



# BRAIN

Repair & Intracranial Neurotherapeutics



Ariennir gan  
**Lywodraeth Cymru**  
Funded by  
**Welsh Government**



Ymchwil Iechyd  
a Gofal **Cymru**  
Health and Care  
Research **Wales**

## 2018-19 Annual Report







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# Foreword

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**“Next year is an exciting one for the BRAIN Unit. Having submitted our bid for continued support from Health and Care Research Wales, we hope to be able to go in an exciting and rewarding new direction from 2020 onwards.”**

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A handwritten signature in black ink, appearing to be 'W Gray', positioned below the portrait of Professor William Gray.

**BRAIN Unit Director, Professor William Gray**

I am pleased to present our 2018- 2019 annual report, showcasing another busy year for the BRAIN unit. This year marks the first of our two-year extension period and our annual report for 18/19 highlights how much we have achieved since inception in 2015.

Growing from strength to strength, our Neuroscience Research Unit (NRU) has successfully completed the first stage of the landmark anti-sense oligonucleotide (ASO) trial for treating Huntington's Disease (HD). The HD team, led by BRAIN Unit deputy director Professor Anne Rosser, and the hard work of the NRU have achieved excellence in ensuring not only that this trial was a success, but also in cementing collaborations with Roche, securing follow-on trials with the company. This work has been a primary factor in ensuring the NRU reaches its goals of becoming financially sustainable, this year seeing a record increase in profit from commercial income of over £60K, all of which is reinvested back into the NRU.

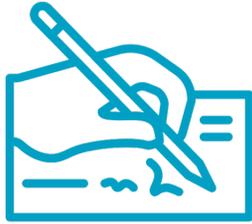
For every £1 invested into the BRAIN unit we attract a further £22 to Wales, thanks to the hard work and dedication of our BRAIN Unit members continuing to push the boundaries of neurological and neurodegenerative treatment and research. Of note, our collaboration with Takeda looking at pathway discovery in human tissue to identify new approaches for treating schizophrenia and other psychiatric disorders, emphasises the importance of good industry collaboration to Wales.

Central to our goal of being able to delivery novel cell, drug and other complex therapies to the human brain is the TRIDENT trial which is well underway. This year we have seen several successes including ensuring the in-house manufacturing device meets all testing requirements and recruiting 16 patients to the study. I look forward to the coming year when this hard work will come to fruition, helping us to understand more about the ability to delivery fetal cells in the brains of HD patients.

Finally, I would like to thank all of the BRAIN Unit members, staff and administrative team for their commitment to developing novel therapeutics and treatment delivery systems for neurological conditions, and hope that you enjoy reading this report.

# Key achievements 2018-19

## Financial



Total Grant Income to Wales  
**£8,793,556.00**



Total Grant Award Income  
**£12,902,875.00**



Return on Investment to Wales:  
**For every £1 invested attract in £22**



Commercial Profit (18/19)  
**£60,400**

## Research



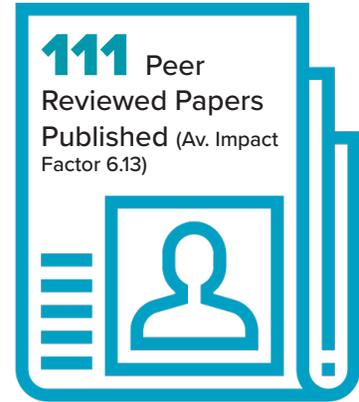
**53**  
Research Submissions



**79.26**  
Highest Impact Factor Published



Research Awards  
(47% success rate)



**111** Peer Reviewed Papers Published (Av. Impact Factor 6.13)



**449**  
Twitter Followers

## Public Engagement and Involvement



**15** New BRAIN Involve members.  
Total **31**



**14,756**  
People Reached through our events and presentations



**37** Public Engagement and Involvement Events and Activities

# Who we are

## The Team

### Director

Professor William Gray - Professor of Functional Neurosurgery at the University Hospital of Wales (UHW), Cardiff

### Deputy Director

Professor Anne Rosser - Professor of Clinical Neurosciences & Consultant Neurologist at UHW

### Administration

Dr Cassy Ashman - Research Manager  
Victoria Saunders- Finance Officer  
Clare Anderson- Administrative Assistant  
Camila Araya-Larrain- Communications Officer

### Neuroscience Research Unit

Professor Khalid Hamandi- NRU Lead and NIHR Speciality lead.  
Belinda Gunning - Research Nurse Manager  
Cynthia Butcher, Dympna Mcaleer, Rajimol Sibichen and Andy Davison - Research Nurses

### Research Associates & Fellows

Dr Erini Messaritaki - Imaging Research Associate  
Dr Feras Sharouf - Clinical Research Fellow  
Dr Cheney Drew- Senior Clinical Trials Manager

### Research Technicians

Dr Samantha Loveless - Biobank Officer (Cardiff)  
Beata Fonferko-Shadrach - Biobank Officer (Swansea)  
Dr Chloe Ormonde and Matthew Barrell - Stem Cell Technician  
Shirin Davies - MRI Physicist  
Dr Anne-Marie McGorrian- GMP Research Technician

# Introduction

Funded by Welsh Government through Health and Care Research Wales, the Brain Repair and Intracranial Neurotherapeutics (BRAIN) is a Research Unit within the Infrastructure, developing novel therapeutics and treatment delivery systems for neurological conditions.

The Unit operates under the directorship of Professor Gray with 31 principle investigators (PIs) and collaborators, with a total grant income of over £34 million since the Unit's inception in 2015.

## Principle Collaborators & Partners

BRAIN is a multi-disciplinary research unit with strong academic and NHS clinical leadership. Based in Cardiff, the Unit's all-Wales brief also involves groups of research excellence in Swansea University and Health Boards across South Wales.

The Wales Neurological Alliance (WNA) is a forum of not-for-profit organisations representing people affected by neurological conditions in Wales. The WNA sit on both the BRAIN and BRAIN Involve executive boards, and continues to support BRAIN Unit activities with its far-reaching membership and input.



### Our Mission

It is our vision to make the BRAIN Unit top-5 worldwide as a pre-eminent centre for international leadership and a Wales and UK national centre for excellence in:

- Delivering novel cell, drug, growth factor and other complex therapies to the human brain.
- Supporting translational research underpinning disease modification and brain repair in people with neurological conditions.

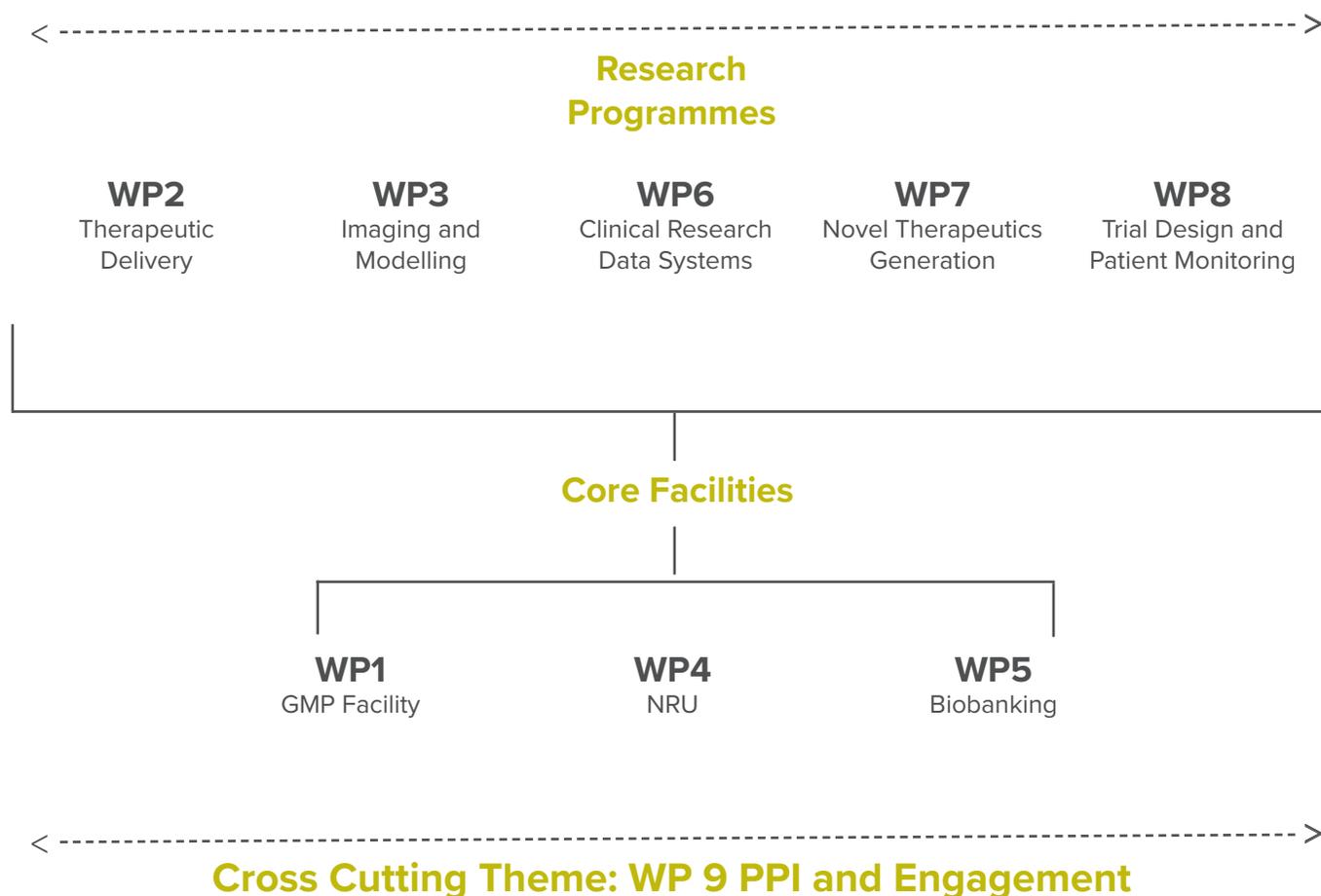
### Our Aims

Through innovation and collaboration, the BRAIN Unit aims to:

- Develop new and refine existing systems for delivery of therapeutics into the human brain.
- Develop the appropriate infrastructure for capturing relevant, high quality patient data to measure real clinical and social impact, as well as continuing to support ongoing mechanistic translational research.
- Build a clinical and health economic outcome, social care and service delivery research portfolio.

# Work Packages and Cross Cutting Themes

## Cross Cutting Theme: NHS, Commercial & Industry Engagement



## Glossary

- **Intracranial-** Within the skull.
- **Neurotherapeutics-** The treatment of disorders that affect the nervous system.
- **In-vitro-** (Latin for "in the glass") studies performed with micro-organisms, cells, or biological molecules outside their normal biological context.
- **Stem Cell-** Cells of the body (somatic cells) which can divide and become differentiated. When an organism grows, stem cells specialize, and take specific functions. For instance, mature tissues like skin, muscle, blood, bone, liver, nerves, all have different types of cells.
- **Striatum-** The striatum, or corpus striatum (also called the neostriatum and the striate nucleus) is a nucleus (a cluster of neurons) in the subcortical basal ganglia of the forebrain. The striatum is a critical component of the motor (movement) and reward (pleasure) systems.
- **Hippocampus-** The hippocampus (Greek for "seahorse") is a major component of the brain of humans and other vertebrates. Humans and other mammals have two hippocampi, one in each side of the brain. The hippocampus is part of the limbic system, and plays important roles in the consolidation of information from short-term memory to long-term memory, and in spatial memory that enables navigation.
- **Cerebrospinal fluid (CSF)-** is a clear, colourless body fluid found in the brain and spinal cord.
- **Peripheral blood mononuclear cell (PBMC)-** is any peripheral blood cell having a round nucleus. These cells consist of lymphocytes (T cells, B cells, NK cells) and monocytes.
- **Neurogenesis-** is the process by which nervous system cells, the neurons, are produced by neural stem cells (NSC).
- **AMPAKine molecules-** A subgroup of AMPA receptor modulators currently being investigated as potential treatments for a range of conditions involving neurological and psychiatric disorders.





# WP 1

## Cardiff Good Manufacturing Practice (GMP) Facility

**Work package aim:** Provide a Human Tissue Authority (HTA) licensed facility to prepare and deliver cell therapies for human use in clinical trials for neurodegenerative diseases.

### Highlights

- The Cardiff Fetal Tissue Bank (CFTB) ethics were successfully renewed in June 2018 for a further 5 years until June 2023.
- We have welcomed three new staff members this year. All new team members have been trained to undertake the various roles which are required to maintain the cleanroom facility. Following successful training, they have all contributed to the work undertaken to complete validation of the tissue processes and will contribute to live cell processing for actual surgeries.
- We have generated new Standard Operating Procedures (SOPs) for Tissue Documentation, Tissue Processing, Hibernation Media change (this is where the liquid, in which the tissue sits, is refreshed), Final Dissociation (creating the final cell product), and Transportation of the Final Product to the surgical site.
- Following finalisation of these SOPs, we have completed validation of all stages of the process in relation to the quality of the tissue.
- Quality checks are performed by taking microbiological samples of tissue washes

before and after processing using blood culture bottles, which when cultured, detect the growth of organisms.

- Contact and settle plates are incubated in the cleanroom for 7 days to allow growth of bacterial colonies which are sent off to Public Health Wales (PHW) for analysis.
- All results must be within GMP limits and the final tissue/cell product must be clean for each run to count as successful.

**In total, 14 fully successful runs were undertaken**

- Testing was also undertaken for tissue transportation, where the tissue was packed and the temperature measured to ensure that the transport box kept the final product within a suitable temperature range. This has taken several months to complete and this has now been submitted to the Human Tissue Authority (HTA) for approval.



### What is a GMP Facility?

A system for ensuring that products are consistently produced and controlled according to quality standards.

These guidelines provide minimum requirements that a manufacturer must meet to assure that their products are consistently high in quality, from batch to batch, for their intended use, to minimise harm to the end user.





## WP 2

# Therapeutic Delivery into Patients

**Work package aim:** Refine existing systems for effective delivery of cell therapy and other therapies into the human brain.

### Highlights

- In July 2018, Dr Sharouf was successfully awarded a Cardiff University PhD position. He is investigating the role of the inflammatory micro-environment on stem cell survival when used as a therapy for Huntington's Disease (HD), continuing his work to ensure the successful delivery of cells in HD patients.
- The BRAIN Unit Director, Professor Liam Gray was invited to speak at the 11th International Conference on Stem Cell and Regenerative Medicine on Nov 27-28, Guangzhou, China. This has given us the opportunity to increase our collaborations with international partners, in particular with the Huntington's Disease network in China for clinical and translational research funding and clinical studies.
- Non-Disclosure Agreements (NDAs) have been signed with PDR in Cardiff Metropolitan University and ArroTek in Ireland, on the development of devices for cell delivery to the human brain, including the TRIDENT study and other studies going forward.
- Profs Rosser, Busse & Gray convened in an international workshop in Barcelona with industry and academia, including leaders from the US and Europe in cell and gene delivery for HD, under the auspices of the European Huntington's Disease Network (EHDN). Outputs were the formation of a task force for cell therapy delivery to identify significant obstacles for translation across technical and regulatory domains.

The TRIDENT clinical trial to deliver fetal cells into the brains of HD participants to replace lost nerve cells has had a successful first year.

- In-house manufactured Device (IHMD) for cell delivery cleared by MEG group at UHW for use in TRIDENT.
- Specification of IHMD confirmed.
- In-vitro testing on IHMD performance completed.
- Sterilisation testing completed on IHMD and passed.
- 16 participants recruited to TRIDENT trial including 1 to the surgical cohort.



### Definitions

**NDAs-** a contract by which one or more parties agree not to disclose confidential information that they have shared with each other as a necessary part of doing business together.

**IHMD-** In-house manufacture refers to medical devices that are made in a healthcare establishment to be used for patients within that establishment.





## WP 3

# MRI and Tissue Modelling of Cell and Drug Delivery

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**Work Package aim:** To utilize high resolution and microstructural Magnetic Resonance Imaging (MRI) scanner and Positron Emission Tomography (PET) scans to support accurate modelling of cell and drug delivery to the brain.



### Highlights

Dr Eirini Messaritaki, our BRAIN Unit imaging researcher, has presented her work at international conferences on several topics:

- How to improve the predictions of drug delivery models.
- Modelling drug delivery on Huntington's disease patients and on brain tumour patients- essential in identifying the optimal placement of catheters so that patients can benefit the most from convection-enhanced drug delivery.
- Assessing the reliability of structural networks- this work is essential in building the framework for assessing the effect of therapeutic interventions in the human brain.

### Achievements

- We have been continuing to assess the effect of therapeutic interventions on brain structure and function including how to correctly measure the tracts in the brain. In addition, we now know what potential changes are observed in structural networks when there is no intervention.
- We have run drug-delivery simulations on the data from HD patients, simulating infusion in the striatum and found we could capture previously unknown effects.
- We are working towards identifying the optimal metrics that will allow us to assess the effect of brain surgery on epilepsy patients that undergo hippocampus resection, who are scanned on the Connectome scanner before and after the resection.





## WP 4

# Neuroscience Research Unit (NRU)

**Work Package aim:** To establish a fully functional clinical research facility at the University Hospital Wales, Cardiff. To support commercial and academic clinical trials.

### Highlights

- The NRU has seen a 17% increase in profit from commercial income between 17/18 and 18/19, beating our aim to increase profit by 10% year on year. This has been reinvested into the NRU.
- NRU Director, Prof Khalid Hamandi has retained his position as Speciality Lead for Neurology after a competitive recruitment process.
- The NRU continues to develop strong links with our partners at CUBRIC. We now have a service level agreement in place with CUBRIC to make it easier to scan patients with neurological conditions at the world renowned imaging centre.
- We continue to work closely with Cardiff and Vale UHB, neurosciences directorate, meeting regularly to discuss operational and financial matters.

- We have successfully recruited two new band 6 nurses and two more are currently in the recruitment process, bringing the nursing team to 6. We have also recruited a Clinical Fellow to post.
- Thanks to the hard work of NRU, C&V UHB and the HD team led by Anne Rosser and Monica Busse, we have successfully collaborated with pharmaceutical partner Roche to continue working on disease modifying treatments in Huntington’s disease.
- On the successful completion of the first Phase 1 study (IONIS/Roche), we are continuing to work with Roche on a further three studies.

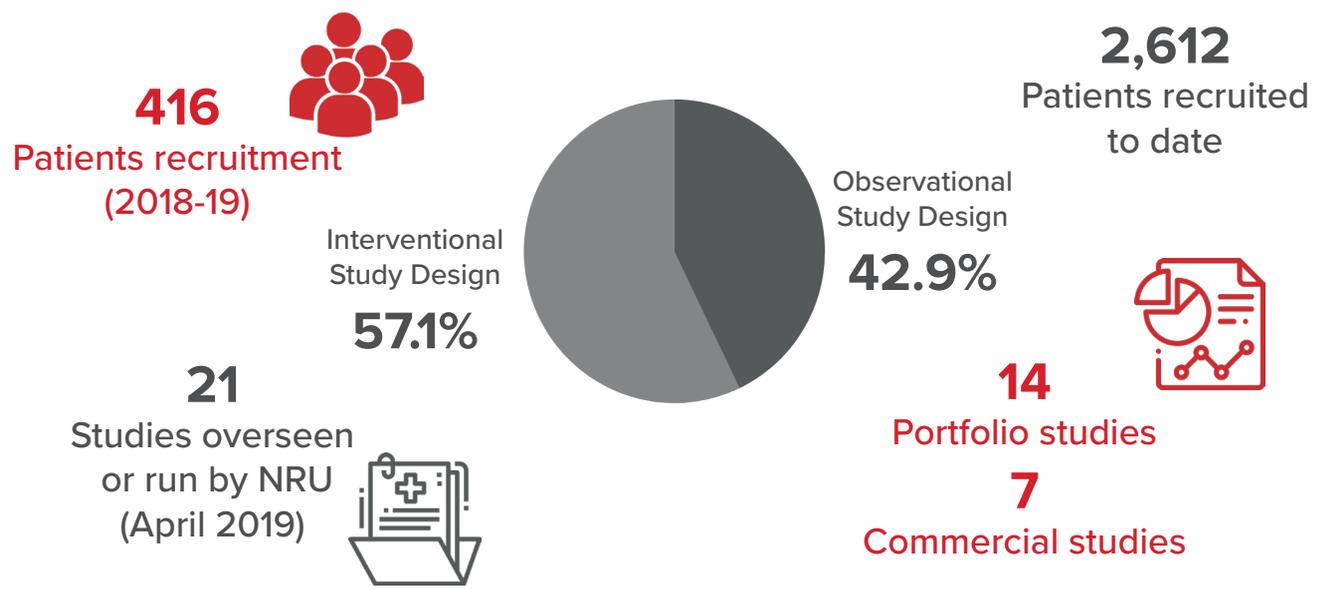
### Roche came to visit in May 2019

“Thank you for the opportunity to connect directly with teams of dedicated and clearly caring professionals. The Roche teams are clearly interested and dedicated in a similar way”

“It has been a pleasure to work alongside the NRU team. The unit continues to grow by increasing studies. I look forward to our continued close working arrangements for the benefit of the Neurosciences Directorate and the patients we support”

*Sarah Lloyd, Neuroscience Directorate Manager, Cardiff and Vale University Health Board.*

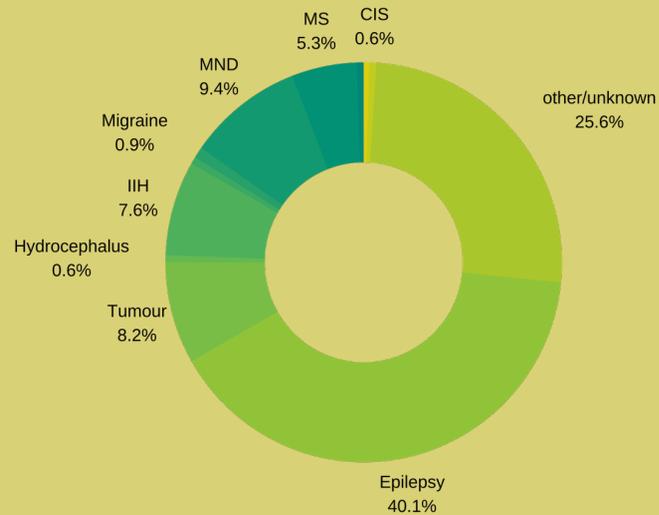
- The MS team were announced Site of the Month for the MS-STAT2 study “The Cardiff team randomised an impressive 6 patients in one day back in March”.
- We have also seen our first student on a C&V UHB Research Spoke placement, who spent some time with the NRU team.



# WP 5 Biobanking

**Work Package aim:** Expansion of sample collection across neurological and neurodegenerative conditions in the Welsh Neurosciences Research Tissue Bank (WNRTB) Cardiff and Swansea Neurology Bank (SNB)

Percentage of patients recruited to WNRTB. The chart shows the types of patients recruited.



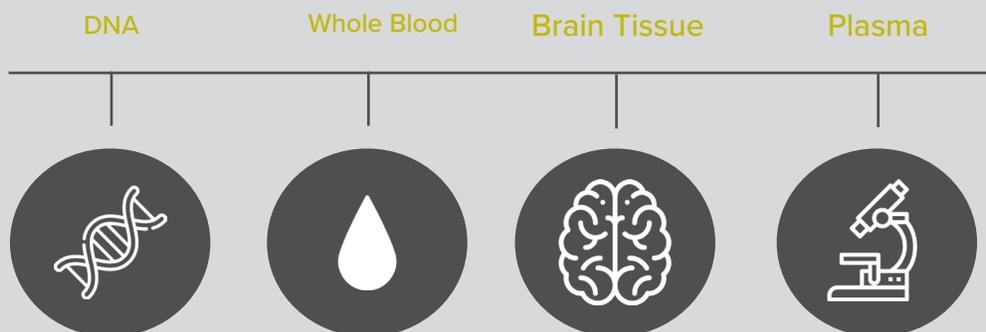
**2,967 Total consents collected from WNRTB and SNB since 2014**



**2,252 samples issued for research from WNRTB and SNB**

## Examples of sample types collected

102,265 Total number of samples acquired from WNRTB and SNB at end April 2019. These included Serum, Plasma, CSF supernatant, DNA, blood, CSF cells, Brain tissue and tears.





## Highlights

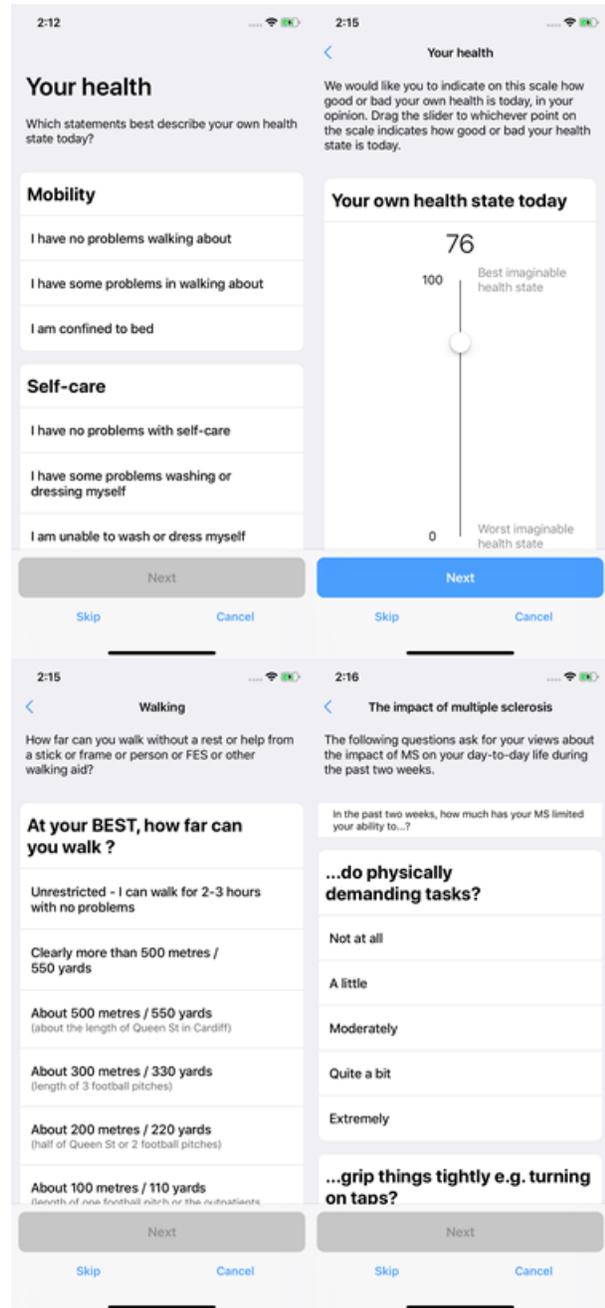
- The Welsh Neuroscience Research Tissue Bank (WNRTB) in Cardiff has had a successful extension to their ethical approval. Ethics have now been extended to April 2024.
  - The Swansea Neurology Biobank (SNB), has collected 297 samples 18/19 beating their target of 200 samples for this year.
  - SNB continues to supply DNA to Epi25k with nearly 300 samples shipped to the Broad Institute, Boston, USA.
  - WNRTB have sourced additional funding to appoint a part time technician who will start May 2019. This role will act to specifically boost recruitment of research patients and diversify the sample collection in Cardiff, with the aim to increase CSF collection and create a research cohort of peripheral blood mononuclear cell (PBMC) isolated from peripheral blood.
  - The SNB, in collaboration with Swansea Bay University Health board, has begun collecting samples from persons affected by Multiple Sclerosis and Parkinson's Disease. This and other core biobanking work is supported by a new research technician funded by the clinical leads.
  - The Cardiff biobank has successfully won a Cardiff and Vale University Health Board, R&D equipment fund award, to purchase analytical scales for use within the biobank laboratory (Jan 2019).
- 
- “The Welsh Neuroscience Research Tissue Bank has developed an excellent in-house traceability system that is efficient and easy to use. It provides details of all 100,000 samples the bank holds, from consent forms to sample information and location”**
- External Human Tissue Authority Audit Report, 2019*
- 
- The SNB is supplying DNA to the BIOJUME study, a large study investigating Juvenile Myoclonic Epilepsy.
  - Both the WNRTB and SNB had excellent feedback from the external Human Tissue Authority (HTA) audit, with no negative comments or shortfalls.
  - The SNB has successfully expanded into Hywel Dda, Cwm Taf and Aneurin Bevan Health boards for the collection of epilepsy samples.

# WP 6 Clinical Research Data Systems

## Highlights

- We have continued to rollout ‘PatientCare’, the combined clinical and research electronic health record system, and now have 31,509 registered patients, recording a total of 368,288 clinical and research encounters across 107 cohorts.
- As a contemporary, prospective, longitudinal clinical electronic patient record, we have recorded 3909 patients with multiple sclerosis, 2339 with Parkinson’s disease, 1066 with essential tremor, 617 with motor neurone disease and 242 with clinically isolated syndrome. This combined clinical and research solution tracks consent for research and links biological samples with deep phenotypic data including longitudinal outcome data.
- The roll out to the Huntington’s disease service is ongoing. We now have all patients seen by the clinical research service in 2019 registered (82 patients) with clinical outcome measures due to be released in the next version of the software in 2019/20.
- The ‘PatientCare’ electronic health record consists of multiple modules, including a clinician-facing web portal, available on every NHS desktop across Wales.
- We have developed bespoke patient-facing portals and mobile applications, including iPad consent for movement disorder clinics. We have a website [www.movementdisorders.wales](http://www.movementdisorders.wales) which Dr Kathryn Peall and Dr Mark Wardle have developed and this enables electronic recruitment, consent, and questionnaire completion for patients. Similarly, we have continued to run an Internet-portal for tracking patients and their outcomes with multiple sclerosis from across the UK.
- Finally, we have been able to start sharing the PatientCare patient recruitment platform to other health boards due to a successful MS Society grant. We will start recruitment at Swansea Bay University Health Board for multiple sclerosis and related disorders.

**Work Package aim:** Develop and implement a clinical research database system that supports clinical care and is integrated within BRAIN Biobanks and the NRU. Providing real time data capture that will also benefit NHS service delivery.

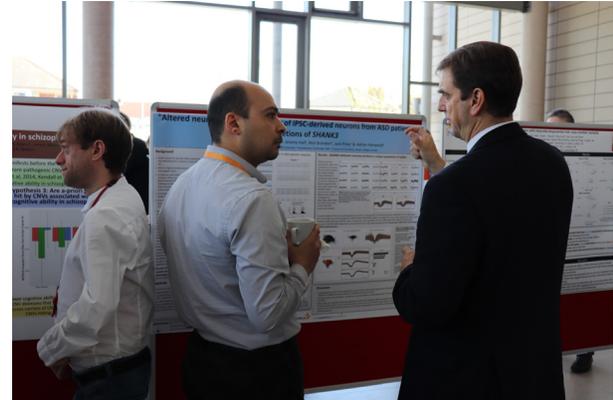
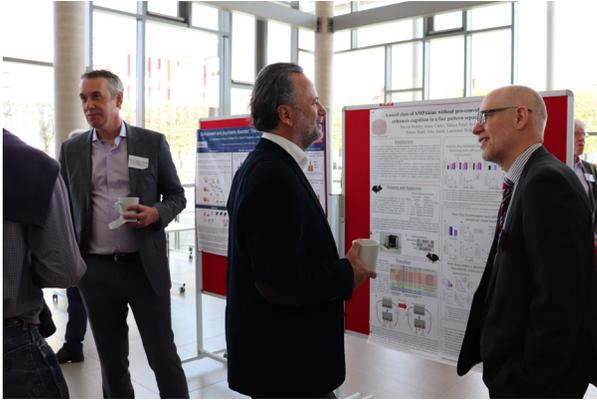


iPad/iPhone mobile application measuring disease-specific outcomes



**Work Package aim:** To support the generation of pre-clinical grade cell therapies, drug development and evaluation of biologically active molecules for potential therapeutic use.

## WP 7 Novel Therapeutic and Devices Generation



This year the BRAIN Unit have jointly formed a drug discovery collaboration with Takeda Pharmaceutical Company Limited (Takeda) to identify new approaches for treating schizophrenia and other psychiatric disorders.

The collaboration will combine the University's large scale genomic data, and world-class expertise in psychiatric genetics, genomics and neuroscience, with Takeda's extensive drug discovery and clinical development capabilities. This academic partnership will allow Takeda access to world-leading biological psychiatry research and the related infrastructure across the University, including the MRC Centre for Neuropsychiatric Genetic and Genomics, NMHRI, National Centre for Mental Health, and the Brain Repair and Intracranial Neurotherapeutics Unit.

BRAIN's involvement is in pathway discovery in human tissue – specifically using primary human tissue cultures generated through the Human Tissue Lab.

We have further cemented our collaborations with the Prof John Attack at the Medicines Discovery Institute (MDI). Work has now commenced with the MDI on testing of novel compounds on Hippocampal neurogenesis.

We have set up a non disclosure agreement (NDA) and industry collaborators have been found to fund some of the work involved. We have now performed the first successful testing of AMPAlike molecules on neural stem cells and work on this will continue into the summer.



## WP 8

# Trial Design, Evaluation and Patient Monitoring

**Work Package aim:** To develop more accurate and reliable testing of mobility and cognitive dysfunction across trials, through developing novel clinic based and remote monitoring.



Working towards our vision of the BRAIN Unit being internationally leading for trial design for intracranial therapies, much of the activity over the year has been focussed on the RfPPB funded **TRIDENT cell transplantation trial**.

Thus far we have successfully:

- Ensured all governance procedures are in place.
- Completed site training.
- Applied for excess treatment costs.
- Set up the trial database.
- Developed qualitative research to support the deconstruction of the trial processes.
- Recruited 15 participants to the observational cohort in TRIDENT.
- Presented our novel trial design at the international Efficiency and Analysis of Trials Using Cohorts and Routine Health Data Symposium.
- Dr Cheney Drew was invited to present TRIDENT as one of 30 selected abstracts at the British Neuroscience Association Festival of Neuroscience meeting in Dublin in April.



### Clinch Token Transfer Test (C3t)

A continually growing dataset of C3t scores and accompanying sensor data is currently being gathered across multiple different national and international sites using modern data collection technology built and maintained in-house in the Centre for Trials Research, Cardiff University. Early analysis of the dataset suggested C3t sensor data may be highly related to clinical scoring of the C3t and potentially predictive of multiple other clinical outcome measures such as chorea and dystonia measures. This is important from a research perspective given the known subjectivity inherent in the clinical assessment of Huntington's disease. License agreements are in place with KU Leuven, Newcastle University and Columbia University. Researchers in these institutions are now exploring the use of this assessment in Parkinson's Disease populations.



Monica Busse was principal investigator of **Roche Natural History Study** a multi-site prospective longitudinal study measuring CSF mutant Huntington protein in patients with Huntington's disease. Cardiff was one of only 5 UK sites (11 international sites) in this pivotal biomarker (including digital biomarkers) study which is part of the ROCHE long term strategy of bringing their anti-oligosenside therapeutic to market as a disease modifying drug for Huntington's Disease. It is expected that the pivotal efficacy study will follow the observational study in summer 2019 (Anne Rosser as Principle investigator).



In October, we were notified that the **DOMINO-HD** grant involving 6 European partners (€2,049,523.75, funding Value to Wales of £409,261) submitted to JPND Multinational research projects on Health and Social Care for Neurodegenerative Diseases was successful. Ten projects were recommended for funding by an independent, international Peer Review Panel based on scientific excellence with input from the JPND advisory board on patient and public involvement. The awards have now been published on the JPND website ([www.neurodegenerationresearch.eu/2018/11/2018-call-results-health-and-social-care-for-neurodegenerative-diseases/](http://www.neurodegenerationresearch.eu/2018/11/2018-call-results-health-and-social-care-for-neurodegenerative-diseases/))

DOMINOHD



**Key Investigators:** Dr Emma Lane, Dr Cassy Ashman and Mr Peter Roberts.

## WP 9 Public Involvement



### BRAIN Involve Community Day

Launched last year, The UK-wide National Standards for Public Involvement provided for the first time a common framework for organisations to develop their involvement of the public in research. They provide indicators allowing identification of areas of strength and areas that need improvement, in order to achieve good, fully-rounded public involvement.

The application of the National Standards for Public Involvement was the focus of the BRAIN Involve Community Day hosted in 24 September 2018.

BRAIN Involve is the Public and Patient involvement group that helps to inform research activities. It is made up of people who are, or have been affected by neurological diseases such as epilepsy, Huntington's disease, Multiple Sclerosis or Parkinson's disease.

The Community Day brought together members of the public and researchers to address the new National Standards for Public Involvement and refresh the group's Terms of Reference to make sure that they met the standards.

Some of the issues highlighted were how to create better opportunities for existing members as well as making researchers more aware of the resources available for their work.

This scoping exercise gave rise to discovering how current and interested members felt about available resources and opportunities and how we can improve our patient and public involvement and engagement with researchers.

The results from the exercise formed the basis of an application to the Wellcome Trust institutional Strategic Support Fund. The grant is aimed at developing better digital resources, including animations, a forum and better access to information for members of the public. If approved this grant would have a measurable impact on patient and public involvement for the unit and would also be of wider benefit for research in Wales, giving digital access to patient and public involvement opportunities in neuroscience related research; something which is not currently available.

## WP 9 Public Engagement

Key investigators: Dr Emma Lane, Dr Cassy Ashman and Mr Peter Roberts



The annual Brain Games Public Engagement event, took place on Sunday 10 March 2019, welcoming record breaking numbers.

Organised, funded and delivered by the BRAIN Unit, NMHRI, CUBRIC and Cardiff University, the annual Brain Games event this year took place on Sunday 10 March. Marking the beginning of Brain Awareness and British Science week, with a record breaking 3,670 people making their way through the doors of the National Museum Cardiff to join in the fun.

A large selection of interactive games and shows were available to the public throughout the day, explaining various scientific concepts relating to the brain and giving children an opportunity to interact and ask questions to some of Cardiff's leading scientific community.

Games included an inflatable brain bouncy castle, stroop mat races, guessing animal brains, shrinking chair optical illusions and many more. These were supplemented with a series of shows throughout the day giving children the opportunity to practice brain surgery alongside qualified surgeons, learn about super hero stem cells and challenge their curiosity.

Running Cardiff University's largest public engagement

event relies heavily on the time of willing volunteers, all of whom came from varied medical and research backgrounds, offering their insights and knowledge to the budding young scientists in attendance.

Attendees braved the queues and gave us some great feedback on the day:

**"I love this event, great activities and friendly, interesting people"**

**"Well done on a fascinating and educational event. So lovely to see the kids learning without even realising they are!"**

We hope those who attended left having learnt more about the diverse research taking place at Cardiff University and feeling inspired to become the neuroscientists of the future.

## Meet the Researcher: Dr Kathryn Peall, Clinical Senior Lecturer

Dr Kathryn Peall's interest in mental health research began during her PhD which was focused on mental health symptoms in a specific type of movement disorder. Other than the psychiatry training she had done at medical school, this was the first time she had the opportunity to concentrate on mental health symptoms, how they affected other medical problems and the impact on day-to-day living.



Kathryn currently has a number of studies taking place in her group, ranging from clinical symptom and natural history studies, to laboratory-based work looking at how specific gene mutations affect the way nerve cells function. This work is all interlinked, focusing on a type of movement disorder known as dystonia, and how changes on a cellular level might affect movement and mental health symptoms.

Kathryn undertakes both clinical and laboratory-based research, allowing the two to feed into each other. On the clinical side, much of her work is influenced by clinical scenarios/symptoms highlighted by patients as causing significant impact to their lives, or being difficult to treat. The aim of all the laboratory-based work is to better understand the causes of dystonia, and to hopefully identify or develop new treatments that might be taken forward to clinical trials.

In terms of changes to attitudes towards mental

health during her career, Kathryn has noticed that principally, there is a willingness to discuss mental health by patients, their relatives and clinical staff. There has been a shift from mental health being infrequently discussed in neurology to clinics, to a topic that is discussed on a regular basis. She has also noticed changes in attitudes to treatment, with greater discussion about the merits of different types of therapy.

The key challenges Kathryn has identified for mental health are trying to understand why mental health problems arise. This involves linking genetic and environmental factors, and then trying to develop systems so that we're able to try and understand the mechanisms that cause mental health problems. Alongside this however, there is also a need to continue to talk about mental health issues and how they affect people, widening the community with which we achieve this.

# Outcomes & Impact

**Objective:** To develop new and refine existing systems for therapeutics delivery into the human brain.

1

A step closer to understanding which devices are appropriate for delivery of therapeutics to the human brain, through the TRIDENT fetal cell delivery trial.

2

Forming collaborations with industry partners PDR and Arrotek for device development and therapeutic development.

3

“TRIDENT Cup” public engagement activity winning the Best Interactive Stand at the Health and Care Research Wales conference 2018, helping to increase awareness of delivering therapeutics to the brain as treatments for neurological disorders.

**Objective:** To build appropriate infrastructure including a dedicated NRU.

1

Improved relationship with NHS colleagues- Excellent feedback from Neuroscience directorate team at Cardiff and Vale UHB

2

Increased economic impact to Wales- record profit from NRU commercial income.

**Objective:** To continue supporting patient data and tissue bio-banking.

1

Increased access to a wider range of samples for researchers to use to study neurological conditions- 102,265 total number of samples held for over 9 neurological diseases and conditions.

**Objective:** To embed into all relevant work-packages cross-cutting excellence in the relation to public involvement and engagement and commercial and industry engagement and collaboration.

1

More members of the public are involved and engaged with BRAIN Unit research- Doubling our BRAIN Involve members in one year; record numbers of people reached through our events and presentations; highest number of twitter followers to date.

2

New relationships with industry partners- Takeda, Arrotek, PDR, Roche.



# Conclusion

Since 2015, when the BRAIN Unit was established, we've strived hard to develop each of our 9 work packages to reach our ultimate aim of developing novel therapeutic and treatment delivery systems for neurological conditions. This year has been no exception and we have seen some fantastic achievements meeting many of our median to short-term outcomes and thus strengthening our impact in Wales and beyond.

Whilst the research landscape is ever changing, we are recognising the importance of good collaboration with a variety of partners in academia, NHS and industry all of which we have improved on in 2018-2019. This is thanks to the hard work of the BRAIN Unit members who ensure visions of both research and financial sustainability are realised.

## Public Perceptions

BRAIN has developed novel ways to engage and inform the public about our research. Over the past 4 years, we have reached nearly 15,000 people across more than 37 events, communicating our often complicated research into rare and complex diseases. The controversial nature of some of the technologies we use such as fetal stem cell research and transplantation into human brain, makes it even more a unique challenge, from which we have learned and continue to learn greatly.

We have a history of successful, dynamic, diverse and far-reaching public engagements events and activities which reach all members of the public from school children to the university of the 3rd Age. We have designed a range of interactive activities to promote a more practical understanding of what we do winning the "Best Interactive Stand" award at the Health and Care Research Wales annual conference for three consecutive years. Our flagship events include the annual Brain Games, attended by over 3500 people in 2019. We have now 31 members to our Public Involvement group BRAIN Involve, who represent the breadth of neurological conditions covered by BRAIN's research. This number has doubled in the past year alone, testament to the increased awareness amongst our principle investigators that good public and patient involvement (PPI) makes good research.

## Looking Forward

We want to build on our achievements over the last 4 years, building and supporting critical infrastructure, leveraging grant funding for both preclinical and clinical research, translation of academic findings and attracting key commercial trials to Wales. Putting in place the elements necessary to generate novel, potentially disease-modifying therapies, for patients with neurological disease in Wales, and providing a robust evidence-base supporting their implementation. This has formed the basis of our ambitious research strategy for 2020- 2025.

We will continue to facilitate and enhance our public events, and we will focus on two key areas of engagement, patients and NHS stakeholders and industry. In addition, it is our aim to embed appropriate and meaningful PPI across all domains of BRAIN. BRAIN Involve, our patient and public involvement panel, has formed an invaluable expert voice, informing our research activities. Our priorities are to expand our PPI provision whilst working towards more effectively meeting the National Standards for Public Involvement in alignment with the needs of BRAIN.

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