DEMENTIA RESEARCH NETWORK IRELAND

Prevention, Cure & Care for Neurodegenerative Diseases

DRNI Early Career Researcher Day

St James's Hospital, Dublin

10th October 2023

ABSTRACT BOOK

Health Research Board

Trinity College Dublin
Coláiste na Tríonóide, Baile Átha Cliath
The University of Dublin

Welcome to the DRNI Early Career Research Day!

We are thrilled to welcome you to the 2023 Early Career Researcher Day, which brings together early career professionals working in neurodegenerative diseases from across disciplines and across the island of Ireland. A major objective for DRNI is to facilitate and support networking and create space for ECRs to meet with their peers and share their research, to promote increased collaboration and career opportunities.

This event was organised by the DRNI ECR Steering Committee:

- Dr Vanessa Moore, DRNI/Trinity College Dublin
- Dr Francesca Farina (Chair), Northwestern University
- Dr Isabelle Killane, TU Dublin
- Carmel Geoghegan, PPI Representative, Dementia Ireland Empowering Communities
- Dr Cassandra Dinius, Maynooth University
- Dr Sarah Nicolas, University College Cork
- Calum Marr, Queen's University Belfast
- Cameron Keighton, University of Galway
- Ying Zhai, University of Galway
- Sinead King, University of Galway
- Dr Aoife McFeely, Tallaght University Hospital

We thank you for joining us and we hope you enjoy the day!

Professor Sean Kennelly
Chair and Principal Investigator, Dementia Research Network Ireland (DRNI)
Clinical Associate Professor, Department of Medical Gerontology, Trinity College Dublin. Consultant Physician in Geriatric and Stroke Medicine, Director of Memory Assessment and Support Service, Tallaght University Hospital.

DRNI supports and facilitates collaborative interdisciplinary research integrating the basic, clinical and social sciences with the aim of bringing about a demonstrable impact on dementia and neurodegenerative disease research, knowledge translation and policy development. DRNI was established in 2012 and is funded by the Health Research Board.

To become a member of DRNI, please contact Vanessa Moore (mooreva@tcd.ie).

PPI Contribution - Dementia Research Advisory Team

DRNI wishes to thank our Public and Patient Involvement (PPI) contributors from the Dementia Research Advisory Team: Janice Nolan Palmer, Ray Creggan, Nuala and Gerry Paley, and Kevin Cullen. The importance of PPI in research cannot be understated, and the presence of PPI representatives was fundamental to this event. We hope that by having PPI representation across judging panels and including the **Best PPI Engagement** prize, our event will encourage all ECRs to engage in PPI as part of their research.

The Dementia Research Advisory Team is a group of people living with dementia and carers/supporters who are involved in dementia research as co-researchers. These Experts by Experience influence, advise, and work with researchers across Ireland. To learn more about the work of the Dementia Research Advisory Team, please click HERE or email ciara.oreilly@alzheimer.ie.

Acknowledgements

DRNI wishes to thank the ECR Day Judging Panel for contributing their time and expertise: Dr Claire McEvoy, Queen's University Belfast; Dr Joanna McHugh Power, Maynooth University; Sean Donal O'Shea, Alzheimer Society of Ireland; Clodagh O'Donovan, Trinity College Dublin; Dr Román Romero-Ortuño, Trinity College Dublin; Dr Caoimhe Hannigan, National College of Ireland.

DRNI wishes to thank the representatives of funding organisations for sharing their knowledge and insights into the funding landscape for ECRs across Ireland: Dr Annalisa Montesanti, Health Research Board; Dr Martha Cahill, Horizon Europe; Dr Roisin Cheshire, Science Foundation Ireland; Emma Stone, Alzheimer Research UK; Dr Anne Marie Miller, Dementia Trials Ireland.

DRNI wishes to thank Brice Cortadi who did the graphic design for the event.

Finally, a sincere thank you to all the ECRs who are attending in-person and virtually, and to those who submitted abstracts to present their research.

Programme

Davis Coakley Theatre, First Floor, MISA Building, St James's Hospital, Dublin 8

09.30-10.00 **Registration**

10.00-10.05 **Welcome**
Dr Isabelle Killane, Technological University Dublin

10.05-11.25 **Public and patient involvement and the lived experience of dementia**
Oral presentations

11.25-11.50 **Coffee break and posters**

11.50-13.10 **Diagnostics, therapeutics, and improving quality of life and healthcare in dementia**
Oral presentations

13.10-14.10 **Lunch and networking**

14.10-15.30 **Dementia risk reduction and prevention**
Oral presentations

15.30-15.50 **Coffee break and posters**

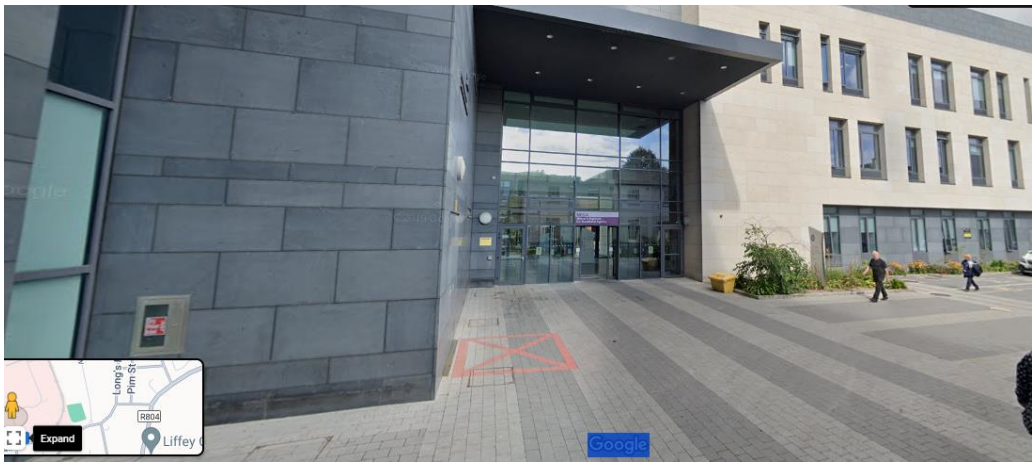
15.50-16.30 **Panel Discussion with funders**
Chair: Dr Francesca Farina, Northwestern University

- Dr Annalisa Montesanti, HRB
- Dr Martha Cahill, Horizon Europe
- Dr Roisin Cheshire, SFI
- Emma Stone, Alzheimer Research UK
- Dr Anne Marie Miller, Dementia Trials Ireland

16.30-16.45 **Prize giving and closing remarks**
Dr Vanessa Moore, DRNI

Venue

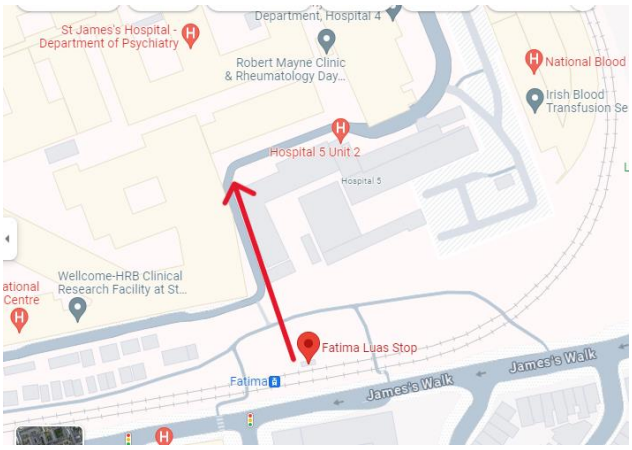
The event is taking place in the Davis Coakely Theatre, First Floor, Mercer's Institute for Successful Ageing (MISA), St James's Hospital, Dublin 8.



Directions to the venue will be signposted from the MISA entrance and from the main St James's Hospital entrance.

By public transport

The easiest way to get to St James's with public transport is via the red LUAS line (which serves both Connolly Station and Heuston Station). The Fatima LUAS stop is the closest to the MISA Building. When you get off the tram, walk across the pathway past the coffee van and in through the back gates. MISA is directly in front of you. There is also a James's LUAS stop, which brings you to the front of the Hospital campus.



The 123 bus stops on the St James's Hospital campus. There is also a Dublin Bike station at the James's Street end of the St James's Hospital campus.

By car

If you are driving, please note that while parking facilities exist, it is very difficult to get a parking spot in St James's Hospital.

Oral presentations

Theme 1:

Dementia risk reduction and prevention

Exploring the epigenome to identify biological links between the urban environment and neurodegenerative disease: an evidence review

Sophie Glover, PhD candidate, School of Medicine, Dentistry and Biomedical Sciences, Centre for Public Health, Queen's University Belfast

The urban environment in which the majority of the global population lives includes characteristic features and pollutants which impact human health. Pollutants including air, noise, soil, water and light pollution are linked to higher risk of mild cognitive impairment (MCI) and dementia. Conversely, features of the urban environment including urban green and blue spaces have been suggested to be of benefit to cognitive function, potentially reducing the risk of MCI and dementia. The biological pathways linking the urban environment to cognitive outcomes are not fully understood. Epigenetics is a molecular biological field which may aid our understanding of the underlying biology linking the urban environment with MCI and dementia. Analysing epigenetic profiles has the potential to reveal causal relationships between the urban environment and MCI through epigenetic mechanisms. This research offers crucial insights into modifiable environmental exposures that could diminish MCI and dementia risk amongst older adults.

The Brain Busters Project! The benefits of Cognitive Stimulation for Adults with Intellectual Disabilities at high risk of developing Alzheimer's disease in the future – A Pilot Randomised Control Trial

Sharon Hardiman, Senior Clinical Psychologist, Saint John of God Community Services Dublin South East

Dr Sharon Hardiman[1], Rory Cousins[2], Dr Aisling Ryan[1], Maria Kennedy[1], Leigh Hagan[1], Dr Flavia H. Santos[3]

[1]Saint John of God Community Services Dublin South East
[2] Saint John of God Research Foundation
[3] School of Psychology, University College Dublin

Adults with Down syndrome (DS) are at significantly increased risk of developing Alzheimer's disease (AD) but there is a distinct lack of research investigating how this risk might be reduced. We used a pilot randomised control trial (RCT) design to assess the feasibility and efficacy of a standardised 14-session group-based Cognitive Stimulation Therapy (CST) programme that we adapted for adults with DS. Participants were adults with DS and moderate ID, aged between 20 – 45 years and were randomised to either the CST (n = 6) or control (services as usual; n = 6) condition. Assessments of cognition (episodic memory, verbal fluency), memory self-efficacy, perceived wellbeing and adaptive behaviour were administered at pre- and post-programme. Preliminary results indicate that CST is both feasible and beneficial for younger adults with DS and moderate ID. It is imperative that larger scale research trials are supported to continue to build evidence in this important area.

LUHMES cells: A new window into therapeutics for Parkinson's Disease

Cameron Noah Keighron, PhD Researcher, School of Physiology, Department of Medicine, University of Galway

Neurodegeneration (ND) is hallmarked by the progressive loss of dopaminergic neurons and/or significant protein aggregates in the brain. Neurodegenerative diseases are a leading cause of death worldwide. The current mainstay of therapeutics includes pharmacological approaches such as levodopa to replace dopamine in Parkinson's Disease(PD) patients. However, these treatments are typically not disease-modifying but do help at least for a period with symptom management. However, there are several limiting factors to the development of novel therapeutics. These include physiologically relevant disease models and therapies able to pass the blood-brain barrier. miRNA-enhanced Extracellular Vesicles may allow for normal development, physiology, and neurogenesis in the central nervous system. Alongside this, they may influence the levels of alpha-synuclein (α-Syn) and other protein aggregates thus reducing associated mitochondrial and oxidative stress. Our work focuses on using the LUHMES (Lund Human Mesencephalon cells) cells, a dopaminergic cell type, in tandem with Extracellular vesicles to explore restoring ATP levels in vitro, reducing superoxide production protein aggregates and restoring native electrophysiological functions in PD.

Gait Speed – A Useful Addition to Dementia Risk Prediction in Midlife? Results from ENBIND

Laura Morrison, MD candidate Trinity College Dublin, Tallaght University Hospital

Introduction: Midlife Type 2 Diabetes Mellitus (T2DM) is associated with a two-fold increased risk of developing dementia in later life, however, knowledge of potential biomarkers indicating the individuals at greatest risk is limited. Methods: ENBIND is a longitudinal study of cognitively-healthy middle-aged adults with T2DM (without microvascular/macrovascular complications) and healthy controls. Gait speed was measured across three tasks (usual speed, maximal speed and cognitive dual-task). Montreal Cognitive Assessment (MoCA) and a custom CANTAB battery were used to assess domain-specific neuropsychological performance with identical assessments repeated after 4 years. Results were analysed using linear regression. Results: 59 individuals (55.8 ± 9 years; 47% female) were followed up. 76.7% (n=23) had midlife T2DM. Individuals with T2DM did not experience greater cognitive decline over 4 years. Baseline "usual" gait speed (not dual-task or maximal speed) was associated with MoCA score at 4 years, which persisted on controlling for T2DM status, age, sex and baseline cognition. Conclusion: "Usual' gait speed in midlife, in a population with known dementia risk factors, may be a useful adjunct to identify those at greatest risk of longitudinal cognitive decline.

Nutritional Adequacy in Older Adults with Subjective Cognitive Decline enrolled in the PROMED-EX Trial

Nicola Ann Ward, PhD candidate, Centre for Public Health, Queen's University Belfast

Nicola Ann Ward[1], Lorraine Brennan[2], Lisette CPGM de Groot[3], Michelle C. McKinley[1], Federica Prinelli[4], Giuseppe Sergi[5], Caterina Trevisan[5], Dorothee Volkert[6], Jayne V Woodside[1], Claire T. McEvoy[1].

[1]Centre for Public Health, Queen's University Belfast
[2]School of Agriculture and Food Science, Institute of Food and Health and Conway Institute, University College Dublin, Dublin, Ireland.
[3]Division of Human Nutrition, Wageningen University, Wageningen, Netherlands
[4]Epidemiology Unit, Institute of Biomedical Technologies, National Research Council (CNR), Segrate (MI), Italy
[5]Department of Medical Sciences, University of Ferrara, Ferrara, Italy,
[6]Institute for Biomedicine of Aging, Friedrich-Alexander-Universität Erlangen-Nürnberg, Nuremberg, Germany.
[7]The Global Brain Institute, Trinity College Dublin, Ireland & University of California San Francisco, USA.

A nutrient-dense diet may be an effective preventative strategy for undernutrition and cognitive impairment. The PROMED-EX randomised controlled trial is testing a PROtein-enriched MEDiterranean Diet, with or without EXercise on nutritional status and cognitive performance in older adults at risk of undernutrition with subjective cognitive decline. This cross-sectional study aims to determine baseline nutritional adequacy of participants enrolled in PROMED-EX. Nutritional adequacy was determined by comparing sex- and age-specific UK Dietary Reference Values (DRV), for nutrients derived from completed 4-day food diaries.

Participants (n=62; 60% female; 68±6years; BMI: 23.3±2.7kg/m2) had high risk of nutrient inadequacy, particularly for Vitamin D, fibre, and selenium. More than 50% failed to meet nutritional adequacy for vitamin A, iodine, iron, magnesium, and potassium, and over 25% had suboptimal intakes for omega 3, folate and calcium.

A protein enriched Mediterranean diet intervention may be beneficial to optimise nutrient status in this population with suboptimal dietary intake.

Real-time EEG Spectral Analysis based on Linear Predictive Coding to Support Dementia Research

Jin Xu, Postdoctoral researcher, School of Computer Science, University College Dublin

This work presents a novel approach for real-time EEG spectral analysis using a modified Linear Predictive Coding (LPC) to aid dementia research. Dementia is a growing global health concern, necessitating advanced tools for early detection and monitoring. Our method leverages LPC to extract spectral features from EEG signals in real-time, allowing for continuous monitoring of brain activity. We demonstrate the effectiveness of our approach through extensive experimentation, showcasing its potential in identifying spectral abnormalities associated with dementia. Real-time analysis enables timely intervention and contributes to a deeper understanding of dementia progression. This innovative technique holds promise for improving the accuracy and efficiency of dementia research, ultimately leading to enhanced diagnostic and therapeutic strategies.

Theme 2:

PPI involvement and the lived experience of dementia

Engaging lived experience in advance care planning through co-operative inquiry

Jennifer Allen, PhD Candidate, School of Social Policy, Social Work and Social Justice, University College Dublin

This presentation focuses on the participatory (PPI) process of a three-stage action research doctoral study focusing on advance care planning in a Mental Health Service for Older Persons (MHSOP), including persons with dementia. The MHSOP is committed to creating a culture of recovery which emphasises lived experience, promoting engagement in co-production and collaboration with service users and families. The PPI element was also guided by the Framework of Public Engagement.

Methodology: Stage two involves a co-operative inquiry group with health care professionals (HCP's) and service users, which involves participants acting together as co-researchers and co-subjects. Stage three will involve stakeholder engagement with day hospital groups and carers of persons living with dementia.

Findings/ Conclusion: The co-operative inquiry group provided a self-identified forum for developing understanding and upskilling in advance care planning processes. Both service users and HCP's engaged extremely well in the collaborative process and recognised the benefits of collaboration. Attention must be taken to creating a relational space that privileges all voices and ensures that service users feel comfortable and valued. The cooperative inquiry process will influence practice and pathways for advance care planning within the MHSOP.

A collaborative multicomponent wellbeing intervention for women caregivers of people living with dementia in Colombia

Sandra Baez, Atlantic Fellow for Equity in Brain Health, Global Brain Health Institute (GBHI), Trinity College Dublin, and Los Andes University, Bogota, Colombia

Caring for people with dementia can be one of the most stressful forms of caring. In Colombia, 80-90% of dementia caregivers are women. However, there is a significant shortage of interventions designed for women caregivers of people living with dementia, particularly for vulnerable populations. This project aims to design a multicomponent intervention to enhance the subjective wellbeing of women dementia caregivers living in low socioeconomic levels in Colombia, using public patient involvement (PPI) at different project stages. This project will consist of three primary aims: (a) identify the most relevant psychosocial factors associated with the subjective wellbeing of women dementia caregivers of low socioeconomic status, and to understand their desires and needs from an ideal intervention; (b) analyse the results from Step I with an expert panel, and design a tailored program; and (c) evaluate and modify the proposed program according to the feedback provided by potential users.

Young Onset Dementia: Examining the experience through Family Systems Theory

Cathal Blake, PhD Candidate, School of Psychology, Dublin City University

Research into young onset dementia (YOD) typically focuses on the issues couples face – i.e., the dyad of carer and the person with young onset dementia (PwYOD). This study examined YOD from the broader family systems approach, focusing on the impact on the entire family.

Methods: Firstly a participatory workshop with members of the Alzheimer Society of Irelands (ASI) Dementia Research Advisory Team (DRAT: n = 3) was conducted to uncover specific issues of relevance to PwYOD that could subsequently be explored through focus groups. Focus groups involved PwYOD and their family members including children (n = 44).

Findings: Five main themes emerged: initial onset of dementia; personal and social impact; behavioural and psychological symptoms of dementia; adaptive support and the shifting family roles.

Conclusion: It is clear from the current data that a diagnosis of YOD results in significant challenges for the entire family system.

What are the research priority topics for Lewy body dementia in Ireland?

Rachel Fitzpatrick, PhD candidate, School of Medicine, Trinity College Dublin

Rachel Fitzpatrick, Irina Kinchin, Panos Alexopoulos, Iracema Leroi

Background: Lewy body dementias (LBD) account for approximately 10-15% of all dementia cases yet remain significantly under-represented in dementia research. To address this gap and ensure that people with lived experience have an opportunity to set the research agenda, we conducted a multi-stakeholder' priority setting partnership' (PSP) study.

Methods: An Irish national collaborative study took a 3-stage approach. Stage 1) AI topic modelling of the global LBD literature to identify the 25 most frequently researched topics about LBD. Stage 2) A scoping review of LBD research priorities to generate a 'long list' of research priority questions (RPQs). Stage 3) An online survey to identify the ten most important RPQs for LBD in Ireland. Participants included adults living with LBD, family carers, and health professionals in relevant specialities who have managed or experienced LBD.

Results: AI modelling yielded 522 abstracts, highlighting the leading research areas in LBD globally, including diagnostic classification, prevalence, clinical data, and biomarker features. A prioritisation survey was undertaken, garnering responses from 46 individuals. Of these respondents, 70% were researchers or healthcare professionals, while 30% were individuals with lived experience. This survey distilled the research focus into ten key RPQs, ranging from LBD's causes and risk factors to its progression, diagnostic challenges, support services, and treatments.

Conclusions The RPQs highlighted evidence gaps in LBD research, encompassing both clinical aspects and the lived experiences of those directly impacted. These findings will steer future research pertinent to the Irish population and beyond, providing valuable insights for researchers and funding bodies.

The Development of a Dance Exercise Intervention for People Living with Dementia and their Care Partners

Niamh Kelly, PhD Candidate, Department of Sport and Health Sciences, Technological University of the Shannon

Supervisors: Dr Clare McDermott[1], Dr Fiona Skelly [1], Dr Kieran Dowd [1], Professor Desmond O'Neill [2,3,] Dr Noel McCaffery[4]

[1]Department of Sport and Health Sciences, Technological University of the Shannon.
[2]Tallaght University Hospital.
[3]Trinity College Dublin.
[4]ExWell Medical.

Dance exercise is an appropriate form of exercise for PLWD and their care partners as it combines endurance, coordination, strength and social interaction1. It provides many of the same benefits as an exercise intervention with added balance and memory enhancements 2. The aim of this study is to develop a person-centred, dance exercise intervention for PLWD and their care partners.

A participant advisory group (PAG) advised on components of the intervention development. The methods were informed by the Medical Research Framework and the Behaviour Change Wheel framework 3, 4 . Focus groups and interviews conducted with PLWD and care partners. From this dance exercise intervention components were developed. The intervention components were presented to a stakeholder expert panel. Their feedback was applied to the intervention.

Content analysis was used to develop themes from the collected qualitative data. The intervention components were informed by combining the information from previous literature and the results of the content analysis.

The Buddy Programme – An Intergenerational Dementia Intervention

Cíara O'Reilly, Masters by Research Candidate, School of Psychology, Dublin City University

In Ireland, 63% of people living with dementia live at home in their community. The most common social supports available to them include day centres, social clubs and befriending services. However, these do not suit all people affected by dementia. It is therefore necessary to provide an alternative support to meet the social and cognitive needs of these people.

Intergenerational programmes refer to opportunities where non-familial young people and older adults are brought together to connect through meaningful activities, with a view to increasing positive attitudes to ageing whilst simultaneously providing space for social connectedness. The Buddy Programme is an online intergenerational psychosocial intervention, partnering people living with dementia with a student "buddy" for 6 weeks, engaging in a shared interest.

This presentation explores the data collected through semi-structured interviews and focus groups, the Person Public Involvement-led design, and results highlighting the strengths and limitations of an intervention of this nature.

Theme 3:

Diagnostics, therapeutics and improving quality of life and healthcare in dementia

A Sex Stratified Approach to Drug Repurposing in Alzheimer's Disease

Chloe Anderson, PhD Candidate, Personalised Medicine Centre, School of Medicine, Ulster University

Alzheimer's disease (AD) is a neurodegenerative condition characterized by the build-up of amyloid-beta plaques and neurofibrillary tangles. Currently aetiology of disease is unknown, but several factors which increase the risk of developing the disease have been identified, including biological sex. Women are seemingly more at risk than men, with 60% of the AD patient population being post-menopausal women. Despite this difference in risk level men and women receive the same treatments for AD.

Here we attempted to stratify the patient population by sex and then preformed differential gene expression analyses to identify dysregulated genes in the AD patient cohorts. These dysregulated genes where then used to create gene signatures for use in sscMap, a gene expression connectivity mapping software, to identify potential drug repurposing candidates for male, female and all patients in order to determine if men and women would benefit from different drugs for AD.

Looking Beyond the Cognition in Dementia: An Innovative Method in Tertiary Care Practice

Swati Bajpai, Atlantic Fellow, Global Brain Health Institute, Trinity Institute of Neurosciences, Trinity College Dublin, and Clinical Neuropsychology, Neurosciences Centre, & Department of Geriatric Medicine , All India Institute of Medical Sciences, New Delhi, India

Introduction: Cognitive therapy is known for improving cognition; however, its implication on everyday functioning lacks empirical evidence. The aim was to examine the efficacy of extended practice (EP) of cognitive tasks over strategy training (ST) in improving the untrained functional tasks.

Methods: A RCT on 53 participants (27= EP group; 26= ST group) of mild Alzheimer's disease, diagnosed as per gold standard. The EP comprised of 56 individual repeated practice trials each of memory and attention tasks. The ST comprised of 8 dyadic sessions of brief instruction on a mnemonic techniques. The trained outcome was PGI-Memory Scale and the untrained outcome was IADL Scale.

Results: Effect size (ES) was calculated at 2, 5, 8 months respectively. Significant difference was evident in EP group over ST on both the memory (estimated ES =1.12 >1.43>1.66) and IADLS (ES = -14.99 > -15.74> -18.35).

Discussion: EP training has potentiality to extend cognitive benefits to functionality and aid better wellbeing.

Predictive Molecular Modelling-Led Investigations of New Therapeutic Strategies for Parkinson's Disease Dementia

Shayon Bhattacharya, Assistant Professor, Department of Physics, University of Limerick and SSPC, The Science Foundation Ireland Research Centre for Pharmaceuticals, Ireland

Shayon Bhattacharya[1], Lily Arrue[1], Jack O'Callaghan[1], Liang Xu[2], Tim Bartels[3], Olena Synhaivska[4], Peter Nirmalraj[4], Damien Thompson[5]

[1] Department of Physics, University of Limerick and SSPC
[2]FDA/National Center for Toxicological Research, Arizona, USA
[3] UK Dementia Research Institute, University College London, UK
[4] Swiss Federal Laboratories for Material Science and Technology, Dubendorf, Switzerland
[5] The Science Foundation Ireland Research Center for Pharmaceuticals

The 140-residue α-synuclein (α-Syn) intrinsically disordered protein is closely associated with the aetiology of Parkinson's disease (PD) and Lewy body dementia formed in the PD patient brains. Misfolding and aberrant self-assembly of the α-Syn protein monomers can produce neurotoxic β-sheet oligomers that further aggregate into insoluble amyloid fibrils. There is no cure for PD, and the toxic oligomers are very short-lived species which makes them difficult targets for development of therapeutics. In this body of work, we identify three potential therapeutic targets in PD through extensive computational molecular modelling guiding experiments: (1) Re-populating α-Syn helical tetramers that are resistant to toxic aggregation, but are found in very low concentration inside the cells - we design a potential therapeutic approach for PD by remodelling α-Syn interactions with different charged cellular membranes to shift the population balance towards more soluble helical α-Syn tetramers by designed charged micellar nanoparticles; (2) Targeting copper (Cu (II)) ions mediated α-Syn toxic β-sheet trimers - our designed atomic scale models of monomer and oligomers at gold-water interface reveal that at low Cu (II) concentration, trimers facilitate typical fibril growth, while at high Cu (II) concentration, atypical annular shaped trimers form as confirmed by liquid-based atomic force microscopy experiments; (3) Targeting a cell surface receptor, lymphocyte activation gene-3 (LAG-3) - LAG3 binds α-Syn preformed fibrils outside neuronal cells and transmits them inside cells through endocytosis leading to cell death; repurposing antibodies used for anticancer therapy against LAG3 could be an efficient strategy to decouple LAG3-α-Syn interactions.

Viscous dynamics associated with hypoexcitation and structural disintegration in neurodegeneration via generative whole-brain modelling

Carlos Coronel-Oliveros, Atlantic Fellow, Global Brain Health Institute (GBHI), Trinity College Dublin; Latin American Brain Health Institute (BrainLat), Universidad Adolfo Ibáñez, Santiago, Chile; Centro Interdisciplinario de Neurociencia de Valparaíso (CINV), Universidad de Valparaíso, Valparaíso, Chile

Alzheimer's disease (AD) and behavioural variant frontotemporal dementia (bvFTD) lack well-understood characterization in diverse, non-stereotypical, and underrepresented populations. Electroencephalography (EEG) is a high-resolution, cost-effective technique for studying dementia globally, but lacks mechanistic models and produces non-replicable results. We developed a generative whole-brain model that combines EEG source-level metaconnectivity, anatomical priors, and a perturbational approach. This model was applied to Global South participants (AD, bvFTD, and healthy controls). We found that metaconnectivity outperformed pairwise connectivity and revealed more viscous dynamics in patients, with altered metaconnectivity patterns associated with multimodal disease progression. The biophysical model showed that connectome disintegration and hypoexcitability triggered the altered metaconnectivity dynamics, and identified critical regions for brain stimulation. We replicated main results in a second subset of participants for validation with unharmonized, heterogeneous recording settings. The results provide a novel agenda for developing diagnostic methods and model-inspired therapies in clinical, translational, and computational neuroscience.

Building the Bridge: Examining the integration of mental and physical health services to a multidisciplinary Parkinson's memory clinic

Heather Dignam, Visiting Scholar, Dementia Research Group, Trinity College Dublin

The aim of this project was to demonstrate the benefit of a multidisciplinary team for those suffering with Parkinson's Disease by examining the first 100 patients referred to the Mind and Movement clinic at St. James' Hospital. Given how psychiatric and cognitive side effects of Parkinson's have been rated as some of the most challenging of the disease, numerous patients struggle to access services aimed at improving the non-motor side effects.

Results: Data collected showed numerous benefits of having a service aimed at bridging the gap between traditional Parkinsons' services and services that treat non-motor effects, with patients being referred to over 15 separate services within the clinic and almost a third having their medications changed by the clinic's consultant psychiatrist.

Discussion: The data show promise for the future of the Mind and Movement clinic, and highlights the importance of multidisciplinary care for the future of treatment for this progressive disease.

This work was conducted under the supervision of Professor Iracema Leroi and Dr. Panos Alexopoulos.

Participant and caregiver experiences of an Activities of Daily Living-focused Cognitive Stimulation program (CS-ADL) for individuals with mild-to-moderate dementia

Simone Ryan, Research Masters student, Department of Occupational Therapy, School of Health Sciences, University of Galway

Background: Non-pharmacological interventions, such as cognitive stimulation, are increasingly being used to address the cognitive and functional deterioration associated with dementia. This study explored the participant and caregiver experiences of CS-ADL, an activities of daily living-focused group cognitive stimulation program for individuals with mild-to-moderate dementia.

Method: A descriptive qualitative design was implemented. Semi-structured interviews were completed with participant dyads consisting of the CS-ADL participant and their caregiver. Data retrieved were analysed through reflexive thematic analysis.

Results: CS-ADL was experienced as an acceptable intervention that positively influenced the everyday life of both dyad members, with benefits reported in the memory, mood, and social interaction of participants. Furthermore, the facilitation style of group facilitators positively influenced participants' engagement in CS-ADL.

Conclusion: This is the first study to explore experiences of CS-ADL, producing a preliminary addition to the evidence-base for this intervention. However, further, large-scale research is required to enhance confirmability and transferability of study outcomes.

Poster presentations

Theme 1:

Dementia risk reduction and prevention

A Life-cycle Model of Brain Health and Lifestyle Health Behaviours

Daniel Araya-Ríos, PhD candidate, Trépel Lab, Trinity College Institute for Neuroscience, Trinity College Dublin

Daniel Araya-Ríos[1], Dominic Trépel[1]
[1]Trépel Lab, Trinity College Institute for Neuroscience, Trinity College Dublin

We present a conceptual framework for understanding the life-cycle development of Brain Health, focusing on Lifestyle Health Behaviours (LHB) and their impact on Brain Health. Research indicates that 40% of dementia cases can be attributed to these modifiable factors, although the exact mechanisms remain unclear. Drawing inspiration from the Nobel Laureate James Heckman's work on the developmental origins of health, this framework views LHB as investments to improve Physical and Brain Health.

The proposed framework posits that as individuals habituate to these LHBs over time, the effort required decreases, thus temporary nudges that ease the effort required can disrupt established habits and promote behavioural change. Our framework anticipates that temporary nudges can reduce the risk of dementia during all stages of life.

This approach provides insights into the interplay between lifestyle choices, habituation, and dementia risk, offering an avenue for future research and preventive strategies.

Functional connectome-based prediction of individual clinical and cognitive scores in midlife population with risk of dementia

Bolin Cao, PhD candidate, Global Brain Health Institute, Trinity College Dublin

It is well acknowledged that Alzheimer's Disease (AD) neuropathology starts decades before clinical manifestations, but the brain mechanism of sporadic AD in midlife remains unclear. Resting-state functional connectivity (FC) is increasingly used to understand early brain changes in AD (Sperling, 2011; van den Heuvel & Sporns, 2019). We asked whether the risk for late-life dementia impacts functional connectivity in cognitively healthy middle-aged individuals.
Methods: Functional Magnetic Resonance Imaging and detailed neuropsychological assessments were obtained for 585 (207/378 female/male) cognitively healthy individuals aged 40-59 years (mean = 50.9), from the PREVENT-Dementia study. Dementia risk was calculated with the Cardiovascular Risk Factors, Aging, and Dementia (CAIDE) score. A novel connectome-based predictive method called NBS-Predict was used to investigate the association between FC and CAIDE scores and its role in cognition.
Results: FC significantly predicted CAIDE scores across the whole cohort ($r = 0.207$, $p < 0.001$). FC within and between the cingulo-opercular network (CON) and sensorimotor network (SMN), as well as between CON and fronto-parietal network (FPN), and between SMN with default mode network (DMN), and FPN contributed the most (Figure 1). Furthermore, we found that in the high dementia risk group (CAIDE > 6) only, FC, mainly in DMN-SMN and DMN-CON (Figure 2), significantly predicted multisensory processing cognitive score ($r=0.114$, $p<0.05$).
Conclusion
Our results show that FC can be used to detect early brain changes associated with the risk of future dementia in cognitively healthy individuals. This method has implications for the early detection of dementia in preclinical populations.

An Audit of Referrals to Sleep Services from General Dental Practice in Ireland

Stephen Paul Kelly, Ennis Dental Health Centre & Faculty of Dentistry, RCSI

Introduction: Identification of modifiable risk factors is key to alleviating cognitive disorder impact on the population. A link has been established between Dementia and Obstructive Sleep Apnea (OSA). Epidemiological studies show high prevalence estimates for OSA in the general population, the majority of which are undiagnosed. Objectives: To assess if a general dental practice is an effective setting for OSA screening. Method: Sleep study reports received by a referring dentist were obtained and analysed. Results: A total of 35 (Male: Female = 20:15) sleep reports were received in response to the referrals. Of these, 27 (77.14%) were positive for sleep apnea (Mild = 11 (31.43%), Moderate = 13 (37.14%), Severe = 3 (8.57%)) with 8 (22.86%) displaying no apnea. Conclusion: Screening for OSA in general dental practice in Ireland is effective. Efforts to explore the viability of a referral pathway from dentists to sleep services is warranted and may serve as part of a wider prevention and risk reduction approach to dementia.

The effect of mindfulness-based intervention on cognitively unimpaired older adults' cognitive function and sleep quality: a systematic review and meta-analysis

Colm Lannon-Boran, PhD Candidate, Maynooth University & National College of Ireland

Objective: This systematic review and meta-analysis aimed to investigate the effect of mindfulness-based intervention (MBI) on cognitively unimpaired older adults' cognitive function and sleep quality. Method: Studies published in English since 2010 were considered for inclusion. Databases searched were PubMed, Embase, Web of Science, and PsycInfo. We included randomized controlled trials (RCTs) with adults over 55 with no known cognitive impairment, that recorded cognitive outcomes and/or sleep quality pre- and post-intervention, and that implemented Mindfulness-Based Stress Reduction (MBSR), or an MBI closely based on MBSR protocol. Results: Seven RCTs fit the inclusion criteria, with 276 participants in MBI groups and 287 in controls. Four studies investigated mindfulness and cognitive function, two investigated mindfulness and sleep quality, and one investigated mindfulness, cognitive function, and sleep quality. Some studies were not reported in sufficient detail to be included in meta-analyses. Results of meta-analyses showed no significant differences between MBI groups vs controls on cognitive measures of executive function, free recall, and delayed recall. Meta-analysis revealed that MBI significantly improved sleep quality compared to controls. Conclusion: Given that poor sleep quality is strongly linked to increased risk of cognitive decline, further research investigating sleep quality's role in the mindfulness-cognitive function relationship in cognitively unimpaired older adults is recommended.

Acting in concert - soluble Tau and Aß in patient brain-derived extracts rapidly and persistently disrupt synaptic plasticity in vivo

Tomas Ondrejcak, Department of Pharmacology & Therapeutics and Institute of Neuroscience, Trinity College Dublin

Tomas Ondrejcak[1], Igor Klyubin[1], Neng-Wei Hu[1,2], Michael J. Rowan[1]

[1]Department of Pharmacology & Therapeutics and Institute of Neuroscience, Trinity College Dublin
[2]Department of Physiology and Neurobiology, School of Basic Medical Sciences, Zhengzhou University, 100 Science Avenue, Zhengzhou 450001, China

Amyloid ß (Aß) and tau, the two central proteins involved in causing Alzheimer's disease (AD), can trigger synaptic dysfunction before apparent synaptic loss occurs in vulnerable brain circuits. Whereas soluble Aß from AD brains are potent synaptotoxins less is known about the synaptotoxicity of soluble tau in the brains of patients with AD or other tauopathies like Pick's disease (PiD). Here, we explore how soluble Aß and tau in extracts of patient brains contribute to persistent disruption of synaptic plasticity in the hippocampal CA1 area of urethane-anaesthetized rats. We found that persistent LTP disruption caused by single i.c.v. injection of aqueous extracts from patient brains was abrogated by immuno-neutralization using either anti-tau or anti-Aß antibodies when administered 2-4 weeks later. These findings support a critical role for diffusible tau in causing rapid onset, persistent synaptic plasticity deficits and in promoting Aß-mediated synaptic dysfunction.

Factors influencing variation in dementia risk literacy in Ireland, a cross-section analysis

Naoise Rasmussen, PhD candidate, Department of Health and Nutritional Science, Atlantic Technological University, Sligo

While knowledge of established risk factors for dementia have been assessed in Ireland, limited research on emerging risk factors has been conducted.

A cross-sectional online study was conducted between November-December 2022 in a sample of the Irish population. A statistical analysis of the measured dementia awareness levels, and how individual and environmental factors contributed to these levels was performed.

Overall, poor knowledge of risk factors and better knowledge of protective factors was observed (n=289). Lower knowledge levels were associated with self-reported low dementia knowledge (p=0.021), self-reported high dementia knowledge (p=0.019), age group 18-34 years (p=0.043) and 35-44 years (p=0.012) relative to the base category of 55-65+ years, gender (female) (p=0.049), and dementia exposure (p=<0.001).

Dementia knowledge was poor. As the levels of awareness vary across several factors, the need for targeted awareness campaigns designed to reach those with the lowest awareness levels are suggested to improve health literacy around dementia.

Sex differences in the associations between the risk for late-life Alzheimer's disease, protective lifestyle factors and cognition in mid-life

Qing Qi, PhD candidate, School of Psychology, Trinity College Dublin

Abstract: It is now acknowledged that Alzheimer's Disease (AD) processes are present decades before the onset of clinical symptoms, but it remains unknown whether lifestyle factors can protect against these early AD processes in mid-life and whether the protective effect varies by sex. To address this gap, 491 participants (40–59 years) data were collected from cognitive tests, clinical assessments, and Lifetime of Experiences Questionnaires. We assessed the impact of lifestyle activities, AD risk, sex, and their interactions on cognition. We replicated the previous finding that more frequent engagement in stimulating lifestyle activities was associated with better episodic and relational memory. We also found only for APOE Ɛ4+ females, higher occupational attainment was associated with better episodic and relational memory. These findings suggest an urgent need for targeted research on female-specific risk factors, to inform personalised strategies for AD prevention and the promotion of female brain health.

Biological Sex Influences Exercise-induced Changes in Memory and Mood in Alzheimer's Disease: A Preclinical Study

Zoe Williams, PhD candidate, Department of Anatomy and Neuroscience, University College Cork

Zoë A.P. Williams[1,2], Sarah Nicolas[1,2], John F Cryan[1,2], Yvonne M Nolan[1,2]

[1]Department of Anatomy and Neuroscience, UCC, Ireland
[2]APC Microbiome Ireland, UCC, Ireland

Exercise may have beneficial effects on the cognitive and mood impairments seen in Alzheimer's disease (AD). However, little research has explored whether the benefits of exercise are sex specific. We explored the effects of exercise (home cage running wheel access) on cognition and anxiety-like behaviours in five-six month old male and female 5xFAD mice (genetic mouse model of AD) and 5xFAD wildtype littermates (controls) (n=8-22). Four weeks after beginning the exercise intervention, behavioural tests were conducted. Voluntary exercise had sex dependent effects on cognition and anxiety-like behaviours, contributing new knowledge to the efficacy of exercise as a mitigation strategy against the behavioural symptoms of AD.

Theme 2:

PPI involvement and the lived experience of dementia

Improving Research with Long-Term Care Facility Residents with Dementia in Ireland

JP Connelly, PhD candidate, School of Medicine, Trinity College Dublin

The number of long-term care facility (LTCF) residents with dementia (RwD) is expected to rise significantly over the next two decades. Combined with a more complex resident profile, this will place huge pressure on LTCFs to maintain care standards. Innovative solutions are urgently needed to meet these increasingly complex care needs but recruitment of LTCFs to research is challenging. This PhD research will ascertain barriers and facilitators to LTCF research participation, identify research priorities concerning RwD and outline a roadmap for prioritising research with this population.

Method: A nationwide survey (n=200) and interviews (n=20) with key LTCF stakeholders (managers/directors of nursing, care staff, RwD and family of RwD) proceeded by focus groups to deliver a roadmap for prioritising research with RwD.

Results: Preliminary findings from the survey (n=67) indicate barriers to participation such as concern about nursing home information falling into wrong hands and belief that the research will not benefit residents. Motivators include trust in the person running the study and easy to understand study objectives and study language. 85% reported yes or maybe to being interested in actively developing research.

Conclusions: By articulating the research landscape in LTCFs, this research will facilitate the design and delivery of more targeted interventions for RwD at all stages of the disease course. This will also begin to lay the foundation for the creation of a research ready network of LTCFs based on the UK's ENRICH model.

Neuromodulation for Cognitive Impairment in Parkinson's Disease: Exploring Patient Acceptance

Ananya Sanagavaram, School of Medicine, Trinity College Dublin

Ananya Sanagavaram[1], Liam Kennedy[1,2,3], Sven Vanneste[1,2,3], Iracema Leroi[1,2,3].

[1]Trinity College Dublin, Ireland
[2]Global Brain Health Institute, Dublin
[3]HRB-CTN Dementia Trials Ireland

Background: Parkinson's disease affects over 10 million people, with cognitive decline in up to 80% of cases (1). No approved interventions exist for Parkinson's mild cognitive impairment (PD-MCI), emphasizing an urgent need for non-pharmacological research (2). Occipital Nerve Stimulation (ONS) shows promise for PD and Lewy Body Dementia.

Methods: A 32-item survey assessed knowledge, attitudes, and perspectives on non-drug therapies, including ONS, in 50 members from Parkinson's Association Ireland (PAI) and Lewy Body Dementia Ireland (LBDI).

Results: A majority (84.2%) considered cognitive impairment in PD important, with 83.4% recognizing the significance of non-drug treatments. Key factors influencing non-drug treatment choices included safety and clinician qualifications. Concerns included electrode wear and 'unnatural' sensations.

Conclusion: This study reveals substantial receptivity to non-drug treatments within the PD population emphasizing the need for further exploration. Ensuring safety and comprehensive information regarding side effects and device usage is vital for promoting patient engagement in these therapies.

Theme 3:

Diagnostics, therapeutics and improving quality of life and healthcare in dementia

Ultra-widefield retinal imaging in Down syndrome: A high-risk population for dementia

Lajos Csincsik, Postdoctoral Research Fellow, School of Medicine, Dentistry and Biomedical Sciences, Queen's University Belfast

Jamie Mitchell[1], Adam Threlfall[2], Tom MacGillivray[2], Jessica Beresford-Webb[3], Madeleine Jane Walpert[3], Tunde Peto[1], Tony Holland[3]; Imre Lengyel[1], Lajos Csincsik[1]

[1]School of Medicine, Dentistry and Biomedical Sciences, Queen's University Belfast
[2]University of Edinburgh, Edinburgh, United Kingdom
[3]University of Cambridge, Cambridge, United Kingdom

Introduction: People with Down syndrome (pwDS) have a high prevalence of early-onset Alzheimer's disease (AD). With the two-fold increase in life expectancy for pwDS, identifying early biomarkers for AD in this patient population is needed. Previously we have shown that using ultra-widefield retinal imaging (UWFI) has the potential to identify peripheral-retinal biomarkers for AD in the general population. In this study, the feasibility and the utility of UWFI in pwDS is investigated.

Methods: UWFI was performed on 24 pwDS and 17 cognitively healthy, age- and sex-matched controls (ctrl). Images were analysed for non-vascular and vascular changes.

Results: There was a lower retinal-vascular-fractal-dimension (RVFD) in pwDS compared to Ctrl, and a positive correlation between cognitive-scores and RVFD in pwDS when peripheral retina was assessed.

Conclusions: UWFI proved feasible in pWD, opening up the potential of detailed peripheral retinal phenotyping and monitoring the progression of AD in this patient population.

Patient and care partner preferences in the management of dementia with Lewy bodies: protocol for a preference elicitation study

Paula Sinead Donnelly, Centre for Public Health, School of Medicine, Dentistry and Biomedical Sciences, Queen's University Belfast

Currently there is heterogeneity in the primary outcomes investigated in dementia with Lewy bodies (DLB) trials, and the perspectives of people affected by DLB do not appear to be reflected in trial design. This study aims to elicit the treatment preferences of those affected by DLB to inform the choice of person-centred trial outcomes.

Using global voluntary sector networks, we will recruit people diagnosed with DLB and their care partners (n = 135). We will disseminate a web-based survey incorporating two preference elicitation techniques from health economics: best-worst scaling and a discrete choice experiment. The study has been designed with people with DLB, and the challenges they face, in mind. People with DLB will therefore have the option of completing an alternative interview survey.

We will determine preferences for treatment characteristics and the trade-offs people are willing to accept between treatment efficacy and risk of adverse effects.

Emerging Drug Treatments for Early Alzheimer's Disease and Suggested Global Prices Based on a Model-based Cost-Effectiveness Analysis

Men Thi Hoang, PhD candidate, Trépel Lab, Trinity College Institute for Neuroscience, Trinity College Dublin

Men Thi Hoang[1], James G. Kahn[1], Dominic Trepel[1]

[1]Trépel Lab, Trinity College Institute for Neuroscience, Trinity College Dublin

Introduction: Numerous disease-modifying treatments (DMTs) for early Alzheimer's disease (AD) are progressing through phase II and III trials, marking significant AD therapeutic advancements. The U.S. Food and Drug Administration (FDA) has accelerated approval for two amyloid-targeting treatments, Aducanumab and Lecanemab, and is assessing Donanemab despite ongoing clinical and economic effectiveness controversies. However, their extremely high prices in the US market ($28,200 for Aducanumab and $26,500 for Lecanemab annually) and the lack of coverage elsewhere raise global accessibility and affordability concerns. This study, therefore, aims to conduct a cost-effectiveness (CE) analysis of the three mentioned DMTs to recommend global pricing based on country-level CE thresholds.

Methods: We constructed a five-state Markov model (i.e., MCI due to AD, Mild, Moderate, Severe and Death states) to estimate the CE of the three mentioned DMTs compared to usual care over the lifetime horizon. To allow direct comparison of trials with different outcome measures, we incorporated crosswalks between the measures. We employed country-level CE thresholds to estimate global pricing points. Robustness for the model was assessed using probabilistic sensitivity and scenario analyses.

Expected results: This ongoing cost-effectiveness analysis will present estimated outcomes including discounted costs, quality-adjusted life years (QALYs) and incremental CE ratios (ICER) for three DMTs in the U.S. as a base case and then adapt to other countries. Threshold analysis will estimate the optimal pricing points which will be summarised in a table for reference.

Conclusion: Our findings are expected to reveal significant price disparities based on global country-level CE thresholds. Thus, there is a crucial need to implement pricing policies tailored to the country level to tackle affordability and inequalities in patient access worldwide.

An Irish Multi-Hospital Longitudinal Study of Discharged Patients with A Diagnosis of Dementia

AnnMarie Kilgannon, Ireland East Hospital Group

Approximately 64,000 people in Ireland are living with dementia. The care of people living with dementia poses increasing challenges in acute inpatient settings, yet a lack of data exists in Ireland and Europe on the distribution and prevalence of dementia across acute hospitals. To date studies indicate a dementia prevalence in adult inpatient admissions of 29% in 6 Cork hospitals and 42.4% in a single London teaching hospital.

Aim: Identify the prevalence of patients aged 65 years and older discharged with a dementia diagnosis from ten acute hospitals within Ireland East Hospital Group (IEHG). Identify the prevalence of patients under 65 years discharged with a dementia diagnosis from ten acute hospitals within IEHG.

Methods: Retrospective longitudinal analysis of IEHG discharge data extracted from NQAIS Clinical from January 2018 to December 2022.

Results: According to data retrieved from NQAIS Clinical for those over 65 years, only 1% of patients discharged from ten acute hospitals within IEHG had a dementia diagnosis in 2018. This figure remained relatively unchanged between 2018 and 2022. A decrease of 0.04% was noted during the COVID-19 pandemic in Ireland from March 2019 to early 2021. Data recorded for patients under 65 years indicates a gradual upward trend from 2018 to 2022.

Conclusions: Ireland has no systematic approach to the collection and analysis of dementia data. This data only includes diagnosed dementia cases, entirely relying on hospital record documentation. These results reinforce the lack of accurate dementia diagnosis recording and coding within the acute setting and highlights the need for improvement of dementia services given the rising number of dementia diagnoses.

Polymeric nanoparticles as drug delivery tools for brain degenerative disorders; in vitro assessment and release properties

Rebecca Maher, PhD candidate, Trinity College Institute of Neuroscience & School of Pharmacy and Pharmaceutical Sciences, Trinity College Dublin

Drug therapies for neurodegenerative disease are limited in their efficacy and tolerability, largely due to poor penetration of drugs across the blood-brain barrier and off target peripheral effects. Polymeric nanoparticles (NPs) are advantageous for brain drug delivery due to their safety profiles, drug-loading capacity, and controlled-release properties. NP-based therapies have the potential to reduce doses required and associated side effects. The aim of this work was to investigate the biocompatibility of NPs synthesised using the FDA-approved poly(lactic co-glycolic acid) (PLGA) polymer in neuronal and glial cultures. These investigations show that PLGA NPs are compatible with primary neuronal and glial cells in vitro. Furthermore, PLGA NPs do not cause glial activation. Future studies will assess the drug release capabilities of these particles prior to selection of appropriate candidates for in vivo screening and testing in preclinical models of neurodegenerative disease.

Targeting Glial β2-adrenoreceptor for immunomodulation of an inflammatory-driven impairment to attentional and working memory performance in rats

Matthew McAuslan, Trinity College Institute of Neuroscience, School of Pharmacy and Pharmaceutical Sciences, Trinity College Dublin

Matthew McAuslan, Danka Kozareva, Fionn Dunphy-Doherty, Jack Prenderville, Andrew Harkin

Neuropsychopharmacology Research Group, Trinity College Institute of Neuroscience, School of Pharmacy and Pharmaceutical Sciences, Trinity College Dublin, Transpharmation Ireland Ltd, Trinity College Institute of Neuroscience

Introduction: Disruption of Locus-Coeruleus-Noradrenergic (LC-NA) transmission is associated with multiple psychiatric and neurodegenerative disorders in humans including Alzheimer's Disease. The LC-NA system regulates various cognitive and executive domains that are impaired in Alzheimer's disease like attention and working memory, however the degeneration of the LC-NA system makes a two-fold contribution to pathology in that noradrenaline additionally has the propensity to regulate the inflammatory phenotype in the brain and modulate microglial activities facilitating amyloid and tau clearance. The β2-adrenoreceptor subtype, highly expressed on cortical glial cells, mediates the anti-inflammatory action of noradrenaline and presents as a viable disease modifying target in Alzheimer's and related dementias. For these investigations a delayed non-matching to position (DNMTP) protocol was employed to assess rodents' attention and working memory performance. Systemic administration of the bacterial endotoxin and inflammogen, lipopolysaccharide (LPS), induced a sickness like behaviour followed by sustained deficits to working memory in the DNMTP task 24-hrs post-administration. Subsequent investigations employing the co-treatment of LPS with the long-acting brain-penetrant β2-adrenoreceptor agonist, formoterol, indicated that formoterol attenuates the deleterious sustained effects LPS had on working memory performance.

Kinetic modelling of the cellular metabolic responses underpinning in vitro glycolysis assays

Nitin Patil, PhD candidate, FOCAS Research Institute, TU Dublin

Nitin Patil[1,2], Zohreh Mirveis[1,2], Hugh J. Byrne[1]

[1]FOCAS Research Institute, TU Dublin, City Campus, Camden Row, Dublin 8, Ireland
[2]School of Physics, Optometric and Clinical Sciences, TU Dublin, City Campus, Grangegorman, Dublin 7, Ireland

The cellular glycolysis pathway kinetics were determined for three different cell-lines, under non-modulated and modulated conditions. The assay demonstrated a two-phase metabolic response, representing the differential kinetics of glycolysis pathway rate as a function of time, and this behaviour was faithfully reproduced by a simplistic numerical model. The model enabled the quantitative comparison of the pathway kinetics of three cell-lines, and also the modulating effect of two known drugs. Moreover, the modelling tool allows the subtle differences between different cell-lines to be better elucidated and augment the assay sensitivity. The study demonstrates that augmenting the relatively simple, real-time, in-vitro assay with the model of the underpinning metabolic pathway adds considerably enhanced insight into the observed differences in cellular systems. The kinetic glycolysis assay augmented with a simplistic numerical model has potential applications for drug discovery/screening in hypometabolic brain cell-lines in dementia.

Exploring Tau protein in Alzheimer's Disease using computational and protein fragment synthesis approaches

Martina Tuberti, PhD candidate, School of Chemical and Biopharmaceutical Science, TU Dublin

Martina Tuberti[1,2], Fintan Kelleher[1] and Gemma K. Kinsella[2]

[1]School of Chemical and Biopharmaceutical Science, Molecular Design & Synthesis Group, TU Dublin, Tallaght
[2]School of Food Science and Environmental Health, TU Dublin, Grangegorman

Neurodegenerative diseases (NDDs) affect millions of people and currently there are insufficient drugs to prevent or treat these conditions. Alzheimer's disease (AD), the most common, is associated with dementia or memory deficit. The causes are still unknown but is correlated with alteration of proteins such as Tau, whose function is the assembly and stabilization of microtubules, which help normal neuronal functions. In AD, this protein loses that capacity and does not bind microtubules, due to posttranslational modifications such as hyperphosphorylation of serine residues which can result in misfolding. Moreover, if the phosphoserine is close to a lysine residue, it might generate a highly reactive dehydroalanine (Dha) residue, capable of crosslinking with glutathione, Lys, His or Cys residues. Computational and solid-phase peptide synthesis (SPPS) approaches are being used to identify and prepare novel phosphoserine peptides, helping to advance our understanding on how the development of Tau aggregation is linked to AD.

Cost-Effectiveness of Sensory Intervention in Irish Nursing Homes: A protocol

Mikael Äijälä, Trépel Lab, Trinity College Institute for Neuroscience, Trinity College Dublin

Mikael Äijälä [1], Iracema Leroi [1], Dominic Trépel [1]

[1] Trépel Lab, Trinity College Institute for Neuroscience, Trinity College Dublin

Introduction: Sensory issues, including those related to hearing, vision, and the sensory environment, are known to have compounding effects on dementia. This study conducts a cost-effectiveness simulation of a range of sensory interventions for residence in Irish nursing home residents to assess their economic implications and potential benefits for improving residents' quality of life.

Methods: Using a Markov model, we simulate residents' health progression with and without the intervention, considering transition probabilities, costs, and quality-adjusted life years (QALYs) to determine the incremental cost-effectiveness ratio (ICER). Analysis of uncertainty will examine the probability of a sensory champion being cost effective and value of future research.

Expected results: The costs and relative effects of various interventions for hearing, vision, and sensory environment will be estimated. The model will produce incremental cost-effectiveness ratios (ICERs), and analysis of uncertainty indicate the probabilities of this intervention being cost-effective.

Discussion: The results aim to inform the design of an intervention (Sensory Champion) in Irish nursing homes to be tested in a randomised control trial.

Thank you for taking part in the 2023 DRNI Early Career Researcher Day!

For comments or feedback, contact Vanessa Moore (mooreva@tcd.ie)

Dementia Research Network Ireland
Mercer's Institute for Research on Ageing
St. James's Hospital, Dublin 8, Ireland
www.dementianetwork.ie