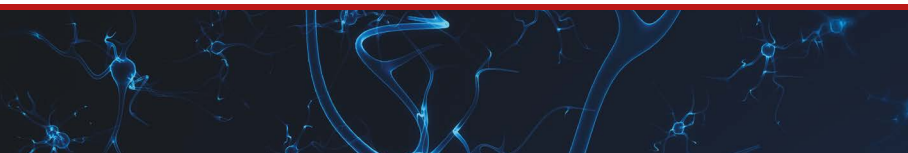
Poster Tour: Cognitive

May 7, 12:30 - 13:30

Hall 3

51. A 48-Month Analysis of the Lecanemab Clarity AD Open-Label Extension in APOE4 Non-Carriers and Heterozygotes: **Michael Rushworth**
52. Autonomic involvement across the spectrum of genetic prion diseases: **Zhilin Jiang**
53. Neurodegenerative outcomes in antidepressant-associated rem sleep behaviour disorder: **John Erskien**
54. Validating Referral Triage Criteria for Functional Cognitive Symptoms in a Cognitive Neurology Clinic: **Arthur Stacey**
55. Night-time activity detected by contactless remote monitoring is associated with falls in dementia: **Anastasia Mirza-davies**
56. When the Past Catches Up: Iatrogenic Creutzfeldt–Jakob Disease With a 39-Year Incubation Period: **Sanjida Chowdhury**
57. The contribution of Apoliproprotein E genetic variation to dementia risk in British South Asians: **Ben Jacobs**
58. A Real-World UK Experience of Disease-Modifying Therapy in Alzheimer's Disease: **Rebecca Kuruvilla**
59. Validating a Clinical Assessment of Working Allocentric Spatial Memory: **Hin Kwan Jeroan Yip**
60. Relationships between sleep actigraphy, subjective sleep, fatigue, and cognition in older adults in Northern Tanzania: **Charlie Nye**



A 48-Month Analysis of the Lecanemab Clarity AD Open-Label Extension in APOE4 Non-Carriers and Heterozygotes

Richard Perry[2], Michael Rushworth[1], Shobha Dhabba[3], Michio Kanekiyo[3], Michael Irazarry[3], Lynn Kramer[3]

[1]Eisai Ltd, [2]Imperial College London, [3]Eisai Inc

Background: Lecanemab is approved in the UK for the treatment of mild cognitive impairment (MCI) and mild dementia due to Alzheimer's disease (AD) in adults who are apolipoprotein E β4 gene (APOE4) non-carriers or heterozygotes.

Methods: In the 18-month, Phase 3 Clarity AD trial, participants were randomised (1:1) to receive lecanemab 10 mg/kg or placebo intravenously every 2 weeks, after which they could enter an open-label extension (OLE) in which all participants received lecanemab 10 mg/kg. OLE assessments included the Clinical Dementia Rating-sum of boxes (CDR-SB) and safety/tolerability. CDR-SB results were compared with a matched historical untreated control (Alzheimer's Disease Neuroimaging Initiative [ADNI] population).

Results: Of 1466 APOE4 non-carrier and heterozygous participants included in Clarity AD (placebo, n=743; lecanemab, n=723), 282 were included in the 48-month analysis. Lecanemab continued to delay disease progression over 48 months: compared with the ADNI control population (N=346), differences in mean change from baseline in CDR-SB were 0.50, 0.77 and 1.31 at 18, 36 and 48 months, respectively, representing 8.4 months of time saved at 48 months. There were no new safety signals.

Conclusions: Ongoing lecanemab treatment through 48 months was associated with increasing treatment difference versus matched control data, consistent with a disease-modifying effect.

Autonomic involvement across the spectrum of genetic prion diseases

Francesca Vitali[1,2], Giacomo Chiaro[1], Zhilin Jiang[1], Tze How Mok[3,4], Simon Mead[3,4], Valeria Iodice[1,5,6]

[1]National Hospital For Neurology And Neurosurgery, [2]Department of Neuroscience, Università Cattolica del Sacro Cuore, [3]Medical Research Council Prion Unit at University College London, UCL Institute of Prion Diseases, [4]NHS National Prion Clinic, National Hospital for Neurology and Neurosurgery, University College London Hospitals NHS Foundation Trust, [5]Department of Translational Neuroscience & Stroke, UCL Queen Square Institute of Neurology, University College London, [6]NIHR University College London Hospitals Biomedical Research Centre

Background: Genetic prion diseases (gPrDs) are fatal neurodegenerative disorders caused by pathogenic PRNP mutations. Fatal familial insomnia (FFI) and PrP systemic amyloidosis (PrP-SA) show prominent autonomic involvement. FFI features selective thalamic degeneration with sleep disruption and cardiovascular sympathetic dysregulation. PrP-SA instead involves systemic amyloid deposition affecting peripheral organs and nerves, causing early gastrointestinal dysfunction, neuropathy, and autonomic failure.

Method: We evaluated cardiovascular autonomic involvement in gPrDs, focusing on FFI and PrP-SA. Five FFI patients, six PrP-SA patients, and three asymptomatic PRNP variant carriers underwent retrospective analysis. Cardiovascular autonomic function was assessed using standardized autonomic function testing (AFT) and 24-hour blood pressure monitoring.

Results: At evaluation (median age 44 years, IQR 33–52), all symptomatic patients reported autonomic symptoms affecting cardiovascular, gastrointestinal, and urogenital systems. FFI patients showed sympathetic overactivity, including supine and nocturnal hypertension and resting tachycardia, with AFT evidence of cardiovagal and adrenergic impairment. PrP-SA patients exhibited combined sympathetic and parasympathetic failure, characterized by neurogenic orthostatic hypotension, reduced heart rate variability, and poor postural tolerance. Asymptomatic carriers demonstrated mild AFT abnormalities without clinical symptoms.

Conclusions: FFI and PrP-SA exhibit distinct autonomic phenotypes reflecting central versus peripheral autonomic dysfunction. Routine autonomic evaluation may facilitate detection and management in gPrDs.

Neurodegenerative outcomes in antidepressant-associated REM sleep behaviour disorder

John Erskine, Madeleine Williams, Elisa Bruno, Mark Edwards, Guy Leschziner, Thomas Pollak, Laura Pérez-Carbonell

Background: Isolated REM behaviour disorder (RBD) heralds development of neurodegenerative disease, specifically synucleinopathies. The prognostic implications of antidepressant-associated RBD are unclear.

Methods: Retrospective cohort study using data from TriNetX, a global, real-world network containing anonymised electronic health records. Patients were aged 50 years or over at time of RBD diagnosis; one cohort had isolated RBD and the second had RBD with antidepressant use within 5 years prior to diagnosis. Cohorts were one-to-one propensity score matched. Primary outcome was comparing emergence of neurodegenerative disease, specifically synucleinopathies (Parkinson's disease, dementia with Lewy bodies, multiple system atrophy) between cohorts, at 1-20 years from RBD diagnosis. Kaplan-Meier analyses assessed probabilities of remaining disease-free.

Results: 14,207 patients were included in each cohort after matching. Average follow-up time was 3.5 years. Patients with antidepressant-associated RBD demonstrated similar risks of phenoconversion for dementia with Lewy bodies (disease-free survival 89.8 vs 87.2%, p=0.316) and multiple system atrophy (87.9 vs 85.6%, p=0.568). Antidepressant-associated RBD patients had a slightly higher risk of phenoconversion to Parkinson's disease (disease-free survival 73.1 vs 74.2%, p<0.001).

Conclusion: antidepressant-associated RBD in older patients is suggested to herald future phenoconversion to a synucleinopathy similar to patients with isolated RBD.

Validating Referral Triage Criteria for Functional Cognitive Symptoms in a Cognitive Neurology Clinic

Arthur Stacey[1], Jeremy D Isaacs[1,2], Weijia Zhang[1], Oliver Cousins[1]

[1]St George's University Hospitals NHS Foundation Trust, [2]Department of Psychology & Neuroscience, School of Health & Medical Sciences, City St George's, University of London

Background: Functional cognitive symptoms (FCS) are a common reason for referral to cognitive neurology. Our service rejects referrals of patients aged < 60 years with none of the following indicators of organic cognitive decline: (1) Informant history supporting cognitive difficulties; (2) Objective decline in ADLs or formal work performance concerns; or (3) Underperformance on a cognitive screening instrument. We sought to validate these rejection criteria.

Methods: Referrals from October 2024 – April 2025 were reviewed for triage outcome. Rejected cases were further reviewed for subsequent patient outcomes.

Results: 41 cases of likely FCS were rejected using our criteria. 10 of these subsequently underwent formal assessment of cognitive symptoms either by our service after re-referral, or in another secondary care setting, with no organic brain disease being identified in any patient. No confirmed cases of organic brain disease were documented in the healthcare records of the other 31 rejected cases after median follow-up of 4.7 months (IQR 3.2 - 6.4).

Conclusions: Our criteria for identifying and rejecting FCS referrals were validated. These allow patients to be safely managed in primary care or other more appropriate services. Further evaluation is underway to validate these triage criteria in a community memory service.

Night-time activity detected by contactless remote monitoring is associated with falls in demention

Ana Mirza-Davies[1,2], Youssef Hbid[1,2], Gaia Frigerio[1,2], Alina-Irina Serban[1,2,3], CRT group[1], David Sharp[1,2]

[1]UK Dementia Research Institute, Care Research and Technology Centre, Imperial College London, [2]Brain Sciences Department, 3Department of Mechanical Engineering, Imperial College London

Disturbed night-time activity is common in people living with dementia (PLWD) and associated with adverse outcomes. We examined the relationship between passively measured night-time activity and falls.

PLWD enrolled in the Minder health management study were monitored using a Withing's Sleep Analyser and in-home motion sensors. Night-time activity was quantified using a rule-based algorithm summarising out-of-bed activity. Group differences were examined between participants with and without disturbed night-time activity. Average night-time activity was calculated over rolling 30-day windows and classified as low or high. Within-person associations with falls in the subsequent 30 days were assessed using mixed-effects logistic regression.

Night-time activity was significantly higher among PLWD reporting sleep disturbance (N=22, Median=19.3 min/night vs N=60, Median=1.5 min/night, U= 997.5, $p<0.001$, r=0.42). Longitudinal monitoring of 158 PLWD over 3,720 person-months identified 247 falls between July 2021 and November 2025. Elevated night-time activity within individuals was associated with increased odds of falling in the subsequent 30 days (OR=1.78, 95%CI 1.15–2.75), with evidence of progressively higher risk with greater activity levels.

Passive sensing can quantify night-time activity in PLWD and may be able to identify periods associated with increased fall risk. This could support best interest decisions, inform clinical assessments and enable timely intervention.

When the Past Catches Up: Iatrogenic Creutzfeldt–Jakob Disease With a 39-Year Incubation Period

Sanjida Chowdhury[1], Melissa Ng[2], Simon Mead[2], Sunday Oghuvwu[3], Sue Lim[1], Saam Sedehizadeh[1]

[1]Nottingham University Hospitals NHS Foundation Trust, [2]University College London, [3]Sherwood Forest NHS Foundation Trust

Introduction: Creutzfeldt–Jakob disease (CJD) is a rare, fatal prion disease, most commonly occurring sporadically but occasionally transmitted through surgical procedures and devices, resulting in iatrogenic CJD (iCJD).

Case Report: A 39-year-old man presented to Queen's Medical Centre, Nottingham, UK with a four-week history of rapidly progressive cognitive and behavioural decline. His family reported impaired executive function and gait disturbance.

At six weeks of age, he developed meningitis complicated by seizures and bilateral subdural empyema. In 1986, he underwent craniotomy with dural repair using a cadaveric dura mater graft (Lyodura).

During admission, he deteriorated rapidly, becoming bedbound, non-verbal, and doubly incontinent. MRI brain demonstrated diffusion restriction in the bilateral basal ganglia with multifocal cortical ribboning, more prominent on the left. EEG showed non-specific encephalopathy. Cerebrospinal fluid was acellular with normal protein, and RT-QuIC was positive. He was referred to palliative care and died in a hospice within two weeks of discharge.

Conclusion: The case highlights the diagnostic value of a detailed lifetime surgical history, particularly childhood neurosurgical interventions that may otherwise be overlooked. Continued vigilance, prompt recognition, and systematic reporting are essential to support surveillance and improve understanding of iatrogenic prion disease in neurological practice.

The contribution of Apoliproprotein E genetic variation to dementia risk in British South Asians

Ben Jacobs[1], Avinash Chandra[1], Arnab Mandal[1], Isabelle Foote[1], Faiza Durrani[1], Sheena Waters[1], Yue Liu[1], Petroula Proitsi[1], Cara Croft[1], Dylan Williams[2], Moneeza Siddiqui[1], Sarah Finer[1], Stuart Rison[1], David A Van Heel[1], Charles Marshall[1]

[1]Queen Mary University Of London, [2]University College London

Understanding the genetic basis of dementia in diverse populations is essential to ensure that efforts to predict, prevent, and treat dementia are equitable. The strongest genetic risk factor for dementia - APOE genotype - has not been assessed in population-scale cohorts of South Asian ancestry.

To test whether APOE variation is associated with all-cause dementia in British South Asians, we analysed data from 51,104 volunteers Genes & Health study. All-cause dementia was defined using electronic healthcare records. APOE genotypes were defined using phased, imputed genotype data. Cox proportional hazards models were used to assess the relationship between APOE genotype and dementia. Population attributable fractions were calculated for each APOE genotype.

Among 614 cases of dementia and 50,490 controls, the APOE β4 allele was associated with all-cause dementia in a dose-dependent fashion (APOE ε4/ε4: Hazard Ratio 2.7, 95% CI 1.7 - 4.2, $P < 0.0001$; APOE ε4/ε3: Hazard Ratio 1.5, 95% CI 1.2 - 1.8, $P < 0.001$). The overall proportion of all-cause dementia cases which could be attributed to this allele was 12.9%.

APOE ε4 - the major genetic risk factor for sporadic dementia in European-ancestry populations - has a similar impact on dementia risk in British South Asians.

A Real-World UK Experience of Disease-Modifying Therapy in Alzheimer's Disease

Rebecca Kuruvilla, Paresh Malhotra, Richard Perry, Paul Jarman, Ross Nortley, James Teo

Cleveland Clinic London

Alzheimer's disease (AD) is the leading cause of dementia in the UK and worldwide. The UK National Institute for Clinical Effectiveness (NICE) evaluation currently does not recommend the disease modifying therapies Lecanemab and Donanemab for mild cognitive impairment or mild dementia due to AD, primarily due to cost-effectiveness considerations. As a UK-based non-NHS independent health provider, Cleveland Clinic London (CCL) has provided these therapies through a multidisciplinary team approach and according to published guidelines since Sept 2024. Here we describe this experience from a real-world UK population.

Within the cohort, 65% of patients are being treated with Donanemab and 35% with Lecanemab. Patients ranged from 56-86 years, with a mean age of 73 years. Most patients had APOE genotypes ε3/ε3 or ε3/ε4. To date, one patient has experienced mild ARIA and continues treatment, and one patient has experienced severe ARIA and discontinued treatment. The mean baseline MMSE score was 25. Further cognitive and qualitative outcome data will be presented.

This study provides an early descriptive account of the use of disease-modifying therapies for AD within a real-world UK healthcare setting. The findings highlight both the feasibility and challenges of implementing these treatments and explores their impact on patients and carers.

Validating a Clinical Assessment of Working Allocentric Spatial Memory

Nathaniel W. Jones[1], Jeroan Yip[2], Gina Gilpin[1], Aysha Mohamed Rafik Patel[1], Charlotte Ash[1], Coco Newton[1], Dennis Chan[1,3]

[1]Institute of Cognitive Neuroscience, University College London, [2]Brighton and Sussex Medical School, [3]Department of Neurology, University Hospitals Sussex NHS Trust

Background: The Four Mountains Test (4MT) is a short clinical assessment designed to probe cognitive deficits in working allocentric spatial memory. Prior studies demonstrated high sensitivity and specificity to conditions selectively impairing hippocampal function such as Alzheimer's disease. However, its construct validity has not been evaluated.

Method: 43 healthy controls (F=27, M=16) aged between 30–65 years completed the 4MT alongside assessments of mental rotation (MR), working memory (WM), and executive function (EF). Correlation and regression analyses between 4MT and each cognitive domain were conducted to gather convergent and discriminant evidence.

Results: 4MT scores of healthy controls were normally distributed. MR and WM significantly correlated with 4MT performance. However, only WM demonstrated significant effect within a multiple linear regression model, and comparison with nested models revealed WM to be a strong predictor of 4MT score. Post-hoc mediation analysis further demonstrated WM to mediate the effect of MR on 4MT performance. Furthermore, increases in EF-related reaction time negatively affected 4MT score.

Conclusion: 4MT relates to both allocentric spatial processing and non-spatial WM, demonstrating construct validity. This supports the application of 4MT in assessing spatial cognitive dysfunction in clinical practice, especially in preclinical stages of Alzheimer's disease.

Relationships between sleep actigraphy, subjective sleep, fatigue, and cognition in older adults in Northern Tanzania

Charlie Nye[1,2], Megan Sison[3], Amour Mkubila[4], Grace Saria Anderson[5], Lachlan Fotheringham[6], Victoria Gabb[1], Jonathan Blackman[1,4], Elizabeth Coulthard[1,4], Bernard Mbwele[7,8], Stella-Maria Paddick[3,9]

[1]University Of Bristol, [2]North Bristol NHS Trust, [3]Newcastle University, [4]Kilimanjaro Clinical Research Institute, [5]Anderson Memorial Rehabilitation and Care Organisation, [6]Cumbria, Northumberland, Tyne and Wear NHS Foundation Trust, [7]University of Dar es Salaam-Mbeya College of Health Sciences, [8]Vijiji Tanzania, [9]Gateshead Health NHS Foundation Trust

Background: Sleep is essential for brain health. Sleep disruption is a potential early marker of neurodegenerative disease and modifiable therapeutic target. Limited data from sub-Saharan Africa means consensus guidelines on sleep measurement may not be relevant. We aim to assess the feasibility of objective sleep measures and their relationship to subjective measures in Tanzania.

Methods: Residents of two villages aged ≥60 years were recruited. Demographic and medical data were collected. Subjective sleep quality, daytime sleepiness, and fatigue were assessed using validated questionnaires. Participants wore wrist accelerometers for one week and completed diaries. Actigraphy data were processed using GGIR to derive total sleep time (TST), sleep efficiency (SE), and wake after sleep onset (WASO).

Results: Of 162 enrolled participants, 140 contributed ≥3 valid nights of actigraphy (mean age 69 years; 67% female; median 6 nights). Sleep disruption was highly prevalent, SE <80% in 67% of participants and WASO ≥60 minutes in 96%. Mean TST was 6.3 hours (SD1.0). Subjective sleep quality, daytime sleepiness, and fatigue were not significantly correlated with actigraphy-derived measures.

Conclusions: Objective sleep disruption was common but poorly reflected by subjective measurement. Further work is needed to understand the relationship of sleep disruption with cognitive health in this setting.