British Neuroscience Association
Making connections

Neuroscience and Mental Health Research: Spotlight on Wales

17 September 2024

Senedd Cymru

British Neuroscience Association

Sponsor: Hefin David (MS for Caerphilly, Chair of the Cross-Party Group on Universities)

NEUROSCIENCE RESEARCH IS VITAL

Neuroscientists in Wales are vitally important to tackling the health challenges of the future.

The British Neuroscience Association (BNA) is the largest UK organisation connecting, representing and promoting neuroscience and neuroscientists across the globe.

A non-profit organisation, the BNA is committed to creating a supportive and inclusive neuroscience community, making connections between academia, industry, the clinic and wider society, and moving world-class neuroscience research up the agenda.

- Hear about the fundamental role neuroscience research plays in developing new approaches to address both clinical and social needs.
- Discover the variety of Welsh neuroscience research from across Wales.
- Meet others interested in collaboration to support and prioritise neuroscience research funding in Wales.

Pierhead, Cardiff Bay

Tues 17 September (11:00-13:30)

office@bna.org.uk

Fundamental neuroscience is key to future health

World-leading neuroscience research in Wales can help us meet the societal challenges we face in the future. The science of the nervous system is essential for understanding what makes us human, preventing and treating neurological and psychiatric disorders, and keeping the UK at the forefront of cutting-edge research internationally. That's why investment in neuroscience research is key, and why we should celebrate the world-leading research happening in Wales.

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We have members across Wales and over 3,000 members overall, whose interests cover the whole range of neuroscience: from molecules to whole animal behaviour to real-life applications in the clinic and beyond.

With world leading research institutions, internationally renowned experts and cutting edge facilities, Wales is driving global advancements in understanding and treating complex brain conditions.

With support from the Senedd, Wales has the potential to become even stronger in neuroscience research.

Professor Tara Spires-Jones

Director of the Centre for Discovery Brain Sciences at the University of Edinburgh and BNA President

100,000 people in Wales

are living with a neurological condition and there are an estimated

2,500 new diagnoses each year [1]

24% of young people in Wales report 'very high' levels of mental health problems [2]

£2 billion

The cost of dementia care in Wales is soaring [3]

Get involved

If you're an MS:

- Raise awareness and talk to your constituents about the importance of research
- Visit a neuroscience project in your constituency or region

If you're a neuroscientist:

- Join the BNA and/or your local group in Wales
- Share your work with your local MS

About neuroscience

Neuroscience is the study of the brain and nervous system in both humans and non-human animals, and in both health and disease.

It is a relatively new field of science, only emerging as a distinct subject in its own right during the 20th century. However, it has grown rapidly and now covers multiple areas including novel technologies, and research into many brain functions and disorders, as well as applications as diverse as education, AI and the law.

The brain is responsible for our thoughts, mood, emotions and intelligence, as well as our physical movement, breathing, heart rate and sleep. In short, it makes us who we are and facilitates almost every aspect of what it means to be alive.

The complexity of the nervous system makes neuroscience inherently highly challenging. Despite an explosion of knowledge over the last century, we are just scraping the surface when it comes to understanding many of its fundamental functions.

Although there has been incredible progress, there is still much left to discover.

The case studies in this booklet show how Welsh reserchers are making significant contributions to our understanding and treatment of complex brain conditions.

Case study: Understanding bilingual and dyslexic literacy

PRIFYSGOL BANGOR UNIVERSITY

Prof Manon Jones
Bangor University

Dr Manon Jones and her team combine EEG and eye-tracking to investigate how children learn to acquire two or more languages, and how having two language systems impacts both the neural correlates of reading and reading style across development. Their research is key to better understanding the difficulties experienced by both children and adults with dyslexia and other reading difficulties.

Combining EEG and eye-tracking not only allows Dr Jones and her lab to identify which words and sentence structures are most difficult, but also capture how brain response is altered when readers struggle with words or phrases. The results of this research has, in turn, informed the development of an evidence-based language and literacy programme for Key Stage 2 children, particularly those that struggle to read. The RILL program (Research on the Instruction of Literacy with Language) was developed with multilingual learners in mind, and is currently being delivered (and assessed) in Welsh and English across schools in North Wales and parts of England.

This program, funded by the ESRC, the Nuffield foundation, and the Welsh Government was initially developed to help children continue to learn to read and write remotely during school closures because of the Covid-19 pandemic. As the programme proved to be effective in improving key literacy skills when delivered remotely, the program has been further developed as a technology augmented intervention that can be delivered by TAs to small groups of children. Randomised control trials in both Welsh and English support the effectiveness of the program, and the team plans to roll the program out across the UK over the next few years.

“The results of this research has, in turn, informed the development of an evidence-based language and literacy programme for Key Stage 2 children, particularly those that struggle to read..“

Case study: Neuroplasticity in hand nerves following injury

Prof Ken Valyear
Bangor University

Hand nerve injury constitutes a significant healthcare challenge. Incidence rates and economic costs are alarming, while patient recovery is typically poor. Sensory and motor impairments, and pain, often persist indefinitely. Rehabilitation is conceptualised as a complex interplay between peripheral and central factors. Understanding how the brain changes and the clinical significance of those changes are urgent priorities.

Contemporary models of functional recovery in nerve repair place a strong emphasis on the brain and its capacity for change. The functional maps of the hand are presumed to reorganise in accordance with animal models, and functional recovery is conceptualised as a process of relearning in the brain. Recovery depends on reversing the changes in hand maps, or facilitating different parts of the brain to adapt accordingly.

By providing the first compelling evidence for altered digit maps after nerve repair in humans, our study validates a core assumption of contemporary therapeutic models—nerve repair indeed alters the cortical maps of the hand. Until now, this had only been shown in animals. Nonetheless, the functional significance of these findings remains unclear. According to our results, altered digit maps do not correlate with impairments in touch localisation or with broader measures of functional impairment. Whether and how functional brain changes in nerve repair relate to patient outcomes remains a question of great fundamental and clinical significance.

This research is funded by the Wellcome Trust and carried out in partnership with hand surgeons Prof. Vivien Lees and Mr. Edwin Jesudason.

Case study: A deeper understanding of social interactions

Prof Kami Koldewyn
Bangor University

Humans are social creatures. Our understanding of the world around us is dictated and shaped through the social interactions that we observe and take part in, so we are excellent at extracting and processing social information. Yet until recently, we have known relatively little about how these skills develop. In the Becoming Social project, Dr Koldewyn and her team explored the roots of our social understanding, by investigating the development of the behavioural and neurobiological systems that support complex social perception.

The team used functional magnetic resonance imaging to understand the development of the brain regions in this network, as well as eye-tracking to look at whether children viewed and processed social scenes differently from adults. This work suggests that, for both adults and children, observed social interactions are processed and understood through a small network of dedicated regions. However, these brain systems, and the ability to parse the complex and nuanced information conveyed in interactions, continues to develop into adolescence.

Ongoing work in the lab investigates how this system, and its development, might be different for individuals who struggle to understand or engage with social interactions. These difficulties can be experienced by not only neurodiverse individuals on the autistic spectrum, but also by those who are socially anxious, socially isolated, or lonely.

"We hope the results of this ongoing work will provide the necessary first steps to understanding how to best support these individuals and provide a crucial piece in our understanding social development."

Case study: Biomarkers in neuropsychiatry

Prof Neil Harrison
Cardiff University

Neil Harrison is a Professor of Psychiatry and Neuroimaging and Consultant Neuropsychiatrist at the Cardiff University. His research focuses on understanding the mechanisms through which the body and the brain interact and how they contribute to neuropsychiatric disorders. Typically, this involves combining diverse blood, cognitive, brain imaging and wearable data, often after experimental drug challenges.

Prof Harrison's research is funded by the Wellcome, MRC and the Hodge Foundation.

He then works with colleagues in drug-development and bioinformatics to identify how these brain or body-based biomarkers can be translated to improve patient diagnosis and accelerate the development of novel drug therapies.

Recent successes include:

1) Working with colleagues in the **Cardiff Medicines Discovery Institute** to incorporate brain imaging into early Phase-I clinical trials and develop target engagement biomarkers that can de-risk Psychiatric drug discovery; and

2) Working with colleagues in the **Cardiff Dementia Research Institute** (DRI) to show that biomarkers from easily collected wearable data can identify people with Parkinson's disease many years before formal clinical diagnosis.

"My fundamental aim is to speed up translation of understanding of disease mechanisms into outcomes that have real world benefits for patients."

Case study: 22q11.2 Deletion Syndrome, a paradigm for mental health research

Prof Adrian Harwood
Cardiff University

Adrian Harwood is a neuronal stem cell biologist, who uses patient-derived induced Pluripotent Stem Cells (iPSC) to study human neurodevelopment and its relationship to mental health. As a Co-Director of the Neuroscience and Mental Health Innovation Institute (NMHII) at Cardiff University, his research group works within a multidisciplinary environment of teams, who study mental health from all research directions.

22q11.2 Deletion Syndrome (22q11DS) is neurodevelopmental disorder (NDD) cause by a large deletion on chromosome 22, affecting many genes. It is the second most frequent genetic syndrome with associated neuropsychiatric conditions, including ADHD, anxiety and psychosis, as well as comorbidity with other health issues, such as congenital heart disease and hypocalcemia. In fact, 22q11DS magnifies risk of developing a psychiatric disorder over that experienced in the broader population, offering a window onto the general causes of mental health conditions.

NMHII's integrated research spans many experimental modalities. Patient iPSC research is establishing the molecular cell mechanisms altered in patients, and this is then translated to animal models for brain function and behaviour, and patient biology with functional brain imaging. This sits in a wider context of genetic studies, deep clinical phenotyping and input from individuals with lived experience.

"To apply our research to the broader patient population we have founded MeOmics, a Cardiff-based spinout company. This has created an iPSC-based experimental Precision Psychiatry platform for improved preclinical drug screening and better patient targeting."

Case Study: DPUK Data Portal

Dementias Platform UK (DPUK) is a multi-million pound MRC funded project, with £7 million of funding being brought into Swansea University. DPUK focuses on three key, human-centered areas in our quest to untangle the complexities of dementia and accelerate progress in research.
Those areas are:

- **The DPUK Data Portal** - A repository of dementia-optimised cohort data
- **The Trails Delivery Framework** - Our engine for matching public volunteers to the most appropriate new research studies
- **The Experimental Medicine Incubator** - Our programme of cutting-edge experimental medicine

Swansea University is home to the DPUK Data Portal which enables the sharing of multi-modal data from more than 3.5 million subjects across the world. This is an essential resource to help scientists and pharmaceutical companies achieve a world free from dementia, by transforming their ability to carry out research and make vital breakthroughs.

Over the past couple of years, DPUK has built up their neuroimaging and genomics infrastructure, enabling important research into neurodegenerative diseases and psychiatric problems. Allowing researchers access to phenotypic data, such as medical history and diet, with the combination of brain images and genomic profiles allows deeper analysis into the causes and prognosis of Dementia. DPUK has also been leading the way in Artificial Intelligence (AI) governance, looking at ways AI models can be developed and deployed safely within a trusted research environment to enable a wide range of AI projects to be developed and deployed responsibly into real world clinical environments.

Case Study: Building a Medicines Discovery Institute to deliver a Bench to Bedside mental health portfolio

Prof Simon Ward
Cardiff University

Prof John Atack
Cardiff University

Simon Ward and John Atack are experienced drug discovery and development scientists with a successful track record of drug hunting across big pharma, biotech and academia. A decade ago, despite the clear and growing need, pharma systematically retreated from mental health drug discovery programmes. In response, Simon & John decided to move to academia to set up a drug discovery unit to continue to advance projects with real potential to benefit patients. They recognised that the industry disinvestment was frustratingly occurring at the same time that advances in genetic disease understanding, patient stratification and biomarkers were finally overcoming many of the barriers to successful clinical translation.

In 2018, they moved the group to Cardiff to create the Medicines Discovery Institute (MDI), building on existing research collaborations and to benefit from the local excellence in fundamental disease understanding embedded in clinical practice. Cardiff University has a strong priority focus on neuroscience and brain health, which aligned with their aspirations and, importantly, also aligned with the strategic priorities of the Wellcome Trust and the Medical Research Council, who have provided significant funding to the MDI.

The group has now grown to employ over 40 scientists and students and has established a portfolio of drug discovery projects from target validation (building off new understandings in disease mechanism) through discovery into early clinical development (working with local clinical scientists and brain imaging experts) by attracting approximately £50M in external funding.

The group has established a successful track record of onward development and commercialisation and is set to make significant impact to the clinical development landscape.

The flagship project targeting cognition in schizophrenia has reached an incredibly exciting and unusual milestone from within a university setting. It started its life with Wellcome Trust funding as a new drug discovery project and has now progressed all the way through to successful completion of Phase 1.

Celebrating Excellence:

Professor Julie Williams announced as BNA Outstanding Contribution to Neuroscience Award winner

We are delighted to announce that Professor Julie Williams has been honoured for her outstanding contributions to the field of genetics, particularly in her groundbreaking work on Alzheimer's disease and dementia. As a leading global figure, Professor Williams' work has not only advanced our understanding of neurodegenerative disorders but has also placed Wales at the forefront of global medical research.

As the Professor of Neuropsychological Genetics and Head of the Neurodegeneration section at Cardiff University's Medical Research Council Centre for Neuropsychiatric Genetics and Genomics, Professor Williams has dedicated her career to unravelling the complexities of Alzheimer's disease. Her landmark discovery of the involvement of synaptic and endosytic genes CLU and PICALM as critical factors in Alzheimer's was a transformative moment in the field, earning recognition as one of TIME's top ten medical breakthroughs of the year.

Professor Williams' influence extends beyond her research. As the former Chief Scientific Adviser to the Welsh Government, the Alzheimer's Research UK and more recently as the Director of the MRC UK Dementia Research Institute at Cardiff, her visionary leadership has been instrumental in shaping global initiatives that have identified over 100 genes associated with Alzheimer's disease.

Prof Julie Williams
Cardiff University

Professor Williams' work has significantly advanced our understanding of the disease, particularly the roles of the immune system, highlighting the roles of microglia and brain inflammation and their effects on synapses, the connections between brain cells which underpin human memory. These discoveries have opened up several new avenues for therapeutic interventions.

In addition to her scientific achievements, Professor Williams is a staunch advocate for diversity in STEM and a mentor to the next generation of researchers. Her efforts to support early career scientists, especially women, have helped ensure a thriving and inclusive scientific community in Wales and beyond.

Professor Julie Williams' exceptional contributions to Alzheimer's research and her dedication to fostering future scientific leaders make her a true luminary. Her work continues to inspire hope for new treatments and, ultimately, cures for neurodegenerative diseases.

Professor Williams will be presented with her award and give a keynote address at the BNA's International Festival of Neuroscience in Liverpool (27-30 April 2025).

Case study: Advanced Therapy Clinical Trials

Professor William (Liam) Gray is an academic neurosurgeon who leads a Biomedical Research Centre focussing on delivering Advanced Therapy Medicinal Products (ATMPs) to the brain in First-in-human clinical trials.

Prof William Grey
Cardiff University

He and his colleagues have been working on translational cell and gene therapies in Cardiff over the last 15-20 years.

Working across Cardiff University and NHS Wales, his team is one of 5 centres worldwide delivering the UniQure AMT-130 gene therapy for Huntington's Disease, a therapy which has just received RMAT approval by the FDA. Interim data has demonstrated a slowing of disease progression in Phase I/II Trials of AMT-130 for Huntington's Disease.

The team are now at an advanced stage of negotiation with a further two sponsors to deliver their gene therapy trials in Parkinson's disease and Fronto Temporal Dementia respectively, to UK and European patients.

Case Study: Understanding lipids

Dr Roberto Angelini
Swansea University

Rob Angelini recently established his lab at Swansea University with the support of an Academy of Medical Sciences Springboard Award to advance his research on Alzheimer's Disease (AD). His lab investigates the critical role of lipids in maintaining synaptic function, and particularly how the APOE gene, a key risk factor for AD, disrupts these lipids' metabolism.

Rob's research is pioneering new insights into the role of plasmalogen lipids in synapse function and how their impairment contributes to AD. The ultimate goal is to develop new therapeutic strategies that could slow or prevent the progression of neurodegenerative diseases.

Case Study: Cholesterol chemistry

The Oxysterol Research Group in Swansea University, led by Yuqin Wang and William Griffiths, focuses its studies on the biosynthesis and metabolism of cholesterol and how intermediates in these pathways are involved in biological processes. About a quarter of body cholesterol is present in brain and unsurprisingly, cholesterol imbalances in the brain are implicated in neurological disorders.

The ORG works with major charities, including the Michael J Fox Foundation and the CHDI Foundation, to identify cholesterol-related biomarkers for different neurodegenerative disorders, and develop new technologies to accurately study how brain cholesterol metabolism varies at different locations in brain.

Collaboration is key: "With colleagues from the University of Edinburgh we are developing a 3D Neurosterol Atlas of the Mouse Brain and with researchers in Cardiff, Manchester and London, we are studying disordered cholesterol metabolism in rare neurological diseases."

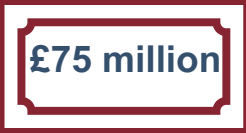
In focus: The UK Dementia Research Institute at Cardiff

Since the UK Dementia Research Institute (DRI) at Cardiff launched in 2017, we have...

Recruited 100+ scientists

Trained 58 PhD students

Attracted over £75m in research funding



Highlights include:

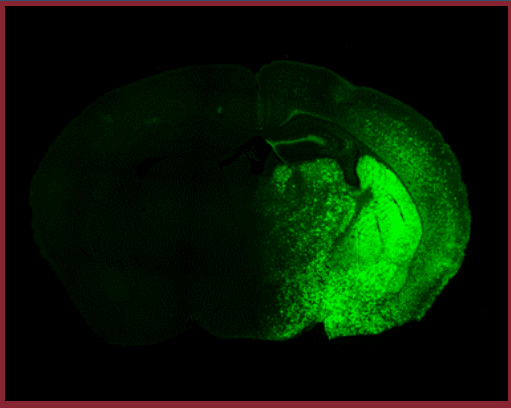
- Through discovering over 100 risk genes for Alzheimer's disease, we have identified new disease mechanisms and are developing novel therapies based on our bodies' immune system.
- We are using cutting-edge gene editing technologies to produce new types of therapy, that if successful could eradicate Huntington's disease and other similar rare diseases in the future.
- We are interrogating big data to identify new patterns and relationships to focus future understanding of disease mechanisms in Parkinson's and Alzheimer's diseases.
- We are now translating our findings by creating spin out companies and collaborating with industry to develop new drugs.

Professor Vincent Dion
UKDRI, Cardiff University

Huntington's disease is a devastating neurodegenerative disease that causes uncontrolled movement, a decline in cognition, and a high incidence of apathy, depression, and suicide. Huntington's disease remains without a treatment beyond palliative care.

Prof. Vincent Dion's lab has been working towards the development of a novel therapy based on cutting-edge technology: gene editing. The goal is to correct the mutation that causes Huntington's disease in brain cells. So far, they have shown success in human stem and brain cells as well as in in vivo disease models.

They are currently evaluating safety and efficacy before being able to set up a first in man clinical trial.



Gene editing treatment (green) injected into one side of the brain of a mouse model for Huntington's disease.

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UKDRI: New Therapies for Alzheimer's Disease

Dr Wioleta Zalek
UKDRI, Cardiff University

Recent genetic studies have highlighted the significant role of inflammation, and specifically the complement system, in numerous neurological diseases including Alzheimer's disease and schizophrenia.

Dr Wioleta Zelek's research focus is to develop novel drugs that specifically target the complement system, aiming to mitigate its harmful inflammatory effects in the brain. These drugs are designed to specifically inhibit the parts of the complement system that contribute to disease progression and pathology.

The major challenge is how to deliver these drugs across the blood-brain barrier (BBB). Effective delivery to the brain is critical for the success of these drugs, as the BBB is a highly selective barrier that prevents most drugs from entering the brain. The Zelek lab is pioneering new delivery methods, including receptor-mediated transport mechanisms, to ensure that these complement-targeting drugs reach the brain in therapeutic concentrations.

Their next steps involve advancing these therapies into clinical trials for Alzheimer's disease, with the hope of providing new, affordable and effective treatments in the near future.

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UKDRI: New Therapies for Parkinson's Disease

Dr Dayne Beccano-Kelly
UKDRI, Cardiff University

Parkinson's is the second most common neurodegenerative disorder in the world and morbidity is on the rise. This makes it vital to identify new interventive therapies to combat the growing health crisis it poses. Importantly, whilst known as a movement disorder, Parkinson's has a number of non-motor symptoms which critically, precede the motor symptoms by years. Understanding those early changes will provide targets for early intervention.

Born in Cardiff, Dayne has returned as a Principal investigator at the UK DRI at Cardiff University. As an electrophysiologist and biochemist, Dr Beccano-Kelly's lab focusses on how the electrical communication between neurons changes in Parkinson's and drives the symptoms observed at the earliest stages of disease.

Using genetic models, his goal is to use state-of-the-art electrophysiological techniques, molecular assays and behavioural readouts to discover the relationships between clinical symptoms and electrical brain activity, and to understand the mechanisms involved and identify new targets for therapies.

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UKDRI:
The Secrets of Big Data

Professor Caleb Webber
UKDRI, Cardiff University

Prof. Caleb Webber is the National UK DRI Director of Informatics and is passionate about transforming healthcare and molecular science through artificial intelligence (AI) and machine learning. These data-driven approaches can unearth answers to questions scientists hadn't yet considered and reveal patterns in vast datasets. This capability allows knowledge from one medical field to be quickly reapplied to another.

His lab's work involves analysing patterns of changing gene expression in different brain cells during Parkinson's and Alzheimer's disease to identify the most effective intervention points. They then map these molecular gene networks onto extensive population datasets to determine which healthcare actions can already modify these networks with measurable benefits. While new treatments are sometimes necessary, transformative healthcare outcomes are often achieved simply by recognizing where one area of healthcare can learn from another.

Building from molecular networks in individual cells up to large healthcare populations requires diverse data science skills and approaches. In collaboration with other data-driven labs, such as those led by Valentina Escott-Price and Peter Holmans, Webber focuses a national UK network of AI expertise on Wales, combined with the exceptional Welsh healthcare records, provides the potential for nationally transformative outcomes.

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THE INTERNATIONAL

BNA2025

FESTIVAL OF NEUROSCIENCE

BNA British Neuroscience Association

27 – 30 April 2025, Liverpool, UK

The International Festival of Neuroscience is coming to Liverpool, a city of poets and playwrights, of artists and music makers…..and of course neuroscientists.

This novel, multi-organisation forum brings together all those with an interest in brain research at a single shared event. From fundamental neuroscience in both academic and commercial sectors, to clinical expertise and patient perspectives in neurology, psychology and psychiatry – we have it all. In both its scientific programme and its breadth of attendees, BNA2025 will celebrate the diversity and scientific excellence of our neuroscience community.

Connecting over 1,500 attendees from 30+ countries, BNA2025 is your opportunity to engage with a global neuroscience community.

Register Today

bna2025.org

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Sources:

1. National Strategic Clinical Network for Neurological Conditions, 2023
2. Health Research Network's (SHRN) Student Health and Wellbeing Surveys in Wales 2021/2022
3. The Hidden Cost of Dementia in Wales, Alzheimer's Society Report, 2024

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