



RESEARCH BULLETIN

*An update on
Epilepsy Ireland's
activities in supporting
Irish epilepsy research.*

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FOREWORD



A chara,

I am delighted to bring you this bumper edition of Epilepsy Ireland's research bulletin!

We have not issued a bulletin during the COVID-19 years, but that is not because we had to delay or postpone our investment in Irish epilepsy research – in fact, it has been quite the contrary.

With your support, despite the challenges which have faced our organisation over the last number of years, we have been able to invest in a varied range of studies and research projects which are of the utmost importance to people with epilepsy and their families. You can read more about each of these in this edition of our research bulletin.

Because of the pandemic, public interest in health research has never been higher. The last two years has shown the importance of scientific advances in health research. We hope that with the projects that you have helped to support, we are laying the

foundations for further advances in the knowledge and understanding of epilepsy.

This is an exciting time for our organisation as we have just recently published our new Strategic Plan for 2022-2026. This plan sets the agenda for our work over the next 5 years. I am pleased to report that the plan includes a strong focus on continuing to invest in epilepsy research. We hope we can continue to depend on your support as we aim to achieve this key marker.

Epilepsy Ireland first began directly investing in Irish epilepsy research in 2009. By 2019, we had invested over €1million in research. With the projects you will read about in this bulletin, thanks to your support, we are now well on our way to our 2nd million.

I hope that you will enjoy reading about the projects which you have helped make possible. Thank you for your continued support for our research activities. If you have any questions or comments, please do not hesitate to contact me by emailing pmurphy@epilepsy.ie.

Yours faithfully,

Peter Murphy

Chief Executive Officer



Best Practice in Transparency and Accountability



RESEARCH ON THE INCIDENCE OF EPILEPSY-RELATED DEATHS IN IRELAND

We are providing up to €25,000 in funding towards a project which will investigate the incidence of epilepsy-related deaths in Ireland and the circumstances surrounding them. The study began in 2020 and is being led by Dr Yvonne Langan, St James' Hospital Dublin.

People with epilepsy have a higher risk of mortality when compared with those in the general population of similar age. These deaths may be related to the underlying condition which caused the epilepsy but also may be due to the very fact of having epilepsy itself. Epilepsy-related deaths include accidents and drowning during a seizure, prolonged seizures (known as status epilepticus) as well as SUDEP.

SUDEP is the sudden, unexpected death of a person with epilepsy where a post-mortem does not identify any other cause of death. The cause of SUDEP is not yet fully understood. While it is understandably one of the most feared aspects of the condition, the risk of SUDEP in any one individual with epilepsy is low and the better a person's seizures are controlled, the lower the risk.

The study is being conducted with the support of the Health Research Board (HRB), who have an established mechanism in place for accessing data held by coroners in Ireland. This mechanism, the National Drug Related Deaths Index (NDRDI) is currently used to identify deaths related to drug and alcohol abuse. By partnering with the NDRDI, the study has now identified deaths in people with epilepsy nationally across



Dr Yvonne Langan of St James's Hospital & Trinity College Dublin who will lead this research.

a full calendar year (2019) and will analyse all available records. Deaths in people with epilepsy will be classified as epilepsy-related or non-epilepsy related. The study will also isolate cases of SUDEP which will then be used to determine for the first time ever, accurate Irish data on the incidence of SUDEP in Ireland. Until now, we have had to rely on estimates based on international studies but by getting recent and accurate information, we hope to increase awareness of SUDEP among people with epilepsy, health professionals and policy makers.

Our new Strategic Plan also makes a commitment to develop strategies to reduce and prevent epilepsy-related deaths. When this research is finalised and published, it will be one of the key foundations for laying the groundwork for these strategies – as for the first time, we will have Irish data on the incidence of epilepsy-related & SUDEP deaths.

This is an incredibly important study which you have helped to make possible, one which could have major implications for the future of epilepsy care in this country.

THE SOCIETAL IMPACTS ON THE LOSS OF A DRIVING LICENSE FOR PEOPLE WITH EPILEPSY

We have invested €15,000 in a study which is investigating the impact of losing a driving license due to a diagnosis of epilepsy. The research is being led by Professor Norman Delanty; Consultant Neurologist at Beaumont Hospital, assisted by Dr Stephen Klaus.

Under Medical Fitness to Drive Guidelines, most people with epilepsy must be free of seizures for one year before they are eligible to drive. More stringent rules apply to driving large vans and heavy goods vehicles such as lorries and buses. Driving restrictions are a major issue for many people diagnosed with epilepsy in adulthood. For people whose seizures are well controlled, losing their licence because of a breakthrough seizure can also be a significant worry. Losing one's licence can affect employment, family responsibilities, social activities, and independence. While we have many testimonies of the personal impact this issue can have, there is currently very little hard data on the extent of this impact. This study will address this evidence by examining:

- The degree of societal impact on patients and their families caused by driving restrictions. This will include patients' views on the restriction, financial impact, perceived social stigma, loss of employment and/ or breakdown of personal relationships.
- Alternative transport means utilised by patients during driving restriction including the use of public transportation and reliance on patient's family members.
- Patients' views on the potential



availability of access to the Free Travel Pass scheme.

- The doctor-patient relationship after the implementation of driving restrictions. Specifically, it will look at patients' views on the medical staff informing them of restrictions and whether second opinion and/or alternative care was sought.

It will also identify and compare the number of Group 1 (Cars, Motorcycles etc) and Group 2 (Larger vehicles such as HGV's etc) drivers within the patient cohort, as well as patients working as taxi drivers, and how they have been affected by driving restrictions.

This is an important study, not only in terms of understanding more about the impact of losing a driver's licence, but also in terms of the support people need as a result. We believe that all people with epilepsy restricted from driving due to their epilepsy should be provided with access to the free travel scheme for the duration the restrictions are in place. This is one of our key advocacy campaigns and it is regularly raised in the Dáil. Your help in funding this study could lead to a breakthrough in this longstanding advocacy campaign by providing data on the points listed which we can use to further enhance our arguments.

CAN DOGS PREDICT SEIZURES?



An Epilepsy Ireland supported study made national and international headlines in 2021 when Dr. Neil Powell of Queen's University Belfast published his study on whether untrained dogs can predict epileptic seizures. The research had been ongoing since 2017 and was published in the scientific journal, *Animals*.

The study focused on 19 pet dogs and explored how they reacted to the emergence of seizure-associated odours. This was done using two specially designed pieces of apparatus called the Remote Odour Delivery Mechanism (RODM). To carry out their investigations, researchers separately delivered epileptic seizure-associated odours and non-seizure associated odours to the dogs and recorded how they reacted to each.

The findings were quite extraordinary with **ALL** 19 dogs displaying behavioural changes when confronted with the seizure related odours compared to non-seizure odours, which led Dr. Powell to conclude, "Our findings clearly showed that all dogs

reacted to the seizure-associated odour whether this was through making eye contact with their owner, touching them, crying, or barking. There is a unique volatile smell linked to epileptic seizures, detectable by dogs who can in-turn warn their owner a seizure is likely to occur. Our research was based on pet dogs with no prior training. If we can train dogs, this has the potential to make a big difference to owners who experience unpredictable seizures and should go a long way in improving not only their safety, but also their quality of life."

The findings of this study were significant. Over the years, we have heard many anecdotal reports from people with epilepsy and their families about their pet dogs displaying such behaviours. However, this study represented the first time that this was replicated in a research setting.

The findings of this project have laid the foundations for what will be a new advocacy campaign for Epilepsy Ireland. Under current legislation, it is unclear whether seizure alert dogs are recognised as service dogs – therefore meaning that a dog that is theoretically trained may not be able to accompany a person with epilepsy in public settings.

With the findings that dogs can be trained to detect seizures, this legislation needs to be changed to ensure that new approaches to seizure detection alongside 'man's best friend' are not prevented by a lack of access.

Because of your support, we now have real-world data of untrained dogs predicting seizures – something which could go on to become a game-changer in the epilepsy community.

You can read more about Dr. Powell's research and its findings by visiting our website.

[▶▶ https://bit.ly/NPDogsRB](https://bit.ly/NPDogsRB)

STUDY UNDERWAY INVESTIGATING NEUROMODULATION

In 2021, we committed funding of €30,656 to research investigating a new type of neuromodulation in epilepsy. The study is being undertaken in the Department of Physiology in NUI Galway.

The research, led by James Britton and Dr. Leo Quinlan, is focused on whether an emerging technology called Transcranial Focused Ultrasonic Stimulation can be used to treat rare, drug-resistant epilepsies such as Dravet Syndrome or Lennox Gastaut Syndrome.

This is a type of non-invasive treatment which has shown potential therapeutic applications in other areas such as Parkinson's, neuropathic pain & Alzheimer's. The researcher is investigating if this technology can be used to regulate the 'firing' of neurons associated with seizures.

The researcher will investigate this in a laboratory environment, using brain cells derived from human patients.



If the technology is shown to regulate the 'firing' of particular neurons, this could lead to the development of potential new treatments. In rare epilepsies like those mentioned, treatment options are limited and therefore it is crucially important that new potential therapies are investigated. Thanks to your support, the potential role of neuromodulation is now being investigated.

This project is being funded in conjunction with the Irish Research Council Enterprise Partnership Scheme. Having begun in 2021, the study is set to last two years. You can watch the lead researcher, James Britton, talk about the study by visiting our website.

▶▶ <https://bit.ly/JBNeuroRB>

NEW STUDY AIMING TO UNDERSTAND MORE ABOUT CDKL5

We are delighted to confirm that this year, we have committed €36,000 in funding over the next four years to a study aiming to better understand CDKL5 Deficiency Disorder (CDD).

This is a rare brain disorder which is characterised by epilepsy and developmental delays – and is a disorder for which no specific treatments exist.

This study will investigate the potential role of gene regulators called microRNAs as novel therapeutic targets. MicroRNAs reduce cellular protein levels and have been linked to epilepsy and brain development. Altering their activity produces powerful therapeutic effects in mice. The project will use different techniques to measure changes

to microRNAs in a mouse model of CDD, understand how microRNAs regulate levels of CDD and use drug-like molecules to manipulate microRNAs and determine if this restores brain function and improves symptoms.

It is hoped that this research will illuminate the role of microRNAs in CDD and enhance understanding of the underlying cellular and molecular mechanisms. Thanks to your support, this research will help to build a knowledge base about a condition for which very little is known.

This project is being funded in conjunction with the Irish Research Council Enterprise Partnership Scheme and has recently got underway in the Royal College of Surgeons in Ireland.

NEW STUDY ON IMPACT AND VALUE OF EPILEPSY WEARABLES FOR SEIZURE MONITORING

Over the last decade, improvements in technology have led to the development of several new seizure-detection devices, many of which can be easily worn to look like a wristwatch. These devices can provide peace of mind to both patients and caregivers in knowing that the alarm will alert a loved one when they might have a seizure. The devices can also be used to provide further details to clinicians about how often a person may be having seizures, helping them to better understand a person's condition. However, there is still a lot that is not known about these devices in terms of their validity in accurately recording and alerting seizures as well as their real-world impact for patients.

One such wearable device for the automatic detection of seizures is the Embrace 2 wrist-worn device by Empatica. This is seen as the leading device on the market by many. This FDA cleared device alerts patients and caregivers to a seizure detected via accelerometer and electrodermal data processed with a machine learning classification model.

To help build data around the unknowns surrounding seizure alarms, we confirmed

in 2022 that we would be supporting a new study in investigating the impact of the Embrace 2. €27,000 will be invested over three years and the research will have 2 key aims:

- What is the validity of the Empatica Embrace2 wearable device in detecting generalised tonic/clonic seizures?
- What value / clinical impact is there in using wearable seizure monitoring devices in the management of epilepsy?

Thanks to your support, this study will help provide real-world data on the use of seizure detection alarms and indeed, potentially help clinicians identify the patients that the alarms can potentially best support.

This project is being funded in conjunction with the Irish Research Council Enterprise Partnership Scheme and has recently got underway in the Royal College of Surgeons in Ireland.

The study had also been made possible thanks to the support of the family & friends of the late Louise Young, who sadly passed away from SUDEP in 2021. Their fundraising efforts in Louise's memory has helped to support this study as we will be using the funds raised to purchase the devices that the study requires.



SUPPORTING RESEARCHERS AND STUDENTS ACROSS IRELAND

Our contribution to research is not just monetary. We are proud to work with researchers and students across Ireland who are seeking to add to the global knowledge base around epilepsy. Requests from researchers are a common feature on our website and social media channels. We have supported many projects across the years through the input of staff and

volunteer time. We continue to work closely with world-leading epilepsy researchers at the FutureNeuro Centre in Dublin – and we feature regular research updates on our website and social media channels. We are also a proud member of Health Research Charities Ireland (HRCI) and we are committed to nurturing the development of epilepsy research in Ireland.

NEW STUDY AIMS TO UNDERSTAND MORE ABOUT SUDEP IN DRAVET SYNDROME

As noted in the article about the study investigating epilepsy mortality in Ireland, one of our key strategic aims is to develop strategies to prevent epilepsy-related deaths.

Dravet Syndrome is a rare type of epilepsy that is severe and drug resistant. It is characterised by prolonged seizures, starting in an infant's first years of life. Sudden Unexpected Death in Epilepsy accounts for approximately 53-61% of deaths in Dravet Syndrome. Nocturnal seizures – which are a significant risk factor for SUDEP – feature regularly in patients living with Dravet Syndrome and linked with severe sleep disturbances.

Sleep disturbances are associated with the disruption of circadian rhythms, the body's internal clock.

Despite efforts, no genetic, biochemical, or circadian signatures have yet been identified for Dravet Syndrome, and the urgent need for interventions to prevent SUDEP in Dravet syndrome remains. This research aims to identify circadian molecular biomarkers associated with

the development of Dravet syndrome and relevant SUDEP-linked phenotypes to, ultimately, predict SUDEP. The study will identify characteristics and molecular signatures in a mouse model of Dravet Syndrome, to identify relevant biomarkers of disease progression and/or SUDEP risk. Following this, the study will seek to recruit Dravet syndrome patients across multiple clinical sites in Ireland to investigate their circadian rhythm profile through actigraphy and electroencephalography (EEG) assessments.

The final part of this project will seek to validate the pre-clinical biomarker findings in plasma samples from DS patients to assess its translational (real-world) potential, while combining circadian clinical datasets.

It is hoped that this research will have a significant impact in potentially preventing SUDEP amongst patients with Dravet Syndrome. Once again, this would not have been possible without your support. We confirmed funding of €32,500 for this study earlier this year.

This project is being funded in conjunction with the Irish Research Council Enterprise Partnership Scheme and has recently got underway in the Royal College of Surgeons in Ireland.

CONGRATULATIONS TO OUR 'TIME FOR A BREAK' DRAW WINNERS!

One of the key ways you have supported our research priorities over the years is via our Time for A Break draw. The monthly draw allows those signed up to the draw to be entered into a competition to win a €300 voucher to use at any of the Select Hotels of Ireland!! We would like to say thank you to all our draw participants and congratulations



to all our winners! We hope you have enjoyed your stays with the wonderful teams at Select Hotels.

NEW RESEARCH TO INVESTIGATE POTENTIAL PATHWAY TO TREATMENT FOR TEMPORAL LOBE EPILEPSY

Temporal lobe epilepsy (TLE) is the most common type of epilepsy in adults, with seizures being the major symptom although individuals may also have anxiety, depression and/or memory disturbances because of their condition.

TLE is very difficult to treat and about 30% of individuals with this type of epilepsy are failed by available treatments. TLE may arise following various brain injuries such as traumatic brain injury, stroke or infection. These brain injuries trigger several disease-causing processes in the brain which eventually culminate in seizure development.

One major change observed following epilepsy-causing brain injuries are large scale changes in the expression patterns of genes in the brain. These changes likely drive many of the other processes because gene expression dictates how our brain cells behave.

This new project will be led by Dr. Gary Brennan of UCD. Dr Brennan's group has previously found that a specific group of molecules called long non-coding RNAs are produced at different rates in the brain following epilepsy-causing brain injury. This group of molecules are critical for almost every cellular activity and may therefore play an important role in the transformation of cells to an epileptic state.

This study will use advanced molecular biology techniques to initially identify the full extent of the dysregulation of long non-coding RNAs in epilepsy and then test



Prof Gary Brennan, School of Biomolecular and Biomedical Science, University College Dublin who will lead this study.

whether we can target these molecules to identify novel therapeutic strategies to treat epilepsy.

It is hoped that the study will greatly increase our understanding of the molecular mechanisms behind epilepsy development and shed light on the therapeutic potential of targeting long non-coding RNAs to treat the condition. Commenting on the study, Dr. Gary Brennan said, "The research asks a very relevant question and could potentially address a huge unmet need for people with refractory epilepsy, for whom existing treatments have been unsuccessful and for whom the burden of epilepsy is significant. It focuses on a novel molecular approach which has not been extensively studied to date. The furtherance of work such as this is key to identifying and understanding new therapeutics to treat (or even reverse) the underlying causes of seizures rather than the seizures themselves."

The study will see an investment of €91,286, over three years. 50% of the funding for this project has been made available by the Health Research Board (HRB) through the Joint Funding Scheme operated by the HRB and Health Research Charities Ireland. Epilepsy Ireland will fund the other 50% which would not have been possible without your support.

PREDICTING AND MONITORING OUTCOMES IN AUTOIMMUNE ENCEPHALITIS (POTA)

Autoimmune encephalitis (AE) is a rare cause of epilepsy. It is an inflammatory disease of the brain. This means that the body's own immune system attacks healthy brain tissue, just like it would if it were infected by a virus or a bacteria, by producing an army of proteins called 'antibodies' which go on to 'attack' healthy tissues.

Seizures in AE typically do not respond well to normal anti-seizure medications. Instead, medications which suppress the immune system are used to treat it. These can have significant side-effects and some patients will continue to have seizures or experience a recurrence of AE-related epilepsy despite treatment. It is difficult to accurately predict who these outcomes will happen to.

This new study which is being led by Professor Norman Delanty, Consultant Neurologist and Director of Epilepsy Services at Beaumont Hospital will aim to find ways of predicting which people with AE are at greatest risk of these outcomes, so that clinicians can better direct them towards appropriate treatments.

The researchers will collect clinical information and samples of blood and cerebrospinal fluid (fluid surrounding the brain and spinal cord) from people with AE and 'control' participants with other neurological illnesses. They will then analyse these samples for proteins (biomarkers) which may help to predict outcomes in AE such as microRNAs, cytokines, and chemokines. Ultimately, this



Prof Norman Delanty, Consultant Neurologist and Director, Epilepsy Service, Beaumont Hospital & Honorary Clinical Associate Professor, RCSI who will lead this research.

will help better understand the disease and potentially lead to the development of new treatments for AE. Professor Delanty commented on the study, "The mechanisms involved in autoimmune epilepsy are poorly understood and better treatments are needed. Identifying biomarkers that predict responses to treatment would be a major step in improving the care of individuals affected. This study could also lead to greater knowledge and use of early precision therapies in future. It offers significant potential not just for patients in Ireland, but around the world."

€149,924 will be invested in this research over three years. 50% of the funding for this project has been made available by the Health Research Board (HRB) through the Joint Funding Scheme operated by the HRB and Health Research Charities Ireland. Epilepsy Ireland will fund the other 50% - again, which would not have been possible without your support.

RESEARCH NEWS IN BRIEF!

DID YOU KNOW?

If you'd like to read more about all the projects we have funded since 2009, you can find out more about these by visiting the Research section of www.epilepsy.ie

OTHER ONGOING PROJECTS

While not discussed in detail in this edition of our research bulletin, there are other ongoing Epilepsy Ireland research projects which you have helped to support. These include:

- The microbiome as an environmental trigger for autoimmune epilepsy
- MicroRNAs in the mechanism of ketogenic diet therapies and as biomarkers in paediatric epilepsy

You can find more information about these by visiting the Research section of www.epilepsy.ie.

EPILEPSY IRELAND ARE PART OF THE NATIONAL PPI NETWORK!

We are local patient partners with the Royal College of Surgeons in Ireland and Dublin City University as part of the National Public & Patient Involvement (PPI) Network. The basis behind PPI is to ensure that health research and general research is carried out "with" patients and the public rather than being 'about' or 'for' them. In short, the goal of PPI is to ensure that patients with long-term health conditions and the public are at the heart of the decision-making process in research that is conducted. We are delighted to be part of this network and look forward to continuing our work with both institutions.

RESEARCHERS

If you are a researcher and would like to get in touch with our team about an epilepsy-related study that you are conducting/planning to undertake and would like input from people with epilepsy or Epilepsy Ireland, visit the link below to find out what we'll need from you!

▶▶ <https://bit.ly/EIReReq>

NEED FURTHER INFO?

If you would like any further information on epilepsy, Epilepsy Ireland, or any of the projects you've read about, please do not hesitate to get in touch with our team by calling **014557500** or by emailing info@epilepsy.ie.

THANK YOU

For the final time in this bulletin, we'd like to say Thank YOU for supporting Epilepsy Ireland's research activities – as mentioned throughout, without you, these investments would not have been possible. We look forward to sharing further information with you about future research developments and outcomes of existing studies.

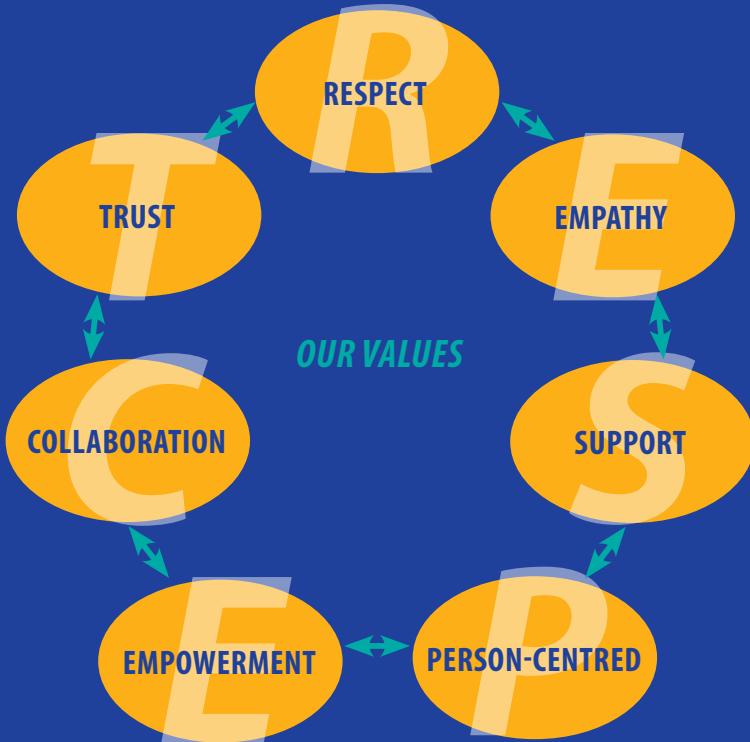


OUR VISION:

To achieve a society where no person's life is limited by epilepsy.

OUR MISSION:

To empower all those affected by epilepsy to achieve their full potential by providing high-quality community-based support and education, raising public awareness, conducting effective advocacy and supporting research.



Rialtas na hÉireann
Government of Ireland



pobal
government supporting communities



Seirbhís Sláinte
Níos Fearr
á Forbairt

Building a
Better Health
Service