs, seminars and improve collaborations within BRR and across ION; improve networking and social opportunities for students
- **Tackle equality awareness** to ensure fair representation in all departmental activities at all levels
- **Develop our communications strategy** with effective departmental admin team support
- **Develop new partnerships with industry** for instance within the QUINIAC framework and BRR spinout initiatives.

2.2 Department of Clinical and Experimental Epilepsy

Epilepsy is one of the most common, serious brain disorders, affecting over 50 million people worldwide.

Our **vision** is to transform the lives of people with epilepsy. Our **mission** is to collaboratively create the world's leading comprehensive epilepsy research and clinical care centre.

The discovery and translational research priorities of DCEE over the next five years are in three broad topics of fundamental importance. There are Discovery Science and Translational projects and programmes that address specific aspects within each priority area.

Priorities	Discovery Science	Translational studies
1. Epileptogenesis: causation of epilepsies	Multimodal studies of synapses, neurone and glial interactions. Genetic components and responses to the environment.	Neuroimaging as a biomarker for epileptogenesis. Identification of novel therapeutic targets.
2. Functional anatomy of eloquent functions and seizures in the brain and effects of epilepsy	High-resolution functional anatomy of language and memory and effects of epilepsy and therapies on cognition. Neuropsychology, fMRI, MEG.	Image-guided precision treatment: surgical, laser, stimulation, focal gene therapy, targeting the epileptogenic zone and sparing eloquent cortex.
3. Neurodegeneration caused by epilepsy	Multimodal studies of excitotoxicity, effects of epilepsy on brain chemistry and pathology.	Identification of in vivo biomarkers, and novel therapies.

1) Epileptogenesis: Understanding the causation and pathophysiology of epilepsy and the processes of ictogenesis and seizure inhibition are of fundamental importance. They will lead to the identification of novel therapeutic targets and disease-modifying strategies.

Discovery basic science:

- Synaptic structure, function and dysfunction. Mechanisms of exocytosis. Quantitative analysis of synapse function and heterogeneity
- Mechanisms of seizures, spreading depression, circuit function. Role of inhibition, relation to spreading depression. Heterogeneity of seizures with different underlying causes
- Identification and design of genetic therapies, target genes and delivery methods.

Discovery clinical science:

- MRI studies of blood-brain barrier breakdown, PharmacofMRI to clarify neurobiological impact of anti-seizure medications
- PET studies of epileptogenesis, with NMDA receptor ligands.
- EEG and video analysis of seizures and physiological parameters related to seizures

Translational studies:

- Implementation of clinical trials of genetic therapies.
- Trials of novel therapies, with small molecules and novel fatty acid dietary supplements.

2) Functional anatomy of functions and seizures and effects of epilepsy: Defining the basis and location of epileptogenic networks and the interaction of these, in terms of structure and function, with the nodes and networks that sustain cognitive function is crucial to understanding the effects of epilepsy on the brain and to devise optimal therapies

Discovery science

- High resolution structural, functional and diffusion MRI to determine connectivity of language and memory networks and relation to epileptogenic networks.
- Serial imaging and neuropsychological studies to understand the impact of epilepsy on brain structure and function.
- Functional assessment of hippocampal memory formation using single unit and local field potential activity.

- Design of novel graphene microelectrodes to characterise seizure networks at a cellular and local level.
- Microwire recordings of single nerve cell activity in vivo with intracranial EEG to clarify mechanisms of seizure generation and spread in vivo.
- Psychological testing using virtual reality whilst recording activity in critical brain areas with intracranial EEG, to clarify functional anatomy of eloquent functions
- Validation of Optically-pumped magnetoencephalography (OPM-MEG) for seizure source localisation and to map eloquent functions with millisecond temporal resolution
- Assays for panomics (epigenomics, transcriptomics, metabolomics, metagenomics) individually to fully characterise gene-based influences on phenotype.

Translational studies

- Multimodal 3D neuroimaging to improve outcome and reduce risks of surgery: Map resection targets, functional MRI and tractography, integrated with neuropsychological assessment to identify critical areas and tracts for language, motor, sensory, memory, vision. Risk stratification and modification of surgical approach to reduce risk and increase the chance of seizure freedom.
- EEG phenotyping to identify foci and networks underlying epilepsy; use AI to automate seizure classification. Development of EEG and physiological measures to reduce the risk of SUDEP.
- Image-guided minimally invasive focal treatment: local genetic modification, laser lesioning, stimulation, integrated with NHNN.
- Stratification for preoperative rehabilitation and post-operative rehabilitation, and implementation of novel “long-distance cognitive rehabilitation.

3) Neurodegeneration caused by epilepsy: Progressive impairment of memory and other cognitive functions is a common consequence of epilepsy and significantly impacts quality of life and employability. There is a pressing need to understand the pathophysiology of these processes, identify pre-symptomatic biomarkers and identify therapeutic targets to prevent these devastating consequences of epilepsy.

Discovery science

- Characterise seizures and interictal epileptic activity mechanisms, with multiplex fluorescence imaging of calcium, voltage, neurotransmitters, and combine imaging with advanced electrophysiology in freely moving animals.
- Clarify the impact of epileptic activity on cognitive function in animal models.
- Determine the genetic predispositions to epilepsy -associated cognitive impairment.
- Correlational studies of clinical neuropsychology, neuropathology, EEG, MRI and PET studies (Tau, amyloid)
- Long-term longitudinal neuropsychology and MRI studies

Translational studies

- Validate imaging biomarkers of presymptomatic epilepsy-related neurodegeneration
- Initiate clinical trials of disease-modifying therapies.

Collaborations: We collaborate closely with NHNN for clinical studies, with key clinical-academic appointments, and integration with BRC. We foster close relations and symbiosis with Epilepsy Society, that underpin our activities at the Chalfont Centre and have a shared vision for future collaboration and creation of new clinical research facilities at Chalfont. We are part of large international consortia, especially in genetics, imaging and neuropathology (ENIGMA, EBBB) that enable studies with sufficient power to address fundamental questions.

PPI: Our close relations with Epilepsy Society enable active PPI with the charity members and presentation at meetings and social media interactions. We have regular meetings with the NHNN epilepsy surgery patient self-help group “BrainBuddy”, which provides invaluable input into formulating research priorities, study design, and presentation of results.

2.3 Department of Clinical and Movement Neurosciences

DCMN was created in July 2018. It has 33 Principal Investigators and over 97 Researchers, Technical and Professional Staff. The active grant portfolio over the last three years has increased significantly from £26.8 M (July 2019) to £33.8M (July 2020) and is now £39.1M (July 2021), a 45% increase in 2 years. DCMN is spread over 5 sites: QSH, 33QS, 1 WS, The Crick and RF campus.

DCMN majors in discovery and clinical translational neuroscience. Discovery science and translational science sit on a continuum in DCMN whereby discovery science programs focus on new findings across genes, molecules, cells and tissue, and the translational science programs translate these discoveries into diagnostics, biomarkers, drug discovery, and ultimately into cohort studies, first in man experimental studies and clinical trials.

DISCOVERY SCIENCE – current and future focus areas

All stages of the translational pipeline are represented for common diseases such as Parkinson's disease (PD), as well as rare atypical parkinsonism (tauopathies), ataxias, and mitochondrial diseases. For each disease area, DCMN research groups harness reverse translation from patient derived cells, patient post-mortem brain tissue, and patient bio-samples to make new discoveries, utilising the UCL QS ION cell repository, the QSBB, the UCL QS Movement Disorders Centre (MDC) cohorts, the Ataxia Centre (AC) and the global ASAP GP2 consortium. DCMN achieves forward translation, taking these discoveries back to human biology and patient benefit through the UCL QS MDC, the LWENC, AC, NIHR BRC, and partnerships across the UK. Three major themes and related questions are:

1. What is the genetic architecture of parkinsonism and related movement disorders?

DCMN researchers discover genes causing familial movement disorders, thus defining the missing monogenic causes of PD, dystonia and related movement disorders. Population genetic approaches to common neurological disease, such as GWAS, define genetic risk loci for sporadic disease, modifiers of penetrance (e.g., LRRK2, GBA, DYT1), and modifiers of phenotype (progression, dementia ataxia, etc.). Gene-environment interactions have been resolved using mendelian randomisation. The genetic and genomic map is being refined and validated using advanced statistical analyses, integration of brain expression and splicing data. Combining genomic mapping with pathology and single cell expression data will define the cell type specificity of monogenic and sporadic disease.

2. How does protein misfolding and protein homeostasis contribute to neurodegeneration in movement disorders?

DCMN researchers investigate structural mechanisms of α -synuclein protein misfolding, through the formation of small soluble aggregates through to fibril deposition in neurons, as well as the functional consequences of aggregate formation. Quantitative single cell and spatial atlases of misfolded protein and their associated networks in brain tissue are being generated. DCMN researchers study the role of tau isoforms, tau expression, regulation, aggregation and function across a range of cell, tissue and animal models. Studying these mechanisms has led to the development of new diagnostics, biochemical and imaging biomarkers, and tractable therapeutic targets from cell biology, leading to small molecule screens and development of novel first in man studies e.g., tau antibodies, ambroxol, exenatide.

3. What are the cellular mechanisms driving neuronal function in health and disease?

DCMN researchers study how lysosomal function is altered in Parkinson's, how and why and how GBA mutations and altered glucocerebrosidase activity, lead to synucleinopathy, and how lipid metabolism within lysosomes influences proteinopathy. Work also investigates the role of mitochondria in health and disease, notably addressing how mitochondria regulate synaptic activity, how mitochondrial bioenergetics interacts with calcium signal transduction, how mitochondrial metabolism, transcription, quality control, and clearance is impaired in disease. This research has led to the development of small molecules and antisense oligonucleotides targeting lysosomal function in PD, mitochondrial DNA homeostasis, the NRF2 pathway, and the permeability transition pore.

TRANSLATIONAL SCIENCE – current and future focus areas

The current and future main areas for research in DCMN will be in PD, the parkinsonisms, other movement disorders and in translational science of brain injury and focus on three broad questions:

1. How to identify and investigate the prodromal and progression phases of PD and other movement disorders for patient stratification for risk and prognosis?

This will concentrate on cohort studies both prospectively (Predict-PD, PROSPECT, RAPSODI, PD FRONTLINE UG2PD, UK BBN, Drug trials, PFP, PROSPECT, 100K Genomes, UK-Biobank, VIP, PROBAND, Discovery, ARSACS) and retrospectively (QSBB cohorts of PD, PSP, MSA, ataxia) integrating clinical (non-motor and motor), imaging, genetic, metabolomic and mitochondrial function, protein aggregation and

microbiome utilizing AI/machine learning. This will enable stratification and identification of factors that predict progression of motor and non-motor symptoms, including monogenic causes and modifiers of penetrance e.g., in PD, dystonia, ataxias and phenotype e.g., dementia. Development of wet and dry state biomarkers in tandem will aid stratification and delivery of clinical trials.

2. How to develop personalized therapies and novel trial design for movement disorders?

We will build on our foundation of delivering novel trial agents and designs (GBA, Edmond J Safra ACT-PD, UCL/Eisai anti-tau antibody therapy for AD), wide collaboration with industry (Eisai, IONis, Vico, Biogen, Merck, NRG, Reata Pharmaceuticals), world class facilities to drive delivery of novel therapeutics in cohorts stratified by genetics and clinical phenotype e.g., progression rate, and the integration of the MDC in DCMN. We will continue development and delivery of genetic therapeutic options to modify disease (LRRK2, GBA PD) or gene replacement therapy (DYT1, Frataxin). Novel functional neurosurgical technology will be developed in tandem to deliver genetic therapeutics stereotactically, or identify targets for stimulation for neurological (PD, tremor, dystonia) and neurobehavioural (Tourettes, depression, OCD, anorexia nervosa) conditions.

3. How to promote optimal recovery after brain injury?

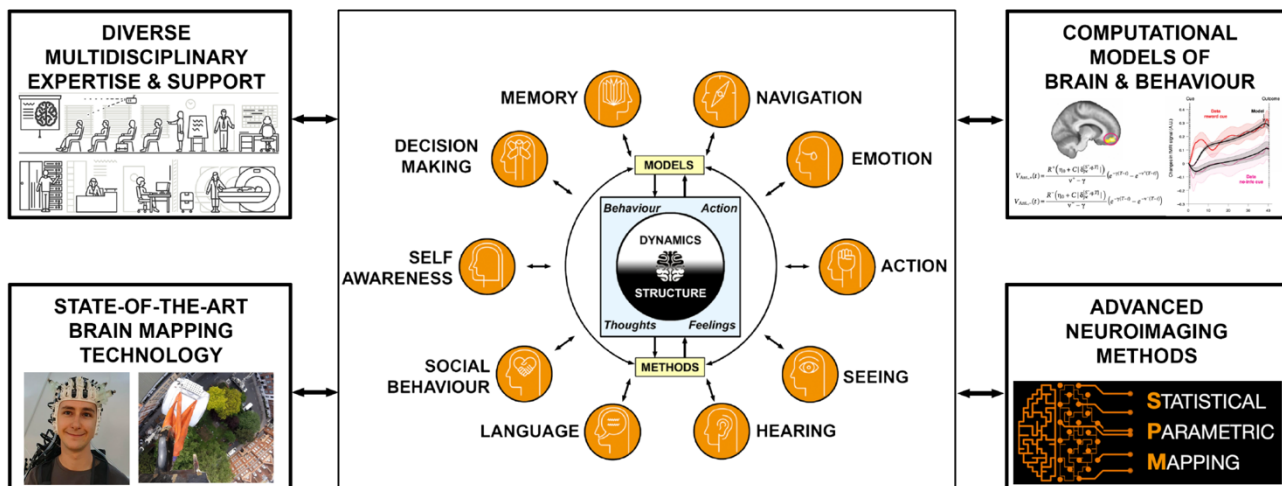
Neurorehabilitation involves complex behavioural treatments with multiple interacting components. Understanding how these components map onto a range of behavioural outcomes, including fine-grained motor, sensory-motor and cognitive-motor behaviours is necessary for developing more effective treatments and understanding how to combine them. A new approach to 'diagnostics' is required to understand how to select specific treatments for individual patients. We will determine whether individual (i) fixed and fluid (plastic) brain states ('Brain-omics') and (ii) complex behavioural phenotypes ('Behaviour-omics') can independently explain individual differences in response to a range of current and novel neurorehabilitation treatments. Modulating brain state (plasticity) can increase learning during behavioural training. We will determine the effect of candidate modulators on both biomarkers of post-stroke plasticity mechanisms (using TMS and M/EEG) and key behavioural outcomes. Candidates include drugs, non-invasive computational neurostimulation, 'enriched environments', cognitive manipulation and time post stroke. This work will establish who and when to target with each approach. We will establish natural history cohorts of stroke and use deep phenotyping to create realistic predictions of functional outcomes. This work is crucial for enabling trial design to employ smaller numbers of patients through stratification based on expected outcome.

INFRASTRUCTURAL STRATEGIC PRIORITIES

Over the next 5 years the main strategic goals of DCMN to support discovery and translational research are 1) the creation of the Parkinson disease Centre for Translational Research (PCTR) whose mission will be to transform our understanding of the causes of the parkinsonisms and deliver the next generation of therapeutics for these diseases. 2) the creation of a Centre for Neurorecovery Research (CNR) whose mission will be to improve outcomes after acquired brain injury through understanding the mechanisms of recovery. Success in these two major themes will foster the growth and ambition to transform translational research in rare disorders.

2.4 Department of Imaging Neuroscience

1. Human Brain Function in Health and Disease



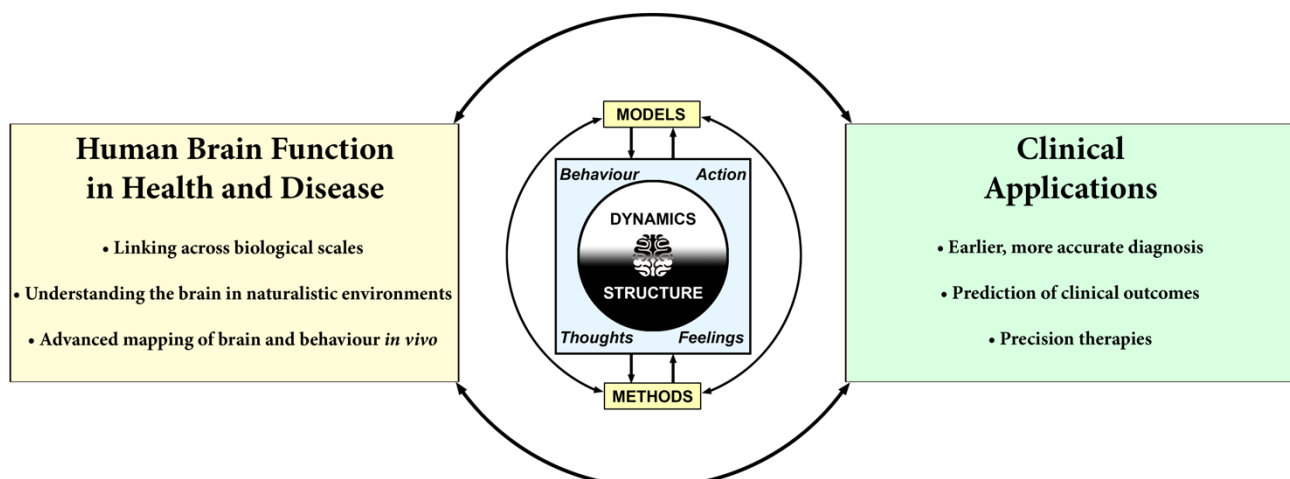
Each brain function is underpinned by complex neural systems. We tackle this complexity by having a broad group of specialised teams that focus on understanding different systems associated with particular functions (e.g. visual perception, memory), and how these change in disease. Investigators acquire different combinations of high-quality, *in vivo*, multimodal brain and behavioural data to address specific questions, and couple these with advanced analytic and computational models of neural dynamics, brain structure, and emergent functions.

Our discovery and clinical scientific priorities are:

DISCOVERY SCIENCE:

Our overarching future priority for discovery science is to develop these methods, skills, and technologies further - To more easily acquire, integrate, and analyse a greater number of multimodal measurements across a wider range of temporal and spatial biological scales, and use these to provide novel mechanistic insights, particularly at the single subject level. This can be divided into three overlapping **discovery themes**:

A. Advanced mapping of brain and behaviour *in vivo* - To define the neural circuitry, dynamics, and functions at multiple scales *in vivo*, and use these to discover the mechanisms of human cognitive processing and behaviour. These include cortical laminar functional MRI to define how different cortical layers contribute to the neural computations underlying perception and motor function; and how higher-order cognitive computational models or algorithms can be validated and advanced with neuroimaging data.



B. Understanding the brain in naturalistic environments - Leveraging Optical Pumped Magnetometer technologies, that generate electrophysiological images of brain or spinal function whilst subjects move and interact naturally, to discover how the brain works in a naturalistic rather than controlled environment. This requires the acquisition and analysis of high dimensional, dynamic and complex data.

C. Linking across biological scales - Includes efforts to use non-human data or observations to inform advanced generative models or hypotheses, combine individual specific *in vitro* human neural models (e.g. iPSC, organoids) with *in vivo* longitudinal data, develop novel methodologies to analyse dynamic biological data including longitudinal clinical/behavioural observations, integrate existing datasets to provide biological annotation of *in vivo* brain data (e.g. receptotopic/genetic maps) and *ex vivo* ultrahigh resolution MRI.

CLINICAL APPLICATIONS

By better understanding human brain function in health, we can apply the same tools, techniques and methods to study neurological, developmental and psychiatric disorders, with a focus on defining: (1) How do these *in vivo* mechanisms change in disease; (2) Can structural and functional brain abnormalities be used to more accurately classify clinical syndromes; (3) How do we translate these discoveries to allow:

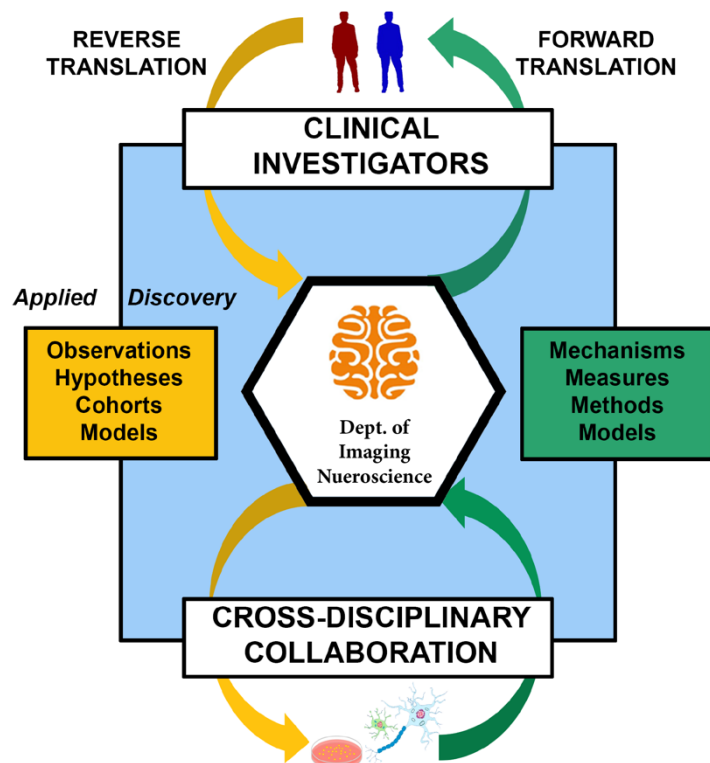
A. Earlier, more accurate diagnosis - Combining multimodal measures of different brain properties, along with other potential measures, to develop ways of identifying individuals with a disease from *at risk* cohorts before overt clinical signs emerge, and to more accurately discriminate potential disease mimics.

B. Prediction of clinical outcomes - Methods to predict long-term clinical events before symptoms emerge and to anticipate disease trajectory more precisely, to help inform treatments and aid discussions with patients and their families e.g., Language recovery after stroke, onset of dementia, vulnerability to future psychopathology, targeting in deep brain stimulation.

C. Precision therapies - Leveraging *in vivo* brain data to identify, and understand, discrete clinical phenotypes who may benefit and respond to targeted therapies, for example, objectively identifying disease phenotypes, predicting response to certain therapies, or linking *in vitro* human models with MRI data acquired in the same individuals to deliver flexible platforms for target identification and testing. This theme integrates the need to provide accurate biomarkers to monitor disease progression in the absence of overt clinical signs

Our approach provides an ecosystem that can flexibly combine clinical expertise and observations with a wealth of knowledge spanning many different brain functions, *in vivo* experimental techniques and analytic methods. This allows us to iteratively formulate, refine and test hypotheses, rapidly adjust and adapt technologies and methods to fit particular needs or questions, leverage collaborators expertise from other disciplines and can provide extremely rich, high-quality, detailed measurements across many different biological scales in the same subjects.

Forming one part of an iterative translational pathway, our framework can naturally integrate with expertise embodied by the dual-hub, where cultivating a partnered approach will allow discoveries to be more rapidly adapted, deployed, tested and refined in the clinical setting.



2.5 Department of Neuroinflammation

The Department of Neuroinflammation brings together researchers with expertise in cell signaling, inflammation, immunology, imaging and clinical trials. Our work covers all stages of the translational pathway, from basic science to clinical trials and routine clinical setting, most of the PIs focus on MS. We bring expertise in immunology, neuroinflammation, imaging and clinical trials to the wider community of neuroscientists at ION and UCL. Our vision is for Neuroinflammation Department to be the international leading centre for translational research in neuroinflammation and neuroimmunology, which has the potential to provide wide benefit across neurological diseases.

A) What are the most important discovery and translational questions now and over next 5 years?

We have grouped these questions in 5 critical areas of research (in red the top research questions):

1. Neuroimmunology

Discovery questions:

- What is the role of innate immunity in the pathogenesis of MS and what are the new immunological targets for novel therapies in MS?
- Can we discover novel biomarkers of peripheral nerve, neuromuscular, neurodegenerative or other diseases, which have clinical application and utility for diagnosis and prognosis?

Translational questions:

- Can we screen novel therapies identified from preclinical studies and initiate first-in-man studies?
- How can clinical, imaging and fluid biomarkers of disease integrate into and influence outcomes of clinical trials and daily care?

2. Microglia and cell signalling

Discovery questions:

- How do microglia respond in neurodegenerative/neuroinflammatory diseases?
- How can we control the response of microglia in MS to enhance their neuroprotective properties?
- Do microglia genes, which regulate inflammation in the progression of AD, affect MS?

Translational questions:

- What are the biomarkers with regard to cell proteins, which are encoded by microglia genes and secreted either as cytokine profile or exosomes?
- Can we develop assays for translational research to target microglial pathways and genes?

3. Tissue energy deficiency

Discovery questions:

- Optimise methods to improve oxygen delivery to inflamed brain tissue that will be hypoperfused and suffer an inadequate oxygen supply, in both MS and neurodegenerative disease.
- Understand how maintaining oxygenation in inflamed tissue protects neurons from slowly progressive degeneration over the lifetime, as we have discovered in animals.

Translational questions:

- Conduct a trial of acute nimodipine therapy in patients with optic neuritis.
- Does therapy that prevents acute and slowly progressive disability in animals translate to protect acute and progressive disability in MS?

4. Global brain properties captured by neuroimaging

Discovery questions:

- What are the new imaging biomarkers of: 1) BBB damage and choroidal abnormalities, and cellular trafficking across these barriers; 2) specific markers of myelin and neuroaxonal damage; 3) brain function and metabolic changes; 4) meningeal pathology; and 5) optic nerve and spinal cord damage?
- Can we unpick biological mechanisms of disease causation and trajectories of disease evolution using MRI, exploiting the specific and different sensitivity to underlying tissue properties of MRI at 3 & 7T?

Translational questions:

- Can we translate insights from histopathology and cells physiology into testable mesoscopic and macroscopic computational models using in vivo imaging data?
- Can we use NHS MRI data (not curated for research) to address clinical questions (around prognosis, treatment response and drug selection) to achieve precision medicine in MS?
- What is the value of OCT in clinical research to monitor MS disease activity and progression and in clinical practice to track/predict disability and guide treatment decisions?

5. Clinical trials

Discovery questions:

- Can we identify a therapy that stops progression in MS?
- Can we develop a real-time QC at imaging sites participating in multi-centre clinical trials to improve sensitivity to changes and assess treatment efficacy?
- Can we predict subgroups of patients who may be more responsive to certain types of treatments for clinical trials patients stratification?

Translational questions:

- Can we improve the interim measures (MRI and non-MRI) of multi-arms, multi-stage (MAMS) trials that can be performed in several (non-academic) centres?
- Can we refine the MAMS statistical methodology to extend it to other diseases?
- Can we develop MAMS design to include MRI-based stratification at recruitment stage?

B) What are the near-term and future capacities, capabilities and new technologies required to deliver your discovery and translational research questions?

Capacities:

- Cross-collaboration with other Departments and BRC for discovery science.
- New registry for patients with newly diagnosed clinically isolated syndrome and MS and enrolment into longitudinal observational studies and future clinical trials.

Capabilities:

- Improve integration of MS research and clinical service at NHNN (including ophthalmology) to: (1) collect a rich standardized dataset of clinical metrics in the NHS, and (2) use MRI for research.
- Improve IT infrastructure, specifically build further (and share) computational power tuned for advanced image analysis and integrated with the MRI scanner.
- Automate QC and data analysis.
- Seamlessly integrate AI into clinical pathways for the diagnosis, prognosis and treatment management.

New technologies:

- New bank of iPSC for production and verification of genotype and phenotype in MS; develop/expand hiPSC technology platform to be used for drug discovery in MS and related inflammatory conditions.
- An in-house mass spectrometry for exosomal proteins and other secreted proteins.
- Standardized imaging acquisitions and analysis pipelines across different studies and different Departments at ION and in the NHS.
- Access to ultra-high field (7T) MRI scanner/s for studying in vivo ensemble tissue properties, not accessible at 3t, with particular reference to metabolism and physiology biomarkers.

Among the proposed initiatives, we agreed that the following will enable our discovery and translation:

1. To increase discovery neuroscience in Neuroinflammation: (i) a senior lead in immunology (and team) and suitable space for the Neuroimmunology lab should be prioritised. The external review of the ION carried out in January 2017 recognised that “*the replacement of Prof Miller with a senior neuroimmunologist will not be sufficient to really impact neuroimmunology and consideration should be given to further appointments in this field in the context of departmental restructuring*”. This is an important strategic development and recruitment, which will lead to a research program that addresses the questions above and cuts across neurological diseases, and will benefit other groups at the ION and UCL-wider community. (ii) **a senior lead in neuropathology**, who will translate insights from histopathology and cells physiology into mechanisms of disease and MRI measures. **2. hiPSC Platform; 3. MRI Research Platform. 4. ION Science Translational Advisory Group**

In addition, we would recommend that the **following aims are prioritised:**

- ❖ **To develop a truly “bidirectional” environment where NHS data (including MRI) can be used for research, and research data, when appropriate, are donated to the NHS for patients’ care.**
- ❖ **Focus on providing secure UCL funding for core staff to work beyond single projects** (physicists, imaging analysis experts and laboratory research staff). The current core staff is insufficient to maintain continuity and drive the full portfolio of research themes, and this has led to significant lost opportunities. The lack of new long-term UCL appointments has also led to stress and anxiety as core staff have continually had to source funding for their own work while supporting the broader team, and to close critical gaps in the Departmental skillset as younger colleagues look to more securely funded research environments to continue their work.
- ❖ **Support early career researchers by:** (i) organizing more events focused on grant writing (such as the Early Career UCL courses/workshops but they are often fully booked); (ii) setting up monthly research “clinics” where senior colleagues offer advice on grant applications, projects and project writing up, and more seminars.(iii) allowing early career researchers to sit in grant review panels; (iv) organising more journal clubs and improving interaction between groups;
- ❖ **Develop robust pathways of recruitment of patients in the NHS and create a registry system using electronic health records.**

2.6 Department of Neurodegenerative Disease

A) What are the most important discovery and translational questions now and over next 5 years?

Research within DND encompasses multiple neurodegenerative disorders: AD, FTD, HD, PD, prion diseases and ageing, and **spans the translational pipeline** from discovery science, therapeutic target identification, drug screening, preclinical studies, experimental medicine to first-in-human and large-scale clinical trials. We aim to enable translation for patient benefit with an iterative pipeline of research from patient to lab and back to patient.

The molecular basis of disease pathogenesis must be understood to optimise therapeutic target identification and we must **capitalise on the clinical resources** available at the ION. Understanding **the genetic basis of disease** provides a foundation for mechanistic investigations. Maximising recruitment of NHNN patients into research (ideally all patients) to allow systematic genome sequencing of every participant would promote the identification of disease-linked genes (causative, risk variants and disease-modifying i.e., influence on age at onset and disease progression). In turn, this will enable the creation of *in vitro* and *in vivo* models (including state-of-the-art iPSC, mouse models) to allow **mechanistic studies** and facilitate the identification of **optimal therapeutic targets** for precision medicine. Determining the extent to which our models recapitulate a given disease will be aided by our access to patient biopsies and biofluids through the clinics at the NHNN and our neuropathological examination of *post-mortem* brains in the QSBB and elsewhere. Departmental priority areas for mechanistic investigation include RNA biology, mitochondrial biology, autophagy/lysosomal biology, cell type vulnerability (neuronal subtypes and glia), proteostasis, lipid metabolism, synaptic biology and membrane integrity. The integration of large-scale 'omics studies will lead to an understanding of how pathogenic dysfunction occurs at the single-cell and network/circuitry levels. Given that the work of DND spans the major neurodegenerative diseases, we are uniquely positioned to harness the power of mechanistic commonalities to cross-fertilise therapeutic development e.g., taking knowledge obtained from the development of immunotherapies and genetic therapies in HD and AD and applying this to other disorders such as prion disease, FTD, PD. The **translation of mechanistic understanding into novel therapies** will be facilitated by increased screening abilities and collaboration with internal (e.g., ARUK DDI, UCL Neuroscience Domain) and external (e.g., Astex, IONis Therapeutics, GSK, Vertex) partners.

To provide the framework for future clinical trials, **detailed evaluation of patient cohorts** must be conducted in parallel to our mechanistic studies and preclinical therapeutic development. We stratify patients based on familial disease-causing mutations and risk variants. Patient cohorts undergo **deep phenotyping** with imaging modalities (structural and functional) and neurological and neuropsychiatric assessments as part of local or collaborative studies (e.g., DIAN for AD, TRACK for HD, GENFI for FTD). This is key to determining when the earliest changes are identifiable and when might be the **optimal time for intervention**. DND has been exceptionally strong in imaging (MR, PET) and 'wet' biomarker development (e.g., NFL, HTT, Abeta, p-tau – in CSF and blood). It is a high priority to expand these biomarker discovery efforts (fluid, imaging, digital, SILK) and to link **biomarker trajectories with clinical outcomes**. Through the LWENC, DND will continue to partner with industry to be world-leading in first-in-human clinical trials.

Complementing the above, expansion of our patient support programmes and development of a Rare Dementia Support Centre will ensure an enriched patient/participant experience and research engagement – and prepare for a new era of disease-modification therapies with associated research opportunities.

B) What are the near-term and future capacities, capabilities and new technologies required to deliver your discovery and translational research questions?

The following would accelerate progress against the questions outlined in (A):

- Expansion of iPSC facilities to increase capacity and incorporate novel methods such as organoids and co-cultures and robotic cultures for screening
- Development of a CRISPR screening platform in human iPSC derived cell types
- Digital imaging and machine learning technologies
- Additional infrastructure for patient sample curation and storage
- Post-mortem MRI imaging capabilities and increased capacity for PET imaging
- Mass spectrometry (proteomics, lipidomics, metabolomics)
- Retention of expertise via staff scientist positions
- Strategic recruitment in areas such as iPSC/screening (technical experts to enable others), neuroinflammation
- Bioinformatics and computational biology support
- Database of samples, models, data available within QS ION
- Increased support for databases – with central QS ION support and a x-department community of expertise for problem solving and economies of scale
- Increased medical statistics support – establish a community/critical mass at QS ION

- Increased support from JRO for contracts and study set up – this is a priority. Major concern is the delay and additional effort required (slow responses and lack of clear pathways) -a reputational risk, a cost in PI and admin time and loss of opportunities.
- Greater capacity for early phase trials
 - Expansion of the CRF
 - Neurosurgical support for safe/enhanced delivery of therapies in the CRF(s)
 - In parallel, appropriate space for non-intensive activities (consenting, administer scales) outside the CRF to free up / optimise use of the CRF
- Greater capacity for observational and multimodel patient studies
- Building on the above, establish a Neurogenetic “NgTP” Centre
 - Partly virtual/partly physical – drawing together strengths across QS ION
 - Attract/retain expertise & accelerate development/ testing of therapies - including increasing CRF expertise in, and capacity for, genetic therapies

2.7 Department of Neuromuscular Diseases

OVERVIEW: The DNMD currently consists of 221 staff and students. This includes 23 Principal Investigators: 16 Professors, 7 ERC Fellows (MRC, Wellcome Trust and MND Association 3yr+ Fellowships), 133 salaried staff and 65 UCL PhD students. In addition, the Department hosts 79 Honorary members, almost all of who are research active, including 9 NHNN Consultants. We currently have 8 visitors working in the Department, bringing the total number of people in DNMD to ~310, supported by an excellent Professional Services Team working across the entire Department (3 FTE), led by Kully Sunner, as well as a bioengineer, Chris Seers. DNMD Research Groups are based across 5 UCL sites: QSH; 8-11 QS; Russell Square House; The Cruciform; The Crick, and our clinical colleagues also conduct research within NHNN. **The Department currently manages 127 active grants totalling £56.4 Million.**

Research within the Department is primarily focused on Neuromuscular Disorders, with groups integrating findings from humans and disease models, and from multiple cell populations, to identify therapeutic targets and test new therapies. Our research teams work along the entire translational pipeline from gene discovery to disease mechanisms to drug discovery and therapy development.

Research within the DNMD covers a wide range of disorders affecting the central nervous system (ALS, SBMA, SMA, and dystonia), peripheral nerves (inherited neuropathies) and muscle (inflammatory myopathies, channelopathies, mitochondrial disease, DMD, and McArdle's Disease). In addition, we have world-leading expertise in a broad range of research areas, with a major strength in gene discovery, RNA biology and dysfunction, brain and spinal cord circuit physiology and pathophysiology, axonal transport, protein homeostasis and glial biology. The DNMD also hosts the ARUK UCL DDI, providing expertise in drug discovery, assay development and medicinal chemistry. In addition, DNMD has an almost unique collection of experts able to generate and deep phenotype the neuromuscular system of novel mouse models of NMD and dystonia. These mice represent an invaluable resource, not only for target identification but also pre-clinical efficacy studies.

DNMD is one of the largest wet lab-based Departments in UCL QS ION and uses a broad range of laboratory techniques, encompassing cellular and molecular biology, in situ transcriptomics, advanced imaging, sequencing, and muscle, nerve, and CNS electrophysiology. The Department also hosts a large number of clinical researchers, whose ability to undertake high quality clinical research is enhanced by their association with NHNN and its unique patient population, which has enabled DNMD researchers to establish stratified cohorts and disease registries, to undertake natural history and biomarker studies, to develop an NMD biobank, as well as undertake experimental medicine and efficacy trials.

KEY RESEARCH QUESTIONS: Although research in DNMD is broadly focused across neuromuscular disease, **four research areas have relevance across several NMDs and are a priority for the Department;** *however these areas are not a ranking of the work done in the Dept:*

i) RNA Biology: What novel insights and therapeutic targets emerge from the study of RNA dynamics in neuromuscular disorders? In particular, the alteration of the cellular distribution and function of **RNA-binding Proteins (RBPs)** is a common theme across several NMDs, including ALS, peripheral neuropathies and IBM. RBPs are involved both genetically and pathologically in these disorders, and their nuclear depletion is a hallmark of disease. Breakthroughs in our understanding of basic mechanisms of RBP function and how these are impaired in disease have now put us on the road to the development of innovative therapeutics.

ii) Gene Discovery, Modelling and Genetic Therapy: Will genetic therapy strategies be effective in NMDs? DNMD has world leading expertise in **neurogenetics**; the identification of new genes permits the generation of **mouse models** and the identification of disease pathways, some of which will be druggable. DNMD has world-leading expertise in the generation and deep-phenotyping of mouse models of NMD, as well as using these disease models in **preclinical trials**. **Genetic therapy** is a growing area of research in DNMD, with several programs aimed at gene knockdown, over-expression or correction of splicing errors currently underway.

iii) Drug Discovery: Can we identify druggable pathogenic pathways to develop effective therapies for NMDs? The DNMD is host to the **ARUK UCL DDI**, which although primarily focused on dementia, has several ongoing drug discovery programs with DNMD research groups, including those focused on axonal transport deficits in ALS as well as protein dyshomeostasis.

iv) Clinical Research: Can we identify biomarkers to i) aid diagnosis and ii) improve stratification, monitor disease progression and thereby improve clinical trials? Clinical research is a core focus of DNMD. Our PIs have particular strengths in biomarker development (MRI; Neurofilaments; miRNA), outcome measures, disease registries and stratified cohorts, as well as designing and undertaking clinical trials.

REQUIRED EXPERTISE AND TECHNOLOGIES:

- Research within DNMD will be significantly enhanced by the establishment of the planned **Core Facilities** in the new ION-DRI Building at GIR, in particular: **Bioinformatics and Biostatistics**; **human iPSC** and **advanced imaging** facilities; the **MRI** core; **tissue processing** and **single cell analysis** facilities, as well as an on-site BSU with a well-equipped **animal behavioural suite**. **Enhanced data storage** is a critical requirement across the entire Department.
- Additionally, as our focus on Gene therapy increases, there is a clear, currently unmet need for **expertise in genetic therapies**, (including ASO and viral vector design and generation), as well as gene editing. DNMD will therefore gain significantly from the planned establishment of the **Gene Therapy Accelerator** and **Science Translation Advisory Group**. Access to **in situ transcriptomics** and **high-throughput screening** would significantly benefit DNMD research programs.
- Almost all groups within DNMD would benefit from increased patient sample collection and storage, with an **expansion of the Brain Bank** to include neuromuscular tissue, and the **NMD Biobank**, to include DNA, RNA and cells (fibroblasts, lymphoblasts). Clinical research remains critically dependent on **Patient Registries & Stratified Cohorts**, and there is a clear need within DNMD to increase our capacity to undertake **Clinical Trials**, with respect to personnel (eg trial coordinators, clinical fellows) as well as space (eg larger gym).
- Finally, **dedicated Enterprise Support** for QS ION would greatly enhance the ability of DNMD researchers to advance their findings towards the clinic.

DUAL-HUB: Regular cross-site seminars; High quality dedicated video links; Newsletters; Social

Events **ERC SUPPORT:** Social events; Grant and Fellowship Workshops; Careers Seminars

PS: ACADEMIC INTEGRATION: (Already very good in DNMD) PS attendance in PI meetings; Newsletter

2.8 UK Dementia Research Institute

The UCL DRI Centre consists of 15 group leaders (GLs), 7 of whom have DRI as their home department. The remaining members of the UCL DRI (have their home department elsewhere in QS ION and their input into this report is covered by their home department).

Each GL was asked to discuss IONs strategic plans with their group to get input from staff at all levels. GLs were then asked to create two slides addressing 1. Their group's most important discovery and translational questions now and over the next 5 years and 2. What would be required to deliver their groups discovery and translational research. A meeting of all GLs was convened on 29/9, chaired by the HoRD, Karen Duff. After the HoRD presented a brief overview of the GLs programmes, and how each programme fits into the UCL DRI Centre overall mission, the 7 home DRI GLs (Bart de Strooper in absentia) presented their slides.

UCL DRI Strategic Plan Priorities, recruitments and enabling technologies/cores

The HoRDs then presented the overall UCL DRI Strategic Plan Priorities which included the following areas of focus:

- Genetics (especially the role of modifiers on disease initiation and progression, cross species integration)
- Disease mechanisms (esp. Down's syndrome, synucleinopathies, tauopathies and Alzheimer's disease)
- Vascular contributions to neurodegenerative disease
- Multi-cell interactions (esp. neuron-glia, and gut/periphery-brain interactions)
- Single cell (and in situ/spatially resolved) -omics (transcriptomics, proteomics, lipidomics) and data analysis.
- Imaging (esp. super-res microscopy, live cell and longitudinal confocal, single particle cryo electron microscopy and subcellular tomography)
- Imaging in human (PET)
- In vivo functional assessment (neural activity, network imbalance and behaviour) in both human and mouse models of disease.
- Deep phenotyping of clinical cohorts (including longitudinal)

To address these priorities, strategic recruitment in the next quinquennial funding cycle is planned for two clinical GLs, and one GL with expertise in rodent in vivo recording and cognitive testing. The following enabling technologies/cores etc were identified as being essential to fulfil the strategic aims of the UCL DRI:

- Biomarker assessment at single molecule resolution (plasma, CSF, including aggregates)
- Brain tissue availability (especially high integrity tissue that's critical for in situ/spatial transcriptomics) and neuropathology expertise; state of the art freezers and automation for sample access to reduce freeze/thaw.
- Histology services (including single and multi-block tissue processing, autostainer and analysis including machine learning to identify cell types of interest)
- BSU with high capacity, excellent infrastructure and reasonably priced services
- Rodent behaviour core
- Functional genomics and CRISPR-editing core to test gene candidates
- Viral vector core including for genetic therapies
- Antibody/nanobody core and support
- Advanced cell (iPSC and direct conversion), tissue (multi-cell type organotypics) and mouse models (chimeras, targeted, transgenic, multigene, knockout) core facilities. Ageing component is important.
- EM/ET (including cryo)
- Flow cytometry facilities and support
- Ultra-sensitive mass spectrometry, including of lipids. Tech and analysis support.
- Access to curated donor data at multiple levels where existing (DNA, imaging, biomarker, epidemiology, biofluids and tissue, derived cell lines, clinical and clinical trial data)
- Bioinformatics and statistics support
- Human physiology assessment (including cognitive testing, sleep).
- Human functional analysis at high spatiotemporal resolution (electrophysiology, engineering, imaging eg MEG/fMRI). Cutting edge recording and data analysis (engineering, human-rodent crossover)

The group was then asked to identify its most important current and future discovery science and translation questions and identify enabling technologies and expertise and partnerships

Discovery key areas of interest included:

1. **Understanding the basis of molecular/cellular heterogeneity** at DNA, and single or multi-cell level, especially in the whole brain (and periphery) context. This allows for better understanding of selective vulnerability to pathogenic mechanisms impacting pathology, neurodegeneration, neural function and/or behaviour, as well as cellular and network interactions. Better understanding of molecular and cellular heterogeneity will improve the efficacy and specificity of therapeutics. Enabling technologies include the DRI's investment in spatial transcriptomics (with Kenneth Harris UC, and the Brain Atlas initiative at Imperial DRI), single cell proteomics and the ultra-sensitive mass spec required for protein (or lipid) detection (with U. Dundee, K. Thalassinou UCL). State-of-the-art, enabled data sciences (currently being expanded at UK DRI, and the dual hub) will be essential. Relationships with the Alan Turing Institute, and international systems groups (Broad, Allen Brain Institute) will expand capabilities.
2. **Understanding the impact of ageing, and the basis of healthy aging/disease resilience.** Enabling resources were identified as part of the QSBB and UK biobank, and the ARUK, and through initiatives such as MNDs enrolment of all patients in research programs which will increase the availability of patient resources.
3. **Understanding the earliest (preclinical and early clinical) stages of a disease** to enable early detection and treatment. Clinical resources (including brain and biofluids) and the longitudinal cohorts (eg. the familial AD, HD, the birth cohorts and others studied at UCL) will be invaluable for this.

The availability of high-integrity tissue (including biopsy or resected pre-mortem tissue), and progressive disease and aging relevant cell and animal models will be key for 1-3. The importance of having a functional, usable and reasonably priced BSU was emphasised and the 'BSU futures' initiative was welcomed. The UCL DRI noted it has good connections nationally, and internationally through participation in international advisory panels, pharma links, and NIH and CZI funded collaborative grants.

Translation areas of interest included

1. **Understanding the basis of human heterogeneity** – this has the potential to give rise to a more effective, personalized medicine approach (or at the least stratification), as well as inform on basic mechanisms. ION has unique and enviable clinical connections, and opportunities to curate and coordinate efforts within and between departments, to deep phenotype patients and controls. Well characterized patient cohorts could be a valuable resource for FIH studies (facilitated by BRC-4) and pharma partners. Being able to perform human/animal model cross species studies to identify gaps and synergies between humans and model systems (mainly rodents, but also non-human primates, flies and worms) was considered important but needs to be supported by data sciences.
2. **Understanding the relationship of biomarkers to disease processes** (including in rodents to interrogate disease process, and in humans in clinical trials). Fluid and imaging biomarkers (PET, MEG, MRI etc) are key to identifying molecular and cellular therapeutic targets, and monitoring the efficacy and off-target effects of drugs. Key partnerships exist with other ION departments.
3. **Developing therapeutic agents based on targets identified through discovery.** These include genetic therapies (ASOs), repurposed drugs, brain activity modulators, small molecules and immunotherapy approaches. Partnerships with pharma (e.g., IONis) and the Drug Discovery Institutes, and the input of the UK DRI's innovation and commercialisation service have been invaluable for taking therapeutic developments forward. More could be done by UCL to reduce paperwork and impediments to materials exchange and commercial opportunities.

Dual Hub, ECR well-being and one team.

Suggestions for enhancing a cohesive, well informed community include an on-site subsidized bar, open till late, with some bar food, to encourage mixing and casual discussion (and conflict resolution) between all levels of academics and professional staff. Data-blitz sessions, speed dating opportunities, quiz nights, regular socials (including events to draw people in) with poster boards for ECRs to showcase their work are all good ways to inform and bond people. Having an ECR (e.g., post-doc) committee with a representative that sits on key committees – ideally with a small budget would also be good.

A dual hub newsletter with searchable function to identify labs housing equipment, technology, expertise, resources would be useful. TV screens positioned at key spots (entrance, elevators, toilets etc) showing upcoming talks and celebrations would help with information sharing that doesn't entail reading more emails. The shared facilities and cores were considered key to the success of the dual hub; presentations by technologist (with perhaps a user group) would showcase what the equipment can do and inform on developments in the technology. One challenge will be to reduce the feeling of two sites (wet lab activities at EDH and clinical activities at QS). A regular shuttle bus between the two, joint seminar series, funding for shared students or postdocs would help.

Appendix 3

Summaries of the Strategic Aims of QS ION Divisions

- 3.1 Division of Neurology
- 3.2 Division of Neuropathology
- 3.3 Division of Neurophysiology
- 3.4 Division of Neuropsychiatry
- 3.5 Division of Neuroradiology and Neurophysics
- 3.6 Division of Neurosurgery

3.1 Division of Neurology

The Division of Neurology is the academic home for all QS ION and NHNN neurologists. The division aims to promote academic research, training and education and provide support for academic careers both of clinical academics and NHS consultants doing research.

The division is uniquely placed to facilitate close working between QS ION and NHNN especially in the areas of education and translation thus supporting the QS ION education and translation strategy.

Division of Neurology achievements since 2019 and plans for next 1-5 years.

Despite the disruption caused by covid-19, the division has continued to deliver its core education programme including the weekly Gowers grand round and the yearly neurology consultant educational away afternoon. The division delivered on its 3 key deliverables from 2019 away day as follows:

1. Review funding for division with aim to increase overall and specifically increase NHNN contribution

The yearly consultant educational away afternoon has become increasingly popular and attracts 65-80 neurology consultants. This number of people meant there was a funding gap as the division gets a small contribution from QS ION each year which no longer covers the increasing costs of travel for patients attending Gowers and the cost of the away day afternoon. In 2019 we successfully applied for a contribution from NHNN to cover the excess costs for the division away afternoon.

Plan going forward: Many NHS NHNN neurologists benefit from the away day and Gowers round so a joint funding model for educational activities going forward is optimal. *See below for division response to Covid-19.*

2. Develop Gowers further as educational asset for QS ION (funding permitting)

We recognised that Gowers round is an unrivalled education opportunity for QS ION / NHNN staff and students but also has the potential to be a much more widely used educational asset. The current consent allows the patients to be videoed but there is no system to record and curate the whole round or to consent to use these recordings more broadly for QS ION educational activities including MSc courses and the increasing number of virtual educational activities. In early 2020, we agreed a plan to put together with the educational unit a business case to partly fund a teaching fellow to take on this role. This was put on hold due to Covid-19 and a new virtual Gowers round was developed in the interim (see below).

Plan going forward: We plan to revisit this plan using the experience we have gained from the virtual Gowers round to develop a hybrid Gowers which can be recorded and curated as described above.

3. Work with QS ION / NIHR / UCLH / CLRN to understand CLRN funding stream

Mary Reilly performed a wide reaching consultation and review and prepared a report on CLRN funding in QS ION / NHNN during early 2020. This report had a number of recommendations to streamline CLNR in QS including appointing a clinical lead. The issue with CLRN understandably became more acute during Covid but has resulted in a permanent loss of CLRN funded staff in QS. The report was sent to Mike Hanna and Chris Turner in May 2020. This led to a meeting with Nick Mc Nally and an agreement to appoint a clinical lead. This has not been activated yet due to covid-19.

Plans going forward: Suggest amalgamate plans for CLRN with those for clinical trials (see below).

Division response to the Covid-19 pandemic

The covid-19 pandemic has had a massive impact on all aspects of QS ION and NHNNs work. The division has responded to the challenges by the following actions.

1. We immediately moved to a virtual format for Gowers round. This has been very popular and has attracted between 110 and 130 attendees weekly. As no-one was travelling and the virtual format allowed everyone to attend this enabled very high-level consultant discussions around cases. We also used the forum of Gowers round to present and discuss the evolving clinical syndromes and management issues (e.g., strokes) seen with covid-19. The virtual format also highlighted the very poor NHNN internet and computer facilities which resulted in access issues for the NHNN clinical SPRs. This problem has been brought to the NHNN management's attention.
2. In 2021 we redesigned our away day afternoon to be virtual and focussed on new therapeutics. This got excellent feedback but there is a very strong preference for this to be face to face going forward.
3. We worked with NHNN to identify and support consultants and clinical research fellows from QS ION to be redeployed for covid-19 work. Doing this highlighted a need for pastoral support for both junior consultant level clinical academics, research fellows and NHNN consultants which we provided to the best of our ability as needed.

Clinical trials in QS ION / NHNN

The recent QS ION PI science strategy away day highlighted a series of problems performing clinical trials in QS and Mike Hanna asked the divisions of Neurology and Neurosurgery to review this for further discussion at the executive away day.

Mary Reilly and Rob Brownstone have further consulted on this and also held a virtual consultation meeting on the 30th November with appropriate and interested PIs. This was very well attended and we have an excellent response to requests for information. We expect the discussion at the exec away day to inform this further but have identified a number of opportunities, barriers, risks and proposed solutions as listed below:

1. **Opportunities**

- QS ION and NHNN have a large number of enthusiastic, dedicated and experienced PIs both in early and late stage clinical trials.
- QS ION has unparalleled basic science and pre clinical science underpinning translation to clinical trials
- The success of the LWEC is remarkable and shows QS can do trials if resourced and supported.
- There is currently a massive increase in trial opportunities especially for genetic therapies for QS.
- We have the opportunity to embrace and develop the newly evolving adaptive and other new trial designs for phase 3 / 4 trials (e.g. MS)
- There are huge opportunities with industry / enterprise to be seen as the go to neuroscience trial centre worldwide
- We have all been very impressed how rapidly JRO were able to set up and deliver covid-19 trials so we know if resourced adequately the issues that have been identified with JRO can be solved.

2. **Barriers**

- JRO has emerged as the top issue for most PIs. The main concerns are delays, no dedicated individual study contact, lack of timely response to emails, no clear pathways, lack of clear differentiation for investigator versus industry led trials. Multiple examples of the above are available.
- Lack of JRO / UCL research services interaction
- Lack of local clinical trial centre / support in Queen Square (advice, statistics, research nurses and coordinators, lack of QS CLRN leadership)
- Lack of clarity / fear re BRC support
- Disappearing CLRN support post Covid / 1 year funding mechanism
- Lack of capacity / staff LWEC – LWEC seen as very successful but needs more resources
- No facilities to do phase 3 / 4 trials in QS. This is needed as many trials need to be here rather than at UCLH due to specialism of investigations and staff needed and to optimise staff use.
- Extra step needed for neuroradiology involvement at QS seen as unnecessary and has slow approval times
- Lack of training for clinical trialists / lack of recognition as academic career
- Lack of Pharmacy support due to insufficient staff e.g., time for EPIC build. Pharmacy staff recognised as being very helpful but overstretched.
- General lack of space for staff
- Feeling that there is no clear representation for QS / neurosciences in JRO

3. **Risks**

- Huge imminent reputational risk to QS ION (already happening)
- We are nowhere near 2nd in the world in neurosciences clinical trials
- Trials being done elsewhere by QS PIs
- QS cannot deliver translational agenda unless something changes
- PIs could move to other institutions
- Dual hub EDH / QS model risk to clinical trials unless QS house developed carefully to accommodate clinical trials including adequate MRI capacity being available on QS site to service trials

4. **Proposed solutions for discussion.**

- a. Need QS clinical trial administrative centre (QSCTC)
Need 2 PA clinical trial lead to include CLRN role (very experienced PIs in QS). Joint ION / NHNN funded.
Need fulltime trial manager to help / advise / liaise with LWEC, CRFs, JRO
Need dedicated part time statistician
Suggest someone from JRO embedded in QSCTC as we need to work more closely with JRO
Suggest whole floor of QSH to include LWEC, phase 3/4 facilities, QSCTC? do we need a QS CTU
- b. Audit neuroscience clinical trial activity versus national and international Neuroscience centres.
- c. Suggest external JRO / UCL research services review
- d. Suggest individual JRO staff given portfolio of trials to report against ie ownership

3.2 Division of Neuropathology

MISSION STATEMENT

Our mission is the continuous innovation through translational research and implementation into clinical diagnostics, and the provision of world-class training and education.

DIVISION OF NEUROPATHOLOGY OVERVIEW

The Division of Neuropathology (DNP) is the largest academic Neuropathology department in the UK. DNP has, 6 consultants and 1 academic vacancy. 3 consultants are UCL employees (Brandner, Thom, Jaunmuktane), and 2 consultants have NHS appointments (Phadke, Merve, both jointly with great Ormond Street Hospitals). 1 academic consultant (Marino) is employed by Queen Mary University. The clinical work is performed in 36 programmed activities. We have currently 3 neuropathology trainees and 2 NIHR clinical lecturers.

Through the affiliation of the academic (Thom, Jaunmuktane, Brandner) and NHS consultants (Phadke, Merve) DNP is closely aligned with key research themes at the Institute, neuro-oncology, neurodegeneration, adult and paediatric neuromuscular pathology, and epilepsy. DNP provides research expertise and infrastructure to ION and diagnostic services to NHNN and provides teaching and education through undergraduate and post graduate courses, and PhD supervision. It drives implementation of research innovation and is provider of essential and sought-after tissue resources for basic and applied research at ION, nationally and internationally.

ACHIEVEMENTS AND GROWTH 2016-2021

- Expansion of regional catchment area for neuropathology diagnostics, acquisition of Romford (BHRUT) neuropathology service.
- Increase of neuropathology training posts from 2 FTE to 3 FTE, and currently 2 NIHR clinical lecturers.
- Developed digital pathology teaching resource from a UCL-wide teaching platform into a national resource by joining the NHS Digital Pathology Portal.
- Molecular pathology service of adult brain tumour grew to the largest highly specialised national services.

STRATEGIC OBJECTIVES 2021-2026

Leadership and impact

DNP is a major hub for diagnostic neuropathology, providing services for NHNN and regional hospitals. DNP is also major provider for specialised brain tumour services in the UK, with regular molecular pathology referrals from over 10 centres nationally. Since 2016 we provide molecular profiling of adult brain tumours using DNA methylation arrays and algorithmic brain tumour classification, with currently over 500 referrals annually. We are in the process of setting up a novel molecular test using Nanopore technology to reduce the turnaround time for complex molecular tests from 3-4 weeks to less than one week. Our leadership is also underpinned by our involvement in authoring guidelines for the Royal College of Pathologists and other national and international organisations.

Training and education

DNP is a major provider for clinical training in diagnostic neuropathology within Health Education England, for London, Kent, Surrey Sussex (London/KSS). Our highly specialised services (molecular pathology, adult and paediatric muscle, peripheral nerves, epilepsy and neurodegeneration) provide an excellent spectrum and critical mass of cases for outstanding training experience. Locally, we are a key partner to provide neuropathology teaching to under-graduate and post graduate trainees. The high quality of our training is reflected in the 2021 GMC survey of UCLH training places where neuropathology ranked second of all specialties.

Such a training environment of clinical excellence has been enabled through a strategic acquisition of neuropathology diagnostic services (Royal free hospital, merger in 2012, Barts Health (2014), Brighton (2014) and Romford (2019)), serving a population of 8.2m, predominantly in diagnostic neuro-oncology. World-class training in diagnostic neuropathology is also enabled through our provision of a state-of-the-art molecular pathology service, with conventional and advanced molecular tests, such as brain tumour methylation profiling. Our strategy aligns with the 2018 establishment of the North London Genome Laboratory Hubs, for which we perform methylation profiling of brain tumours.

FOCUS AREAS

Digital pathology and image analysis

DNP already has 10 years' experience in generating digital pathology slides for training, education, and research, and more recently for diagnostic neuropathology of neuromuscular diseases. Over the last 10 years,

we have provided image analysis solutions for experimental pathology (contribution to over 50 publications), and we were part of a digital pathology CRUK accelerator award (2015-2020). DNP is also part of a North Central London bid for a digital pathology solution, bringing together UCLH, GOSH, Royal Free Hospital and Whittington Hospital on a joint digital pathology diagnostic platform. The data acquired through diagnostic pathology will provide the underpinnings for machine learning and artificial intelligence-powered analysis of digital images, a key area for the upcoming BRC renewal and these technologies form an important basis for forward-looking pathology training, and benefit from workforce retention through multisite and remote working.

Molecular pathology

This has been the most significant growth area in DNP over the last 5 years. DNP is at the forefront for molecular diagnostics of adult brain tumours in the UK. Between 2017 and 2020 we participated in the Queen's University Belfast-led Cancer research UK accelerator program, enabling us to send two biomedical scientists and one neuropathology trainee for a master's degree in molecular pathology. Both our NIHR clinical lecturers (Clarke, ICR Sutton and Millner, QMUL) work jointly between their host institutions and our department and DNP on aspects of molecular pathology of brain tumours.

Research and collaborations with clinical divisions

- Four domains will remain a strong research focus over the next five years: Brain tumours (with focus on molecular diagnostics and basic research, integration with BRC theme Neuro-oncology); Neurodegeneration, jointly with QSBB; Neuromuscular diagnostics and research (neuropathies, adult and paediatric muscular disorders); and epilepsy. Obtaining significant research funding across all domains remains a priority in the future.
- DNP continues to foster strong collaborations with the Division of Neuroradiology (27 peer-reviewed publications in 10 years and 3 joint book chapters). Significant potential by integrating digital pathology with radiology. Machine learning analysis of digital pathology and correlation with radiology images in several ongoing projects.
- Potential synergies with neuro genetics (Houlden) for Nanopore technology.
- Clinical neurology disciplines (neuropathies, stroke, neurodegeneration).

OPPORTUNITIES

The reconfiguration of the Queen Square House in the context of the opening of the EDH offers significant opportunities to rethink the synergies between the currently distinct tissue-based diagnostic and research activities, i.e., neuropathology (NHS), UCL IQPath (histology research, clinical trial and image analysis service), and Queen Square Brain Bank. A unified laboratory platform can realise significant savings, foster collaboration, can be managed with a unified tissue governance structure and enable lean laboratory management.

3.3 Division of Neurophysiology

Medical Staff. The Division of Neurophysiology has 9 consultants (5 FT, 4 PT), total of 6.7 FTE. Of those only 2 consultants (Diehl and Koltzenburg) have university PAs (total of 1 FTE). One consultant (Chowdhury) recently received a 0.2 FTE CARP award to contribute diagnostic work to first-in-human clinical studies of gene therapies in epilepsy. The division received funding for HEE for two additional physician trainees increasing the number from 4.4 to 6.4. There are 26 physiologists. We received accreditation as training centre for STP (MSc equivalent) and HSST (doctorate equivalent) and received 3 funded positions. HEE approached us to ask for further funding for 2 HSST positions starting in autumn 2022. Our goal over the next 5 years is the successful completion of 1 STP trainee (3 year course) and 1 HSST trainee (5 year course) and establishment of a constant stream of physiologists in training.

Education. The award of these training positions recognizes the comprehensive training programme of the Division. The latest GMC Trainee Survey of 2021 returned a “positive outlier” score in 10 out of 19 domains. This reflects about 10% of all positive outliers of UCLH and puts us well on top of all 66 departments of UCLH.

The Division provides regular teaching to the pan London Calman Neurology days and UK-wide Neurophysiology teaching days. With other divisions it provides regular presentation to the Gowers Round. Under the supervision of two consultants (Cordivari, Li) a comprehensive three-month-long teaching program was established. It was also attended by neurology trainees and had contributions from GOSH and other divisions (Neuroradiology). We have plans to establish this series as a yearly feature and will open it up for trainees and teachers across the UK. A challenge for the education is the relative lack of coverage of basic neurobiology in clinical neurophysiology and, I suspect, in other Divisions as well.

Clinical Service. The Division continues to provide an efficient high-quality service and maintained this as F2F service during the pandemic. During the alpha wave we saw at some point as many as 40% of all F2F first patient encounters of the NHNN. At the end of 2021 there is a 100% compliance with diagnostic waiting time – one of the few departments across UCLH. Maintaining an efficient diagnostic service supports the research of Divisions and Research Departments and tries to establish a seamless transition from clinical service to research support. On the telemetry unit It supports the research of DCEE for microwire single nerve cell recordings and direct electrical brain stimulation. The division supports advanced clinical services and research on peripheral neuropathy, muscle disease, including channelopathies and neurophysiological diagnostics for the prion service. There are also close links with researchers of the Functional Neurosurgery Group and the new HSST training will provide service and receive training for the next 5 year period. The Division provides diagnostic support for clinical trials with researchers in Department of Neuroinflammation, Division of Neurology for natural history studies and novel therapies. There are plans to support work in the LWENC. This work enables and facilitate research of other departments and division.

Clinical Trials. While the Division supports clinical trials it does so using conventional techniques. A future challenge is the establishment of novel translation biomarkers of target engagement of neuroactive drugs or pharmacodynamic assessment of access to different neural compartments. Opportunities would be combinations of functional neurophysiological assessments with neurotransmitter studies using MRS or comparing receptor occupancy of drugs with direct functional readouts.

Research. One research area focuses on mechanisms of Sudden Unexpected Death in Epilepsy (SUDEP). This showed that people with uncontrolled seizures and those who later died of SUDEP have structural MRI volume increases and decreases in regions critical for cardiovascular regulation. Increases in amygdala and BA 25, and decreases in posterior thalamus, cerebellum and periaqueductal gray. Heart rate and breathing recordings during seizures showed that atrophy of thalamus, cerebellum and brainstem relates to the degree of peri-ictal hypoxia. Future work will continue investigations of cardiovascular and respiratory parameters during seizures with the view to optimize individualized prediction tools for SUDEP and assess effects of therapeutic interventions.

Another research focus is the development of innovative stimulus paradigms and software for the use of transcranial magnetic stimulation (TMS). Based on prior work on peripheral nerve and muscle excitability and in collaboration with DNMD (Bostock) a standardized stimulation and analysis software package was developed. The protocols support conventional amplitude TMS and threshold tracking TMS which allows for the first time the direct continuous monitoring of corticospinal motor excitability. Paired pulse TMS protocols have emerged as biomarker for the assessment in ALS and this diagnostic tool is already established in routine clinical practice. A goal for the next 5 years is the establishment of a core facility using the integration of novel fast TMS hardware, innovative software, brain navigation and robotics to provide one system for research and clinical use. Over the next 5 years opportunities are establishment of advanced diagnostics of neurodegenerative diseases such as ALS, dementia or dystonia and response to therapy. Other applications include basic mechanisms of sensorimotor control, measuring target engagement of drugs in clinical trials and allowing automated non-invasive cortical mapping.

3.4 Division of Neuropsychiatry

The Division of Neuropsychiatry:

- Supports QS ION translational research by being a partner in neurological and neurosurgical clinical trials.
- Provides a bridge between the UCL Institute of Mental Health (IoMH) and QS ION for research and teaching.
- Enables recruitment for trials via NHNN clinical activity.

Neurosurgery and Movement Disorders Research

The Division, with the Unit of Functional Neurosurgery (UFUN), led the first UK study of DBS for severe OCD, funded by the MRC. This has had international reach and led to data sharing with international colleagues. In 2021, NICE approved this as a research procedure.

The Division is a full partner with the UFUN on a current MRC/EME/NIHR funded study of deep brain stimulation for severe Tourette's syndrome. Recruitment is by the academic neuropsychiatry-led National Tourette Clinic and patient assessment and care is by admission to NHNN Hughlings Jackson neuropsychiatry ward. The aim is to provide evidence for NICE guidelines and NHS provision.

Psychiatrist Harry Costello was awarded WT Training Fellowship for PhD on depression in Parkinson's disease. This involves joint working across FBS: ICN (Roiser), QS ION (Joyce); IoMH (Howard).

The Top Hat Trial, funded by Parkinson's UK, for hallucinations involves PIs from IoMH (Howard, Reeves [lead]) and QS ION (Weil, Joyce, Schrag).

The NIHR BRC Mental Health Theme resubmission: The Division and UFUN contributed a subtheme on Neurosurgery for Severe Mental Illness.

Future Activity:

To work with NHS England Highly Specialised OCD Service in studies of focussed ultrasound for OCD.

Neuroinflammation and Psychosis Research

MRC EME/ NIHR funded multicentre trial of the anti-inflammatory minocycline (Deakin, CI and Manchester lead, Joyce UCL lead). Completed.

MRC funded SINAPPS2 RCT of immunotherapy of antibody-associated psychosis (leads: Coles Cambridge, Lennox Oxford, IoN: Joyce, Zandi PIs). Aims (if positive) to provide NHS immunotherapy for psychosis.

The Division led the establishment of a neuropsychiatric reporting system and database, with RCPsych and ABN, for COVID-19 research.

NIHR APG funded CIRCuiTS study: Implementation of cognitive remediation in early intervention for psychosis services. (Co-PIs: Wykes KCL, Joyce IoN). Aims to obtain NICE approval to introduce CRT in NHS.

Teaching and Administrative Activity

The Division is represented on the Institute of Mental Health Executive Board (Joyce, Dolan) and the NIHR BRC Mental Health Theme Executive Board (Joyce). The Division provides teaching to QS ION MSc, IoMH MSc and Neuroscience BSc courses (Joyce)

Future of Academic and Clinical Neuropsychiatry at Queen Square:

Neuropsychiatry supports many clinical services at NHNN, especially movement disorders, and thereby their research. We are behind other UK neuropsychiatry centres in terms of consultant numbers/PAs. More research opportunities will undoubtedly arise at the QS ION with the increased national interest in mental health. There is increasing interest from trainee psychiatrists rotating through our service in applying for training fellowships in neuropsychiatry and from other trainees wishing to spend their weekly research days with us. Academic output will undoubtedly increase with more senior academic clinical neuropsychiatrists.

3.5 Division of Neuroradiology and Neurophysics

MISSION STATEMENT

The Division of Neuroradiology and Neurophysics (DNN) promotes academic neuroradiology and neuroimaging physics at Queen Square. Since its inception, its core objectives have been to support its members in all aspects of their professional career, to provide an environment for the academic and clinical members to interact and to ensure an open and constructive engagement between MR groups across the QS ION. It therefore functions effectively as a cross-cutting theme spanning activities ranging from basic scientific developments through to clinical implementation.

Membership. The DNN brings together Academic Neuroradiologists, Physicists, Computer Scientists and Radiographers at the UCL Institute of Neurology, and research-oriented Clinical Neuroradiologists, Clinical Scientists and Radiographers at the NHNN.

The imaging groups represented in the Division are: the Neuroradiological Academic Unit, the NMR Research Unit of the Queen Square MS Centre, the Epilepsy Imaging research group and the Wellcome Centre for Human Neuroimaging; furthermore there is representation and involvement of the Faculty of Engineering Centre for Medical Imaging Computing (CMIC).

STRATEGIC OBJECTIVES

- **Strategic involvement**

The Division provides strategic advice and support exemplified by leading the ION *MR Review and Recommendations* to the 2017 External Review Panel (2018), developing the rationale for the *GIR Research Infrastructure: Requirement for 3T and 7T MRI* in 2021 and providing strategic depth by reaching across faculties to establish structural links with CMIC and conceiving the Quantitative Neuroradiology Innovation and Adoption Centre (QUINIAC) as a cross-faculty and cross-institution (UCL/UCLH) initiative.

In particular, members of the Division have leadership roles in all existing and planned London-based 7T facilities: the FIL, the London Ultra-high Collaborative Scanner (LOCUS) at St. Thomas's, as well as the GIR MR Facility. Indeed, Profs Callaghan, Golay, Wheeler-Kingshott, Thornton, & Yousry are all involved with either or both 7T scanners.

Gray's Inn Road (GIR) MRI facility

The Division has taken a leading role in the development of the GIR MRI facility, where UCL and UCLH scanners will offer the perfect opportunity to achieve a timely and world-leading translation of novel imaging methods to clinical practice

Academic Radiography Building on the existing expertise the GIR facility will offer the perfect opportunity to further expand academic radiography

Knowledge Transfer

Strategically significant has been the early assessment of commercial avenues which led to the launch of 2 spinouts (Gold Standard Phantoms & QS Analytics).

- **Education**

Education has been a central theme of the DNN, including

1. MSc in Advanced Neuroimaging A complete portfolio is now available, with an increasing number of students (13 in 2008 to 31 in 2021).
2. UK 7T users meeting in London in June 2019, at the time when both London 7Ts were just going through installation and acceptance.
A follow-up Clinical 7T meeting is currently being arranged.
3. Deliver Physics short course on Devices and MR Compatibility, developing to be world leading, initiated 2017 & planned again for 2022
4. Expand Applied MR Physics courses to other divisions
5. Establish with the Division of Neuropathology a Brain-cutting course
6. Expand the International Academic Neuroradiological Fellowship programme for overseas Neuroradiologists.

- **Communication and Collaborative Research**

Open and constructive communication has been key to the success of the DNN, enabled through bi-monthly meetings of the Steering Group, Annual Meetings of all members and regular workshops. Successful examples, which we will continue to develop, are:

1. Aligned governance structures including MR safety frameworks
2. Harmonised MRI protocols and quality control frameworks, within and external to the Division and FBS across UCLH BRC sites, and aligned with national initiatives such as the Dementias Platform UK.
3. Collaborative research projects based on specific expertise in one team shared with the other teams such as Sodium imaging, & multi-platform multi-parametric mapping (MPM)
4. Provision of neuroradiology and MR Physics support to MRI research groups (Dementia, MS, Neuromuscular, Epilepsy, Neuroscience)

- **People**

Highlights include the successful promotion of members of the Division such as Prof Martina Callaghan as well as the establishment of new academic and clinical posts, including a) the creation of the 1st Academic Clinical Scientist post as a joint appointment between CMIC and the Lysholm Department of Neuroradiology, reflecting a strategic alliance between the faculties of Brain Sciences and Engineering; b) the appointment of Dr David Thomas to a new Academic post to the GIR Facility and QUINIAC. These developments are critical to the validation and clinical adoption of new imaging tools.

- **Partnering with QS Divisions**

Neuropathology: The DNN has a long history of collaboration on the level of education and research, the latter focusing on imaging post-mortem tissue. It is planned to develop reciprocal educational activities which will include basics of neuropathology & brain morphology and basic MR physics and clinical imaging.

Neurology, Neurophysiology, Neurosurgery, Neuropsychiatry: Once the above is established the educational framework will be expanded to include all QS Divisions.

The activities and successes of the Division and its leadership in a number of developments, such as the GIR imaging facility, are central to the success of neuroimaging research at Queen Square and the Faculty of Brain Sciences.

SUMMARY OF STRATEGIC OBJECTIVES 2022-26

- **Establish GIR as the world-leading translational and clinical adoption MR facility**
- **Institutionalise the harmonised working relationships between the MR scanner groups**
- **Establish Academic Radiography**
- **Integrate computer scientists in the Division**
- **Education**
 - Further transform the MSc in Advanced Neuroimaging to be the leading UK course
 - Establish an educational programme with the Division of Neuropathology
 - Expand MR Physics courses

3.6 Division of Neurosurgery

Vision: To develop and implement novel, safe, and effective treatments to advance neurosurgical care.

Mission: The Division of Neurosurgery through its close partnership with the NHNN is committed to advancing neurosurgical care for the current and next generations of patients through world class research, excellent training and education, and top-quality clinical care.

2019 Goals and Achievements since then, with a forward look for next several years

As with all Divisions, SARS-CoV-2 had a significant impact on the Division, disrupting clinical care, research, and teaching. Although recovery is not yet complete, activity has been increasing.

We have two broad themes of priorities for the next 5 years:

1. Build mechanism-based research from the ground up: integrated academic training programmes

Progress:

- We have been recruiting academic clinical fellows annually, and currently have 3 (one in each of ST1, ST2, and ST3), each with different interests (pre-clinical, clinical, and engineering).
- In 2019, we recruited our first NIHR clinical lecturer, whose research programme is in the pathobiology of brain cancer, studied in his lab at the Cancer Institute. A second clinical lecturer began in Feb 2021 with expertise in movement disorders and lab work on animal models of dystonia in QSH. A third CL began in Aug 21, with lab work also in neuro-oncology, working at the Crick.
- Three trainees completing PhDs 2021/2022 (2 at ICH-GOSH, 1 at QS).

Beyond 2021:

- We will recruit another ACF in 2022, and at least two more in the next 5 years.
- We have secured another NIHR CL position for 2023, and will aim to secure 1 position every 2 years.
- We will explore locally-funded ACF and CL positions, aiming to add at least 2 additional positions in the next 5 years.
- We will continue to mentor our young academics with respect to both fellowship and project grants, integrating them into research departments.
- We will expand our support of ancillary activities, such as our new “academic journal club” to discuss key issues across the academic pillars of neurosurgery.
- We will develop and expand an MRes (Neurosurgery) programme, which has been approved and will launch in 2022.
- We will increase our participation and those of our trainees in Gowers rounds.
- We will develop a simulation centre for neurosurgical training.

2. Nudge the culture: targeted consultant recruitment, specialty research days, and increased collaboration (QS ION, UCL, and beyond)

Progress:

- We have had only one academic recruitment in the last few years, but he is on a soft academic salary. We have recruited another academically trained and excellent neurosurgeon, but he has no protected academic time.
- We had one subspecialty research day in CSF disorders, but were interrupted by Covid-19. We held an informal research day on brain-computer interfaces.
- Our collaborative activity has improved, e.g., in CSF with neurology; in vascular with Dept of NPP, and in oncology with the Cancer Institute and the Crick. We are deeply integrated with the engineers in WEISS.

Beyond 2021:

- Recruitment is the #1 issue and goal of the Division. To be successful, the clinical culture needs to be penetrated, and we will continue to chip away at it.
- We aim to secure an academic salary for our academic neurosurgeon on soft money.
- We aim to secure a 50% clinical position for our completing CL – we have already secured a 50% academic post at the Cancer Institute.
- We aim to secure academic time (e.g., through fellowships) for our academic neurosurgeon who is currently full time clinical.
- We will recruit 2-3 more academic neurosurgeons, with goal of ~1/4 of neurosurgeons with significant academic commitments.

- We will have another CSF research day in 2022, and a neuro-oncology research day in 2022. These will be annual or biannual events. We aim to add other specialties over the next two years. We will continue to strengthen our collaborations with the Cancer Institute and the Crick, and will enhance relationships with our colleagues at ICH-GOSH.