NEURACLIN 2017

PROGRAMME

PLACE: South Tess Institute of Learning, James Cook University Hospital, Middlesbrough, TS4 3BW

DATE: 20th September, 2017

Welcome to the 2017 meeting of **NEURACLIN**

Mission Statement: **NEURACLIN** is a network of North-East based Neuroscience and Research oriented Academics and Clinical workers. The aim of this network is to bring Academics and Clinical workers together, with a view to making it easier both to share knowledge and to collaborate on research projects. **NEURACLIN** will primarily focus on memory-affecting disorders, including but not limited to Dementias and Epilepsy.

Programme of the Meeting

All talks and refreshments are in the David Kenward Lecture Theatre.

9:45-10.30	Arrival and coffee in the David Kenward Lecture Theatre
9.50-10.20	[Private NEUROSIG Meeting in Room 20 Learning and Research Institute, ending about 10.20]
10.30-10.40	**Dr Stephen Evans, Dr Colin Lever, Dr James Dachtler** NEURACLIN organisers *Welcome address, Agenda*
10.40-11.25	**Prof. Jan Oyebode,** University of Bradford *Cognitive Rehabilitation for People with Early Dementia*
11.25-11.50	**Dr Alan Bowman,** NHS South Tees and Teeside University *Applying signal detection theory to the study of visual hallucinations in Lewy body disorders*
11.50-12.20	Coffee break and networking
12.20-12.45	**Dr Eleanor King,** Newcastle University *Peripheral Inflammation in Prodromal but not Established Lewy Body and Alzheimer's Dementias*
12.45-13.10	**Dr Claire Garwood,** University of Sheffield *Consequences of impaired insulin/IGF1 signalling in astrocytes: A role in Alzheimer's disease*
13.10-14.00	**Buffet Lunch**
14.00-14.45	**Keynote Talk: Prof. Nigel Hooper,** University of Manchester *Challenges and opportunities for Alzheimer's research*
14.45-15.10	**Dr Paul Donaghy,** Newcastle University *Amyloid PET and FP-CIT SPECT in Lewy Body Disease*
15.10-15.30	**Dr James Dachtler, Dr Colin Lever and Dr Stephen Evans,** Durham University and NHS South Tees *An introduction to Durham Against Dementia*
15.30-16.00	Coffee Break and networking
16.00-16.25	**Dr Stephen Hall,** University of York *Modelling spike and wave absence epilepsies; Thalamus or Cortex?*
16.25-16.45	**Lyn Rodgers,** Alzheimer's Society *The role of the Research Network in the Alzheimer's Society*
16.45-17.00	Closing remarks by the organisers
17.00-17.30	Refreshments and networking

Abstracts of Talks

10:40-11:25 Prof. Jan Oyebode, University of Bradford

Cognitive Rehabilitation for People with Early Dementia

Cognitive rehabilitation (CR) is a person-centred intervention that involves the application of knowledge derived from cognitive and clinical psychology, to help people with mild levels of cognitive impairment due to dementia, to achieve personally relevant goals that help them to maintain their independence and engagement with life.

In this talk I will give background to show why this is an appropriate approach to use in dementia care. I will give information about the principles and nature of the intervention and will summarise research evidence on effectiveness, focusing on the recent GREAT study in which I was a co-investigator. This multi-centre randomised controlled trial was run in 8 centres across England and Wales to find out whether cognitive rehabilitation helps to improve everyday functioning. It was NIHR funded and led by Professor Linda Clare. 427 participants completed the trial and were followed up at 3 months and 9 months after the intervention sessions ceased. Findings will be released at the end of July 2017.

11:25-11:50 Dr Alan Bowman, NHS South Tees and Teeside University

Applying signal detection theory to the study of visual hallucinations in Lewy body disorders.

Visual hallucinations are a common, distressing, and disabling symptom of Lewy body and other diseases. Current models suggest that interactions in internal cognitive processes generate hallucinations. However, these neglect external factors. Pareidolic illusions are an experimental analogue of hallucinations. They are easily induced in Lewy body disease, have similar content to spontaneous hallucinations, and respond to cholinesterase inhibitors in the same way. We used a primed pareidolia task with hallucinating participants with Lewy body disorders (n = 16), non-hallucinating participants with Lewy body disorders (n = 19), and healthy controls (n = 20). Participants were presented with visual “noise” that sometimes contained degraded visual objects and were required to indicate what they saw. Some perceptions were cued in advance by a visual prime. Results showed that hallucinating participants were impaired in discerning visual signals from noise, with a relaxed criterion threshold for perception compared to both other groups. After the presentation of a visual prime, the criterion was comparable to the other groups. The results suggest that participants with hallucinations compensate for perceptual deficits by relaxing perceptual criteria, at a cost of seeing things that are not there, and that visual cues regularize perception. This latter finding may provide a mechanism for understanding the interaction between environments and hallucinations.

12:20-12:45 Dr Eleanor King, Newcastle University

Peripheral Inflammation in Prodromal but not Established Lewy Body and Alzheimer’s Dementias

Aims and Hypothesis

This study aimed to characterise systemic inflammatory mediators in established Dementia with Lewy Bodies (DLB) and Alzheimer’s disease (AD), as well as in their prodromal, Mild Cognitive Impairment (MCI) phases. We

hypothesised that inflammatory markers in patients with DLB would be similar to that in AD, and would be raised in patients with MCI compared to controls.

Background

There is growing evidence for the role of systemic inflammation in AD particularly at the pre-demetntia and early stages of AD, however the systemic inflammatory profile in DLB has never before been investigated.

Methods

We obtained plasma samples from patients with DLB (n=37), AD (n=20), MCI with DLB profile (n=38), MCI with AD profile (n=20) and healthy comparison subjects (n=20). Samples were stored at -80C, and the following inflammatory biomarkers measured using Roche Cobas c702 and Meso Scale Discovery V-Plex Plus: high sensitivity C-reactive Protein (hs-CRP), Interferon (IFN)-gamma, Interleukin (IL)-10, IL12-p70, IL-13, IL-1beta, IL-2, IL-4, IL-6, IL-8 and Tumor Necrosis Factor (TNF)-alpha.

Results

We found significantly higher levels of IL-10, IL-1beta, IL-4 and IL-2 in both MCI groups (p□0.001), whilst there was no significant difference in inflammatory markers between dementia groups and controls. Furthermore, increased disease severity was associated with lower levels of IL-1beta, IL-2 and IL-4 ($p < 0.05$).

Conclusions

We have shown for the first time that in both DLB and AD, increased peripheral inflammation occurs early at the MCI disease stages, and returns back to the same level as controls at the dementia stage.

12:45-13:10 Dr Claire Garwood, University of Sheffield

Consequences of impaired insulin/IGF1 signalling in astrocytes: A role in Alzheimer's disease

The insulin/insulin-like growth factor 1 (IGF1) signalling pathways are associated with longevity and play essential roles in cell growth, survival and metabolism. In Alzheimer's disease there are alterations in this signalling pathway but why this occurs and what it means for 'brain health' are not well understood. We have previously reported that there are changes in the insulin/IGF1 signalling pathway in astrocytes in human brain with progression of Alzheimer's disease pathology. Astrocytes play a central role in modulating the brain environment and changes in this signalling pathway is likely to impact their ability to function effectively. We have recently developed models in human astrocytes to understand the functional implications of reduced signalling through this pathway and the potential impact that this has on disease development and progression.

14:00-14:45 Prof. Nigel Hooper, University of Manchester

Challenges and opportunities for Alzheimer's research

Alzheimer's disease (AD) is the most prevalent age-related dementia that, as yet, has no disease-modifying treatment. Central to the pathological process in AD is the deposition of amyloid-β in extracellular amyloid plaques and the accumulation of tau in intracellular neurofibrillary tangles. However, the molecular and cellular mechanisms that initiate these pathologies are far from clear, and likely occur 15-20 years before the onset of clinical symptoms. I will highlight the challenges we face in identifying those at risk of developing AD and the current lack of treatments. I will describe how research using human induced pluripotent stem cells (iPSCs) provides opportunities for

investigating the underlying biological mechanisms in human neurons and how neurovascular dysfunction contributes to neurodegeneration. I will also discuss potential links between diabetes and AD.

14:45-15:10 Dr Paul Donaghy, Newcastle University

Amyloid PET and FP-CIT SPECT in Lewy Body Disease

Dementia with Lewy bodies (DLB) is the second most common form of neurodegenerative dementia after Alzheimer's disease (AD). Molecular imaging techniques such as PET and SPECT are increasingly being used to gain insights into the pathophysiology of neurodegenerative diseases and as biomarkers to identify disease in its early stages.

The AMPLE study investigated amyloid deposition in DLB using ^{18}F-Florbetapir PET. The effect of amyloid deposition on clinical presentation and imaging findings in DLB will be presented.

The LewyPro study investigated ^{123}I-FP-CIT SPECT in prodromal DLB. ^{123}I-FP-CIT SPECT is known to be effective in differentiating DLB from AD. The accuracy of this scan does differentiate between prodromal DLB and prodromal AD will be presented.

15:10-15:30 Dr James Dachtler and Dr Colin Lever, Durham University and Dr Stephen Evans, NHS South Tees

An introduction to Durham Against Dementia

We at Durham are particularly interested in the development of new neuropsychological tests to detect dementia earlier. We argue that the widespread, national rollout of screening tests for the earliest forms of dementia for use in primary care cannot, for financial or logistical reason, be biological (i.e. MRI, cerebrospinal fluid or genetics). As such, we are currently working with NHS South Tees, NHS Cumbria and NHS Tees Esk and Wear Valley to pilot new cognitive tests that can predict conversion from mild cognitive impairment to Alzheimer's disease (the 'Detecting Dementia Earlier' project).

However, we have plans to utilise Durham's strength in psychological research (e.g. EEG, social behaviour, gait analysis) to longitudinally assess ageing local populations from the local community to understand which are the best psychological tests to predict those at risk of dementia, years before they would otherwise come in contact with the NHS. Our end goal is to create a longitudinal psychological test, that much like a breast or prostate exam, could be delivered by your GP annually from when you reach a critical age (e.g. 50). The enable these goals, Dachtler, Lever and Evans are launching Durham Against Dementia on the 21st November, with a keynote speech delivered by James Pickett, Head of Research for Alzheimer's Society.

We will briefly introduce Durham Against Dementia, it's aims, and will welcome anyone that wants to become involved in the project prior to launch.

16:00-16:25 Dr Stephen Hall, University of York

Modelling spike and wave absence epilepsies; Thalamus or Cortex?

Patients with a diverse range of epilepsies, in particular absence type epilepsies, demonstrate electrographic events termed spike and wave discharges (SpW). SpW are linked to pathology of the thalamocortical axis and a thalamic mechanism has been elegantly described. However, recent studies have shown a neocortical focus, both in models

of SpW and in patients. SpW events are known to be heterogeneous, which means that the SpW frequency, rhythmicity, amplitude distribution and clinical accompaniment can vary dramatically among different seizure pathologies. As such, the frequency of SpW has been used to subclassify absence epilepsies; typical absence, in which SpW frequency is 3-4Hz and atypical absence, which shows a slower 1-2Hz frequency.

Our work demonstrates that SpW can be generated *in vitro* in an isolated neocortical slice preparation, using an acetylcholine and serotonergic antagonist, d-Tubocurarine. The frequency of this activity is akin to that of atypical absence and the model does not respond to known anti-epileptic drugs used to treat typical absence pathologies, such as Ethosuxamide and Sodium Valproate. However, using more novel anti-epileptic drugs demonstrated to be effective at treating atypical absence pathologies (Levetiracetam and Rufinamide), we can effectively reduce SpW. In contrast, using *in vitro* slices which contain the thalamus and its projections to the neocortex, we can generate SpW in the neocortex by antagonising $GABA_A$ receptors within the thalamus. These SpW are markedly different to those generated in the isolated neocortex preparation and Ethosuxamide is effective at supressing them.

These data suggest that the heterogeneity of absence type epilepsies may be due to the origin of the SpW; it is possible that *both* the thalamus and the neocortex can be the foci. Furthermore, they also highlight the importance of the correct clinical treatment of absence type epilepsies, given the differences in the pharmacological profile of each model.

16.25-16.45 Lyn Rodgers, Alzheimer's Society

The role of the Research Network in the Alzheimer's Society

Alzheimer's Society particularly values the input from its lay member network, referred to as the Research Network. Alzheimer's Society is a pioneer in public involvement in dementia research. The Research Network, established in 1999, now includes a team of over 280 carers, former carers and people living with dementia.

Alzheimer's Society's philosophy is that people with dementia and carers can make a unique and valuable contribution in every stage of research. The knowledge and passion of those affected by dementia ensures that our research funding is allocated to projects that address the real needs and concerns of people with dementia and their carers.

Increasingly, Research Network volunteers play an active role in dementia research funded outside Alzheimer's Society. They co-design research projects, sit on steering groups, take part in focus groups and act as co-applicants in our partnership projects. Within Alzheimer's Society, all applications contain a 4 page lay application. All lay applications are reviewed and scored by our Research Network volunteers. Research Network scores are taken into account, with peer review scores, to shortlist applications for discussion by our Grant Advisory Panel and Grant Advisory Board.

Lyn will be discussing the role of the Alzheimer's Society Research Network, and more generally, how and why she became involved in dementia research.