ABSTRACT BOOKLET 2024

AUSTRALIAN DEMENTIA RESEARCH FORUM 2024

3-5 JUNE 2024

Australian Dementia Network
REGISTRY. CLINICS. TRIALS.

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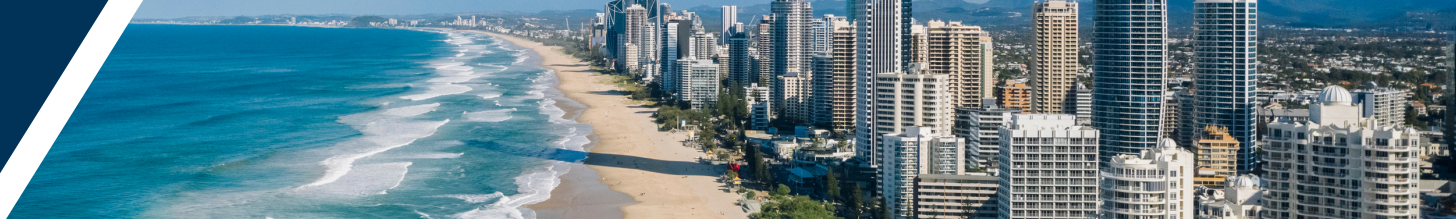

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Framework for Best Practices and Institutional Readiness in the Advent of Anti-Amyloid Therapy for Early AD in Asia

Dr. Christopher Chen

Background

Advances in Alzheimer's disease (AD) research over the past few decades have led to a paradigm shift in therapeutic approaches from management of clinical symptoms to disease-modifying treatments (DMTs) that target the underlying pathophysiology of AD. In particular, anti-amyloid therapies, in early AD, have the potential to slow down clinical progression of AD.

As these therapies obtain regulatory approval and become available, we need to transition to clinical care pathways that enable identification of patients early in the course of AD and deliver DMTs efficiently and safely.

Apart from infrastructure-related requirements, such as diagnostic assessments including biomarkers for AD, infusion centres for delivering the currently available DMTs and protocols for monitoring response and potential side effects, rigorous and all-encompassing education at all levels (specialists, primary care, ancillary healthcare staff, patients, caregivers) will be the cornerstone to achieving optimal outcomes with these DMTs. In this talk, we will examine some of the essential changes that are needed in our healthcare systems as we transition from symptomatic treatment of AD to DMTs.

Celebrating 10 years of Cognitive Stimulation Therapy in New Zealand

Dr. Gary Cheung

Background

Cognitive stimulation therapy (CST) is a structured and manualized evidence based psychosocial group treatment specifically developed for people with mild to moderate dementia. The effects of CST appear to be of a comparable size to those reported with the currently available anti-dementia drugs.

A cost effectiveness study found that CST for people with dementia is more cost-effective than usual treatment. CST was developed in the UK and is recommended in the NICE dementia guidelines. It has been adopted in at least 38 countries including New Zealand, and its uptake in Australia has been gradual. This presentation summaries our 10 years of experience of implementing CST in New Zealand, including adaptation to Māori, the indigenous population of New Zealand, and Pacific peoples.

KEYNOTES

Unravelling the Role of Tau Tangles in Neurodegenerative Diseases

Professor Karen Duff

Background

Pathology composed of abnormal tau protein (tauopathy) is a key and feature of many neurodegenerative diseases and syndromes. In Alzheimer's Disease (AD), tauopathy occurs with amyloid (Abeta) plaques whereas in FrontoTemporal Dementia linked to chromosome 17 (FTD-tau) tauopathy is the main feature. Tauopathy is also associated with several syndromes and infectious diseases, possibly through a chronic inflammatory response. What causes tauopathy to be initiated in neurodegenerative diseases is unclear, however, it is known that particular cell types and brain regions are initially susceptible and as disease worsens, tauopathy spreads through the brain along anatomical trajectories which are characteristic of a particular disease. The tau protein shows high levels of complexity, and the diversity of tau forms contributes to the diversity of dementias which feature abnormal tau. Using a combination of techniques, human tissue and new cell and mouse lines that model the earliest stages of AD or FTD, we have examined the mechanisms by which tauopathy is initiated and spreads, and how tau interacts with other pathological proteins such as Abeta. Data will be discussed in the context of the leading hypotheses in the field to provide an overview of what we know of the earliest events in tau pathogenesis in neurodegenerative disease.

Locus Coeruleus Imaging to Identify Pre-Preclinical Alzheimer's Disease

Dr. Heidi Jacobs

Background

Alzheimer's disease (AD) is characterized by a long asymptomatic stage during which the two pathologic hallmarks, beta-amyloid and tau depositions, accumulate, lead to neurodegeneration and the manifestation of clinical symptoms. Being able to effectively delay disease progression will require early intervention, before irreversible damage has occurred. There is thus need for a biomarker that can predict who is likely to accumulate AD pathology and show a decrease in cognition in the following years. Given that autopsy data reported presence of hyperphosphorylated tau in the locus coeruleus (LC) early in adulthood and before cortical involvement, we aimed to evaluate the LC – using structural and functional neuroimaging – as a promising early marker of AD risk.

Methods

We used data from Harvard Aging Brain Study+ (n=214) where individuals underwent 3T MRI-LC imaging, 18F-Flortaucipir (FTP)-PET imaging, PiB-PET imaging and longitudinal cognitive assessments. Of these individuals, 77 underwent repeated LC imaging and repeated FTP-PET imaging. In addition,90 individuals underwent functional MRI during a face-name memory task (novel versus repeated contrast).

Results

Lower LC integrity was associated with greater entorhinal tau and PiB-related cognitive decline (starting earlier than the identified PiB threshold). Longitudinal data revealed that lower LC integrity preceded accumulation of tau in the medial temporal lobe, and that the relationship between lower baseline LC integrity and lower follow-up cognitive performance was mediated by accumulation of medial temporal lobe tau. Lower novelty-related activity in the LC was associated with faster cognitive decline and entorhinal tau deposition. Finally, when comparing LC integrity, PiB and hippocampal volume in all PiB- individuals, LC integrity was the best predictor of entorhinal tau accumulation and disease progression.

Discussion/ Conclusion

Our findings highlight that LC changes reflect early pathologic changes relevant to AD and that LC imaging holds promise as early marker of AD. Remaining open questions will be discussed.

Frontotemporal Dementia

Professor Peter Nestor

Background

Frontotemporal dementia encompasses a range of clinical presentations and different pathologies, the defining feature being a predilection for degeneration of frontal and/or temporal lobes. The majority have one of two histopathologies, namely either with tau or TDP-43 containing inclusions. Compared to other forms of degenerative dementia, it has the highest risk of being dominantly genetically inherited although it is important to stress that for the majority of people diagnosed with a form of frontotemporal dementia, it will not have a genetic basis. Clinically, the disease typically presents with either language dysfunction—in turn subdivided into semantic or non-fluent types—or a syndrome of altered personality and behaviour denoted as "behavioural variant' (bvFTD). Furthermore the clinical syndromes of frontotemporal dementia can, in some people, overlap with motor disorders. For instance, the progressive non-fluent aphasic presentation is often underpinned by tau pathology and, with time, features of progressive supranuclear palsy or corticobasal syndrome may emerge. Likewise, frontotemporal dementia can co-exist with motor neuron disease. There are presently no evidence-based therapies for frontotemporal dementia; management is supportive.

Aside from the paucity of therapeutic options, a major ongoing research challenge is to tackle the misdiagnosis rate, particularly in the case of bvFTD—delay in diagnosis of actual bvFTD as well as misdiagnosis of non-degenerative diseases

Opening a New Era for the Diagnosis and Treatment of Alzheimer's Disease

Dr Stephen Salloway

Background

Recent scientific advances have opened a new era for the diagnosis and treatment of Alzheimer's disease (AD), transforming the way we view and manage AD. Increasingly, we will treat AD like other major chronic diseases, such as heart disease and cancer, with a focus on early detection, risk reduction, coordination of care and disease-modifying treatments. Thanks to the courageous contribution of thousands of research volunteers we know that the plaques and tangles of Alzheimer's disease begin accumulating in the brain 15-20 years before memory loss begins. PET scans and tests of spinal fluid and blood can reliably measure changes in amyloid and tau providing a molecular confirmation and staging of Alzheimer's disease. Recent studies in patients with early AD have demonstrated that treatment with amyloid-lowering monoclonal antibodies can lower amyloid plaques below the cut-off for AD in the majority of patients. This produces a mild but clinically significant slowing of decline in cognition and daily functioning. The main side-effect of amyloid-lowering antibodies are fluid shifts in the brain called ARIA (amyloid-related imaging abnormalities). ARIA tends to occur early in treatment, is usually asymptomatic and transient, but more serious cases can occur. The main risk factors for ARIA are number of ApoE4 alleles, dose of the drug and underlying cerebral amyloid angiopathy. Patients with early AD need to be selected for treatment after carefully weighing risks and benefits with the patient and family. Monitoring and management of ARIA should follow the guidelines in the Appropriate Use Recommendations (Cummings, JPAD, 2023). These advances are just the beginning, the future of AD care will rest on risk detection, care navigation, brain health interventions and combination treatments targeting key components of the AD pathological cascade.

KEYNOTES

Building Your Best Day for Healthy Brain Ageing and Dementia Risk Reduction

Associate Professor Ashleigh Smith, Mr. Kirk Erickson, Ms. Audrey Collins, Ms. Maddison Mellow, Ms. Dorothea Dumuid, Ms. Frini Karayanidis, Mr. Timothy Olds

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Background

Physical activity, sleep, and sedentary behaviour collectively referred to as the 24-hour Activity Cycle (24HAC), have been independently associated with brain health, cognition, and future dementia risk. However, the behaviours that make up the 24HAC are not independent; rather, they are interdependent and mutually exclusive. Spending more time in one behaviour leaves less time for others, and together these behaviours interact to influence cognition, brain health and dementia risk. The purpose of this keynote presentation is to highlight initial findings exploring the associations between time-use composition, cognition, and brain health in older adults, using the baseline data of two large studies (ACTIVate (Australia) and IGNITE (USA)). A secondary purpose is to broadly discuss the importance of social determinants of health and participant diversity in 24HAC and dementia risk reduction research.

Methods

Baseline data from ACTIVate (n=378, 67% female, 16.6 ± 3.2 years education) and IGNITE (n= 587, 70% female, 16.3 ± 2.2 years of education) were used to independently examine the relationships between 24HAC and cognition using a compositional data analysis approach (CoDA). We hypothesised that 24HAC, and in particular time spent in moderate-vigorous physical activity (MVPA) relative to sleep, sedentary behaviour (SB) and Light Physical Activity (LPA), would be associated with better cognition across cognitive domains.

Results

24HAC was associated with cognition in several initial analyses (but not all). The baseline activity footprint (highly active VS highly inactive participants), brain volume, and certain activity types/contexts (i.e., not only intensity) appear important for cognition.

Discussion/ Conclusion

There is great potential for using CoDA approaches to explore associations between 24HAC, cognitive, brain health and dementia risk. Future studies should consider modeling time-use longitudinally. Given the infancy of these data analysis approaches, considerations of several social determinants of health which likely impact the 24HAC remain under-explored.

The Australian Dementia Network: Critical Dementia Data Infrastructure

Prof Henry Brodaty [1], Prof Susannah Ahern [2], Kasey Wallis, Stephanie Ward [3], Xiaoping Lin [4]

[1] (FRANZCP, PhD), [2] (FRACMA, PhD), [3] (FRACP, PhD), [4] (PhD)

Background

The Australian Dementia Network (ADNeT) Registry is a clinical quality registry that aims to capture population-level data of people with newly diagnosed dementia or mild cognitive impairment (MCI) for quality improvement purposes. Established in 2018, as of December 2023 the ADNeT registry has baseline clinical information from 64 participating services regarding 4,283 participants (66% with dementia, 34% with MCI) and post diagnostic surveys from 1,493 participants and 1,210 carers. It provides descriptive public Annual Reports and 6-monthly benchmarked reports to participating clinics.

Methods

This presentation will discuss the various ways that the ADNeT registry is becoming critical dementia data infrastructure with potential to improve outcomes via:

1. Quality improvement
2. Sharing data for research
3. Use as platform for research and data linkage

Results

The ADNeT Registry has very high data completeness, with nearly all items reaching 90%. Clinical Quality Indicators are developed based on best practice recommendations, and Annual Reports provide comprehensive data on dementia diagnosis and post-diagnostic management and referral. Site reports highlight differences in cohort characteristics, support health service accreditation requirements, and identify opportunities for improvement, particularly regarding access. The registry is developing a Monoclonal Antibody Therapies (mABs) module to monitor the safety and effectiveness of novel treatments such as mABs. The registry is commencing sharing data for quality improvement and research purposes, and will develop processes for researcher access to consented participants. The Registry is engaging with the Australian Institute of Health and Welfare (AIHW) by using its data to support Dementia Action Plan monitoring, and is working toward integrating registry data with AIHW as an enduring asset.

Discussion/ Conclusion

Established as a clinical quality registry, the ADNeT registry not only supports provider quality improvement, but is developing processes that will enable it to becoming critical infrastructure that supports and enhances dementia research across Australia.

Cognitive Interventions Update

Kerryn Pike [1], Alex Bahar-Fuchs [2], Loren Mowszowski [2], Alessandra Lee [3], Inga Mehrani [2], Alison Hutchison [1], Sharon Naismith [1]

[1] Professor, [2] Dr, [3] M

Background

Despite the evidence that cognitive interventions benefit older adults, there remains a research-to-practice gap where these interventions are not readily available in clinical practice. In this session we will describe our work in addressing this gap through the Australian Dementia Network (ADNeT) Cognitive Interventions Working Party.

Methods

We conducted a scoping review of international practices in implementing cognitive interventions for older adults. We also conducted a national survey of clinicians and trainees regarding their needs and preferences for delivering cognitive interventions. The findings were used to develop a clinician training package, consisting of six online modules and an in-person workshop, for neuropsychologists in Australian memory clinics. Clinicians' experience of the training was evaluated using a short survey.

Results

The scoping review demonstrated the general lack of use of formal implementation frameworks, although the RE-AIM framework was used by several, and has been adopted for our work. We have also incorporated important components of implementation success identified including good stakeholder relationships and engagement, a manualised intervention flexible enough to adapt to the context, and ensuring facilitators are well-trained, confident, and enthusiastic. Our stakeholder survey indicated clinician desire to offer interventions but insufficient training, skills, and confidence. We recruited 17 clinical neuropsychologists from six memory clinics throughout Australia for the clinician training. Most clinicians reported being satisfied with the training. Suggested improvements included addressing technical issues with the online modules and reducing their length, as well as expanding the workshop across two days.

Discussion/Conclusion

The ADNeT Cognitive Interventions Working Group is addressing the evidence-practice gap in cognitive intervention research in Australia. We are currently revising the training package with plans to create a Community of Practice to continue supporting the implementation of cognitive interventions in memory clinics throughout Australia.

Co-Designing and Implementing a Virtual Memory Clinic for Regional and Rural Australia

Susan Kurrle [1], Matthew Paradise [2], Simone Simonetti [2], Sharon L Naismith [1], Lee Fay Low [1], Jessica Parkhouse [3], Lisa Vaccaro [2], Inga Mehrani [2], Johannes Michaelian [2], Henry Brodaty [1], Dimity Pond [1]

[1] Professor, [2] Dr, [3] Ms

Background

While 34% of older Australians live in rural/regional areas, only 15% of multidisciplinary memory clinics are located in these regions and offer limited services. This presents a barrier to timely diagnoses, treatment and post-diagnostic support. This study aims to co-design and pilot a virtual memory clinic model of care for early forms of cognitive decline.

Methods

In 2023, focus groups and interviews were conducted with health professionals, people with lived experience of dementia and other stakeholders in order to develop an ideal model of care, with sufficient flexibility for different healthcare contexts around Australia. The model of care developed involves partnership between the virtual clinic and regional services including GPs. Medical and allied health practitioners (AHPs) will deliver services via telehealth with on-site nurses or AHPs providing in-person support and facilitating local service integration. The model of care incorporates both video-conferencing and face-to-face components. For this initial pilot feasibility study, the model of care has been specifically 'localised' for Echuca, Victoria via a series of meetings and face-to-face workshops. Outcomes will evaluate the model against the ADNeT Clinical Quality Registry quality indicators, experience of care, and the impact on assessment, diagnosis and treatment rates. Cost effectiveness and factors related to successful implementation will also be examined.

Results

The virtual memory clinic model commenced in the Echuca region in May 2024. Training with GPs and AHPs has been undertaken to raise awareness and build capacity for regional dementia assessment and post-diagnostic services. Key progress to date will be presented and discussed, including factors related to successful implementation.

Discussion/ Conclusion

Findings from this project will support Federal and State governments and regional services in understanding the effectiveness of virtual memory clinics, potentially justifying further iterations of the virtual memory clinic model for use in other states and territories.

Blood Based Biomarkers for Alzheimer's Disease in Primary Care

Christopher Rowe [1]

[1] Professor

Background

There is clear evidence that the benefit from amyloid monoclonal antibody therapy for AD is greatest in early stage disease. The current average 3 year delay between onset of symptoms and diagnosis is no longer acceptable and earlier detection in primary care is the solution. Blood based biomarkers (BBB) for AD have arrived and are being marketed to both specialists and GPs. Education of GPs on their appropriate use and application of the results is essential to maximize cost-benefit and avoid harm. With funding from the Commonwealth Department of Health and Aged Care, ADNeT has commenced a study in Adelaide, Newcastle and Melbourne that will educate GPs, provide access to plasma pTau217+, and assess the impact of the BBB in clinical practice on accuracy and confidence in diagnosis of Alzheimer's disease and earlier referral to specialist care.

Is it Just Amyloid?

Amy Brodtmann [1]

[1] Monash University

Background

Co-pathologies are the norm in Alzheimer's disease. People diagnosed with classical amnestic AD in life will have multiple brain pathologies on post-mortem. More than 80% have associated vascular disease, and 60% have more than 4 types of brain pathology, including Lewy bodies, small vessel disease, and TDP-43/hippocampal sclerosis. Canonical features of AD – such as rapid forgetting and hippocampal atrophy – may be more associated with TDP-4 pathology and LATE (limbic associated TDP-43 encephalopathy) than tau and amyloid deposition. Younger people with AD have less co-pathologies but may present with atypical features such as a dysexecutive profile without significant memory impairment or posterior cortical atrophy. This suggests that tau and amyloid are not the sole contributors to the cognitive profile of people with late-life AD. Clinically, people with AD often have features of small vessel disease and prior strokes, meaning that a diagnosis of mixed vascular and Alzheimer's dementia is common. Conversely, people with a diagnosis of dementia with Lewy bodies usually have concomitant AD pathology. This talk will present an overview of pathologies other than Alzheimer's that determine clinical phenotypes.

Is it Really Amyloid?

Bryce Vissel [1], Gideon Caplan [2]

[1] Professor, [2] Associate Professor

Background

The amyloid hypothesis has driven drug development strategies for Alzheimer's disease (AD) for over 25 years. Recent results from clinical trials of antibodies that target β-amyloid (Aβ) for AD have created excitement, accelerated drug approval and been heralded as corroboration of the amyloid cascade hypothesis. But is it?

Method

Considerable epidemiological evidence highlights weaknesses of the amyloid hypothesis. The net effect on clinical outcomes by anti-amyloid antibodies, particularly on cognition and "hard' downstream outcomes, despite their apparent strong effect on amyloid further undermine their use case to clinicians. While Aβ may contribute to disease, the genetic and biochemical data and the mixed disease pathology observed in the majority of patient brains strongly suggest a different and more complex aetiology.

Results

Extensive data cited in support of the amyloid hypothesis, including genetic links to disease, can be interpreted without necessarily invoking a primary role for Aβ in AD. Rather, the data point to Aβ and amyloid playing only a partial aetiological role, despite the importance of amyloid in the definition of AD, and suggest that among other priorities, we need to fundamentally understand the mechanisms driving ADL and cognitive loss in order to solve the disease. Many other avenues seem to offer more promise including synapse loss, neurodegeneration and metabolism.

Discussion/ Conclusion

While a role for Aβ cannot be ruled out, the extremely limited net benefits of anti-amyloid therapy, after decades of trials and multi-billions of research dollars, points to a strong mandate to expand our view of pathogenesis beyond Aβ and tau in order to understand and ultimately solve AD. Care must be taken in considering the use of the new anti-amyloid drugs.

Amyloid Reduction- Can we Achieve it?

Michael Woodward [1]

[1] Associate Professor

Background

We now have effective therapies that lower brain amyloid in those with mild Alzheimer's Disease (prodromal and mild dementia) - achieving normal amyloid levels in many patients in less than 6 months. Two are likely to soon be TGA-approved here: lecanemab and donanemab. Not only do these lower amyloid, they also slow cognitive and functional decline and if used early enough in the disease process may actually reverse the decline that has already occurred. There are practical issues to be resolved- proving the patient is amyloid positive to begin with, finding appropriate infusion centres, monitoring safety and deciding on endpoints. Then there is funding. But for the first time ever we have therapies that directly target the underlying disease process.

Blood-Based Proteomic Profiling for Longitudinal Cognitive and Neuroimaging Outcomes, within an Asian Memory Clinic Cohort

Vera Yuen Cai [1], Hyungwon Choi [2], Christopher Li Hsian Chen [2], Dr Ming Ann Sim [2], Arthur Mark Richards [2]

[1] Chinese University of Hong Kong, [2] National University of Singapore

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Background

The prognostic role of plasma proteomics for longitudinal cognition and neuroimaging outcomes within an Asian memory clinic cohort with a high prevalence of cerebrovascular disease remains un-investigated.

Methods

A prospective cohort of Singaporean memory clinic subjects was followed-up for 5 years. Annual neuropsychological assessments were performed, with cognitive decline defined as a Clinical Dementia Rating Scale Sum-of-Boxes (CDR-SB) ≥2 increment from baseline. Cerebral small vessel disease (CSVD) markers (white matter hyperintensity (WMH) volume, lacunes, cerebral microbleeds (CMBs)) and neurodegeneration (grey matter volume) markers were evaluated on 2-yearly serial brain magnetic resonance imaging (MRI) scans. 768 plasma proteins were profiled at baseline using the Olink platform, and their associations with cognitive and MRI outcomes were evaluated using multivariate regression models.

Results

Of 545 subjects (mean age 72.7±8.0 years, 43.7% male, 57.7% baseline cerebrovascular disease, 22.6% no cognitive impairment, 37.6% cognitive impairment no dementia, 39.8% dementia), the incidence of cognitive decline was 35.8% (N=195). Of the significant proteins associated with cognitive decline, Osteopontin (adjusted hazard ratio (AHR) 1.67, 95% C.I. 1.34-2.09, adjusted p-value=0.0001l), GPR37 (AHR 1.28, 95% C.I. 1.13-1.46, adjusted p-value=0.0022), and CKAP4 (AHR 1.81, 95% C.I. 1.33-2.45, adjusted p-value=0.0022) were the top 3 most significant proteins, and were independently associated with cross-sectional grey matter volume, WMH volume, and CMBs (all p<0.05, Figure 1). Longitudinally, Osteopontin and GPR37 also independently predicted progression of one or more CSVD parameters (all p<0.05, Figure 2). Over-representation analysis of biological processes in all significant proteins revealed enrichment of cell adhesion, inflammatory response and signal transduction (Figure 3).

Discussion/ Conclusion

Our early findings shed insight into late-stage protein biomarkers and proteomic signatures for cognitive decline, which warrant further validation and mechanistic elucidation as potential therapeutic targets.

Cognitive Activity Participation as a Dementia Prevention Strategy

Allen Lee [1]

[1] The Chinese University of Hong Kong

Background

Staying cognitively active may help older adults prevent dementia. However, findings from epidemiological studies are mixed, and the underlying mechanisms are not well understood.

Methods

In collaboration with the Department of Health of the Government of Hong Kong, our team conducted a territory-wide longitudinal epidemiological study to examine the association between cognitive activity participation and dementia incidence, independent of other lifestyle practices and health-related factors. Moreover, with the support of Research Grants Council (grant number: 24114519), we performed a randomized controlled trial to test the effect of increasing cognitive activity participation on cognition and functional connectivities in older adults with subjective cognitive decline (but without mild cognitive impairment or dementia).

Results

Our epidemiological study found that those with regular participation in cognitive activities were at a lower risk of development dementia years later. This association remained significant even after excluding those who developed dementia shortly after baseline and controlling for other lifestyle behaviours and a wide range of health problems and limitations. Furthermore, our RCT showed that cognition was maintained and the default mode network was strengthened at 6 months among participants with increased cognitive activity participation. The adherence rate was high, and no serious adverse effect was reported.

Discussion/ Conclusion

Our research work suggests that engaging in more cognitive activities is a safe and effective non-pharmacological intervention for better brain health in older adults who are not yet experiencing mild cognitive impairment or dementia. Our findings highlight the importance of advocating for older adults to stay cognitively active in late life.

Large Scale Case-Finding of Dementia in the Community - Can AI Solve it All?

Ming Yan, Yaping Zhang, Xin Xu, Xindi He, Ting Pang, Xuhao Zhao, Christopher Chen, Ruofei Hu, Haoxuan Wen, Guohai Xu

Background

To investigate the psychometric properties, administration efficiency and implementational feasibility of a previously piloted voice recognition-based digital cognitive screener for dementia detection in a large-scale community of elderly participants.

Methods

Eligible participants completed the demographic, lifestyle investigations and the DCS. Domain-specific and global cognition was assessed by a comprehensive neuropsychological test battery. Diagnosis of mild cognitive impairment(MCI) and dementia was made based on the clinical dementia rating. Completion rate and administration time for the DCS were recorded. Correlation between the DCS and domain-specific and global cognitive performance were assessed. Receiver operating characteristic (ROC) analyses examined the discriminate validity of the DCS in detecting MCI and dementia. A cost-consequences analysis was conducted to compare the screening efficacy of DCS with two traditionally administered cognitive assessment tools, the Mini-Mental State Examination(MMSE) and the Montreal Cognitive Assessment (MoCA), was conducted.

Results

Among a total of 11,186 participants, the completion rate of the DCS was 97·5% with a conduction time of 5·6-6·1 minutes, regardless of gender, age and education stratifications. DCS total score was significantly associated with domain-specific and global cognitive z-scores. Area under the curves (AUCs) of the DCS were 0·95 (0·92, 0·99) and 0·83 (0·79, 0·88) for dementia and MCI detection, respectively. There was no significant difference on the AUCs among different age- and education-stratified subgroups. Comparing with the MoCA and MMSE, DCS resulted in time savings of 35·4%-36·0% and 30·7%-31·2% for identifying dementia cases, as well as 22·6%-22·8% and 16·2%-16·4% for identifying MCI cases.

Discussion/ Conclusion

Our findings demonstrated that the DCS was an effective and efficient tool for case-finding of dementia and MCI in a Chinese community. The large-scale implementation of the DCS among older Chinese adults could be an practical cognitive screening strategy to improve the management of healthcare resources.

Adult Children of Patients Having Alzheimer's Dementia: Preclinical Stage of AD?

Yuan-Han Yang [1]

[1] Kaohsiung Medical University

Background

Individuals with his parents having Alzheimer's dementia (AD) have a 4 to 10 times higher risk of developing AD compared to those without family history. We are going to report the demographic and biological characteristics of adult children (AC) of AD parents with its clinical significances in Taiwan.

Methods

AC of AD patients age from 50-79 years old were recruited from the neurological outpatient department of Kaohsiung Municipal Ta-Tung Hospital, Taiwan. The paired individuals, adult children and parents have received annual following up in clinical, neuropsychological, and neuroimaging including PET/CT with 18F-Florbetaben (FBB) imaging session, using DiscoveryTM MI DR PET/CT system (General Electric Medical Systems, Waukesha, Wisconsin, USA), plasma biomarkers, amyloid beta 1-40, amyloid beta 1-42, total-tau, and P-tau181measured by ELISA. The study was approved byKaohsiung Medical University Hospital Institutional Review Board [ ]. Written informed consent was obtained from all participants before including in this study.

Results

63 AC with age 59.3 ± 5.8 years, female predominant (76.2%), baseline MMSE 28.3 ± 1.8, CASI 94.7 ± 3.4, and having at least one of APOE e4 allele 34.9%, have recruited. 19 voluntary participants (25.4%) completed 18F-FBB PET.

9 of 19 (47.4%) were classified as amyloid-positive based on visual assessment, rated by a senior board-certificated nuclear medicine physician with experience in interpretation of 18F-FBB PET who evaluated all images according to the guideline of 18F-FBB PET interpretation, blind to all clinical information.

Discussion/ Conclusion

AC of AD patients have higher proportion of having APOE4 allele and higher proportion of having amyloid PET (+). It may imply AC does increase the risk of developing AD, and AC with amyloid PET (+) could be preclinical AD.

Improving Dementia Data in Australia: National Dementia Data Improvement Plan 2023-2033

Sonya Glasson [1], Melanie Dunford [1]

[1] Australian Institute of Health and Welfare

Background

Dementia is a substantial heath, aged care and societal challenge. Currently over 400,000 Australians are estimated to be living with dementia, and with population ageing, this is predicted to double in the next 35 years. Despite this, many dementia data gaps persist. Accurate and timely evidence is crucial to inform how we respond to this challenge. In response, the Australian Institute of Health and Welfare (AIHW)'s National Centre for Monitoring Dementia (NCMD) aims to ensure that there is robust information to provide timely, accessible and policy-relevant statistics on dementia through systematic reporting of available data and improving current, as well as developing new, data sources.

Methods

The AIHW's NCMD consulted with key data custodians, policymakers, and an established dementia expert advisory group consisting of researchers, clinicians, peak bodies and a consumer representative on existing data gaps, priorities and activities to fill data gaps. A 10-year National Dementia Data Improvement Plan 2023-2033 was developed which outlines activities to improve national dementia data over the next 10 years to monitor dementia and provide an evidence base for effective policy development, service provision and planning.

Results

Through these consultations, 5 main goals and 14 key data gaps which limit national policy development and service planning were identified. Forty data improvement activities to address the key data gaps were also developed. Additionally, criteria to prioritise the data improvement activities was developed to assist enablers of the National Dementia Data Improvement Plan 2023-2033 (e.g., the National Health and Medical Research Council) on how to focus their efforts.

Conclusion

Achieving one or more of the 5 main goals would greatly improve the data available to effectively deliver and evaluate policies and services aimed at improving the lives of people with dementia and their carers in Australia.

Geographical Variation in Health Service Use by People Living with Dementia

Megan Fraser [1], Dr Ann-Kristin Raymer [1], Dr Ingrid Evans [1]

[1] Australian Institute of Health and Welfare

Background

People living in regional and remote areas of Australia face particular challenges in accessing services for dementia diagnosis, treatment and support. Similarly, people living with dementia in areas of relative socioeconomic disadvantage face barriers to accessing timely and appropriate services. There is a need for better evidence to inform policy and service responses to support people living with dementia across all geographical and socioeconomic areas of Australia.

Methods

The current research uses a multi-source enduring linked dataset to identify Australians with dementia and explores variations in health and aged care service use across geographical and socioeconomic areas. A cohort of 158,730 people with a dementia record were assigned to study groups based on their place of residence in 2019: permanent residential aged care or the community. Analysis variables include general practitioner and specialist attendances, medicines dispensed, emergency department visits and hospital stays, and respite residential aged care use.

Results

The remoteness and socioeconomic area people with dementia live in impacts their health service use. People living with dementia outside major cities and in lower socioeconomic areas had fewer specialist appointments and lower rates of dispensing of dementia-specific medicines, but higher rates of polypharmacy and other indications of health comorbidities compared with those in more urban and advantaged areas. Residential respite care was mostly used in the lead up to entering permanent care, with the lowest rates of use being in remote areas.

Discussion/ Conclusion

Linked data can bring together information from a range of sources to improve our ability to understand service use among people living with dementia and identify disparities at the local level. These insights can be used to better plan and deliver services to ensure equitable and timely access to appropriate treatment and support and improve outcomes for all Australians living with dementia, their families and carers.

Dementia Awareness Survey - Examining Public Knowledge and Perceptions Towards Dementia and Dementia Risk Reduction

Melanie Dunford [1], Dr Sarang Kim [1]

[1] Australian Institute of Health and Welfare

Background

There is a poor community understanding of dementia and people often do not know how to reduce their risk or delay the onset of dementia. Stigma about dementia is common, which can lead to delays in timely diagnosis and treatments. This survey explored public attitudes towards, and knowledge of, dementia and people living with dementia from a nationally representative sample of Australian adults.

Methods

A total of 5,445 people aged 18 and over completed the survey between 24 July to 15 August 2023 measuring dementia stigma (Dementia Public Stigma Scale), knowledge of dementia (Dementia Knowledge Assessment Scale (DKAS)) and dementia risk reduction (Knowledge of Dementia Risk Reduction (KoDeRR)), and actions taken for dementia risk reduction.

Results

Australians' overall dementia knowledge level was low (DKAS M= 20.7; CI: 20.4 -21.0). Yet, Australians have a reasonable awareness of some key risk factors of dementia (more than 70% identified being physically, cognitively, and socially active as risk factors of dementia) but less certainty in others. Only 36.4% of people are engaging in one or more actions/behaviours for dementia risk reduction. Australians hold varying levels and types of stigma towards dementia and/or people living with dementia. People indicated that they do not feel relaxed (20%) around people with dementia and believed that people with dementia should always be supervised (66.7%). The level of dementia knowledge was weakly correlated with the level of dementia-related stigma ($r(5386) = -.25$, $p = <.001$).

Discussion/ Conclusion

This survey was the biggest survey of its kind suggesting that there is a need to educate Australians about dementia and dementia risk reduction. The findings from the survey will inform national policy priorities for the next 10 years under the National Dementia Action Plan and inform the design and implementation of dementia awareness-raising initiatives and other relevant interventions.

Pursuing Dementia Detection for Better Prevalence Estimation with Artificial Intelligence Techniques in Electronic Health Data

Richard Beare [1], Helene Roberts [2], Jenny St Sauver [3], Simon Bell [3], Kristy Sisostorm [2], Chris Moran [1], Ming Liu [2], Velandai Srikanth [3], John Clark Kennedy [4], Alicia Lu [2], David Ung [2], Jenni Ilomaki [2], Walter Rocca [3], Elizebeth Le [5], Amanda Thrift [3], Nadine Andrew [1], Taya Collyer [2]

[1] Associate Professor, [2] Dr, [3] Professor, [4] Mr., [5] Ms.

Background

Unstructured data in health records are not routinely available for the purpose of capturing the presence or probability of dementia in health records. We aimed to develop algorithms using routinely-collected structured and unstructured EHR data to reliably identify cases of diagnosed dementia, as a key step towards incorporating such data in prevalence estimation.

Methods

Data were sourced via the National Centre for Healthy Ageing Data Platform, a curated, EHR-derived data warehouse. Individuals aged >60 years with dementia were identified through hospital specialist dementia clinics. A comparison group with EHR records and without dementia was recruited from the community. Clinical experts (Neurology, Geriatric Medicine) informed variable and concept selection. Algorithms were developed via two work-streams; a traditional biostatistical approach fit logistic regression models using structured data, and a data science stream used Natural Language Processing (NLP) to fit diverse models to the unstructured (text) data within the EHR, for the same individuals.

Results

Of 1,082 individuals (368 with dementia), 860 had text available. Among a range of NLP-derived models, Random Forest performed best in assigning dementia status [AUC 0.80, specificity 89.7%, sensitivity 80.3%]. In the traditional biostatistics stream, 15 structured variables were included in the final model, covering demographics, health service attendance, medications, and ICD-10 Codes [AUC 0.85, specificity 72.2%, sensitivity 80.60%]. An algorithm combining data from both streams performed better than either stream alone [AUC 0.95, specificity 83.2%, sensitivity 92.5%].

Conclusions

Artificial intelligence techniques applied to unstructured electronic health data and guided by human clinical expertise may be powerful tools in capturing the probability of dementia at scale, supplementing traditional approaches using structured data. This novel approach may yield practical and scientific advantages for dementia prevalence estimation. Validation is required in real-world settings, in whom the a priori probability of dementia is less-crisply delineated.

Tracing Kynurenine's Footprints in Alzheimer's Disease

Benjamin Heng [1], David Lovejoy [1], Ralph Martins [1]

[1]Macquarie University

Background

The kynurenine pathway (KP) is a critical biochemical pathway responsible for production of essential energy (NAD). However, it is often dysregulated in neuroinflammatory diseases such as Alzheimer's disease (AD).

Methods/ Results

Our first study, involving 20 AD patients and 18 healthy controls, showed quantifiable changes in KP activity within brain can be reflected in plasma of AD patients. Notably, these plasma KP alterations significantly correlated with cerebrospinal fluid p-tau and t-tau, highlighting the pathway's involvement in AD progression. Subsequent studies using the KARVIAH and AIBL cohort further reinforce this notion by demonstrating the correlations between KP metabolites and other pathological features of AD. In the KARVIAH cohort study, elevated levels of kynurenine and anthranilic acid were observed in female patients with high neocortical amyloid-b load. When incorporated into a predicative model alongside major risk factors age and APOE e4, these metabolites demonstrated high specificity and sensitivity in identifying patients with high neocortical amyloid-b load. Meanwhile in the AIBL cohort study, we noted elevated 3-hydroxylkynurenine, 3-hydroxyanthranilic acid and 3-hydroxyanthranilic acid/anthranilic acid ratio in patients prior progression to dementia or with an increased risk of cognitive impairment. Conversely, the neuroprotective metabolite picolinic acid was significantly lower in the same group of patients. Interestingly, the 3-hydroxyanthranilic acid/anthranilic acid ratio showed a distinct profile between progressors and non-progressors or those progressing to dementia.

Discussion/ Conclusion

Overall, these three studies underscore the potential role of KP in AD progression and its utility as a predictor for or cognitive changes.

Connecting the Peripheral Lipidome with Alzheimer's Disease and it's Risk Factors

Kevin Huynh [1]

[1] Baker Heart and Diabetes Institute

Background

Increasing evidence suggests metabolic disruptions as key factors to late onset Alzheimer's disease (AD) pathogenesis. The two strongest risk factors for late-onset AD are age, and different alleles of the APOE gene, encoding for apolipoprotein E, a protein that plays a critical in lipid metabolism in the body. Lipids are critical amphiphilic metabolites that are involved in all processes of life, but notably with central and peripheral immunity. Here we investigated the relationship between peripheral lipidome, both plasma/serum and peripheral blood mononuclear cells, to investigate the changes to lipids with both ageing and APOE genotype in the context of AD.

Methods

We performed targeted lipidomics profiling of plasma and serum samples from several large cohorts, including the Australian Imaging Biomarkers and Lifestyle Study (AIBL, n = 1112), the Alzheimer's disease Neuroimaging Initiative (ADNI, n = 800) and the Busselton Health study (BHS = 4384). Lastly, we profiled the lipidome of peripheral blood mononuclear cells in the AIBL study (n = 1112) to study the changes to peripheral immune cells in AD and its risk factors.

Results

Cross-sectional and longitudinal plasma associations highlight lipid related signatures associated with AD, ageing and APOE genotype. A major signature was identified with several lipid classes, but notably within the ether lipid groups. Leveraging the BHS study together with AIBL and ADNI, we identify a potential role in resilience arising from the APOE e2 allele mediated by plasma ether lipids, but no such effect with the APOE e4 allele. Lastly, investigation into PBMC lipid pools, controlling for differences in immune cell populations, identified substantial differences associated with ageing and AD.

Discussion/ Conclusion

As age and APOE remain the largest identified risk factor for late onset AD, identifying how these factors interact and impact different metabolic areas will shed light on additional mechanisms with AD development.

Development of A Novel Immunogenetic Molecular 'Fingerprint' Associated with Alzheimer's Disease

Prof. Colin Masters (AO) [1], Mr. Rizwan Khan [2], Prof. Ralph Martins (AO) [3], Dr. Monique A David [2], Dr. Utpal K Adhikari [2], A/Prof. Mourad Tayebi [2]

[1] Florey Instiute of Neuroscience & Mental Health, [2] Western Sydney University, 3Macquarie University

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Background

Mounting evidence highlights a pivotal link between adaptive immunity and neurodegenerative disorders, particularly Alzheimer's disease (AD). Dysregulation of adaptive immune responses intensifies AD pathology and neuroinflammation, as identified by recent Genome-Wide Association Studies (GWAS) pinpointing immune-related genes associated with heightened AD risk. Despite this, a comprehensive exploration of the role of the adaptive immune system in AD is lacking.

Methods

Our objective was to deepen our understanding of the interplay between adaptive immunity and AD through comprehensive analysis of B and T cell repertoires in AD animal models and patients, utilizing both Sanger sequencing and Next Generation Sequencing (NGS) techniques.

Results

In the APP/PS1 mice B cell repertoire, we observed a significant increase in mutations within the immunoglobulin FWR region of the IGK chain. Remarkably, significant alterations in the SHM profile were identified within the FWR, accompanied by an evident over-utilization of two immunoglobulin genes, IGKV4-91 and IGKV4-74.

Subsequent analysis of human B and T cells unveiled underutilization of two BCR V genes, increased gene usage for the IGK chain, and heightened gene usage for the IGL chain in AD. Additionally, the AD cohort exhibited a significant rise in T-cell receptor alpha (TRA) and beta (TRB) diversity, with elongated junction lengths for TRB compared to healthy controls. Notably, altered gene usage patterns were identified in multiple TRA and TRB genes, suggesting an abnormal behaviour of the adaptive immune system in AD.

Discussion/ Conclusion

Collectively, our findings underscore an aberrant adaptive immune response in AD. Furthermore, the molecular signatures identified in AD-associated immunoglobulin genes may serve as potential biomarkers, offering promise for early AD detection and forming a robust panel for establishing an AD molecular 'fingerprint.' This research contributes crucial insights into the intricate relationship between adaptive immunity and AD, paving the way for targeted therapeutic interventions and diagnostic advancements.

Exploring the Utility of Plasma MicroRNA for Early Diagnosis of Alzheimer's Disease

Assoc. Prof. Joanna Williams [1, 2], Dr. Christopher Fowler [3, 4], Prof. Colin Masters [3, 4], Ms Diane Guévremont [1, 2], Dr. Nicholas Cutfield1, [5], Prof. Warren Tate1, [6], Prof. Wickliffe Abraham1, [7], Prof. Ralph Martins [4, 8]

[1] Brain Health Research Centre, [2] Department of Anatomy, University of Otago, [3] The Florey Institute, The University of Melbourne, [4] Australian Imaging, Biomarkers and Lifestyle (AIBL) Research Group , [5] Department of Medicine, University of Otago, [6] Department of Biochemistry, University of Otago, [7] Department of Psychology, University of Otago, [8] Department of Biomedical Sciences, Macquarie University

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Background

A class of regulatory RNA, microRNA, control a wide range of neuronal functions which are dysregulated in Alzheimer's disease (AD). MicroRNA are highly stable in blood plasma and can be measured by routine technologies. Accordingly, they may represent robust, stable, and easily accessible biomarkers capable of reflecting amyloid pathology, as well as multiple other aspects of AD physiology. Indeed, in previous work we identified specific plasma microRNA that change with AD progression.

Methods

Focusing on a group of cognitively normal individuals from the AIBL cohort, we have explored the expression of these microRNA in association with amyloid-β (Aβ) load as determined by positron emission tomography. The group was stratified by centiloid score where n=84 individuals (73.4 ± 4.4 years; 43:41 female:male) were considered Aβ-positive (69.26 ± 32) and n=93 (73.8 ± 5.0 years; 47:46 female:male) were considered Aβ-negative (-0.64 ± 6.3). MicroRNA expression was assessed using custom TaqMan microfluidics arrays. Following data normalisation, and identification of differentially expressed microRNA (empirical Bayes moderated t-tests; fold change > ± 0.2; $p < 0.05$), multiple logistic regressions were performed using the Backward: Wald method and goodness of fit was evaluated using the Hosmer-Lemeshow test ($p > 0.05$). The receiver-operating characteristic curve, area under the curve (AUC) was calculated to assess the ability of specific microRNA to predict membership of the groups ($p < 0.05$).

Results

We found 13 differentially expressed microRNA, nine of which significantly contributed to the model. These included miR-29c-3p and miR-335-5p identified in our pilot study1. The diagnostic ability (AUC) of the nine microRNA was determined as 0.877 which increased to 0.910 with inclusion of ApoE status in the predictive model.

Discussion

These results suggest that this microRNA signature alone or in combination with ApoE status may be a useful additional tool for detecting the earliest stages of AD.

The Effectiveness of a Culturally Adapted Dementia Prevention Animation on Ethnically Diverse Participants' Knowledge of Dementia Prevention

Dr Marina Cavuoto [1, 2], Dr Kathleen Doherty [3], Dr Andrew Gilbert [1, 4], Dr Claire Eccleston [3], Professor Bianca Brijnath [1, 5, 6], Dr Josefine Antoniades [1, 2], Ms Simona Markusevska [1], Ms Kayla Lock [1], Dr Carolina Navarro Medel [7]

[1]National Ageing Research Institute, [2] Monash University, [3] University of Tasmania, [4] La Trobe University, [5] University of Melbourne, [6] University of Western Australia, [7] University of Chile

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Background

Despite increased dementia risk in culturally and linguistically diverse (CALD) populations, prevention messages rarely reach these communities. We co-designed a dementia prevention animation with 9 CALD groups in Australia. This article investigates the impact of the animation on communities' dementia prevention knowledge.

Methods/ Results

A before-and after survey conducted between January and June 2021. The survey was online and in-person, involving a final sample of 502 participants from the Arabic-, Hindi-, Tamil-, Cantonese-, Mandarin-, Greek-, Italian-, Spanish-, English- and Vietnamese-speaking communities. Dementia knowledge was measured using a modified component of the dementia risk reduction knowledge (KoDeRR) questionnaire in English and relevant languages. We measured change in dementia knowledge using paired sample t-tests, and examined predictors of change in dementia knowledge through a series of hierarchical regressions.

Results

Mean performance on the 20-item KoDeRR significantly increased after viewing the animation (M pre = 18.9, SD = 7.0; M post = 21.9, SD = 6.9; t(501) = -10.89, p < .001), although the effect was considered small (Hedge's g = 0.44). Examination of the individual languages in which the survey was taken revealed a significant increase in dementia knowledge in most languages after viewing the animation (ps <05; except for English, and Hindi and Tamil, which had particularly small sample sizes of less than 5). After controlling for age, gender, and baseline KoDeRR score, completing the survey in a language other than English was associated with a larger increase in KoDeRR score compared to completing the survey in English (except for Hindi). Neither language spoken at home, age, or time lived in Australia predicted change in dementia prevention knowledge.

Conclusions

Animations co-designed with ethnically diverse communities to improve awareness of dementia prevention resulted in increased dementia knowledge in most of the included language groups.

Dementia Awareness and Inclusivity in Multicultural Communities: Lessons Learned from an Australian Education Initiative

Gabriela Caballero [1], Eman Shatnawi [1], Canterbury Bankstown Dementia Alliance [2], Genevieve Steiner-Lim [1], Diana Karamacoska [1], Emorfia Tsouros [1]

[1] Western Sydney University, [2] Canterbury Bankstown

Background

Culturally and linguistically diverse people remain under-served and under-represented in Australian dementia research and interventions. Ongoing work in Western Sydney, Australia, has found that stigma and misperceptions about dementia remain highly prevalent especially among non-English speaking communities. A multisectoral collaboration, known as the Canterbury Bankstown Dementia Alliance, was formed to address these issues.

Methods

Together with alliance members who have living and caring experiences of dementia, we co-created a multilingual dementia education initiative involving the annual delivery of awareness raising information sessions and an exhibition to connect people with research and support services. The impact of these initiatives was evaluated using an implementation science framework involving multi-method research.

Results

To date, the initiative has reached over 2,000 people from English, Arabic, Vietnamese, Cantonese, Mandarin, and Greek speaking backgrounds. The barriers that we encountered with these initiatives included: problematic translations of the word 'dementia' across the different languages; lack of culturally appropriate surveys and research tools; and low literacy levels that prevent engagement with written materials. To aid awareness raising efforts, we implemented the following enablers: referring to memory loss and Alzheimer's disease instead of dementia in advertisements; obtaining different avenues of funding to develop culturally appropriate educational material and surveys with community groups; employing bilingual advocates to co-facilitate information sessions with a field expert; incorporated personal stories during presentations; and embedded the alliance's activities into our professional roles to ensure commitment and continuity.

Discussion/ Conclusion

This presentation will highlight how multicultural communities can be engaged in dementia research and education to combat stigma, promote help-seeking, and foster inclusivity.

“It's all About your own Willpower”: Exploring Perspectives on Brain Health and Healthy Ageing Among Ider Chinese Adults

Joyce Siette [1]

[1] MARCS Institute for Brain, Behaviour and Development, Western Sydney University, NSW, Australia

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Background

In the context of a global ageing population, an in-depth understanding of how older adults perceive and maintain brain health is crucial for tailoring effective public health interventions. Limited research has explored these perspectives, particularly within culturally and linguistically diverse communities. This study aims to capture unique cultural, societal, and personal considerations that influence cognitive well-being, providing novel insights for the development of culturally sensitive brain health awareness interventions for Chinese older adults.

Methods

Qualitative interviews were employed to elicit participants' views on healthy ageing, their understanding of brain health, and the practices adopted for cognitive well-being. The study engaged Chinese older adults (n=22), with an average age of 71.2 years (SD=4.3, range: 66-81). Deductive thematic analysis was applied to identify patterns in responses.

Results

Participants articulated diverse perspectives on the significance of brain health, spanning concerns about memory loss, societal pressures, and the impact on overall quality of life. Motivations to explore brain health emerged from personal experiences and perspectives, highlighting the importance of culturally sensitive approaches to brain health promotion. Chinese older adults also identified concerns about the negative impact of cognitive decline on quality of life and associated stigma. Cultural factors played a significant role, influencing attitudes towards seeking professional help, engaging in cognitive activities, and maintaining social connections. Motivations for preserving brain health included a desire for independence and the fear of burdening family members. Participants expressed receptiveness to government, community, and healthcare professional support in enhancing brain health.

Conclusion

This research establishes a foundation for holistic strategies, fostering inclusive and effective brain health initiatives for diverse ageing populations. By comprehending cultural nuances and individual motivations, policymakers, healthcare professionals, and community leaders can work together to navigate the complexities of cognitive well-being and advance initiatives for promoting brain health.

The Effectiveness of the Chinese iSupport for Dementia Program on the Quality of Life for Family Carers and People with Dementia

Mingxia ZHU [1], Jing Wang [2], Julie RATCLIFFE [3], Rujun HU [4], Chia-Chi CHANG [5], Huali WANG [6], Shahid ULLAH [3], Lily Xiao [3], Timothy KWOK [7], Henry BRODATY [8], Bianca BRIJNATH [9], Hui-Chen (Rita) CHANG [10]

[1] Kiang Wu Nursing College of Macau, [2] Xi'an Jiaotong University, [3] Flinders University, [4] Zunyi Medical University, China, [5] Taipei Medical University, [6] Peking University, [7] The Chinese University of Hong Kong, [8] University of New South Wales, [9] National Ageing Research Institute , [10] Western Sydney University

Aims

To determine the effectiveness of the Chinese iSupport for Dementia program on the quality of life for family carers and people with dementia.

Design

A multicentre randomized controlled trial.

Methods

We recruited Chinese family carers of people with dementia to the study from eight study sites in Australia and greater China. The multicomponent intervention included self-learning using the web-based iSupport manual, facilitator-enabled virtual peer support and access to dementia care resources. The intervention was delivered virtually and lasted for 6 months. We observed the outcomes for another 3 months after the intervention. Our primary outcome measure was quality of life of family carers and people with dementia. Our secondary outcomes measures included carer self-efficacy, social support, changed bahaviours of people with dementia, carers' distress reaction to the changed bahaviours, unplanned hospital admissions and emergency department presentations of people with dementia.

Results

In total, we recruited 266 family carers to the study, with 131 in the intervention group and 135 in the usual care group. Most carers were women with a mean age of 53 years and resided with the people with dementia. The intervention demonstrated improved mental-health-related quality of life for family carers. However, the intervention did not show effectiveness on the physical-health-related quality of life for carers and did not show effectiveness on the quality of life for people with dementia. Moreover, the intervention demonstrated effectiveness on carers' self-efficacy in controlling upsetting thoughts and reduced distress reactions to changed behaviours of people with dementia at 6 months post-intervention. We found no intervention effect on other secondary outcome measures in the study.

Conclusion

The Chinese iSupport for Dementia program can be delivered by trained facilitators virtually. The program can improve Chinese family carers' mental-health-related quality of life and mental health.

A Dementia Model of Care for Residential Aged Care - Co-Design and Model Development

Daniella Rigoni [1], Marta Woolford [2], Niluksha Morawaka [1], Darshini Ayton [2], Phillipa Horsman [1]

[1] Baptcare, [2] Monash University

Background

Residential aged care (RAC) homes have a significant role in promoting and maintaining the health and well-being of residents. A model of care responds to an identified need and defines and conceptualises how care is delivered based on evidence and best practice. This project, which aimed to develop a dementia model of care (DMC), was initiated by Baptcare in response to recommendations from the Australian Royal Commission into Aged Care Quality and Safety.

Methods/ Results

Participatory action research consisting of a staff survey, focus groups and interviews with staff, residents and family members and environmental audits of 8 RAC homes via Dementia Training Australia BEAT-D App. Thematic analysis and descriptive statistics conducted on qualitative and quantitative data respectively.

Results

Data was obtained from 241 survey results, 16 focus groups (11 staff, 1 volunteer, 3 resident, 1 family); 36 interviews (28 resident, 5 family, 4 staff) and 8 environmental audits. Themes and domains were:

1) Integration and coordination of care - connect residents to what matters
2) Training - Promote lifelong learning
3) Workforce and clinical care - Deliver individualised clinical care
4) Dementia friendly environments - create a place where residents belong
5) Person-centre care - support fullness of life

Intervention ideas for each domain included designated care teams, communication processes, improved resident profiles for staff to know and understand residents, Montessori for Ageing and Dementia Care to promote person-centred care over task-based care. These interventions were identified from the literature and data and workshopped with advisory, governance and stakeholder groups.

Discussion/Conclusion

An academic and aged care provider partnership to develop a model of care has led to the development of an evidence-informed, co-designed, holistic model of care.

Deploying Robots to Provide Interactive Activities for People Living with Dementia in Aged Care Facilities

A/Prof. Jun Jo [1], Prof. Wendy Moyle [1], Mr Dongjun Wu [1], Dr. Lihui Pu [1], A/Prof. Rene Hexel [1]

[1] Griffith University

Background

Dementia is a progressive disease significantly impacting social interaction and activity engagement. Robots have been introduced to provide interactive activities for people living with dementia. However, deploying robots to provide interactive activities is challenging in aged care facilities due to the need for expensive human facilitation and oversight.

Methods

We implemented intelligent technologies (e.g., deep learning) to develop a robot program called "Adam' to offer interactive activities, including chat, exercises, and games via a human-like robot. An intervention protocol was developed to offer these activities to people living with dementia without human facilitation. Eleven participants with mild to moderate cognitive impairment participated in robot-led activity sessions three times a week for five weeks. Each robot session was individual and lasted for 10-15 minutes. The verbal, visual and behavioural engagement activities were video recorded and analysed. All participants shared their experiences through individual semi-structured interviews. The attendance rate of Adam's session and the frequency of interactions were evaluated.

Results

Participants reported a positive attitude toward the robot design and activities in the interviews. A high (86.1%) attendance rate for the robot sessions was achieved. We observed a high visual engagement (98.5%) in Adam's activities during the sessions, and behavioural engagement in robot-led activities increased over the five weeks. Participants could independently engage in Adam's activities, and most (97%) Human-Robot Interactions were free of human facilitation. Minor human facilitation (e.g., restarting the program) was primarily attributed to unpredictable program crashes (1.9%). Findings also provided a transparent equipment cost of approximately AUD 4729 when used in the aged care setting.

Conclusions

Deploying a technology-driven human-like robot is feasible to lead interactive activities for people with dementia at aged care facilities. Future research could consider different implementation strategies that address multi-level determinants of Adam's implementation based on the authentic context.

What Behaviours, and What Strategies? An Exploration of Behaviour Support Plans in Residential Aged Care

Henry Brodaty [1], Jennifer Hewitt [2], Kylie Wales [2], Theresa Flavin [3], Amy Tan BPharm [2], Meredith Gresham [2], Jacqueline Wesson [2]

[1] Scientia Professor , [2] Dr, [3] NA

Background

Behaviour support plans (BSPs) for people in residential aged care (RAC) were mandated through legislation in 2019 for those who require, or may require, restrictive practices. This legislation aims to reduce and potentially eliminate restrictive practice use.

People living with dementia will be impacted: up to 90% experience changed behaviours; 54% of people in RACs have dementia; and approximately 20% experience cognitive decline without a diagnosis.

There is no research examining practices implementing BSPs since legislation was introduced. Our exploratory study encompasses BSPs, behaviour support policies, staff views, identifying practices, themes, barriers and enablers. We report here on BSPs.

Methods

RAC providers recruited via professional networks were requested to include two sites, submitting three BSPs for residents from each site. Age, gender and diagnosis from redacted plans were extracted, with legislation and best practice used as a framework to against which to analyse identified behaviours and non-pharmacological strategies prescribed.

Results

Preliminary results are presented. Seven providers (24 sites) across eastern Australian states submitted sixty BSPs, varying in format, content, and length (range 1-27 pages). Residents were mostly female (n=41; 68%), aged 84 years (mean; +/-8.0; range 65-98), and according to BSPs, had dementia/cognitive impairment (n=57; 95%). Agitation and 'wandering' were the most frequently reported behaviours. Restrictive practices were common (n=46, 77%), including chemical restraint (n=14; 30%), environmental secure unit restraint (n=14; 30%), or both chemical and environmental restraint (n=15; 33%).

Behaviour support strategies were variable: many included generic strategies (e.g. offering drinks/snacks); with detailed tailored strategies and clear resident support preferences less common.

Conclusions

Implementation of behaviour support legislation as reflected in care planning documentation appears to be inconsistent, in terms of what constitutes 'behaviour' and how care staff use BSPs to support residents. Positive framing of behaviour support is limited. Strengthening supports for the sector is urgently indicated.

Understanding the Barriers and Facilitators to Small-Scale Dementia Care - A Scoping Review

Dr Stephen Isbel [1], Dr Diane Gibson [1], Dr Nathan D'Cunha [1], Robyn Lewis [1], Dr Kasia Bail [1]

[1] University of Canberra

Background

Small-scale residential dementia care is an innovative approach to providing care in a home-like setting for 6-15 residents by staff with broad caring roles. This model of care has the potential to benefit people with dementia, their families, the staff, and the wider community, but more information is needed to understand the characteristics of care and to clearly describe its potential benefits.

Methods

To identify the barriers and facilitators to small-scale dementia care, a scoping review was undertaken by searching MEDLINE, CINAHL, PsycINFO, Scopus, Web of Science, and CENTRAL from database inception to October 2023. Empirical studies were included if they were peer-reviewed, published in English and investigated long-term small-scale dementia care for 6-15 residents.

Results

In total, 44 studies were identified and synthesised into five focus areas: People with dementia (n=19), families (n=2), staff (n=12), the built environment (n=8) and other studies focussing on a program of care or studies including two or more study populations (n=3). Studies included quantitative (n=29), qualitative (n=13) and mixed (n=2) methodologies. Barriers and facilitators were identified in each focus area that either support or limit the implementation of small-scale dementia care. A key facilitator identified was the presence of a clear philosophy of care that guides the planning of small-scale care. A key barrier relates to the ability of the care organisation to adjust staff roles to deliver small-scale care.

Conclusions

Small-scale dementia care was described as beneficial for people with dementia, families, staff and the wider community. Awareness of the barriers and facilitators may assist aged care providers to establish or adapt care settings that place the person with dementia at the centre of care, provide greater opportunities for meaningful engagement and activities of daily living, while also creating a home-like environment which prioritises relationship building at all levels.

The Importance of Post-Diagnostic Support: a Panel Discussion

Kaele Stokes [1]

[1] Dementia Australia

The importance of post-diagnostic support: a panel discussion

In this panel discussion, participants will outline what good post-diagnostic support looks like, why it is important – not just for quality of life but in supporting research and research translation – and just what services can make a lasting difference.

Providing post-diagnostic support is vital to enabling people to live well with dementia.

This is best achieved by the provision of a tailored, flexible model of care that offers information and support for people recently diagnosed with dementia and, when available, their carer and/or family.

This type of post-diagnostic support can help people increase their understanding of dementia, plan support services and networks, develop personal and lifestyle strategies to help them live well and prepare and plan for any changes.

Another key aspect of post-diagnostic support is the timely referral and help accessing mainstream services and programs, including My Aged Care and the National Disability Insurance Scheme (NDIS).

Dementia Australia is the provider of post-diagnostic disease management support and the first point of call or entry into the service system.

Dementia Australia's post-diagnostic support service ensures that every person, pre, during and post-diagnosis is able to access the resources, supports and services available as well as assisting in them to access other services and allied health.

This includes people of all ages, living with all forms of dementia as well as for people with mild cognitive impairment.

Dementia Australia provides support for people living with dementia immediately following their diagnosis with reliable and expert information, advice and a wide range of programs to live well with dementia.

DeepSUVR: Using Temporal Constraints to Improve SUVR and Centiloid Quantification

Duygu Tosun [1], Christopher C Rowe [2], Tim Cox [3], Jurgen Fripp [3], Michael W. Weiner [1], Ashley Gillman [3], Vincent Dore [3], Pierrick Bourgeat [3], Manu Goyal [4], Pamela LaMontagne [4], Tammie Benzinger [4], Colin Masters [5], Victor L Villemagne [6]

[1] San Francisco Veterans Affairs Medical Center, [2] Department of Molecular Imaging & Therapy, Austin Health, [3] CSIRO Health and Biosecurity, [4] Mallinckrodt Institute of Radiology, Washington University School of Medicine, [5] The Florey Institute of Neuroscience and Mental Health, University of MelbourneThe Florey Institute of Neuroscience and Mental Health, University of Melbourne, [6] Department of Psychiatry, The University of Pittsburgh

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Background

PET quantification using the Standardised Uptake Value Ratio (SUVR) is hindered by noise, spill in, and specific binding in the reference region. We evaluate a novel deep learning method which learns from noise in longitudinal trends to correct the SUVR and improve quantification.

Methods

3098 participants with 2+ visits in AIBL/ADNI/OASIS (8826 scans) had their Amyloid PET images spatially normalised and quantified using the Centiloid SPM pipeline. A deep learning network (DeepSUVR) was trained to predict a SUVR correction factor (CF) for each spatially normalised image. For each iteration, the prediction was run on 2 random timepoints from the same participant, resulting in 2 Adjusted Centiloids computed using SUVR*CF and each tracer's standard Centiloid transform. A loss function was defined to penalise unexpected temporal changes: Centiloid decreasing over time, Centiloid deviating from the curve Centiloid/Year vs mean Centiloid. The loss also included a penalty for over-correction. The model was trained using a subset of ADNI/AIBL (2037 participants) and evaluated in terms of longitudinal consistency on the remaining ADNI/AIBL participants and on OASIS data. The correlations between head-to-head tracers in the OASIS and GAAIN calibration datasets were also computed.

Results

DeepSUVR increased the correlation between each pair of 11C-PIB/18F-Tracers in the GAAIN calibration dataset and between pairs of 11C-PIB/18F-Florbetapir in OASIS (from R2=0.86 to R2=0.92). Using DeepSUVR, the correlation between Centiloid/Year vs mean Centiloid increased from ρ=0.39 to ρ=0.48 in AIBL/ADNI and ρ=0.47 to ρ=0.51 in OASIS.

Conclusions

We have proposed a novel deep learning technique to correct SUVR estimation based on noise in longitudinal trends. The longitudinal constraint led to higher agreement between tracers in the head-to-head GAAIN/OASIS datasets and higher longitudinal consistency. Importantly, while the model was trained using pairs of images, the prediction is run on single images. Future work will evaluate this approach on tau tracers.

Genome-wide CRISPRi Screening Reveals Regulators of Alzheimer's Tau Pathology Shared Between Exosomal and Vesicle-Free Tau Seeds

Adam Briner [1], Gabriel Hand [1], Jürgen Götz [1], Juan Carlos Polanco [1], Yevhen Akimov [2], Avinash Fernandes [1], Giuseppe Balistreri [2]

[1] University of Queensland, [2] University of Finland

Background

The aggregation of tau protein is a defining feature of Alzheimer's disease (AD) and other tauopathies. Tau pathology is believed to be driven by free tau aggregates, and tau carried within exosomes, which propagate trans-synaptically and induce tau pathology in recipient neurons through a corrupting seeding process. Control of tau propagation by targeting either exosomes or vesicle-free tau has been proposed as a viable therapeutic strategy. It is, therefore, crucial to identify regulators of tau pathology that control both forms of tau seeding.

Methods

Tau transgenic mice were used to isolate sarkosyl insoluble vesicle-free tau and brain-derived exosomes (Polanco et al. JBC 2016). Optimized genome-wide CRISPR libraries (Sanson et al. Nat Commun 2018) were screened in tau biosensor cells.

Results

We identified ANKLE2, BANF1, NUSAP1, EIF1AD, and VPS18 as top validated regulators that restrict tau aggregation initiated by both exosomal and vesicle-free tau seeds. Interestingly, both ANKLE2 and BANF1 more robustly affected tau seeding caused by exosomal tau than free aggregates. Furthermore, none of our validated hits affected the uptake of either form of tau seeds, supporting the notion that they operate through a cell-autonomous mechanism downstream of the seed uptake. Lastly, validation studies with human brain tissue revealed that several of the identified protein hits are downregulated in the brains of AD patients, suggesting that their decreased activity may be required for the emergence or progression of tau pathology in the human brain.

Conclusions

We have validated novel cellular regulators that oppose the formation of tau aggregates. Some of these genes are downregulated in AD patients, which may imply a functional role in the emergence of tau pathology in humans. Future experiments will reveal how these genes regulate tau aggregation and why tau seeds within exosomes are more affected by specific genes.

Towards Restoration of Proteomic Balance: Tau Antibodies' Impact on a Mouse Model of Tauopathy

Godfrey Nkajja [1], Jürgen Götz [1], Ashley J. van Waardenberg [2], Phillip J. Robinson [3], Swara Tapaswi [1], Pranesh Padmanabhan [1], Rebecca Nisbet [4], Esteban Cruz [1], Mark E. Graham [5]

[1] Clem Jones Centre for Ageing Dementia Research (CJCADR), Queensland Brain Institute (QBI), The University of Queensland, [2] i-Synapse, [3] Cell Signalling Unit, Children's Medical Research Institute, The University of Sydney, [4] The Florey, The University of Melbourne, [5] Synapse Proteomics, Children's Medical Research Institute, The University of Sydney

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Background

The microtubule-associated protein Tau is a driver of neuronal dysfunction in Alzheimer's disease and numerous other tauopathies. In this process, Tau initially undergoes subtle changes to its abundance, subcellular localization and a vast array of post-translational modifications including phosphorylation, that progressively result in the protein's aggregation and dysregulation of multiple Tau-dependent cellular processes.

Given the various loss- and gain- of functions of Tau in disease and that brain-wide changes in the proteome characterize Alzheimer's disease, we asked whether these two pathological phenomena are interlinked and whether targeting Tau restores proteomic dyshomeostasis observed in the disease.

Methods

To this end, we generated a novel pan-Tau antibody, RNJ1, that preferentially binds human Tau and neutralizes proteopathic seeding activity in multiple cell-lines, and benchmarked it against a clinically tested pan-Tau antibody, HJ8.5 (murine version of tilavonemab). We next evaluated both antibodies, alone and in combination, in the K3 mouse model of tauopathy, showing reduced Tau pathology and improvements in neuronal function following 14 weeks of treatment, without obtaining synergistic effects for the combination treatment.

Results

To gain insight into molecular mechanisms contributing to improvements in neuronal function, we employed quantitative proteomics and phosphoproteomics to first establish alterations in K3 mice relative to WT controls at the proteome level. Quantitative proteomics revealed deregulation of metabolic and microtubule-associated proteins in K3 compared to wild-type brain, in line with previously reported functional defects in multiple tauopathy models. Importantly, both treatments, in particular RNJ1, reversed protein and phospho-protein dyshomeostasis for both increased and decreased proteins in the K3 brain, shifting levels towards wild-type. Gene Ontology- analysis further confirmed that proteins undergoing reversal are involved in biological pathways affected in K3 mice.

Conclusions

Our study suggests that restoration of proteomic balance with Tau immunotherapy links target engagement and treatment efficacy.

Unraveling the Early Trajectory of Cortical Tau Accumulation Using 18F-MK6240

Tim Cox [1], Victor Villemagne [2, 3], Pierrick Bourgeat [1], Azadeh Feizpour [3], Kun Huang [3], Vincent Dore [1, 3], Christopher Rowe [3], Antoine Leuzy [4, 5], Samantha Budd Haeberlein [5], Jurgen Fripp [1]

[1] CSIRO, [2] University of Pittsburgh, [3] Austin Health, [4] C-Path, 5Enigma

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Background

Tau PET is instrumental in tracking the longitudinal progression of Alzheimer's disease (AD). 18F-MK6240 is a high affinity tracer targeting the 3R/4R paired helical filaments of tau in AD. We aimed to evaluate the early phase of the natural progression of tau accumulation using 18F-MK6240.

Methods

231 participants: 100 cognitively unimpaired (CU) Aβ- (Centiloid<25CL), 58 CU-Aβ+, 73 cognitively impaired Aβ+ (41 with mild cognitive impairment (MCI) and 32 with dementia) from the AIBL cohort were followed-up with 18F-MK6240 PET over one to four years (median 2.2years). Meta-Temporal CenTauR (CTR) were generated using CapAIBL and CU CL<15, N=120 and AD (typical AD tau pattern, MMSE>24, CL>50 & age<75, N=39) as 0 and 100CTR anchored points. Abnormal level of tau was defined at 2 standard deviations above the CU Aβ- (13CTR). Linear differential equations (ODE) were employed to model the mean natural history of CTR based on tau accumulators (CTR>13 or CTR rate>0) only. Given the limited numbers of individuals with CTR>100, our analysis concentrated on the early phase of the tau accumulation (CTR<100).

Results

Figure1A illustrates a linear relationship between the average and the rate of CTR, with a R of 0.72. Tau accumulation spanned from 0.5CTR/yr at 13CTR to 12.2CTR/yr at 100CTR, with a standard deviation of the residuals at 2.4CTR/yr. Figure1B displays the individual's trajectories projected on the ODE model. We estimated that, on average it takes 15.1 (CI:[12.6-17.9]) years for an individual crossing 13CTR to reach 100CTR.

Conclusions

Longitudinal 18F-MK6240 is a robust tool for estimating progression of tau accumulation. Our findings indicate that it typically takes around 15 years to reach the tau levels associated with mild AD once tau starts aggregating in the neocortex. These findings shed light into the initial stages of cortical tau accumulation, relevant for early diagnosis and therapeutic interventions in AD.

The PTAU217 Interactome in Human Alzheimer‘s Disease Brain Tissue from APOE3 and APOE4

Manon Thierry [1], Eleanor Drummond [2], Tomas Kavanagh [2], Jackeline Ponce [3], Thomas Wisniewski [1], Beatrix Ueberheide [3]

[1] Center for Cognitive Neurology, Department of Neurology, Grossman School of Medicine, New York University, New York, NY, 10016, USA, [2] Brain and Mind Centre and School of Medical Sciences, University of Sydney, Camperdown, NSW, 2050, Australia., [3] Proteomics Laboratory, Division of Advanced Research Technologies and Department of Biochemistry and Molecular Pharmacology, New York University Grossman School of Medicine, New York, 10016, USA

Background

Hyperphosphorylated tau (pTau) in Alzheimer’s disease (AD) brain tissue is a complex mix of multiple tau species that are variably phosphorylated on up to 55 epitopes. Phosphorylation of specific epitopes appears to alter the functions of tau. The unique roles of individual pTau species can be explored through protein interaction (“interactome’) studies. The aim of this study was to analyse the interactome of pTau217 for the first time, which biomarker studies suggest is one of the earliest accumulating tau species in AD.

Methods

pTau217 interactors were identified in human brain tissue from 10 AD cases using affinity purification-mass spectrometry. Cases were balanced for ApoE ε3/ε3 and ε4/ε4 genotypes (n=5 each) to explore if ApoE influences pTau protein interactions. Results were compared to our previous pTauS396/S404 interactome dataset to determine if individual pTau species have different interactomes.

Results

579 proteins were significantly enriched by pTau217 co-immunoprecipitation. Of these, 23 proteins were identified as bona fide pTau217 interactors, including known pTau interactors SQSTM1 and ubiquitin. Phosphorylation analysis of tau enriched by pTau217 vs pTau396/S404 co-immunoprecipitation confirmed enrichment of different pools of tau, with pTau217 displaying fewer phosphorylated epitopes, hinting that pTau217 may be an earlier generated species. Despite these differences, 15 bona fide pTau217 tau interactors also interacted with pTauS396/S404 suggesting close similarities in interactomes (Fisher’s exact p = 2.3x10-14). Common interactors notably included five subunits of an E3 ubiquitin ligase not previously been linked to tau or AD. 46 and 28 pTau217 interactors were identified in ApoE ε3/ε3 and ApoE ε4/ε4 cases respectively and these significantly overlapped (16 common interactors; Fisher’s exact p = 4.3x10-24).

Conclusions

pTau217 interacts with many similar proteins to pTauS396/S404. Our results highlight a strong interaction between multiple pTau species and a novel E3 ubiquitin ligase, which may have an important role in AD and potentially tau degradation.

Alteration of the Amyloid Precursor Protein (APP) Trafficking by Familial Alzheimer's Disease Mutation Featured by Quantitative Live-Cell Microscopy

Paul A. Gleeson [1], Lou Fourriere-Chea [1], Jingqi Wang [1]

[1] The University of Melbourne, Bio21 Institute

Accumulation of amyloid plaques in the brain is a hallmark of Alzheimer's disease. Plaques are formed by the aggregation of soluble secreted amyloid β (Aβ) generated after a proteolytic processing of the amyloid precursor protein (APP) by the protease ß-secretase (BACE1). Membrane transport and protein sorting underpin the initial events associated with enhanced Aβ production in neurons and which seed the onset of Alzheimer's disease, but remain poorly defined. Therefore, defining the intracellular route of newly synthesized BACE1 and APP is essential to understand the regulation of Aβ production, the development of Alzheimer's disease and design novel therapeutics.

By combining cell biological techniques and high-resolution imaging, we observed that APP and BACE1 are sorted into different post-Golgi transport pathways in HeLa cells and primary mouse neurons. Moreover, using super-resolution and live-cell imaging, we have shown that the partitioning of APP and its secretase BACE1 early in the secretory pathway is critical to regulate APP processing [1]. We used the Retention Using Selective Hooks (RUSH) to synchronise APP trafficking. By combining live-cells and immunoblot analysis, our temporal-spatial analysis of APP anterograde trafficking and processing has revealed different intracellular locations for the preferential secretase cleavage and Aβ production of wild-type APP and familial APP mutants with the Golgi as the major processing site for the pathogenic Swedish APP mutation [2,3]. We are currently exploring BACE1 and APP trafficking in primary human neurons following our recent organelle mapping of human iPSC-derived neurons [4].

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Amyloid Induced Hyperexcitability in Default Mode Network Drives Medial Temporal Hyperactivity and Early Tau Accumulation

Joseph Giorgio [1], Jenna Adams [2], Anne Maass [3], William Jagust [1], Michael Breakspear [4]

[1] Helen Wills Neuroscience Institute, University of California, Berkeley, Berkeley, CA 94720, USA, [2] Department of Neurobiology and Behavior, University of California, Irvine, Irvine, CA 92697, [3] German Center for Neurodegenerative Diseases (DZNE), Magdeburg 39120, Germany, [4] School of Psychological Sciences, College of Engineering, Science, and the Environment, University of Newcastle, Newcastle, NSW 2305

Background

In cognitively intact older adults (OA) the presence of AD pathology disrupts normal cortical processes subserving the ability to recognise repeated stimuli. To uncover this, we used generative modelling of functional and molecular imaging probing how AD pathologies affect these processes.

Methods

66 subjects (45 cognitively normal OA, 21 Younger Adults) performed an fMRI task involving novel and repeated scenes and objects. 42 OA had measures of ABeta using PIB-PET and cross-sectional entorhinal cortex tau (EC-tau) measured using flortaucipir (FTP)-PET. We decomposed the fMRI data into functional networks and then used Dynamic Causal Modelling (DCM) to infer cortical interactions supporting responses to repeated stimuli. We used a hierarchical approach to uncover how individual differences in these interactions are related to AD pathologies. Finally, in a subset (n=32) with multiple measures of EC-tau we ran leave one out validation to use these network interactions to predict rate of longitudinal tau accumulation.

Results

Networks with BOLD activity significantly related to the task design were selected for DCM analysis. We modelled these time-courses as a fully connected system allowing stimulus repetition to modulate any connection. We observed very strong evidence that AD pathologies shift the functional interactions between MTL and DMN from inhibitory to excitatory when stimuli are repeated. These changes are driven by local pathologies with ABeta disinhibiting the input to the DMN from the MTL and EC-tau disinhibiting the input to the MTL from the DMN. Finally, we show excitation of the MTL by the DMN when stimuli are repeated is predictive of rate of tau accumulation ($r(30)=0.45$, $p=0.005$).

Conclusions

We find that AD pathologies disrupt local cortical processing of repeated stimuli with ABeta increasing the gain of the DMN, which in turn over stimulates the MTL in an excitatory feedback loop, a potential mechanism for EC-tau accumulation.

Polygenic Scores for Alzheimer's Disease Risk and Resilience Predict Age at Onset of Amyloid-β

Colin Masters [1], Andrew Saykin [2, 3], Carlos Cruchaga [4, 5], Eleanor O'Brien [6, 7, 8], Pierrick Bourgeat [9], Ben Goudey [1], Timothy Cox [10], Simon Laws [6, 7, 8, 11], Shane Fernandez [6, 7, 8], Christopher Rowe [1, 12], Vincent Dore [10, 13], Tenielle Porter [6, 7, 8, 11], Victor Villemagne [6, 14], James Doecke [8, 9]

[1] Florey Institute, University of Melbourne, Parkville, Victoria, Australia, [2] Indiana Alzheimer's Disease Research Center, Indiana University School of Medicine, Indianapolis, IN, USA, [3] Center for Neuroimaging, Department of Radiology and Imaging Sciences, Indiana University School of Medicine, Indianapolis, IN, USA, [4] Department of Psychiatry, Washington University, St. Louis, MO, USA, [5] NeuroGenomics and Informatics, Washington University, St. Louis, MO, USA, [6] Centre for Precision Health, Edith Cowan University, Joondalup WA, [7] Collaborative Genomics and Translation Group, Edith Cowan University, Joondalup WA, [8] School of Medical and Health Sciences, Edith Cowan University, Joondalup WA, [9] Australian e-Health Research Centre, CSIRO, Brisbane, Qld, Australia, [10] Australian e-Health Research Centre, CSIRO, Melbourne, Victoria, Australia, [11] Curtin Medical School, Curtin University, Bentley WA, [12] Department of Molecular Imaging & Therapy, Austin Health, Heidelberg, Victoria, Australia, [13] Department of Molecular Imaging & Therapy and Centre for PET, Austin Health, Heidelberg, Victoria, Australia, [14] Department of Psychiatry, University of Pittsburgh, Pittsburgh, Pennsylvania, USA

Background

Genome-wide association studies (GWAS) have identified genetic variants associated with Alzheimer's disease (AD) risk, but genetic variation in onset and progression of AD pathology is less understood. Accumulation of brain amyloid-β (Aβ) is a key pathological hallmark of AD, beginning 10 - 20 years prior to cognitive symptoms. We investigated the genetic basis of variation in age at onset (AAO) of brain Aβ by comparing the performance of polygenic scores (PGSs) based on AD risk and resilience with a Aβ-AAO trait-specific PGS.

Methods

1122 participants from the Alzheimer's Dementia Onset and Progression in International Cohorts (ADOPIC) study underwent genome-wide SNP genotyping and assessment of brain Aβ using positron emission tomography (PET) imaging at two or more timepoints. AAO was the estimated age at which participants crossed the 20 centiloid (CL) threshold for high Aβ. We utilised AD risk and resilience GWAS summary statistics and conducted a GWAS for AAO using a cross-validation approach. We used PRSice to identify optimal PGSs for Aβ-AAO for risk (PGSRisk), resilience (PGSResilience) and Aβ-AAO (PGSAAO)

Results

PGSRisk and PGSResilience were significantly associated with Aβ-AAO, such that higher PGSRisk and lower PGSResilience were associated with an earlier Aβ-AAO. PGSRisk showed the strongest association and explained more variance in Aβ-AAO than did PGSAAO. When stratified by APOE ε4 carriage, the strongest genetic risk factor for AD, the association of PGSRisk with Aβ-AAO was stronger among ε4 non-carriers, whilst PGSResilience, was more strongly associated with Aβ-AAO in ε4 carriers.

Conclusions

PGS based on genetic risk and resilience for AD are both significant predictors of the age at which people are estimated to cross the threshold for high brain Aβ burden. Predicting the age at which a person will pass this threshold would enable treatment at an earlier stage, when it may more effectively delay or prevent symptom onset.

The Role of Diet in Moderating the Relationship Between Depression and Brain Amyloid Load

Hilal Salim Said Al Shamsi [1], Samantha L. Gardener [1, 2, 3], Stephanie R. Rainey-Smith [1, 2, 3, 4, 5], Hamid R. Sohrabi [1, 2, 4, 6], Kevin Taddei [1, 2], Colin L. Masters [7], Christopher Rowe [7, 8], W.M.A.D. Binosha Fernando [1, 2], and Ralph N. Martins [1, 2, 4, 6].

[1] Centre of Excellence for Alzheimer's Disease Research and Care, School of Medical and Health Sciences, Edith Cowan University, Joondalup, Western Australia, Australia. [2] Alzheimer's Research Australian, Ralph and Patricia Sarich Neuroscience Research Institute, Nedlands, Western Australia, Australia. [3] Lifestyle Approaches Towards Cognitive Health Research Group, Murdoch University, Murdoch, Western Australia, Australia. [4] Centre for Healthy Ageing, Health Futures Institute, Murdoch University, Murdoch, Western Australia, Australia. [5] School of Psychological Science, University of Western Australia, Perth, Western Australia, Australia. [6] Department of Biomedical Sciences, Macquarie University, Sydney, New South Wales, Australia. [7] The Florey Institute of Neuroscience and Mental Health, University of Melbourne, Melbourne, Victoria, Australia. [8] Department of Molecular Imaging, Austin Health, Heidelberg, Victoria, Australia.

Background

Recent advances in our understanding of lifestyle choices and brain health emphasize the crucial link between diet, cognitive well-being, and Alzheimer's biomarkers such as brain amyloid beta (Aβ). This study aimed to assess dietary patterns as a moderator of the relationship between depression, anxiety, and brain Aβ in older adults.

Methods

Cross-sectional data from cognitively unimpaired older adults (n=524, age ≥60 years) enrolled in the Australian Imaging, Biomarkers, and Lifestyle study (AIBL) were included. Participants completed a food frequency questionnaire, self-report measures of depression and anxiety, and underwent Positron Emission Tomography imaging to quantify brain Aβ load. Scores for three dietary patterns, 1) Mediterranean diet (MeDi), 2) Dietary Approaches to Stop Hypertension (DASH) diet and 3) western diet were generated for each individual. Moderation and simple slope analyses were used to examine the interactions between dietary patterns, depression, anxiety, and brain Aβ load.

Results

Individuals with DASH diet adherence below the mean exhibited a positive association between depression and anxiety, as assessed by the Hospital Anxiety and Depression Scale (HADS), and brain Aβ load (β=2.992, SE=0.917, p<0.001, and β=1.807, SE=0.664, p=0.007, respectively). The association between anxiety and brain Aβ load was also observed in Apolipoprotein E ε4 allele carriers with lower than mean DASH diet adherence (β=4.479, SE=1.552, p=0.005). MeDi and western diet did not moderate the relationship between mood and brain Aβ.

Conclusions

Our findings highlight the role of DASH diet adherence as a potential moderator of the relationship between mood and brain Aβ load, such that a healthier diet may ameliorate the effect of suboptimal mood on markers of brain health. Our findings also emphasize the importance of genotype-specific approaches to mood-brain Aβ-diet research and highlight the need for further investigation.

Estimating Pre-Symptomatic Episodic Memory and Executive Function in Community-Dwelling Adults using Unsupervised Online Hand Movement Analysis

Eddy Roccati [1], Quan Bai [2], Jane Alty [1], Anna King [1], Aidan Bindoff [1], James Vickers [1], Katherine Lawler [3], Larissa Bartlett [1], Xinyi Wang [1], Son Tran [2], Rebecca St George [4]

[1] Wicking Dementia Centre, University of Tasmania, [2] School of Information and Communication Technology, University of Tasmania, [3] Discipline of Physiotherapy, La Trobe University, Melbourne, [4] School of Psychological Sciences, University of Tasmania

Background

Finding affordable and accessible methods to detect Alzheimer's disease in asymptomatic older adults is crucial for targeting specialist new biomarker tests and advancing drug development. Motor impairment precedes memory decline in Alzheimer's disease and new computer technologies enable home-based movement analysis. This study evaluated the accuracy of unsupervised online hand movement analysis to predict cognitive performance in cognitively asymptomatic older adults.

Methods

1,140 community participants without cognitive symptoms (65.7 ± 7.4 years old; 73% female) from the ISLAND cohort in Tasmania completed online TAS Test tests at home: a 40-second single key tapping test, a 60-second 2-key tapping test, and a 40-second 3-key sequence tapping test. Participants also completed validated CANTAB cognitive tests of episodic memory, working memory and executive function. Frequency, variability, key press duration and accuracy scores were calculated for each tapping test. Generalized linear models examined associations between tapping motor features and cognitive performance, adjusted for confounders including age, sex, depression, anxiety and education. ΔAIC > 2 denotes statistical significance.

Results

Combinations of hand motor features from the single key (R2adj = 8.0%, ΔAIC = 3.7), 2-key (R2adj = 7.9%, ΔAIC = 2.8), and 3-key sequence tapping tests (R2adj = 8.2%, ΔAIC = 8.4) improved estimation of episodic memory performance relative to models with demographic and mood confounders only (R2adj = 7.3%). Only the motor features of the 3-key sequence tapping test improved estimation of working memory (R2adj = 6.3%, ΔAIC = 2.5). Tapping features of single key tapping tests (R2adj = 15.8%, ΔAIC = 8.3) and 3-key sequence tapping tests (R2adj =16.5%, ΔAIC = 13.7) improved the estimation of executive function performance.

Conclusions

Brief, unsupervised online hand motor tests improve estimation of asymptomatic episodic memory and executive function in older adults, offering a cost-effective, language-agnostic and home-based method for risk stratification in the community.

More than a One-Hit Wonder: Exploring Synergistic Effects of Genetic and Environmental Risk Factors in the Progression of Cognitive Impairment in Parkinson's Disease

Angus McNamara [1], Dr Irina Baetu (PhD) [2], A/Professor Lyndsey E. Collins-Praino (PhD) [1]

[1] School of Biomedicine, The University of Adelaide, [2] School of Psychology, The University of Adelaide

Background

Factors that predict risk/rate of progression of cognitive impairment in Parkinson's disease (PD) are largely unknown. A number of genetic (e.g. GBA mutation; APOE4 allele) and environmental (e.g. history of traumatic brain injury (TBI); pesticide exposure) risk factors have been proposed, but whether they act synergistically to increase risk/worsen progression of cognitive impairment is unknown. This study assessed whether such risk factors, alone or in combination, were associated with baseline differences in biomarkers or cognitive function in newly-diagnosed PD or predictive of cognitive function at 5-year follow-up.

Methods

Data (n=208) were extracted from the Parkinson's Progression Markers Initiative. A composite cognitive score was derived from principal components analysis. Baseline differences in cognitive function and CSF levels of alpha-synuclein, amyloid beta and hyperphosphorylated tau (p-tau) were assessed using a series of two-way ANOVAs for the following combinations of risk factors: 1) TBI+pesticide exposure; 2) TBI+GBA mutation and 3) TBI+APOE4 allele. Prediction of cognitive ability at 5-year follow-up was assessed via multiple linear regression, with predictors including demographic information (age/sex/education), baseline cognitive function, genetic and environmental risk factors and the interactions between risk factors.

Results

At baseline, there was a significant interaction between TBI history and pesticide exposure for CSF levels of both alpha-synuclein ($F(1,137)=4.023;p=0.0468$) and p-tau ($F(1,178)=4.641;p=0.0326$). Similarly, there was a significant interaction between TBI history and APOE4 allele for CSF levels of p-tau ($F(1,178)=4.623;p=0.0329$). No other interactions were significant. Cognitive function over a 5-year follow-up was predicted by both pesticide exposure and the interaction between TBI and pesticide exposure, explaining 62% of the variance.

Conclusions

Established risk factors for PD can act synergistically to worsen underlying brain pathology and may have utility for predicting long-term prognosis of cognitive dysfunction. This highlights the importance of collecting a thorough life history from individuals at time of diagnosis.

Pre-Symptomatic Blood Tests to Detect Neurodegeneration and Predict Dementia Risk: Public Perceptions Across the Life-Course

Eddy Roccati [1], Anna King [1], Hannah Fair [1], Sladana Pavkovic [1], Jessica Collins [1], Jane Alty [1]

[1] Wicking Dementia Research and Education Centre, College of Health and Medicine, University of Tasmania

Background

Pre-symptomatic blood tests to detect neurodegeneration are a rapidly developing innovation in dementia prevention and diagnosis, with applications across the life-course. However, relatively little is known about the publics' attitudes to adopting this innovation. We therefore aimed to understand public opinions about undertaking pre-symptomatic blood tests for neurodegeneration across the life-course.

Methods

We collected quantitative survey responses from 3385 participants recruited from the Understanding Dementia Massive Open Online Course in February 2019. Patterns in responses across life stages were analysed using linear mixed effects models, binomial regressions, and multinomial regressions, with Tukey adjusted post-hoc contrasts. Confounders were adjusted for in all analyses (education, gender, working with people living with dementia, having family member(s) living/lived with dementia).

Results

Participants reported that pre-symptomatic blood tests would be utilised by themselves (92.6%) and by others (71.3%). Participants believed that follow-up support is required after results indicating neurodegeneration (99.7%), and that additional awareness campaigns are needed to prepare for this innovation (93.8%). Later-life participants (age >65) were significantly less positive about pre-symptomatic blood testing to understand brain health than mid-life (age 45-65) or young adult (age <45) participants ($p<0.001$). Compared to participants in other life-stages, participants in later-life were significantly more positive about testing themselves, but were significantly less positive about other people's uptake of testing ($p<0.001$). Participants in later-life were also significantly more positive about becoming involved in research after a test indicating neurodegeneration (comparison: mid-life and young adult, both $p<0.001$). Compared to participants in later-life, young adult participants were significantly more likely to believe that additional public awareness campaigns are needed to prepare people for pre-symptomatic blood tests to detect neurodegeneration ($p<0.001$).

Discussion/Conclusion

Attitudes to pre-symptomatic blood testing for neurodegeneration vary across the life-course, highlighting the need for a targeted approach to raise public awareness and preparedness for this developing innovation.

Meeting the Need for Valid Mid-Life Dementia Risk Assessment: Development and Validation of Risk Scores for a Midlife Specific Dementia Risk Tool

Kaarin Anstey [1], Md Hamidul Huque [1]

[1] School of Psychology, University of New South Wales

Background

Although many key dementia risk factors emerge at midlife, most available risk assessment tools for dementia are based on data from older adults. The only validated midlife risk tool, CAIDE, was developed almost two decades ago. Therefore, there is need to develop a midlife risk score for dementia using current risk factor knowledge.

Methods

Participants aged 40 to 64 from the UK Biobank comprised the sample. This was divided in development and validation samples, using a 60:40 ratio. Cox proportional hazards regression was used to evaluate the regression coefficients of the risk factors stratified by sex in the development sample. All the risk factors of dementia available in the CogDrisk were considered because the CogDrisk utilizes most recent dementia risk factor information. The regression coefficients were converted and the CogDrisk tool for midlife was developed. Multiple imputation was used to address missing data. We evaluated the midlife CogDrisk risk tool by estimating ROC curves (95% CI) in the validation sample and compared it with the CAIDE.

Results

208,473 and 138,991 participants were included in the development and validation sample, respectively, with mean follow-up 13 (sd=1.7) years. During the follow-up 1330 and 876 dementia cases were identified in the development and validation samples, respectively, through data linkage. In the validation sample midlife-CogDrisk resulted in AUC (95% CI) of 0.75 (0.73, 0.77) and 0.72 (0.69, 0.74) for males and females, respectively. For CAIDE these figures were 0.63 (0.61, 0.66) and 0.64 (0.61, 0.67).

Discussion

The midlife CogDrisk resulted in an acceptable ROC and outperformed the only other midlife risk tool. The midlife CogDrisk can be implemented online with the existing CogDrisk for older adults. This increases the applicability of the CogDrisk assessment with the potential for wide usage in primary care and public health from mid to late-life.

What Factors Should be Prioritised for Dementia Prevention? A Meta-Analysis of Population Attributable Fractions (PAFs) Related to Modifiable Risk Factors

Ms. Aysegul Kafadar [1], Mr. Jacob Brain [1], Mr. Louie Cochrane [1], Prof. Blossom Stephan [2], Prof. Mario Siervo [2]

[1] University of Nottingham, [2] Curtin University

Background

Dementia is a global public health priority. There are 57 million cases worldwide including over 450,000 cases living in Australia. Identification of key modifiable risk factors is important to inform the development of dementia risk mitigation and prevention strategies. We therefore undertook a systematic review and mate-analysis to determine the population-attributable fraction (PAF) for dementia associated with modifiable risk factors.

Methods

Ovid, EMBASE, MEDLINE, and PsycINFO were searched (covering all literature to 29th of June 2023), for studies that had reported PAFs for modifiable risk factors for later life dementia. A random-effects meta-analysis was used to calculate a pooled PAF estimate for each risk factor and their combinations.

Results

Out of the 4,024 articles identified, 74 were included. In total, 61 modifiable risk factors were assessed including studies from high-income as well as low- and middle-income countries. Results from the meta-analyses showed high pooled unweighted PAF% values for low education (17.2%; 95%CI: 14.4-20.0%), hypertension (15.8%; 95%CI: 14.7-17.1%), hearing loss (15.6%; 95%CI: 10.7-20.5%), physical inactivity (15.2%; 95%CI: 12.8-17.6%), obesity (9.4%; 95%CI: 7.3-11.6%) and smoking (9.1%; 95%CI: 7.1-11.0%). Using weighted PAF% values, low education (9.3%; 95%CI: 7.2-11.4%), physical inactivity (7.3%; 95%CI: 3.9-10.6%) and hearing loss (7.2%; 95%CI: 5.5-8.9%) had the highest values. A seven-factor model combining low education, hypertension, obesity, smoking, physical inactivity, depression, and diabetes had a pooled weighted PAF% of 32.0% (95%CI: 27.3-36.8%), globally.

Discussion/Conclusion

Urgent governmental policies are needed to advance dementia prevention efforts, emphasising a life-course approach. These policies should prioritise education, foster health-promoting environments, and promote the enhancement of overall health to mitigate the disease burden associated with dementia. The seven-factor model, showing a high pooled weight PAF% value, highlights the multifactorial nature of dementia risk and the potential for tailored prevention strategies aimed at addressing co-occurring risk factors.

Effects of Dual-Task Functional Power-Based Training on Cognitive Function in Older Adults at Increased Falls Risk: An 18-Month Cluster Randomised Controlled Trial.

Dennis Taaffe [1], Jamie Tait [2], Robin Daly [2], Timo Rantalainen [3], Catherine Milte [2], Gavin Abbott [2], Keith Hill [4], Rachel Duckham [2, 5, 6], Kerrie Sanders [7], Luana Main [2], Caryl Nowson [2]

[1] Exercise Medicine Research Institute and School of Medical and Health Sciences, Edith Cowan University, Joondalup, Australia, [2] Institute for Physical Activity and Nutrition, Deakin University, Geelong, Australia, [3] Faculty of Sport and Health Sciences and Gerontology Research Center, University of Jyväskylä, Jyväskylä, Finland, [4] Rehabilitation Ageing and Independent Living (RAIL) Research Centre, Monash University, Melbourne, Australia, [5] Clinical Leadership Effectiveness and Outcomes, Northern Health, Epping, Australia, [6] Australian Institute for Musculoskeletal Science, Department of Medicine, Western Health, the University of Melbourne, Melbourne, Australia, [7] Department of Medicine, Western Health, the University of Melbourne, Melbourne, Australia

Background

Age-associated functional and cognitive decline are linked to increased dementia risk. High velocity power-based exercise can improve function in older adults and cognitive training shows mixed findings for improving cognition, but their combined impact remains uncertain. This 18-month cluster randomised controlled trial examined whether dual-task functional power training (DT-FPT) improves cognition in older adults, and whether intervention responses vary by apolipoprotein-E (APOE) and brain-derived neurotrophic factor (BDNF) polymorphisms.

Methods

22 independent-living retirement communities (300 residents, ≥65y at increased falls risk) were randomised to 12-months of group-based DT-FPT (6-months supervised + 6-months maintenance, 45-60 minutes, 2/week) performed simultaneously with cognitive and/or motor tasks, followed by 6-months follow-up, or usual care control (CON). Executive function, working memory and reaction time/attention were assessed using CogState at baseline, 6, 12 and 18-months. Z-scores were created to form composites for psychomotor-attention, learning-working memory and global cognition. BDNF and APOE polymorphism data were obtained from blood samples.

Results

Overall, 223 (74%) participants completed the 18-month intervention; mean exercise adherence was 50% at 6-months and 40% at 12-months. There were no group differences for the change in any cognitive outcome after 6 or 12-months, except for a net 0.20 SD (95%CI, 0.03, 0.36) benefit in reaction time/attention for DT-FPT versus CON at 6-months (P=0.020). At 18-months, there was a 0.14 SD (0.004, 0.27) benefit to the learning-working memory composite for DT-FPT (P=0.044), whereas CON exhibited a 0.26 SD (0.09, 0.43) benefit for executive function (P=0.003). Genotype interactions were observed for the learning-working memory composite, with benefits for DT-FPT vs CON in APOE non-e4 carriers at 12-months [0.22 SD (0.05, 0.39)], and BDNF Met-carriers at 18-months [0.42 SD (0.15, 0.69); both P<0.05].

Discussion/Conclusion

DT-FPT in older adults at increased falls risk produced no consistent cognitive benefits, potentially due to modest program adherence, but this may vary by genotype.

Validation of Multiple Linked Administrative Datasets to Identify People with Dementia

Professor Rory Wolfe [1], Associate Professor Joanne Ryan [1], Dr Fleur de Crespigny [2], Associate Professor Robyn L. Woods [1], Professor Annette J. Dobson [3], Michelle Wilson [1], Thao Vu [2], Dr Leon Flicker [4], Dr Michael Waller [3], Dr Osvaldo P. Almeida [4]

[1] Monash University, [2] Australian Institute of Health and Welfare, [3] University of Queensland, School of Public Health, Faculty of Medicine, Brisbane, QLD, Australia, [4] Western Australia Centre for Health and Ageing, Medical School, University of Western Australia, Perth, WA, Australia

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Background

Accurately measuring the prevalence of dementia (including Alzheimer's disease) is important for chronic condition management and service planning. Routinely collected linked administrative data presents an accessible and inexpensive method to estimate the prevalence of dementia. The aim of this study was to examine the accuracy of identifying people with dementia in linked administrative data compared with adjudicated cases of dementia from a community-based clinical trial.

Methods

We created the National Linked Dementia Dataset—the most comprehensive linked administrative dataset containing people with dementia in Australia at the time of linkage and used it to develop algorithms which identified people with dementia. These algorithms were tested against adjudicated cases of dementia (both confirmed and not confirmed) in the ASPirin in Reducing Events in the Elderly (ASPREE) clinical trial to help determine optimal sensitivity and specificity.

Results

The algorithm that provided the highest sensitivity and positive predictive value estimates on balance without excluding ASPREE trial participants with suspected (but not confirmed) dementia was having at least one record for dementia in a minimum of two sources or two records with dementia in one source based on truncating the timeframe of the ASPREE trial to one year (from the first date of randomisation).

Conclusion

Linked administrative data can identify people with dementia with moderate accuracy. This is a promising start but requires enhancement before it can be used for estimating the prevalence of dementia.

Examining the Acceptability and Usefulness of Positive Behaviour Support (PBS) Training for Staff and Family Members Supporting People with Dementia in Residential Aged Care: A Pilot Study

Sau Cheung [1], Olivier Piguet [1], Claire O'Connor [2], Alinka Fisher [3]

[1] FRONTIER, Brain and Mind Centre, The University of Sydney, [2] University of New South Wales, [3] College of Nursing and Health Sciences, Flinders University

Background

Non-pharmacological interventions are recommended to address behavioural and psychological symptoms of dementia (BPSD). Positive behaviour support (PBS) education has shown promise in supporting family members to provide effective behaviour support in home settings, resulting in changed behaviours, and improved relationships and quality of life. This study examined the acceptability and usefulness of PBS training in building capabilities of support staff and family members providing behaviour support to people living with dementia in residential aged care.

Methods

We conducted a mixed-methods pilot across three residential aged care organisations. The training consisted of two components: (1) online training for clinical leaders from each participating organisation (n=8), which was conducted online (via Team) across four 3-hour sessions, and (2) training for family members (n=37) and support staff (n=18), conducted in-person across three 2-hour sessions. The acceptability and usefulness of the program was evaluated using pre- and post-training questionnaire assessments.

Results

Support staff and family members reported increased confidence in providing behaviour support, with 96% indicating it would support their practices across settings. Key training benefits reported by participants were their new understanding of PBS principles and process (e.g., focussing on why behaviours occur, and using this knowledge to inform effective strategies). Concerns were raised about the adequacy of current systems to efficiently translate newly acquired knowledge into practice, and a majority (89%) expressed the need for further behaviour support training.

Discussion/Conclusion

This pilot provides preliminary evidence for the acceptability and usefulness of PBS training in residential aged care. This research has informed practice and research recommendations towards building effective behaviour support systems and practices in residential aged care organisations, including the importance of clear roles and responsibilities across behaviour support teams, and establishing service culture and systems that value and enable collaborative PBS practices.

Prevalence of Guideline Recommended Care Provided to Aboriginal People Living with Dementia Who Attend Aboriginal Community Controlled Health Services

Mr Phillip Naden [1, 2], Dr Megan Freund [3, 4], Prof Alan Clough [5], Kim Whitely [6], Mr Steve Blunden [3, 4, 7], Prof. Nola Ries [8], Mr Robert Daviis [3, 4], Dr Peter Silberberg [9]

[1] Coonamble Aboriginal Health Service, [2] Rural Health Research Institute, Charles Sturt University, [3] Health Behaviour Research Collaborative, School of Medicine and Public Health, Faculty of Health and Medicine, University of Newcastle, [4] Equity in Health and Wellbeing Program, Hunter Medical Research Institute, [5] College of Public Health, Medical and Veterinary Sciences, [6] The Remote Aboriginal Health Corps, [7] Durri Aboriginal Corporation Medical Service, [8] Faculty of Law, University of Technology Sydney (UTS) & UTS Ageing Research Collaborative, [9] Rekindling the Spirit Health Service

Background

Dementia prevalence is indicated to be 3-5 times higher for Aboriginal and Torres Strait Islander peoples compared to non-Indigenous Australians. It is important that Aboriginal and Torres Strait people living with dementia receive care consistent with best practice guidelines. This study explored the care recorded as being received by Aboriginal people who attend Aboriginal Community Controlled Health Services (ACCHS) and are living with dementia.

Methods

A manual search of the electronic medical records of patients aged 45+ attending nine ACCHSs was undertaken to identify those living with dementia. Patients living with dementia were defined as those with medical record documentation of: dementia; Alzheimer's disease; frontotemporal dementia; multi-infarct dementia; vascular dementia; Lewy body dementia; Pick's disease; or senile/senility. A trained ACCHS staff member recorded care provided under six domains: disease management plan including dementia; health assessment in past 12 months; assessment of dementia-related problems; medications for symptom management; referral to aged care services; and advance care planning.

Results

70 patients were identified as living with dementia (<1% of audited records). Of these, 61% had a management plan inclusive of dementia, 41% a cognitive assessment in the past 12 months; 37% had been prescribed dementia medications; 69% had been referred to an aged care service; 26% had an Enduring Guardianship discussed or noted as completed; and 24% had an Advance Care Directive discussed or noted as completed. Assessment of dementia-related problems ranged from 23% (elder abuse) to 70% (pain).

Conclusion

The prevalence of dementia detected (<1%) was less than expected given the comparatively high prevalence of dementia reported in population level studies (12-14%). A significant proportion of patients did not receive care in line with guidelines, particularly related to advance care planning. Effective strategies to increase the timely detection of dementia and the routine delivery of appropriate care should be examined.

Associations Between Social Factors and Access to Home Care Packages Prior to Moving to Permanent Residential Aged Care in Australia

Keith Evans [1], Craig Whitehead [2], Maria Crotty [2], Gillian Caughey [1], Maria Inacio [1], Megan Corlis [3], Stephanie Harrison [1]

[1] South Australian Health and Medical Research Institute, [2] Flinders University, [3] Australian Nursing and Midwifery Education Centre

Background

Older adults consistently report a preference to age in place i.e., to live at home for as long as possible. Government-subsidised home care packages aim to support older adults to achieve this. The objective of this study was to examine individual-level social factors (e.g., location, housing, carer support) associated with access to home care packages prior to entering permanent residential aged care, in the overall population and in people living with dementia.

Methods

A cross-sectional study was conducted using the Registry of Senior Australians (ROSA) Historical Cohort, which includes integrated national health, aged care, and social welfare data. Individuals in ROSA aged ≥65 years with first-time aged care eligibility assessments between 01/01/2010 and 31/12/2019 and entered permanent residential aged care before 30/06/2020 were included. Stepwise logistic regression models were used to examine associations between social factors and access to home care packages prior to entering permanent residential aged care, adjusting for age, sex, and health conditions.

Results

390,770 individuals (median age 84.6 years, 59.4% female, 48.8% living with dementia) were included. Of these, 25% accessed home care packages prior to permanent residential aged care. Lower SEIFA Index of Relative Socioeconomic Advantage and Disadvantage (Odds Ratio 0.91, 95% confidence interval (CI) 0.89-0.93), not owning a home (0.77, 95% CI 0.76-0.78), having a preferred language other than English (0.87, 95% CI 0.85-0.89), living alone (0.89, 95% CI 0.88-0.91) and having informal carer support (0.95, 0.93-0.98) were associated with lower odds of accessing home care packages prior to permanent residential aged care. In people living with dementia, living alone and informal carer support were not significantly associated with access to home care packages.

Discussion/Conclusion

Only one-quarter of older adults entering residential aged care accessed home care packages prior to entering. Social factors may have an important impact on home care package access.

Emergency Hospital in the Home for People Living with Dementia

Ann-Marie Crozier [1], Linda Koria [1], Leanne Kearney [1], Vasi Naganathan [1], Sarita Lo [1]

[1] Sydney Local Health District

Background

The Emergency Hospital In The Home (EHITH) Model of Care (MOC) was implemented in 2022 within the Sydney Local Health District (SLHD) to manage urgent low acuity health conditions in older adults at home as an alternative to Emergency Department (ED) presentations. This MOC is particularly appealing for people living with dementia and their caregivers as time in ED can cause distress for people with dementia and hospital admission can result in a decline in health and function. This study explores the characteristics and management pathways of people with dementia who were referred to the EHITH MOC.

Methods

Descriptive analysis of the characteristics of the people with dementia who were referred to the EHITH MOC and additional information including sources of referrals, immediate assessment outcomes, and short-term hospital utilisation.

Results

234 people living with dementia were referred to the EHITH MOC between February 2023 and January 2024 with a mean age of 83.2 years (SD =9.7 years), and 125 (53%) were males. Referrals originated from the SLHD Residential Aged Care Facilities outreach program (32.5%, n=76), New South Wales (NSW) Ambulance paramedics (29.1%, n= 68), General Practitioners (11.1%, n=35), NSW Virtual Clinical Care Centre (4.7%, n=11), and other sources (22.6%, n=26). Almost 89% (n=208) of individuals were assessed and managed by the EHITH clinicians with 89% (n=186) assessed and managed at home, and 10.6% (n=22) conveyed to the hospital. Of the 91.3% (n=191) of individual followed up by 28 days post the EHITH encounter, 38.2% (n=73) had at least one ED visit, and 35.6% (n=68) had at least one hospital admission.

Discussion

The EHITH MOC shows promise in addressing urgent cases among people living with dementia by reducing ED visits and hospital admissions. Further evaluation is needed to assess the clinical outcomes and economic feasibility of this MOC.

Investigating the Interaction Between Psychological Trauma and Behaviours and Psychological Symptoms of Dementia

Daniel Whiting [1], Mustafa Atee [1, 2, 3, 4], Monica Cations [5], Tom Morris [1, 3, 6]

[1] The Dementia Centre, HammondCare, [2] Curtin University, [3] University of Sydney, [4] Edith Cown University, [5] Flinders University, [6] University of Canberra

Background

Behaviours and psychological symptoms of dementia (BPSD), such as depression/aggression, are common and can lead to negative health outcomes. Causes of BPSD are complex, but are typically unrelated to the disease process e.g., pain is a leading cause of BPSD but is not a primary symptom of dementias.

Identifying causes of BPSD is fundamental in resolving these symptoms. However, not all causes of BPSD are well understood or identified.

For instance, while up to 70% of older adults are estimated to have experienced a traumatic event, and that dementia onset can lead to its re-emergence, little is known about the interaction between trauma and BPSD. In this paper we aimed to describe the occurrence and impact of BPSD in people with or without a history of psychological trauma.

Methods

This was a 5-year, retrospective observational study (1 January 2018 and 31 December 2022) utilising data of referrals to national BPSD programs of Dementia Support Australia (DSA). Presence of psychological trauma was determined by trained DSA consultants after reviewing the referral's social/medical history, and/or if it was identified during DSA assessment. BPSD were assessed with the Neuropsychiatric Inventory (NPI). Referrals with evidence of psychological trauma were grouped "Trauma' and those without "No Trauma'. Regressions examined group differences, controlling for age and sex.

Results

"No Trauma' group included 39,347 referrals and "Trauma' group 2,259 referrals. "Trauma' group demonstrated significantly higher average BPSD severity and associated caregiver distress and was more likely to demonstrate higher odds of experiencing 8 of 12 symptom domains (e.g., psychotic and affective symptoms) of the NPI.

Discussion

This large study lends further support of the interaction between psychological trauma and the occurrence of BPSD. This warrants the need for timely support and targeted intervention for people with dementia with a previous history of psychological trauma.

Memory Clinic Implementation of Cognitive Interventions for People with Mild Cognitive Impairment

Sharon Naismith [1], Alessandra Lee [1], Loren Mowszowski [1], Alison Hutchison [2], Inga Mehrani [3], Kerryn Pike [4], Alex Bahar-Fuchs [2]

[1] University of Sydney, [2] Deakin University, [3] University of New South Wales, [4] Griffith University

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Background

Despite compelling research evidence for the effectiveness of cognitive interventions for people with mild cognitive impairment (MCI), they remain largely inaccessible in clinical practice. The Australian Dementia Network (ADNeT) Cognitive Intervention Working Party has been tasked with bridging this evidence-to-practice gap in memory clinics in Australia.

Methods

We used the findings from our scoping review and national survey of clinicians and trainees, to develop a clinician training package as our implementation strategy. Clinical neuropsychologists and their managers from six sites completed surveys at baseline and following six months of supported implementation at their site. Surveys covered current practice, clinician knowledge and confidence related to cognitive intervention, clinician work satisfaction, organisational readiness for implementing change, and perceived barriers and facilitators to implementation.

Results

Seventeen clinical neuropsychologists from six memory clinics throughout Australia participated in the clinician training. Five of these sites have commenced offering cognitive interventions to clients with MCI. Preliminary results will be reported, including implementation success, in terms of changes in the number of people with MCI who have been offered and received a cognitive intervention. Clinician changes in knowledge, confidence, and work satisfaction will be presented, as will changes in organisational readiness for change, and perceived barriers and facilitators to implementation.

Discussion/Conclusion

This project has increased the availability of cognitive interventions for people with MCI in five memory clinics across four states of Australia. The learnings from this pilot study will inform future larger scale implementation of cognitive interventions throughout memory clinics. This will enable the provision of tailored cognitive support for people with MCI, reducing the impact of cognitive impairment, and enabling them to participate independently for longer and live meaningful lives.

Filling a Gap in the Post-Diagnostic Care Pathway for Dementia in Australia via the Integrated Rehabilitation for Early-Stage Dementia (iREADi) Program: A Novel Post-Diagnostic Early Intervention Education, Rehabilitation and Support Program for People Living with Dementia and their Carers

Christine Sender-Ivanov [1], Dr Wendy Longley [1]

[1] SESLHD War Memorial Hospital

Background

Other chronic medical conditions have post-diagnostic care pathways in Australia, why not dementia? Timely access to integrated rehabilitation for those affected by newly diagnosed dementia has been identified by WHO and National Standards for Action on Dementia as a gold standard. In 2018, the Uniting War Memorial Hospital (UWMH) determined to fill that gap via the development of a novel outpatient education, rehabilitation and support program.

Methods

iREADi was designed via input from expert clinicians, local health district stakeholders and service providers, and, most importantly, people affected by dementia, using a collaborative participant co-design approach. The UWMH's Management of Dementia 'MOD' Squad, a specialist multidisciplinary dementia rehabilitation team, launched the new integrated rehabilitation for early-stage dementia "iREADi" Program as an outpatient service in 2020.

Results

The iREADi program is for both people living with dementia (PLWD) and their Carers. It consists of:
An in-person, 9-week small-group dementia rehabilitation and education course
Cognitive rehabilitation
A 3-month Individual goal-based rehabilitation phase
Ongoing care-coordination by a dementia nurse consultant
Linkages with local services and supports
Fostering of post-Program social networking amongst iREADi graduates
Despite COVID, between September 2020 and January 2024, 189 participants successfully completed the Program. Service delivery data, qualitative, and 'real-life' outcomes show iREADi is feasible and requires modest resourcing. It is acceptable to PLWD and their carers, garnering overwhelmingly positive participant feedback. Statistical evaluation of quantitative outcomes is in progress.

Discussion/Conclusion

Participant co-design is the secret of iREADi's success. Informed and empowered graduates experience greater confidence in living with dementia, combating stigma, and continuing to participate actively in their communities. iREADi's anticipatory and multidisciplinary rehabilitation approach identifies early opportunities in preventative care-coordination, enabling participants to adjust their lifestyle to better manage their condition whilst they are still 'well', rather than later in their dementia trajectory through crisis intervention.

Antidementia and Psychotropic Drug Use in Older People with Dementia in Australia: A National Data Linkage Study

Edward Lau [1], Edwin Tan [1], Weisi Chen [1], Yun-Hee Jeon [1], Christine Lu [1], Sarah Hilmer [1]

[1] The University of Sydney

Background

People with dementia are high users of psychotropic medications; however, national estimates of antidementia and psychotropic medication use are lacking in Australia. This study aims to estimate the national prevalence of antidementia and psychotropic medication use, and sociodemographic factors associated with their use, in Australians living with dementia.

Methods

This was a nationwide data linkage study using 2021 Census and Pharmaceutical Benefits Scheme (PBS) data. All people aged 65 or above with dementia (self-reported in Census or dispensed an antidementia drug) were included. Medication use was defined as at least one dispensing during the 3-month period following the Census (August–October 2021). Prevalence of antidementia and psychotropic medication use, including antipsychotics, benzodiazepines and Z-drugs, antiepileptics, opioids and psychostimulants, was calculated. Sociodemographic factors associated with medication use were explored using multivariable logistic regression models.

Results

Of the 177,809 older people living with dementia included, 58.6% were using at least one psychotropic medication. Antidepressants were the most commonly used psychotropics (41%), followed by opioids (20%) and antipsychotics (13%). Antidementia medications were used by a quarter of people with dementia (26%). People with dementia living in a higher socioeconomic area were more likely to use antidementia medications (odds ratio (OR): 1.22; 95% confidence interval (CI): 1.17–1.28), while less likely to use psychotropics (OR: 0.91; 95%CI: 0.88–0.95) compared to people living in a lower socioeconomic area. Conversely, those living in regional areas were more likely to use psychotropics (OR: 1.06; 95%CI: 1.03–1.10), while less likely to use antidementia medications (OR: 0.80; 95%CI: 0.77–0.83) compared to people living in metropolitan areas.

Discussion/Conclusion

Psychotropic medication use is common in people with dementia in Australia. Disparities in access to healthcare may be associated with the use of antidementia and psychotropic medications.

Genetic Correlation and Casuality Assessment Between Alzheimer's Disease and Asthma

Simon Laws [1, 2, 3], Tenielle Porter [1, 2, 3], Giuseppe Verdile [3, 4], Ayeisha Milligan Armstrong [1, 2, 3, 4], Olasunkanmi Bamidele[2, 5], Emmanuel Adewuyi [2]

[1] Collaborative Genomics and Translation Group, School of Medical and Health Sciences, Edith Cowan University, Joondalup, Perth, WA 6027, Australia, [2] Centre for Precision Health, Edith Cowan University, Joondalup, Perth, WA 6027, Australia, [3] Curtin Medical School, Curtin University, Bentley, Perth, WA 6102, Australia., [4] Curtin Health Innovation Research Institute, Curtin University, Bentley, Perth, WA 6102, Australia, [5] Faculty of Pharmaceutical Sciences, University of Ilorin, Ilorin, Nigeria

Background

Observational studies have suggested a co-occurring relationship between Alzheimer's disease (AD) and asthma. However, the aetiology and biological mechanisms underlying AD and its potential association with asthma, an autoimmune condition, remain unclear.

Methods

We examine the genetic relationship between AD and asthma by analysing large-scale genome-wide association study (GWAS) summary data from international research consortia and groups. We conducted a linkage disequilibrium score regression (LDSC) analysis to assess AD's genome-wide (global) genetic correlation with asthma. We also performed a two-sample Mendelian randomisation (MR) analysis to investigate the potential bi-directional causal relationships between AD and asthma. We performed additional analyses for possible (partial) replication of our genetic correlation and causality findings on the side of both AD and asthma.

Results

Our LDSC-based genetic correlation estimates revealed a positive and significant global genetic correlation (rG) of AD with asthma (rG = 0.19, SE = 0.04, P = 5.57 x 10-6). We used additional asthma GWAS data for replication testing with consistent significant results across all data. We observed a similar pattern of correlation estimate direction in our (partial) replication testing for AD (clinically diagnosed cases), although only one of the asthma GWAS data's results was significant (likely due to a smaller sample size). Based on the inverse-variance weighted (IVW) model, our MR analysis found no evidence for a significant causal association between AD and asthma. This MR result was consistent with AD or asthma as an exposure or outcome variable, respectively. Sensitivity testing using other MR approaches produced results similar to our IVW model, supporting no evidence of a causal association between AD and asthma.

Discussion/Conclusion

Our study reveals a significant genetic correlation but non-causal association between AD and asthma, implicating the presence of shared genetic mechanisms and biological pathways in both conditions.

Innovative Small Molecule Approaches to Boosting Proteostasis in Alzheimer's Disease

Prof. Ralph N Martins [1], Ajish Ariyath [1], Dr. Warnakulasuriya Mary Ann Dipika Binosha Fernando [1], Dr. Prashant Bharadwaj [1]

[1] Edith Cowan University

Background

Autophagy is over activated in Alzheimer's disease brain, but still activating autophagy has received most attention, however recent evidence suggests that ubiquitin-proteasome system can clear aggregate proteins and a potential therapeutic target for AD and protein misfolding diseases.

Methods

We previously developed an assay using the MC65 AD cell model and demonstrated that Amyloid Precursor Protein (APP) derived carboxy terminal peptides (APP-C99) and amyloid-β protein (Aβ) is rapidly cleared in this model. Using this model, we screened a library of small molecule proteostasis modulators and identified IU1, a USP14 inhibitor that improved cell survival and promoted Aβ clearance. Our study investigated whether new analogues of IU1 provides better neuroprotection in AD. Screening of 71 novel small molecule proteostasis inhibitors using this cell model, discovered a novel lead compound C51. This compound effect on autophagy, proteasome activity, and APP-C99/Aβ clearance were further analyzed using techniques involving immunofluorescence staining, toxicity analysis, western blotting, and proteasome assays.

Results

Initial study used an in-silico artificial intelligence screening platform from Atomwise to design and develop novel small molecule USP14 binding ligands. Cell studies have shown promising results with compound C51 from the screened library of proteostasis modulators in alleviating AD proteostasis dysfunction, protein aggregation and regulating autophagy clearance. Cell survival by IU1 was 40% which was improved to 55% using C51, where it reduced accumulation of APP-C99 and Aβ. Also, reduced levels of autophagy markers LC3 and p62, restored proteasomal activity in the AD cell model.

Conclusions

Ours, is the first report of using IU1 in an AD model as USP14 inhibitor. The novel IU1 analogue C51 looks more promising and hold potential as candidates for pre-clinical validation in AD. The next steps involve testing therapeutic efficacy, target engagement, and brain bioavailability in AD animal models.

Lumipulse Plasma pTau217 Accurately Detects and Stages Alzheimer's Disease and Rises with Early Tau Aggregation

Ralph N. Martins [1], Christopher Fowler [2], Eddie Stage [3], Pierrick Bourgeat [4], Colin L. Masters [2], Natasha Krishnadas [2], Victor L. Villemagne [5], Larry Ward [2], Joanne Robertson [2], Jurgen Fripp [4], Anthony W. Bannon [3], Manu Vandijck [6], Vincent Doré [7], Azadeh Feizpour [2], Christopher C. Rowe [8], James D. Doecke [4]

[1] Australian Alzheimer's Research Foundation, Perth, [2] The Florey Institute of Neuroscience and Mental Health, [3] AbbVie, [4] CSIRO, Brisbane, [5] University of Pittsburgh, [6] Fujirebio, [7] CSIRO, Melbourne, [8] Department of Molecular Imaging & Therapy, Austin Health

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Background

Plasma assays for phospho-tau 217 (pTau217) accurately detect amyloid and tau. This study tests the performance of a novel pTau217 assay, run on a widely available, fully-automated immunoassay platform, for predicting amyloid and tau pathology in Alzheimer's disease (AD).

Methods

Participants included 156 cognitively unimpaired (CU), 100 with mild cognitive impairment (MCI) and 132 with dementia, with plasma pTau217 Lumipulse® assay, 18F-NAV4694 amyloid-beta (Aβ) PET and 18F-MK6240 tau PET data. Discriminative performance for Aβ PET status, tau PET status, PET-based Braak stages and AD biological PET stages was assessed using ROC analysis. In a subset of participants with Centiloid <150, the entorhinal, amygdala and meta-temporal (MetaT) tau SUVR and pTau217 levels were modelled as a function of Centiloid.

Results

Compared to Aβ- (Centiloid<25) CU, pTau217 increased two-fold in Aβ+ CU, four-fold in Aβ+ MCI and six-fold in Aβ+ AD. It correlated with Centiloid ($\rho = 0.75$) and tau SUVRMetaT ($\rho = 0.78$). Applying a single threshold to pTau217, accuracy was 87% for correct classification to Aβ- vs. Aβ+ while the accuracy of a two-threshold approach was 92% excluding the 17.8% indeterminant results. Area under curve (AUC) for Aβ- vs Aβ+ was 0.93 and for tau- vs tau+ (MetaT) was 0.94. AUC for Braak 0-III vs. Braak IV-VI was 0.96 and for moderate/high neocortical tau vs. mesial-temporal/no-tau was 0.97. Rise in plasma pTau217 slightly lagged the rise in amygdala 18F-MK6240 binding and paralleled the rise in MetaT 18F-MK6240 binding, consistent with our previous report using Janssen p217+tau.

Conclusion

Plasma pTau217, measured on Lumipulse® platform, was a strong predictor of Aβ and tau PET status and may provide cost-effective biological PET staging of AD. A rise in pTau217 may reflect early formation of neurofibrillary tangles (NFT) rather than a direct physiological response to brain Aβ plaques prior to NFT formation.

Olfactory Stem Cells as a New Model for Investigating Potential Biomarkers for Alzheimer's Disease

Alexandre S Cristino [1], Katja M Kanninen [2], Laura M Rantanen [3], Riikka Lampinen [2], Anthony R White [3], Maina Bitar [3], Harley Robinson [3]

[1] Griffith Institute for Drug Discovery, Griffith University, Brisbane, QLD, Australia, [2] A.I. Virtanen Institute for Molecular Sciences, University of Eastern Finland, Kuopio, Finland, [3] Mental Health Program, QIMR Berghofer Medical Research Institute, Brisbane, QLD, Australia

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Background

Alzheimer's disease (AD) is a neurodegenerative disorder with an increasing incidence worldwide. There are currently no treatments to cure or effectively slow the progression of AD. To address this, patient-derived cell models of AD that co-relate with early clinical features observed in AD could be valuable to gain a better understanding of the disease and develop new treatments. Impaired olfaction is one of the earliest symptoms and a significant predictor of conversion to AD from mild cognitive impairment (MCI), a prodromal AD condition. Found deep within the nasal cavity, olfactory stem cells provide a window into the brain. Their inherent ability to form neuroglia makes these cells potentially an ideal model system to examine the early pathophysiological changes that take place in AD.

Methods

Human olfactory neurosphere-derived (ONS) cell lines were generated using olfactory mucosal biopsies from age-, gender- and ApoE genotype-matched cognitively healthy individuals (HC), patients with AD, and individuals with MCI (n=6 for each group). Transcriptomics and proteomics analyses were performed to identify global gene and protein changes and associated pathways between HC, MCI and AD ONS cells, and to discover potential disease biomarkers.

Results

Transcriptomic results revealed several differentially expressed genes associated with cognitive changes, AKAP6 being the most significantly altered. Proteomics analysis highlighted especially differentially expressed proteins, such as NDUFS4 and TMSB4X, and disease pathways associated with altered cell metabolism, mitochondrial function and actin cytoskeleton organisation in AD ONS cells compared to MCI and HC.

Conclusion

This study demonstrated the potential of patient-derived ONS cells to provide a cell-based model for AD biomarker discovery. Importantly, we identified potential novel genes, proteins, and disease pathways that may have a role in AD, especially MCI to AD transition, and could possibly be utilised as prognostic biomarkers for AD. However, further studies are required.

ISLAND Campus: Opt-In Intervention of Fee-Free University Education Reduces Modifiable Risk Factors for Dementia and Improves Cognition throughout Tasmania

Dr Hannah Fair [1], Eddy Roccati1, Anna King [1], Jane Alty [1, 2], James Vickers [1], Aidan Bindoff [1], Jessica Collins [1], Kathleen Doherty [1], Alex Kitsos [1]

[1] Wicking Dementia Research and Education Centre, [2] Royal Hobart Hospital

Background

We know early-life education reduces dementia risk, yet there is great potential for risk reduction in later-life through interventions, even for people with low early-life educational attainment. In 2019, we launched ISLAND (Island Study Linking Ageing and Neurodegenerative Disease) Campus, offering free university study to participants, with flexible in-person/online learning models removing educational, socioeconomic and geographical barriers. Here we investigate our core hypothesis: that engagement in later life education leads to improvements in modifiable risk factors for dementia and cognition.

Methods

ISLAND Campus participants were optimal matched on age and gender to non-Campus participants via propensity score method.. Participants completed online surveys on background health, demographics, modifiable dementia risk via customised Dementia Risk Profile (DRP). Cognition was measured online via the validated Cambridge Neuropsychological Test Automated Battery Paired Associates Learning (PAL) and Spatial Working Memory (SWM) tasks. Impact of the opt-in educational intervention was tested in R via ANCOVA.

Results

Included were 986 participants (intervention = 493, control = 493), mean age 61.2 years, 71.2% female, 11.7 mean years of education). Intervention/control participants were similar on socioeconomic status, however intervention participants had significantly higher history of prior university study completion (76.1%) than controls (59.8%). Intervention participants enrolled in a variety of university degrees, the most common were Diploma of Family History (n = 103, 20.8%) and Diploma of Arts (n = 74, 15.0%). Over four years of follow-up, intervention participants significantly improved episodic memory (PAL) and their risk factor profiles as measured via the DRP ($p < 0.001$), indicating a significant change towards lower dementia risk.

Conclusion

We found free later-life university education was associated with improvements in modifiable dementia risk factors over time and cognition. Intervention participants displayed significantly higher baseline education than control participants, therefore later life educational interventions should be targeted at individuals with lower baseline education.

Hearing Loss, Social Isolation and Depression in Participants Aged 50 Years or Over in Tasmania, Australia

Aidan Bindoff [1], Larissa Bartlett [1], James Vickers [1], Lynette Goldberg [1], Mohammad Shoaib Hamrah [1]

[1] Wicking Dementia Research Education Centre

Background

Hearing loss (HL) in adult life is one of the most prevalent health conditions and is associated with several chronic diseases. HL can lead to reduced social activity and perceptions of supportiveness within social networks. This study explored the effects of corrected vs. uncorrected HL on social support, and social isolation, anxiety, and depression.

Methods

A cross-sectional study was undertaken by 7,442 Australian residents aged 50 years or over as part of the Island Study Linking Ageing and Neurodegenerative Disease (ISLAND). Respondents were grouped into those with no reported HL, those with corrected HL (managed with hearing aids and other listening devices), and those with uncorrected HL.

Results

HL was reported by 1,274 participants (17.1%). There was a higher proportion of females when compared to the No-HL group (25% male, 75% female). Compared with participants with corrected or no-HL, those with HL (n= 548, 7.4%) reported significantly smaller (p=.007) and less supportive social networks (p = .001), higher self-reported anxiety (p<.001) and depression (p<.001) symptoms. For all outcomes, correction of HL mitigated these negative effects. The only significant contrast between participants with HLcorrected and No-HL was on the depression scale (SMD = .10, p = .039). Depression symptoms were more common in those with HLcorrected than No-HL.

Conclusions

Uncorrected HL was associated with poor mental health and social isolation, compounding the risk for dementia. Correcting for HL appeared to mitigate these outcomes except for depression. Longitudinal studies are needed to track the effects of HL correction over time. Hearing status needs to be assessed when people present with mental health concerns, so health professionals can make appropriate referrals and provide appropriate advice and support.

Do People from Culturally and Linguistically Diverse (CALD) Background Take Longer Times to Receive a Dementia or Mild Cognitive Impairment Diagnosis: Findings from the Australian Dementia Network (ADNeT) Registry

Xiaoping Lin [1], Kasey Wallis [1], Susannah Ahern [1], On behalf of ADNeT Registry Steering Committee [2], Stephanie Ward [1, 3, 4], Henry Brodaty [3], Mohammad Honardoost [1]

[1] Monash University, [2] ADNeT Registry, [3] University of New South Wales, [4] The Prince of Wales Hospital

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Introduction

People from culturally and linguistically diverse (CALD) backgrounds account for one third of Australians living with dementia. However, high-quality national data about this group are lacking to inform evidence-based policy and service delivery. The Australian Dementia Network (ADNeT) Registry is a clinical quality registry that provides robust, systematically collected data on diagnosis and early management of people with dementia or mild cognitive impairment (MCI), including people from CALD backgrounds.

Methods

Registry data from March 2020 to Sept 2023 (3634 participants excluding First Nations participants) were analysed. Participants were categorised into three CALD status based on country of birth and preferred spoken language: non-English-speaking CALD (366, 10%), English-speaking CALD (451, 12%), and non-CALD (2817, 78%). Outcome variables included age at referral, time from referral to diagnosis, time from referral to first appointment, and time from first appointment to diagnosis.

Results

Overall median age at referral was 78 years and median days was 131 days from referral to a memory and cognition diagnostic clinic to diagnosis, 75 days from referral to fist appointment, and 28 days from first appointment to diagnosis. Both English- and non-English-speaking CALD backgrounds were associated with longer time from referral to diagnosis (154/158 vs 123 days, $p<0.001$) and longer time from first appointment to diagnosis (46/70 days vs 18 days, $p<0.001$), remaining significant after adjusting for demographic and health factors. There was no association between CALD status and time from referral to first appointment, $p=0.6$. Non-English-speaking CALD background was associated with older age at referral (77 vs 78/80 years, $p<0.001$), although the association disappeared after adjustment.Conclusion: Data from the ADNeT Registry suggest that people from CALD backgrounds experience delays in the diagnosis of dementia or MCI. These delays may preclude them from accessing timely post-diagnostic services and novel disease modifying treatments on the horizon.

"It's Really Important That We Do Have a Voice." Residents' Perspectives on the Factors that Promote and Support Mental Health within Aged Care Homes

Associate Professor Nadeeka Dissanayaka (PhD) [1], Dr Claire Burley (PhD) [2], Dr Rachel Brimelow (PhD) [1], Dr Deborah Brooks (PhD) [1], Dr Deepa Sriram (PhD) [1]

[1] The University of Queensland Centre for Clinical Research, [2] University of New South Wales, Centre for Healthy Brain Ageing

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Background

Over 50% of people living in residential aged care (RAC) have a dementia diagnosis; 57% report at least one diagnosed mental health disorder. However, mental health practices in RAC are generally poor, and mental health services not routinely available. There are currently no mechanisms to monitor and promote mental health for people living in RAC, including those with mild cognitive impairment or dementia. To address this gap, we are developing a Mental Health Care Indicator Tool (MHICare Tool) for RAC using co-design methods with key stakeholders, including residents.

Methods

Three focus groups and one interview were held in-person with 12 residents from two care homes in New South Wales. Discussions were facilitated by an experienced researcher following a semi-structured topic guide, with a second researcher taking notes. Residents were asked to consider areas of mental health care and practice most important to them. Discussions were audio-recorded, transcribed and imported to NVIVO qualitative software for thematic analysis.

Results

Participants included residents with and without mild cognitive impairment (n=4; n=8 respectively), aged 72-90 years. Three quarters were female; a third had prior experience of mental health conditions. Factors identified as important for the mental health of residents included: 1) staff attitudes (e.g., patient, caring, cheerful, approachable); 2) staff understanding of residents' mental health history and needs; 3) staff communicating with each other regarding residents' mental health; 4) staff maintaining safety from 'dangerous' behaviour of other residents; and 5) residents' having access and choice to attend activities that promote positive mental health.

Discussion

Factors considered most important by residents reflected 'staff attitudes, values and behaviour', 'staff time, care and communication' and 'access to activities that promote mental health' domains. Findings have been incorporated with those from interviews with aged care staff and family carers to develop draft indicators for the MHICare Tool.

The Right to Rehabilitation for People with Dementia - Developing Solutions through Co-Design

Catherine Devanny (MPH) [1, 2, 3], Dr Monica Cations (PhD) [4], Dr Claire O'Connor (PhD) [5, 6, 7], Prof Alan Petersen (PhD) [8], Kate Swaffer (MSc) [9], Prof Helen Skouteris (PhD) [10], Prof Lee-Fay Low (PhD) [11], Dr Barbara Barbosa Neves (PhD) [12], Dr Natasha Layton (PhD) [2, 13], Prof Terry Haines (PhD) [2, 14], Prof Velandai Srikanth (PhD) [1, 2, 3], Dr Den-Ching A Lee (PhD) [2, 13], A/Prof Michele Callisaya (PhD) [2, 3, 15], A/Prof Nadine Andrew (PhD) [2, 3], Prof Keith Hill (PhD) [2, 13], Prof Grant Russell (PhD) [16], Dr Taya Collyer (PhD) [2, 3]

[1] Peninsula Health, VIC, [2] National Centre for Healthy Ageing, VIC, [3] Peninsula Clinical School, Monash University, VIC, [4] College of Education, Psychology and Social Work, Flinders University, SA, [5] School of Psychology, University of NSW, NSW, [6] Hammond Care, NSW, [7] Neuroscience Research Australia, NSW, [8] Sociology, School of Social Sciences, Monash University, VIC, [9] University of South Australia, [10] Health and Social Care Unit, School of Public Health and Preventive Medicine, Monash University, VIC, [11] Faculty of Medicine and Health, University of Sydney, NSW, [12] Sydney Centre for Healthy Societies, University of Sydney, Sydney, NSW, [13] Rehabilitation Ageing and Independent Living Research Centre, Monash University, VIC, [14] School of Public and Allied Health Care, Monash University, VIC, [15] Menzies Institute for Medical Research, University of Tasmania, TAS, [16] Department of General Practice, School of Public Health and Preventive Medicine, Monash University, VIC

Introduction

People with dementia have a human right to equal access to quality health care. However, many people living with dementia lack access to evidence-based rehabilitation for promoting function and quality of life. The aims of this study were to 1) explore barriers to access to dementia rehabilitation; and 2) identify solutions which improve access to rehabilitation.

Methods

People living with dementia and care partners (n=13) and professional staff (n=13) were invited to participate. Experience-based co-design across three virtual workshops was used to understand barriers and solutions to improve access to rehabilitation treatments. The Levesque Access to Health Care Framework was applied to findings regarding barriers and to assist selection of solutions.

Results

Attendance was 92.3% across the three workshops. Barriers were identified at a person-level (including lack of knowledge, transport, cost of therapies and difficulty navigating health, aged-care and disability services) and at the health professional, service and system-level (including health professional low dementia knowledge and negative attitudes, inequitable funding models, and non-existent or fragmented services). Solutions focused on widespread education and training in the area of dementia rehabilitation, including ensuring people with dementia and their care partners know about rehabilitation therapies and that health professionals, aged care and disability co-ordinators know how to refer and deliver interventions. Dementia care navigators, changes to Commonwealth aged care and Medicare funding models, and specific dementia rehabilitation programs were also recommended.

Conclusions

Barriers to accessing rehabilitation for people with dementia exist at multiple levels and will require a whole community and systems approach to ensure change.

Barriers and Facilitators of Social Participation in Older Adults with Mild Cognitive Impairment (MCI)/Early Dementia and their Carers/Supporters

Wing-Yin Leung [1], Diana Matovic [1], Viviana M. Wuthrich [1], Abhirami Viju [1]

[1] Macquarie University Lifespan Health & Wellbeing Research Centre

Background

MCI/early dementia and carer/supporter populations experience social isolation, yet there is limited understanding of their barriers and enablers to social participation, investigated in the present study.

Methods

In survey and focus group studies, older adults with MCI/early dementia (nsurvey=11, MageSurvey=75.36, nfocusGroup=7, MageFocusGroup=68.43) and carers/supporters (nsurvey=27, MageSurvey=73.63, nfocusGroup=13, MageFocusGroup=70.08,) answered open-ended questions about changes to social participation after diagnosis/caring, associated distress, barriers and facilitators. The survey also measured these variables quantitively, and social isolation, loneliness, depression and anxiety symptomology, and caregiver burden.

Results

MCI/early dementia and carer/supporter participants reported, respectively, social isolation (55%, 26% above clinical cutoffs), loneliness (100%, 70%), depressive (11%, 15%), and anxiety (73%, 81%) symptomology, moderate/major difficulties staying socially connected (45%, 37%) and were moderately/very upset by this (40%, 31%). Barriers from quantitative data for MCI/early dementia participants were forgetting people's names (91%), keeping up (73%) or being left out of conversations (55%), motivation (55%) and transport (55%). Facilitators were social groups (55%), their carer/supporter encouraging them to stay socially active (55%), and educating friends about their circumstances (46%). Most carers did not experience barriers (26%). Facilitators were dedicated friends who maintained contact (63%), understanding friends (56%), social groups (33%), and organisations like Dementia Australia (33%). Across the qualitative data, major themes for people with MCI/early dementia were negative feelings (e.g., embarrassment, guilt; 40%), others not understanding/ostracism (40%), practical/transport issues (70%), impaired cognitive processing (40%), and as a facilitator proactive social behaviour (e.g., joining new groups; 44%). Carers reported behavioural and psychological symptoms in dementia (31%), missing social/wellbeing activities (41%), practical/transport issues (43%), and facilitators including friendships/family (40%) and organisations (38%).

Discussion

MCI/early dementia and carer/supporter populations experience practical and psychological barriers to social participation. Interventions should target these barriers and increase facilitators including educating friends/family, and provide psychological skills for MCI/dementia-related embarrassment and joining new groups.

The Oral and Gut Microbiome Signatures of Older Australians with and without Dementia and Comparisons to International Data

Dr Xiaotao Jiang [1], Eunice Cheng [1], Dr Fatima El-Assaad [1], Professor Emad El-Omar [1], Dr Michelle Fitzmaurice [1]

[1] UNSW Microbiome Research Centre, School of Clinical Medicine, UNSW Medicine & Health, St George & Sutherland Clinical Campuses

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Background

Dementia is a chronic, progressive neurodegenerative syndrome resulting in cognitive decline beyond that of biological ageing, which interferes with daily life. Growing evidence has implicated the microbiome in the pathogenesis of dementia.

Methods

We recruited eight Australians with dementia and 40 age-sex-matched, cognitively-well controls as part of the Healthy Optimal Australian Microbiome Study. Oral and stool samples were collected and underwent shotgun metagenomic sequencing to identify microbial signatures associated with dementia.

Results

Oral samples from dementia patients demonstrated a marginal increase in microbial community richness compared to controls ($p=0.049$), although inter-community analysis was not different. Five phyla, 29 genera and 49 species in oral samples, and 18 genera and 34 species in stool samples were significantly different for cognitive status ($p<0.05$, adjusted p-value(padj)<0.2). These included the taxa Collinsella and Veillonella, which may contribute to the neuroinflammation associated with dementia. Pathogenic bacteria common in periodontitis were also enriched, highlighting a potential association between periodontitis and dementia, and a modifiable risk factor for dementia. Functional pathways related to inflammation were also identified.

We re-analysed Laske et al.'s 2022 German microbiome study of Alzheimer's Disease and cross-validated our results. No significantly differential taxa or functional pathways were consistent in the stool samples of dementia groups from both countries, indicating a potential geographic influence on microbial signatures.

Conclusion

This Australian-first study identified microbial signatures associated with dementia including several novel taxa and some that were consistent with literature. Both Australian and German cohorts demonstrated that dysbiosis occurs in dementia and is characterised by the enrichment of pro-inflammatory bacteria whose effects may be mediated by the metabolites they produce. Periodontal pathogens were enriched in dementia, revealing a potential contribution of oral disease in neurodegeneration. Further understanding of these signatures may contribute to the development of personalised microbiome-based dementia preventive and therapeutic strategies.

Modelling CLN3 (Juvenile Batten) Disease in iPSC-Derived Neurons Implicates Interrelated Pathways in Protein Homeostasis and Neurite Arborization

Natalie King [1], Ineka Whiteman [2], Sharn Perry [3], Sueanne Chear [3], Anthony Cook [3], Adelene Chiam [3], Elizabeth Read [3], Emma Wilkinson [3], Alex Hewitt [4], Jana Talbot [3], Anna King [3], Brad Sutherland [1]

[1] University of Tasmania, School of Medicine, [2] Batten Disease Support and Research Association (Austrtalia), [3] University of Tasmania, Wicking Dementia Centre, [4] University of Tasmania, Menzies Institute for Medical Research

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Background

CLN3 (Juvenile Batten) disease is a fatal lysosomal storage disorder causing blindness, epilepsy and dementia, and has no cure. The progressive and disruptive effect on the brain impacts the child's ability to learn, play, and interact with family and friends, resulting in high care needs that are borne by parents and siblings.

Methods

We have established an induced pluripotent stem cell (iPSC) line from a person with compound heterozygous mutations in CLN3 (E295K and 1 kb deletion). We subsequently used CRISPR/Cas technology to generate isogenic iPSC lines, in which the 1 kb deletion allele has been restored to the consensus allele. We have differentiated these cell lines into neurons, and used multi-electrode arrays to quantify neuronal activity differences, and proteomics to identify proteins and pathways differentially expressed. We are currently progressing functional and proteomic studies of glia (astrocytes and microglia), and cells of the blood-brain barrier, including pericytes and endothelial cells.

Results

Quality control assays including tests for pluripotency, genomic integrity, and CRISPR/Cas 'off-target' effects indicate these cell lines to be suitable for disease modelling. By comparing iPSC-derived cortical neurons, we identified disease-related changes relating to neuronal activity, as well as protein synthesis, trafficking and degradation.

Discussion/Conclusion

Our data implicate inter-related pathways in protein homeostasis and neurite arborization as contributing to CLN3 disease. We are now complementing these studies by generating iPSC-based models of other CLN3 gene variants, including a homozygous 1 kb deletion model, and compound heterozygous models with combinations of the 1 kb deletion and various point mutations. Moreover, we are now including studies of other genetic diseases causing childhood dementia, and we anticipate a greater understanding of the molecular similarities and differences between these diseases, and in relation to adult onset neurodegenerative disease, will increase opportunities for pre-clinical development of new therapies.

Investigation of Blood-Brain Barrier Transporter Dysfunction in Sporadic Alzheimer's Disease: Insights from Patient PISC-Derived Models

Lotta E Oikari [1], Anthony R White [1], Juliana C S Chaves [1, 2]

[1] Cell and Molecular Neurodegeneration, Mental Health and Neuroscience Program, QIMR Berghofer., [2] School of Biomedical Sciences, Faculty of Health, Queensland University of Technology, QUT, Brisbane, QLD, Australia.

Background

Alzheimer's disease (AD) is a leading cause of global dementia, primarily impacting individuals aged 65 and older, known as late-onset or sporadic AD (sAD). It is characterized by the accumulation of βeta-amyloid protein aggregates and neurofibrillary tangles formed by tau protein. Recent research underscores the critical association between AD and blood-brain barrier (BBB) dysfunction. The BBB, primarily composed of brain endothelial cells (BECs), pericytes, and astrocytes, serves as a guardian for the brain by regulating substance passage. Transporter-mediated regulation at the BBB is pivotal, with dysregulation implicated in neurodegenerative diseases, including AD. Non-invasive methods, such as focused ultrasound (FUS) mediated BBB opening have been investigated as a new therapeutic to potentially modulate transporter activity to enhances drug delivery.

Method

The present study used human-induced pluripotent stem cells (hiPSCs) from the apolipoprotein E (APOE4) high-risk and (APOE3) low-risk sAD patients to derive brain endothelial-like cells (iBECs) and astrocytes (iAstrocytes). The expression of key BBB transporters in these BBB cells were investigated. FUS combined with microbubbles (MBs) was used to modulate BBB transporters based on promising results from previous studies.

Results

The results demonstrated notable differences in BBB transporter expression between APOE4 and APOE3 BBB cells, particularly those involved in amyloid beta clearance. Interestingly, following treatment with FUS+MB, iAstrocytes in APOE4 exhibited higher expression levels of BBB transporters compared to APOE3 immediately after treatment. Notably, untreated samples showed initially lower expression of BBB transporters in APOE4 compared to APOE3, suggesting a potential compensatory increase in the levels of dysregulated transporters due to FUS treatment.

Conclusions

The findings highlight the potential of using hiPSC-derived iBECs and iAstrocytes in elucidating phenotypic disparities in the BBB of high-risk and low-risk sAD patients. Moreover, hiPSC-derived BBB models also allow to study the potential therapeutic effects of FUS, allowing for translatable research outcomes to AD patients.

A Novel Approach to Alzheimer's Disease through the Gut Microbiome

D. M. Sithara Dissanayaka [1, 2], Stephanie R. Rainey-Smith [1, 2, 3], Ralph N. Martins [1, 2, 4], W. M. A. D. Binosha Fernando [1, 2]

[1] Centre of Excellence for Alzheimer's Disease Research & Care, School of Medical and Health Sciences, Edith Cowan University, Joondalup, WA 6027, Australia, [2] Alzheimer's Research Australia, Ralph and Patricia Sarich Neuroscience Research Institute, Nedlands, WA 6009, Australia, [3] Centre for Healthy Aging, Murdoch University, Murdoch, WA 6150, Australia, [4] Department of Biomedical Sciences, Faculty of Medicine, Health and Human Sciences, Macquarie University, Sydney, NSW 2109, Australia

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Background

Recent research indicates that gut dysbiosis plays an important role in Alzheimer's disease. Alterations in the gut microbiota and their metabolites may influence the progression of AD via the gut-brain axis. The understanding of this dynamic interplay offers promising avenues for developing novel diagnostic and therapeutic strategies aimed at reducing the impact of AD by targeting the gut microbiota. It is therefore intended that in this study the gut microbes of AD patients at different stages of the disease (preclinical, mild cognitive impairment (MCI)) be comprehensively characterized, so that a faecal microbiota profile at the species level can be developed as an indicator for clinical identification of the progression of the disease.

Methods

Study participants were selected from highly characterised cohorts and collected faecal samples according to the sample collection instructions. A metagenomic study will be carried out in this study to examine taxonomic composition and gut microbiota function in cognitively normal individuals as well as individuals with preclinical AD.

Results

The faecal samples of people with AD have been shown to have decreased microbial diversity and compositionally distinct microbiota. Several studies have demonstrated that patients with MCI and AD have altered microbiome compositions compared with healthy controls. Patients with AD have reduced alpha diversity, decreased abundance of taxa that produce beneficial metabolites, and an increase in taxa that produce proinflammatory and toxic compounds. A significant difference exists between the beta diversity of ADs and HCs.

Discussion

Research into the gut and brain concerning AD progression and AD pathology remains very inconsistent with the reported data. Therefore, evaluation of the potential role of microbiota taxonomy in faecal in the early detection of preclinical AD may lead to the development of novel directions in the investigation of the potential role of the gut in AD progression.

Poorer Online Cognitive Performance is Associated with Genetic Risk for Alzheimer's Disease and Brain Phenotypes in Healthy Mid-Life and Older Adults

Nicholas G. Martin [1], Gail A. Robinson [1], Renate Thienel [2], Michelle Lupton [3], Kerry McAloney [4], Michael J. Breakspear [1], Amelia Ceslis [4], Lina Gomez [4], Luis M. Garcia-Marin [5], Caroline Faucher [5], Miguel E. Renteria [2], Jessica Adsett [6], Brittany L. Mitchell [2]

[1] Prof, [2] Dr., [3] A.Prof, [4] Mrs., [5] PhD. Candidate, [6] Miss.

Background

Self-administered online cognitive testing offers a cost-effective and flexible alternative to in-person neuropsychological assessments. We used the Creyos platform to assess cognitive function in a large sample of middle aged and older adults participating in the Prospective Imaging Study of Aging (PISA).

Method

2,162 participants (70% female, aged 42-75 years) completed 12 tasks covering memory, executive function, language, and visuo-spatial domains. We generated polygenic scores (PS) using GWAS summary stats for Alzheimer's disease (AD) (APOE excluded) as well as intracranial volume and nine subcortical brain region volumes. We tested for an association of PS and the presence of APOE ε4 allele with cognitive test scores with using a logistic regression model in GCTA, accounting for sex, age, ancestry and relatedness among individuals.

Results

We identified nominal associations of AD PS with reduced performance on four out of twelve of the cognitive tests covering executive function, memory and visuo-spatial domains (two examples being; Monkey ladder β=-0.027, SE=0.013, p=0.023; Paired Associates β=-0.030, SE=0.014, p=0.014). There was no effect of APOE. We identified suggestive associations of a genetic propensity to a larger volume of brainstem, hippocampus and ventral diencephalon with better performance on tasks covering executive function and language. Association analysis using latent variables (from principal component analysis) of the cognitive data to reduce dimensionality will also be presented.

Conclusion

We show preliminary evidence of the effect of genetic risk for AD and subcortical brain volumes with cognitive phenotypes in middle aged and older individuals. The identification of cognitive changes associated with AD risk and prodromal disease gives important insights into AD development throughout the life span. Our results highlight the utility of online cognitive testing as a cost-effective alternative to in person testing as a pre-screening approach to identify those at high risk of Alzheimer's disease.

Exploring a Novel Hand-Motor Biomarker Across the Dementia Continuum: Integration and Validation of TAS Test in the ISLAND Cognitive Clinic

A/Prof. Quan Bai [1], A/Prof. Jane Alty [2], Ms. Xinyi Wang [2], Dr. Katherine Lawler [3], Dr. Son Tran [1], Prof. Alastair Noyce [4], Dr. Katharine Salmon [1], Prof. James Vickers [2], Dr. Rebecca St Goerge [5], Mr. Aidan Bindoff [2]

[1] School of Information and Communication Technology, University of Tasmania, Hobart, TAS, Australia, [2] Wicking Dementia Research and Education Centre, University of Tasmania, Hobart, TAS, Australia, [3] La Trobe University, Melbourne, VIC, Australia, [4] Queen Mary University of London, London, England, United Kingdom, [5] School of Psychological Sciences, University of Tasmania, Hobart, TAS, Australia

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Background

There is an urgent need for accessible, quick and low-cost methods to aid identification of people across the dementia continuum. Current cognitive assessments are time consuming, and specialist. Emerging evidence shows that simple hand movement tests could aid risk stratification. We evaluated the new online TAS Test key tapping test in the ISLAND Cognitive Clinic (Tasmania, Australia), for classifying dementia, mild cognitive impairment (MCI) and subjective cognitive decline (SCD) from control subjects.

Methods

212 participants (69.0 ± 9.3 years old) were recruited from the ISLAND Clinic, including 50 with dementia, 54 with MCI, 26 with SCD, and 82 cognitively healthy controls. An interdisciplinary team provided consensus cognitive diagnosis. Addenbrookes Cognitive Examination (≥95) was administered to healthy controls. Participants completed a 60-seconds alternate key tapping test on the TAS Test website during their standard visit. We analysed frequency, variability, key press duration, and accuracy scores. Regression models incorporating motor features, adjusted for age and sex, were compared to null models containing only age and sex using area under ROC curves (AUC).

Results

Hand tapping motor data improved the classification of individuals with dementia (AUC = 0.89, 95% CI = [0.84, 0.95], p=0.025), MCI (AUC = 0.8, 95% CI = [0.73, 0.87], p=0.002), and SCD (AUC = 0.75, 95% CI = [0.63, 0.86], p = 0.004) compared to cognitively healthy controls. Additionally, motor features aided in distinguishing dementia (AUC = 0.9, 95% CI = [0.84, 0.97], p = 0.024) and MCI (AUC = 0.79, 95% CI = [0.67, 0.91], p = 0.022) from SCD, though not dementia from MCI (p = 0.221).

Conclusion

The 60-second simple keyboard tapping test has shown promise as an effective mean of differentiating individuals with SCD, MCI, or dementia from healthy controls. This suggests its potential as a novel, cost-effective, and accessible triage tool and motor biomarker in clinical settings.

Detection of Subtle Cognitive Decline in Pre-Symptomatic Community-Dwelling Older Adults Using Unsupervised Online TAS Test Hand Reaction Time Tests

Prof. James Vickers [1], A/Prof. Quan Bai [2], Dr. Katherine Lawler [3], Dr. Eddy Roccati [1], Mr. Aidan Bindoff [1], Dr. Son Tran [2], Dr. Larissa Bartlett [1], A/Prof. Jane Alty [1], Prof. Anna King [1], Ms. Xinyi Wang [1], Prof. Alastair Noyce [4], Dr. Rebecca St George [5]

[1] Wicking Dementia Research and Education Centre, University of Tasmania, Hobart, TAS, Australia, [2] School of Information and Communication Technology, University of Tasmania, Hobart, TAS, Australia, [3] La Trobe University, Melbourne, VIC, Australia, [4] Queen Mary University of London, London, England, United Kingdom, [5] School of Psychological Sciences, University of Tasmania, Hobart, TAS, Australia

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Background

At a population level, accessible and affordable tools for detecting preclinical Alzheimer's disease (AD) would advance neuroprotective drug development and clinical trials. Subtle declines in episodic memory are evident in individuals with preclinical AD, and studies have indicated that motor function analysis may identify this early stage of AD. However, the potential of self-administered hand motor tests to detect this pre-symptomatic period remains unclear. In our study, we evaluated how unsupervised reaction time tests predict cognitive performance in cognitively asymptomatic older adults.

Methods

We recruited 894 community participants (66.2 ± 7.46 years, 71.0% female) from the ISLAND cohort study, a component of the Australian Dementia Network (ADNeT). These individuals reported no cognitive symptoms. They completed a validated online cognitive test (CANTAB) assessing episodic memory, working memory, and executive function. Additionally, they undertook simple and five-choice reaction time tests via the TAS Test website, in an unsupervised setting such as their homes. Reaction time was measured in milliseconds, with test failure defined as a reaction time exceeding 2 seconds. We employed hurdle linear mixed models to explore associations between reaction time, test failure, and cognitive performance, adjusting for the choice of test (single or five-choice).

Results

Higher episodic and working memory errors, and worse executive function scores were associated with test failure (episodic memory log-odds = 0.135, $p < 0.001$, working memory log-odds = 0.130, $p = 0.002$, and executive function log-odds= 0.132, $p < 0.001$). There was no significant association between cognitive test scores and reaction time on successful trials (episodic memory $p = 0.438$, working memory and executive function models would not converge).

Conclusion

In a cognitively asymptomatic older cohort, we observed that test failure in online reaction time tests was associated with cognitive test performance across three domains. These low-cost, brief, and unsupervised tests have the potential to facilitate risk stratification in community cohorts.

An AI-Assisted Analysis of Finger Tapping: Investigating Association of Hand Movement with Cognitive Impairment

Dr Katherine Lawler [1, 2], Associate Professor Michele Callisaya [3, 4], Associate Professor Jane Alty [1, 5, 6], Kaylee Rudd [1]

[1] Wicking Dementia Research and Education, University of Tasmania, [2] School of Allied Health, Human Services and Sport, La Trobe University, [3] Menzies Institute for Medical Research, University of Tasmania, [4] Peninsula Clinical School, Monash University, [5] School of Medicine, University of Tasmania, [6] Royal Hobart Hospital, Hobart, Tasmania

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Background

Motor function can be used as a potential biomarker for early stages of dementia. Evidence shows a strong association of cognition with gait characteristics and emerging evidence also suggests its associations with hand motor function. Availability of remotely accessible smart devices with cameras make test of upper limb movement a viable and affordable screening tool on population-level in dementia investigations. We aimed to assess the association of video recorded self-paced thumb/index finger tapping with cognitive impairment in subjective cognitive impairment (SCI), mild cognitive impairment (MCI), dementia and cognitively healthy control (HC) groups.

Methods

Participants with SCI (n = 60), MCI (n = 112) and dementia (n = 77) were recruited. Consensus diagnosis was given after a comprehensive assessment by an interdisciplinary team. Eighty-six HC participants were also recruited. Participants were video recorded while tapping their index fingers to their thumbs at a comfortable pace for 10s. RapidMotionTrack- a deep-learning based markerless motion tracking system - was used to extract measures of frequency (number of taps per second), speed (maximum speed - MS), amplitude (coefficient of variance (CV) of amplitude), time (mean intertap interval - ITI) and rhythm (intra individual variance - IIV). Variables were analysed using logistic regression, adjusted for age, sex and years of education.

Results

Measures of frequency and speed of self-paced finger tapping were not associated with cognition. Rhythm and CV of amplitude were associated with diagnosis of dementia. Measure of amplitude and ITI were associated with MCI. ITI was associated with a diagnosis of SCI.

Conclusion

Impairment of finger tapping features varies across the dementia continuum. Measures of amplitude, rhythm and time appear to discriminate cognitive impairment. Further understanding of these features can assist with developing an upper limb screening tool to detect dementia in its earlier stages.

The Link Between Depression and Risk of Incident Dementia: An Umbrella Review and Meta-Analysis

Maha Alshahrani [1], Mario Siervo [1], Serena Sabatini [2], Blossom Stephan [1], Jacob Brain [3]

[1] Dementia Centre of Excellence, Curtin enAble Institute, Faculty of Population Health, Curtin University, Perth 6102, Australia., [2] School of Psychology, University of Surrey, Guildford, UK., [3] Institute of Mental Health, Mental Health and Clinical Neurosciences, School of Medicine, University of Nottingham, Nottingham, UK.

Background

Depression is increasingly recognised as a potential risk factor for cognitive impairment and dementia. The 2020 Lancet Commission on Dementia Prevention, Intervention and Care suggested that approximately 4% of dementia cases globally may be attributable to a history of late-life depression. However, uncertainties persist regarding the temporal relationship between depression and dementia. It also remains debated whether depression is a prodromal symptom of dementia or an independent risk factor for cognitive decline. Therefore, the aim of this umbrella review was to synthesize existing evidence on the association between depression and the risk of incident dementia, including its subtypes.

Methods

The study protocol was registered on PROSPERO. PubMed and OVID (Embase and PsycINFO) databases were searched covering all literature to January 24, 2023. Eligible articles included systematic reviews, with or without meta-analysis, focusing specifically on the association between depression and the risk of incident late-life dementia (age ≥65). Random-effects meta-analysis was used to pool the results linking depression to dementia (all-cause and Alzheimer's disease) across the included studies.

Results

From the initial 13,321 articles identified, 12 were included in the review. Most studies report a significant association between depression and increased risk of later-life dementia.

However, findings varied depending on the early onset of depression and longer follow-up time. The pooled results of effect size estimates revealed significant associations for both all-cause (1.855, 95% CI: 1.731-1.978) and AD (1.956, 95% CI: 1.668-2.243).

Conclusion

Depression increased risk of incident dementia by two-fold. However, the relationship is complex, with varying impacts based on factors such as depression severity and timing. Further work is needed to determine the precise nature of the relationship between the two conditions to better inform the development of risk reduction and prevention strategies.

Discrepancies in Self-Administered MIND Diet Surveys Compared to Dietitian-Administered Versions Among the AU-ARROW Study Participants.

Ralph N Martins [1, 2, 3], Malika G Fernando [1], Juliana Chen4, Manohar Garg [1], Samantha L Gardener [2], Carolina B Castro [3, 5], Stephanie Fuller [1]

[1] Macquarie University, [2] Edith Cowan University, [3] Australian Alzheimer's Research Foundation, [4] University of Sydney, [5] Murdoch University

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Background

The Mediterranean-DASH Intervention for Neurodegenerative Delay (MIND) diet is a combination of both Mediterranean and Dietary Approaches to Stop Hypertension (DASH) diets, which has shown promise in improving cognition and delaying neurodegeneration. The MIND diet emphasises plant-based while limiting animal and high saturated fat foods. However, concerns about reporting discrepancies during self-administered dietary surveys persist. This study assesses reporting errors in a self-administered MIND diet survey compared to the same survey administered subsequently by a dietitian in the AUstralian multidomain Approach to Reduce dementia Risk by prOtecting brain health With lifestyle intervention study (AU-ARROW).

Methods

Data from 70 cognitively-unimpaired adults, screened for the AU-ARROW study were analysed (58% female; age 66.7±4.3years). Scores from a self-administered MIND diet survey were compared with subsequent scores obtained from a dietitian-administered MIND diet survey.

Results

The overall MIND diet survey scores did not differ between the self-administered and dietitian-administered versions ($p=0.091$). However, the study participants over-reported consumption of olive oil ($p<0.001$), fried and fast foods ($p=0.001$), sweets and pastries ($p=0.005$), cheese ($p=0.023$) and whole-grains ($p=0.005$) compared to the scores from dietitian-administered survey. The participants under-reported fish ($p=0.011$) and poultry ($p=0.007$) consumption.

Conclusion

While the overall MIND diet scores did not differ significantly for the dietitian- or participant self-administered surveys, the discrepancies within individual food categories may stem from insufficient knowledge of food portion sizes, and miscalculations of seasonal variations in food and differing food habits of participants. Moreover, social desirability and reporting bias could have influenced the over or under-reporting of certain foods deemed healthy or unhealthy. Recognising and rectifying reporting errors is crucial for ensuring accuracy of dietary assessments. Providing nutrition education to participants for the AU-ARROW study participants concerning food portion size estimations delivered by a dietitian may minimize reporting errors.

Initial Outcomes of a Randomized Controlled Trial (RCT) for a Multidomain Lifestyle Intervention Study to Reduce Dementia Risk in Healthy Older Adults: The LEISURE Study

Anthony Villani [1], Ana Boucas [2], Daniel Hermens [2], Bonnie Quigley [2], Alexandra Metse [1], Jacob Levenstein [2], Jim Lagopoulos [2], Thomas Pace [2], Ciara Treacy [2], Sophie Andrews [2], Mia Schaumberg [1]

[1] School of Health, University of the Sunshine Coast, [2] Thompson Institute, University of the Sunshine Coast

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Background

Multidomain lifestyle trials are a promising way to reduce dementia risk in older people, however the effects of the novel combination of diet, exercise, sleep and mindfulness has not been examined. The LEISURE study is an RCT which targets these lifestyle factors in healthy older Australians, testing effects of a 12-week intervention on dementia risk with follow up assessments one-week, 6-months and 24-months post-intervention. The current study reports immediate post-intervention outcomes.

Methods

99 older participants aged 50-84 were randomised into either a) a group-based intervention targeting Mediterranean diet, exercise, sleep, and mindfulness, or b) an education control. All participants completed assessments including fitness, cognition, neuroimaging, molecular biology, self-report diet and sleep and mood measures, with relevant data used to calculate a dementia risk score (CogDrisk). Mixed-model repeated-measures ANOVAs compared groups on the primary outcome (change in dementia risk), and secondary outcomes including change in fitness, diet, sleep, mood, cognition, blood biomarkers and gross neuroanatomical volumes.

Results

81 participants (Mage=65.00, SD=8.13, 65 women, 42 controls) completed baseline and immediate follow-up timepoints. Compared to controls, intervention participants did not significantly reduce their dementia risk (p=.23), however, they significantly improved their single-leg balance (p=.03), diet quality (p=<.001), total sleep quality (p=.006), and triglyceride levels (p=.003). No significant changes were seen in the other domains. Across both groups, change in dementia risk was related to change in ventricular volume (r=.33, p=.005), such that participants with larger risk reductions had less ventricular volume increase.

Discussion/Conclusions

In healthy older people, a multidomain dementia risk reduction RCT targeting diet, exercise, sleep and mindfulness did not significantly reduce dementia risk immediately post-intervention, possibly due to low baseline levels of risk. Nonetheless, significant improvements were seen in key lifestyle and health factors. Next steps include planned analyses of longitudinal outcomes.

Development and Validation of the CogDrisk Short Form for Assessing Risk Factors for Dementia

Dr Ranmalee Eramudugolla DPsych [1, 2], Dr Scherazad Kootar PhD [3], Ms Meiwei BSc Li [1, 2], Prof Kaarin Anstey PhD, FASSA, FAHMS [1, 2], Dr Md Hamidul, Huque, PhD1, [2]

[1] University of New South Wales, [2] Neuroscience Research Australia, [3] Sydney Children's Hospital

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Background

The CogDrisk provides a comprehensive assessment of dementia risk factors. We developed a short form (SF) of the CogDrisk for situations where time and resources are limited. We evaluated its validity by comparing the total score and individual items with the long form (LF).

Methods

The research team developed the draft short form questionnaire by identifying shortened versions of measures and eliminating questions that did not contribute to the algorithm. The SF was revised after a pilot study that identified ambiguities in some questions. The final SF was compared to the LF using an online survey. Participants were recruited via a survey company Qualtrics with the sample stratified by age (40-64, 65+) and sex (male, female). Using a repeated-measures, counterbalanced design, participants completed the SF before the LF, or vice versa. Descriptive statistics, and intraclass correlations (ICC) were used to evaluate the agreement between versions.

Results

647 participants (50.2% female, Mean Age 62.2, age range 40-89) completed the study. 16.8% completed the school certificate or below, and 26% completed post school qualifications. The total CogDrisk score was 10.0 (SD=5.5) and 10.2 (SD = 5.6) for the SF and LF respectively and the ICC was ICC = 0.96. The LF questionnaire took 15.3 minutes, and the SF questionnaire took 9.8 minutes to complete. Fish intake, insomnia and depression had the largest discrepancies with percentage agreements of 79%, 87% and 89% respectively. Other items had >95% agreement between SF and LF except for loneliness (94%), hypertension (94%), high cholesterol (93%), Atrial Fibrillation (91%) and cognitive activity (90%).

Discussion/Conclusions

The very high agreement between the SF and LF shows that CogDrisk-SF is valid for use in research and clinical practice. Where greater depth of information is desired on demographics, alcohol consumption, cognitive engagement, diet, and sleep habits, the LF is recommended.

Implementing Dementia Risk Assessment in Australian Adults: Real World Data From 6241 Respondents on the CogDrisk Website

Hamidul Huque PhD [1, 2], Kaarin Anstey PhD [1, 2], Michael Cartright [2], Scherazad Kootar [3], Marita Long MBBS FRACGP [4], Meiwei Li [1, 2], Ranmalee Eramudugolla DPsych [1, 2]

[1] University of New South Wales, [2] Neuroscience Research Australia, [3] The Children's Hospital at Westmead, [4] Rivergum Village Medical Centre

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Background

Little is known about dementia risk assessment in the real-world. Understanding the characteristics of people who use publicly available dementia risk assessment informs dementia prevention strategies. This study describes the real-world implementation of CogDrisk dementia risk assessment from April to December 2023.

Methods

The CogDrisk website was developed to include an 'opt-in' for respondent data to be included in research. In 2023, CogDrisk was reported in scientific publications and associated media articles. Information on CogDrisk was provided to General Practitioners via Dementia Training Australia workshops, and HealthEd workshops, with more than 10000 GPs participating in a webinar or workshop at which the CogDrisk tool was described. Descriptive analysis of the data was conducted.

Results

The sample comprised 6200 (59% female, <1% non-binary/other) respondents who consented to their data being saved and used for research. 6.0% were aged 18-40, 67.4% were aged 40-64 (midlife) and 26.4% were aged 65-97 (late-life). 39% were born overseas and 61.4% had a university degree. Frequencies of key risk factors in midlife were high cholesterol 23.1%, diabetes 8.1%, head injury 15.0%, hypertension 29.8%, atrial fibrillation (afib) 7.9%, current smoking 4.3% and pesticide exposure 26.5%. In late-life key risk factors were diabetes (8.6%), head injury (16.2%), hypertension (29.6%) afib (7.9%) and pesticide exposure (24.9%). The mean (SD) CogDrisk score was 4.1 (4.3) for midlife, 9.4 (5.9) in late life. Using estimates from published validation studies, 28% of the sample aged 65 and above have high dementia risk (CogDrisk score>12).

Discussion/Conclusions

Free, digital risk assessment for dementia is being implemented in Australia providing evidence-based feedback to inform consumers and GPs on how to reduce risk. These real-world data are restricted to those agreeing to research. Future work is needed to identify the complete usage, CogDrisk is reaching those at high risk of dementia in late life.

Evaluating Diet Quality in AU-ARROW Study Participants Based on MIND Diet Adherence

Carolina B. Castro [3,4], Samantha L. Gardener [4,5,9], Hilal Salim Said Al Shamsi5, Juliana Chen [1,2], Malika Fernando [2], Stephanie J. Fuller [2], Belinda M. Brown [3], Ruey Leng Loo [6], Farzana Jahan [3], Sharon L. Naismith [1], Miia Kivipelto [7], Victor L. Villemagne [10], Stuart Grieve [1], Paul Yates [8], Nicola J. Armstrong [11], Manohar L. Garg [2], Ralph N. Martins [2,3,4,5], and Hamid R. Sohrabi [2,3,4,5].

[1] University of Sydney, Camperdown, NSW, Australia, [2] Macquarie University, NSW, Australia, [3] Centre for Healthy Ageing, Murdoch University, Murdoch, WA, Australia, [4] Alzheimer's Research Australia, Perth, WA, Australia, [5] Edith Cowan University, Perth, WA, Australia, [6] Australian National Phenome Center, and Center for Computational and Systems Medicine, Health Futures Institute, Murdoch University, Perth, WA, Australia., [7] FINGERS Brain Health Institute, Stockholm, Sweden and Karolinska Institute, Stockholm, Sweden, [8] Austin Health, Heidelberg, Victoria, Australia, [9] Lifestyle Approaches Towards Cognitive Health Research Group, Murdoch University, Murdoch, WA, Austral, [10] University of Pittsburgh, Pittsburgh, Pennsylvania, USA, Austin Health, Heidelberg, Victoria, Australia, [11] Curtin University, Bentley, WA, Australia

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Background

Understanding modifiable dementia risk factors is crucial to reducing disease incidence, leading to preventive initiatives including the AUstralian multidomain Approach to Reduce dementia Risk by prOtecting brain health With lifestyle intervention (AU-ARROW). AU-ARROW investigates the impact of a 2-year multidomain lifestyle intervention incorporating physical activity, MIND diet adherence, brain training, health monitoring, and social engagement on cognitive decline. We report the dietary characteristics of eligible and ineligible participants.

Methods

Volunteers completed a MIND diet screener as part of the screening process assessing eligibility, requiring a score of ≤9 out of 14, i.e., poor quality diet. Eligible participants underwent a baseline assessment including the Cancer Council of Victoria food frequency questionnaire (CCVFFQ) and a neuropsychological battery. A MIND diet score was calculated for each individual for each of the two dietary questionnaires (Screener and CCVFFQ).

Results

Whilst ineligible participants were excluded partly due to not having a 'poor diet', their current diet was still inadequate, with several areas to improve according to the MIND diet.

Within eligible participants, the lowest MIND diet component adherence was leafy greens and grains in both diet scores. There was general compliance (>75%) to components of fast and fried foods, red meat and products, butter in the Screener MIND diet, and other vegetables, and butter in the CCVFFQ MIND diet.

There were no gender differences in adherence to Screener MIND diet components. More females adhered to MIND diet components of fast and fried foods ($p=0.016$), and red meat and products ($p=0.011$), therefore consuming fewer unhealthy foods, than males in the CCVFFQ MIND diet.

A higher score on the Screener MIND diet was associated with better performance in episodic memory delayed recall, and verbal fluency ($p<0.05$).

Discussion

These results highlight the necessity for dietary enhancements among both eligible and ineligible participants, focusing on gender-specific improvements.

Barriers and Enablers to Cognitive Assessment in Parkinson's Disease: Perspectives of Clinicians and People Living with PD

Dr Peter Worthy (PhD) [1], Dr Deborah Brooks (PhD) [2], Dr Leander Mitchell (PhD) [3], Dr Kirstine Shrubsole (PhD) [4], Associate Professor Nadeeka Dissanayaka (PhD) [2]

[1] The University of Queensland, School of Electrical Engineering and Computer Science, [2] The University of Queensland Centre for Clinical Research, [3] The University of Queensland, School of Psychology, [4] The University of Queensland, School of Health & Rehabilitation Sciences

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Background

Most people living with Parkinson's disease (PD) will eventually develop cognitive impairment and Parkinson's disease dementia (PDD). However, people with Parkinson's disease are usually seen in Movement Disorders or Neurology Clinics where the focus is on motor symptoms rather than cognition. Whilst people living with PD rate cognitive impairment as a high concern, there are currently few opportunities for cognitive assessment within routine PD clinical care. This qualitative study therefore aims to better understand the barriers and enablers to delivering and receiving a cognitive assessment from the perspectives of clinicians, health professionals and people impacted by PD.

Methods

We are currently conducting qualitative semi-structured interviews with a purposive sample of clinicians and health professionals (e.g., neurologists, medical registrars, psychiatrists, geriatricians, neuropsychologists, movement disorders nurses; n=10) and people living with PD who have lived experience of cognitive assessments (n=10). Interview questions have been informed by the Theoretical Domains Framework (TDF) and the Consolidated Framework for Implementation Research (CFIR). Data collection and analysis is ongoing and utilises both an inductive and deductive framework analytic approach informed by the pre-existing orienting concepts and emergent themes.

Results

We will present the findings from the interviews with clinicians, health professionals and people living with PD.

Discussion

The findings from this study will be used to inform the implementation of a new 'PDCogniCare' intervention (incorporating best practice guidelines with an online platform to improve access to cognitive assessments in PD), that aims to enhance the utility of neuropsychological evaluation for earlier and effective diagnosis of dementia in Parkinson's disease.

Associations Between Brain Structure and Dual Decline in Gait and Cognition

Sadhani Karunarathna [1], Jane Alty [2, 3, 4], Monique Breslin [1], Taya Collyer [5, 6], James McDonald [2, 4], Richard Beare [5, 6, 7], Michele Callisaya [1, 5, 6], Velandai Srikanth [5, 6, 8]

[1] Menzies Institute for Medical Research, University of Tasmania, Hobart, Tasmania, Australia, [2] Wicking Dementia Research and Education Centre, University of Tasmania, Tasmania, Australia, [3] School of Medicine, University of Tasmania, Hobart, Tasmania, Australia, [4] Royal Hobart Hospital, Hobart, Tasmania, Australia, [5] Peninsula Clinical School, Central Clinical School, Monash University, Melbourne, Victoria, Australia , [6] National Centre for Healthy Ageing, Melbourne, Victoria, Australia, [7] Developmental Imaging, Murdoch Children's Research Institute, Royal Children's Hospital, Melbourne, Victoria, Australia, [8] Departments of Medicine and Geriatric Medicine, Frankston Hospital, Peninsula Health, Melbourne, Victoria, Australia

Background

Dual decline in gait and cognition is associated with an increased risk of dementia, with combined gait and memory decline exhibiting the strongest association. However, little is known about the underlying brain correlates. Therefore, we aimed to examine the associations between measures of brain structure and dual decline in gait and cognition.

Methods

Participants over 60 years were randomly selected from the electoral roll into the Tasmanian Study of Cognition and Gait. We used baseline MRI and three serial gait speed and cognitive assessments (memory, processing speed-attention, verbal fluency) performed on average 2.5 years apart. Participants were classified into four groups depending on tertiles of annual decline in gait speed and each cognitive measure (non-decliners, gait-only decliners, cognition-only decliners, and dual-decliners). Multinomial logistic regression was used to examine the associations of baseline brain volumes (grey matter, white matter, and hippocampal) and cerebral small vessel disease (white matter hyperintensities, subcortical infarcts, enlarged perivascular spaces, and microbleeds) with dual gait and cognitive decline for each cognitive domain.

Results

The mean age of participants was 70.9 ± SD 6.7 years (n = 267). Lower baseline grey and white matter volume and higher white matter hyperintensity volume increased the risk of being a dual decliner in gait and both the memory and processing speed-attention groups (all $p < 0.05$). Lower hippocampal volume ($p = 0.047$) was only associated with increased risk of being a dual decliner in the gait and memory group. No significant associations were found between MRI measures and the gait and verbal fluency dual decliners.

Conclusion

Neurodegenerative pathology and white matter hyperintensities are involved in dual decline in gait and both memory and processing speed-attention domains. Smaller hippocampal volume may also contribute to dual decline in gait and memory, but not dual decline in gait and other cognitive domains.

Identification of Objective Cognitive Decline in Preclinical Alzheimer' Disease

Rodrigo Canovas [1], Paul Maruff [2], Christopher JFowler [3], Stephanie Rainey-Smith [4], Colin L. Masters [3], James D Doecke [5]

[1] Australian E-Health Research Centre, CSIRO, Parkville, VIC, Australia, [2] Cogstate Ltd, Clinical, Melbourne, VIC, Australia, [3] The University of Melbourne, The Florey Institute, Melbourne, VIC, Australia, [4] Edith Cowan University, School of Medical and Health Sciences, Centre of Excellence for Alzheimer's Disease Research & Care, Joondalup, WA, Australia, [5] Australian E-Health Research Centre, CSIRO, Herston, QLD, Australia

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Background

Alzheimer's disease (AD) is characterised by the accumulation of amyloid-β (Aβ) and tau. Prior to clinically recognisable symptoms, there is a preclinical period characterized by subtle but relentless cognitive decline. There remains a need to understand how characteristics of the cognitively unimpaired (CU) can influence the nature, magnitude, and variability in this decline. We used a novel approach to identify CU adults who are at risk of cognitive decline (arCD) and then measured changes across different cognitive domains over the following 15-years.

Methods

Neuropsychological test data from 1,479 CU participants from the Australian Imaging, Biomarkers and Lifestyle (AIBL) study of ageing was analysed using an unsupervised multivariate mixture modelling framework accounting for age, gender and APOEe4 allele status to identify participants arCD from those no-risk CU (nrCU). Linear mixed-effects models(LMMs) were used to compare the change over time for six cognitive composite scores (AIBL Pre-clinical Alzheimer's Cognitive Composite(AIBL-PACC), episodic-recall, attention and processing, executive-functioning, language, and recognition) between the risk groups.

Results

Of 1,479 CU participants, 1,055 had data from ≥3 visits and ~44%(N=465) were classified as arCD. LMMs indicated that arCD and nrCU groups showed no significant different rate of change for each cognitive composite ($p>0.05$). However, when the risk groups were reclassified according to APOEe4 allele or PET-Aβ status, the differences between slopes for those arCD/nrCU cognition and PET-Aβ-/+ groups become significantly different for episodic recall (nrCU Aβ- vs Aβ+ $b=-0.050$, arCD Aβ- vs Aβ+ $b=-0.085$, $p=0.024$) and AIBL-PACC (nrCU Aβ- vs Aβ+ $b=-0.054$, arCD Aβ- vs Aβ+ $b=-0.093$, $p=0.009$).

Conclusion

At baseline, nrCU adults who were APOEe4+/PET-Aβ+ declined at the same rate as those arCD that were APOEe4+/PET-Aβ+, although the level of impairment necessary to be classified as arCD in such adults required ~15 years longer for the nrCU group.

Association between Anxiety, Stress, and Cognition in Middle-Aged Adults: Exploratory Factor Analysis Across Multiple Anxiety and Stress Measures

Ivana Chan [1], Paul Maruff [1, 2, 3], Yen Ying Lim [1]

[1] Turner Institute for Brain and Mental Health, School of Psychological Sciences, Monash University, [2] Florey Institute of Neuroscience and Mental Health, [3] Cogstate

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Background

Anxiety and stress have been identified as potential risk factors of cognitive impairment, but research examining this association in midlife has been limited.

Methods

The current study examined the associations between anxiety and stress symptoms, and cognition in middle-aged cognitively unimpaired adults (n = 2,463) enrolled in the Healthy Brain Project. Exploratory factor analysis was conducted on items in the Anxiety Subscale of the Hospital Anxiety and Depression Scale, Anxiety and Stress Subscales of the Depression, Anxiety and Stress Scale, and Perceived Stress Scale. Cognition was measured using the Cogstate Brief Battery (CBB).

Results

The solution that resulted in the best fit to the data comprised five factors which explained for 48% of the variance: Over-Reactivity, Panic, Low-Control, Tension and Intolerance. Panic-related symptoms were significantly associated with both poorer attention and memory. Having clinically meaningful anxiety symptoms, or both anxiety and stress symptoms, was associated with poorer memory.

Conclusions

Anxiety and stress symptoms may be linked to a heightened risk of developing cognitive impairment. Specifically, panic-related symptoms may play a significant role in the relationship between anxiety symptoms and cognition. Limitations include: 1) cross-sectional nature of the study limited ability to ascertain direction of causality; 2) individuals with major psychiatric conditions were excluded from the study, thus limiting external validity of the current findings; 3) HBP sample has a higher proportion of individuals with a family history of dementia compared to the general population, hence the sample presents with an increased risk of developing dementia and generalizability of our findings may be limited.

Enhancing Utility of Neuropsychological Evaluation for Earlier and Effective Diagnosis of Dementia in Parkinson's Disease: PDCogniCare Project

Peter Worthy [1], Peter Nestor [1], Nancy Pachana [1], John O'Sullivan [2], Ji Hyun Yang [1], Helen Tinson [3], Kumar Sivakumaran [1], Alexander Lehn [3], Annette Broome [3], Gerard Byrne [1], Leander Mitchell [1], Dana Pourzinal [1], Syed Afroz Keramat [1], Jacki Liddle [1], Donna Spooner [2], Martie-Louise Verreynne [1], Stuart Robertson [4], Elizabeth Beattie [5], Nadeeka Dissanayaka [1], Kirstine Shrubsole [1], Mark Chatfield [1], Deborah Brooks [1], Tiffany Au [1], Daniel Bailey [1], Sharon Naismith [6], Rodney Marsh [2]

[1] The University of Queensland, [2] Metro North Health, [3] Metro South Health, [4] OPN 365 Pty Ltd, [5] Queensland University of Technology, [6] University of Sydney

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Background

Dementia is observed in 80% of people with advanced Parkinson's disease (PD) and is a primary concern for people living with PD and their families. In addition to reducing quality of life, dementia has far-reaching impacts such as an increased risk of falls and carer burden, as well as earlier institutionalisation. Despite this, dementia in PD is often undiagnosed until the situation becomes unmanageable and options for cognitive support are no longer viable. PDCogniCare aims to develop a technologically advanced solution to enhance the utility of cognitive evaluation for earlier and effective diagnosis of dementia in PD.

Methods

The PDCogniCare intervention utilises a tailored co-designed digital platform to (i) integrate best practice guidelines for cognitive evaluation in PD, (ii) track and identify individuals at high-risk of dementia, and (iii) assist clinical review. A standardised cognitive assessment tool-kit, for both in-person and telehealth delivery, will be incorporated in the guidelines. Psychologists including postgraduate trainees will be trained to deliver cognitive assessments for people with PD according to the guidelines. PDCogniCare will be evaluated within two hospitals using a hybrid II effectiveness-implementation trial design. The in-built process and economic evaluations will inform translation to clinical care and business models for commercialisation. Our multidisciplinary team is partnered with ADNET, software industry, consumers and community organisations, and Queensland Health hospitals to facilitate digital development, testing, and rapid translation to clinical practice.

Results

Results to date of each PDCogniCare workstreams will be presented.

Discussion

This project will deliver a robust evidence-base for a new PDCogniCare intervention to improve diagnosis of dementia in PD. Simultaneously, it will provide (i) a strategic plan for implementation in health services, (ii) a program to upskill the psychological workforce for PD dementia care, and (iii) health economics of PD dementia.

What is the Prevalence of Dementia in Australia?

Kaarin Anstey [1], Leon Flicker [2], Osvaldo Almeida [2], Michael Waller [3], Annette Dobson [3]

[1] University of New South, [2] University of Western Australia, [3] University of Queensland

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Background

Dementia Australia estimates there are more than 421,000 Australians living with all forms of dementia in 2024. The Australian Institute of Health and Welfare (AIHW) estimate for 2022 was 401,300. In contrast, the estimate obtained from the 2021 Australian Census for people with the long-term condition of 'dementia (including Alzheimer's)' was 189,162.

Methods

We compared published age and sex specific data from the 2021 Census, which included all people in the community, hospitals or aged care homes; the NPS MedicineWise General Practice Insights Report 2018-19 which reported data from a national sample of 9% of Australian general practitioners providing information on 13% of all Australian patients; and AIHW estimates based on earlier prevalence estimates from other countries multiplied by Australian population data.

Results

The age and sex standardised estimates for people aged 60 years and older were: 3.1 per 1,000 from the Census, 2.1 per 1,000 from MedicineWise, compared with 6.7 per 1,000 from the AIHW. The corresponding estimates for total numbers of people living with dementia and aged 60 or more for 2021 are: Census 181,574; MedicineWise 123,818; AIHW 395,788.

Discussion

To understand the effectiveness of prevention of dementia in Australia we need to track trends in incidence and prevalence rates. This requires valid and reliable data. Research is needed on the strengths and weaknesses of various data sources, including the AIHW's National Integrated Health Services Information (NIHSI) analysis asset (using linked records from hospitals, medication prescriptions, aged care services and death certificates) and repeated Australian censuses. This could include cross-validation using linked standardised clinical register data. However, a major gap is the lack of linkable GP data.

"It is a Lifestyle...This is it": Drivers of Behaviour Change Towards Dementia Risk Reduction in Rural Older Adults.

Ms. Laura Dodds [1], Assoc. Prof. Celia Harris [1], Asst Prof. Kay Deckers [2], Dr. Joyce Siette [1]

[1] MARCS Institute for Brain, Behaviour and Development, Western Sydney University, NSW, Australia, [2] Alzheimer Center Limburg, School for Mental Health and Neuroscience (MHeNs), Maastricht University, Netherlands

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Background

Despite increasing recognition of the value of multidomain dementia risk reduction initiatives, a gap remains in understanding how individual, social, and contextual factors influence the intent towards and extent of behaviour change for better brain health among older adults.

Methods

Semi-structured telephone interviews (N=40) were conducted with adults aged >55 in rural and/or remote Australia following a 9-month Brain Bootcamp Frontiers intervention which focused on implementing behaviour change for increased brain health. Participants described their experiences with the program including factors that influenced their likelihood of implementing and maintaining the suggested lifestyle changes. Utilising the Theoretical Domains Framework (TDF) as a guide for analysis within the capability, opportunity, and motivation domains, transcripts were independently reviewed by two analysts. Thematic codes were iteratively identified, refined, and organised within the TDF domains.

Results

Mean age of participants was 70.2 (SD=6.6) years, majority were female (69.7%), and lived in a rural area for an average of 30.3 years (SD=17.9) with most obtaining > 12 years of education. In terms of capability, participants identified the significance of personal attributes and self-awareness, continuous acquisition of knowledge, “connecting the dots’, and reaffirming the importance of maintaining overall health in influencing uptake and behavioural change. Opportunities that facilitated behaviour change involved realising the value of connection and community, avoidance of future negatives, and leveraging rural networks, all of which were also identified as vital elements for achieving initiative outcomes and recommended as advantageous for subsequent iterations. Motivation levels were influenced by social comparison and external accountability, adherence to rituals and routines, individual resilience and resourcefulness, as well as the internalisation of values and skills.

Discussion/Conclusion

Findings contribute to a more comprehensive grasp of intervention effectiveness and feasibility in real-world scenarios, guiding the optimisation and tailoring of future dementia risk reduction initiatives to diverse population groups.

Effect of Scanner on Beta Amyloid Quantification in a Head-to-Head Comparison of 18F-NAV4694 Centiloid Measurements between Biograph Vision, Gemini and Biograph mCT

Timothy Cox [1], Jurgen Fripp [2], Natasha Krishnadas [3, 4], Kun Huang [3], Victor Villemagne [3, 5], Rosita Shishegar [6], Shenpeng Li [1], Azadeh Feizpour [3, 4], Ashley Gillman [2], Svetlana Bozinovski [3], Christopher Rowe [3, 4], Rob Williams [7, 8], Graeme O'Keefe [3], Vincent Doré [1, 3], Pierrick Bourgeat [1]

[1] The Australian e-Health Research Centre, Commonwealth Scientific and Industrial Research Organisation, [2] The Australian e-Health Research Centre, Commonwealth Scientific and Industrial Research Organisation, Brisbane, Australia, [3] Austin Health, Melbourne, Australia, [4] The Florey Institute of Neuroscience and Mental Health, Melbourne, Australia, [5] University of Pittsburgh, Pittsburgh, USA, [6] The Australian e-Health Research Centre, Commonwealth Scientific and Industrial Research Organisation, Parkville, Australia, [7] University of Melbourne, Melbourne, Australia, [8] National Imaging Facility, Melbourne, Australia

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Background

New generation PET scanners achieve superior resolution and sensitivity, but the implications on beta amyloid (Aβ) quantitation are not well understood. The Centiloid (CL) scale was introduced to promote consistent Aβ burden quantification, but was not intended to control for hardware or reconstruction changes. In this work, we compare paired Centiloid measurements between the Siemens Biograph Vision and one of Siemens Biograph mCT or Philips Gemini.

Method

28 AIBL participants underwent MPRAGE-MRI and 18F-NAV4694 imaging on two scanners (of Vision, mCT or Gemini) within a year, reconstructed per the ADNI protocols for each scanner. Centiloid was quantified using the standard SPM framework and corrected for expected accumulation between scans. We investigated difference in Centiloid and effectiveness of PET resolution harmonisation, i.e., smoothed to 6mm-equivalent point spread function using estimates from Hoffman scans. Statistical significance was evaluated using empirical, one-sided, non-parametric bootstrap estimates.

Results

Even with harmonisation, Centiloid from Vision was found to be significantly higher than from Gemini ($p=0.000$) and from mCT ($p=0.031$); the difference followed a linear association with slope>1 ($p=0.000$ and $p=0.010$, respectively). The difference at 0CL was negligible, but at 100CL (Gemini) was +10.5% and at 100CL (mCT) was +11.7%. Resolution harmonisation only reduced ~20% of scanner differences at most.

Conclusion

Scanner changes led to different Centiloid quantification, with difference proportional to the participant's Centiloid itself. The standard resolution harmonisation procedure did not correct for scanner difference. For high-amyloid individuals, the measured difference between Vision and Gemini or mCT (> +10%) was greater than the expected annual accumulation rate and so significant for longitudinal studies. Some scanners may exaggerate measured changes in Centiloid, or longitudinal scanner changes may mask or amplify changes. The fact that the effect between scanners was found linear is promising that scanner calibration methods are possible, further investigation is warranted.

Plasma Ergothioneine Levels in Cognitively Normal Individuals with Low or High Neocortical Amyloid

Irwin Cheah Kee-Mun [1], Barry Halliwell [1], Pratishtha Chatterjee [2, 3], Shaun Eslick [3], Sarah Jerome [3], Ralph N Martins [3, 4]

[1] National University of Singapore, Singapore, [2] Florey Institute, University of Melbourne, Melbourne, VIC, Australia, [3] Macquarie University, Sydney, NSW, Australia, [4] Edith Cowan University, Perth, WA, Australia

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Background

Alzheimer's disease (AD) is a debilitating neurodegenerative disorder characterised by the accumulation of amyloid beta (Aβ) plaques and hyperphosphorylated tau protein neurofibrillary tangles in the brain. Ergothioneine (ET) is a potent antioxidant with additional cytoprotective attributes and has shown potential as a therapeutic for neurodegenerative disease. ET can cross the blood-brain barrier and may exert beneficial effects to the brain via antioxidant and other neuroprotective mechanisms. Therefore, we examined associations between plasma ET and its metabolite hercynine with blood-based AD biomarkers.

Methods

Cross-sectional analysis was performed on samples collected from cognitively normal men and woman aged 65-90yrs from the Kerr Anglican Retirement Village Initiative in Ageing Health (KARVIAH) cohort. Data were sub-grouped by neocortical amyloid load (NAL), where a standardized uptake value ratio of >1.35 indicated high NAL. Plasma ET and hercynine were measured by liquid chromatography-mass spectrometry. Plasma Aβ1-40, Aβ1-42, GFAP, and NFL were measured by ultra-sensitive Single Molecule Array assay platform. pTau181 and pTau231 were measured via enzyme-linked immunosorbent assay.

Results

One hundred plasma samples were analysed from a low NAL group (n=65) and high NAL amyloid group (n=35). There were no significant differences in ET or hercynine between the groups. Following partial correlation analysis, a positive correlation was observed between plasma ET ($r = 0.38$, $p = 0.03$) and hercynine ($r = 0.43$, $p = 0.02$) with Aβ42/40 in the high NAL group only, after adjustment for age and gender.

Conclusion

Evidence suggests that ET may protect the brain from oxidative damage and neuroinflammation. This analysis indicated that ET and hercynine were higher in individuals with higher AB42/40 ratio, in the high NAL group only, suggesting that high ET may protect cognition. Clinical trials will be imperative to understand the significance of ET in prevention.

The Impact of Lifetime Music Experience on Hippocampal Subfields, Prefrontal Cortex, and Cognitive Function in Older Adults at Risk for Dementia

Hannes Almgren [1, 2], Andrew C. McKinnon [1, 3], Sharon L. Naismith [1, 3, 4], Nicole Espinosa [1, 3, 4]

[1] Healthy Brain Ageing Program, Brain and Mind Centre, University of Sydney, [2] School of Biomedical Engineering, Faculty of Engineering, University of Sydney, Sydney, Australia, [3] School of Psychology, Faculty of Science, University of Sydney, [4] Charles Perkins Centre, University of Sydney; Camperdown, Sydney NSW, 2050 Australia

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Background

Playing music throughout life can promote neuroplasticity and protect against cognitive decline. Most of the research on this topic has been performed on professional musicians; however, music experience across the lifespan may also have a protective effect on cognition and brain health in non-professional musicians. This study investigates the effects of lifetime music experience on hippocampal subfield volumes, prefrontal cortical thickness, and cognition in older adults at risk of dementia.

Methods

237 individuals aged >50 years (mean age = 68.60, females = 67.5%, MMSE = 28.91) with (n=122) and without (n=115) a history of music experience were recruited from a memory clinic. All participants underwent tests of memory (Logical Memory subtest of the WMS-III and Rey Auditory Verbal Learning Test; RAVLT) and executive functioning (DKEFS Colour Word Interference Test condition 3; CWIT, and Trail Making Test part B; TMT). We also acquired MRI data (n=138) from which hippocampal subfield volumes were derived using the automated segmentation of hippocampal subfields (ASHS) software. FastSurfer software package was used to compute the prefrontal cortical thickness. Multiple Pearson's partial correlational analyses adjusting for age were carried out to examine the association between music experience, hippocampal subfields, prefrontal cortex, and cognition.

Results

There were small yet positive correlations between music experience and executive functioning (TMT, r=0.15; p=0.021 and CWIT, r=0.16; p=0.018) and verbal learning (RAVLT 1-5, r=0.14; p=0.031). However, memory was not significantly correlated with music experience. There were no differences in hippocampal subfield volumes and prefrontal cortical thickness between those who did and did not have musical experience.

Conclusion

Older adults with music experience showed significantly better executive functioning and verbal learning than those without. However, this improvement was not associated with differences in hippocampal subfield volumes or prefrontal cortical thickness. Further research is needed to understand the effect of music experience on other MRI markers.

The Role of Social Networks in Promoting Dementia Risk Reduction Among Hard-to-Reach Populations

Kathleen Doherty [1], Maree Farrow [1], Claire Eccleston [1], Hannah Fair [1]

[1] Wicking Dementia Research and Education Centre, College of Health and Medicine, University of Tasmania

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Background

Interpersonal conversations provide health information to people from hard-to-reach populations, including men and people with lower levels of education. Dementia risk reduction is one area of health where education is needed, especially among these groups who tend not to be reached by formal dementia risk education. We therefore examined the role of informal interpersonal communication in broadening the reach of dementia risk information, using network data collected from "Preventing Dementia' massive open online course participants.

Methods

A subset of course completers in May 2020 provided comprehensive data on their information sharing behaviour ("network mapping participants'; n=37), including the demographic profile of all people with whom they reported sharing dementia risk information. All course and feedback survey completers in May 2023 ("sharing overview participants'; n=874) reported the number of people with whom they shared information, and the demographic groups represented among those recipients. Data were analysed using summary statistics and binomial generalized linear models with type II ANOVA omnibus tests.

Results

Among network mapping participants, 97% reporting sharing information, each providing information to 2-45 network members, reaching 437 people in total. Similarly, 88% of sharing overview participants reported information sharing, each providing information to 1-455 network members, reaching 7790 people in total. Both groups reported sharing information with men and with people with lower education levels. In May 2020, receiving information from an interpersonal source (reported by information sharers) rather than from the formal course was significantly associated with gender ($\chi 2=26.9$, $p<0.001$) and education level ($\chi 2=106.9$, $p<0.001$), with men and people with less education being more represented in the group of interpersonal information recipients.

Discussion

Both participant groups reported high levels of information sharing, with substantial reach among hard-to-reach populations. In combination with qualitative investigations, this suggests that leveraging interpersonal conversations may increase the reach of dementia risk information.

Best Practice Diagnosis of Cognitive Decline in People with Parkinson's Disease

Dr Dana Pourzinal [1], A/Prof Nadeeka N. Dissanayaka [1, 2, 3], Dr Kirstine Shrubsole [4, 5], Prof Nancy A. Pachana [2], Dr Jihyun Yang [1], Dr Daniel X. Bailey [1, 6], Dr. Syed Afroz Keramat [6], A/Prof Jacki Liddle [7, 8], Dr Leander K. Mitchell [2], Helen Tinson [9], Dr Deborah Brooks [1]

[1] UQ Centre for Clinical Research, Faculty of Medicine, The University of Queensland, Herston, Australia,, [2] School of Psychology, The University of Queensland, St Lucia, Australia, [3] Department of Neurology, Royal Brisbane & Women's Hospital, Herston, Australia, [4] Queensland Aphasia Research Centre, The University of Queensland, Herston, Australia, [5] Speech Pathology Department, Princess Alexandra Hospital, South Brisbane, Australia, [6] Centre for Health Services Research, The University of Queensland, Herston, Australia, [7] School of Health and Rehabilitation Sciences, The University of Queensland, St Lucia, Australia, [8] Occupational Therapy Department, Princess Alexandra Hospital, South Brisbane, Australia, [9] Psychology Department, Princess Alexandra Hospital, South Brisbane, Australia

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Background

Cognitive deficits and cognitive decline are often under-investigated in people with Parkinsons disease (PD) due to the myriad of other symptoms this condition involves. While guidelines for the diagnosis of mild cognitive impairment (PD-MCI) and dementia (PDD) have been developed, there is little information to guide clinicians in the processes around evaluation (e.g. pre-, post-, and re-test procedures). This abstract presents the results from a systematic reviews which will form the basis of Best Practice Guidelines for Cognitive Evaluation in Parkinsons Disease for the PD-Cognicare study.

Methods

The search included five academic databases and four international grey literature databases with search terms of "Parkinsons disease', "cognition' and "guidelines/recommendations'. Articles were limited to full text, in English, published between 2003-2023, and requiring at least one relevant recommendation for inclusion.

Results

In total, 28 articles yielded recommendations for neuropsychological evaluations (n=17), for diagnosis (n=11), for treatment (n=18) and for care (n=9) for people with PD. Guidelines predominantly refer to the Litvan criteria for PD-MCI (2012) and Dubois criteria for PDD (2007) however little guidance is given on how often cognition should be retested especially for those with no objective deficits. Guidelines did not specify which neuropsychological tests showed the best evidence for PD assessment. Despite the complex clinical presentation of people with PD in the later stages when dementia is most prevalent, the least recommendations were found for the domain of care.

Discussion

While guidelines cover a range of areas, there are some gaps regarding how the guidelines could best be operationalised for people with PD. Currently published guidelines offer few recommendations for neuropsychological tests, care considerations and referral pathways specific to cognitive decline in PD. The PD-Cognicare Guidelines aim to fill these knowledge gaps is planned to be completed in late 2024 to early 2025.

A Mixed Methods Examination of the Impact of Dementia on Occupation Violence in Hospital

Dr Gillian Stockwell-Smith [1], Alan Scanlon [2], Dr Fred A Graham [1, 2], Prof Ruth Hubbard [1], Dr Daniel X. Bailey [1], Michelle Lang [1], Dr Syeda F Zahir [1], Prof Len Gray [1]

[1] Centre for Health Services Research, The University of Queensland, Herston, Australia, [2] Princess Alexandra Hospital

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Background

Within hospitals, older people are more likely to experience adverse outcomes, this is especially true for people with cognitive impairment. People with cognitive impairment, dementia and delirium may experience significantly changed behaviours such as agitation, depression, anxiety, aggression and in some cases delusions and hallucinations. Some incidents may escalate into patient-patient violence and patient-staff violence, together termed occupational violence (OV). Despite the relative infrequent occurrence of such incidents, they can result in injuries, significant distress for patients, families, and staff and place a strain on hospital resources. Little is known about the factors that precipitate these incidents; hence it is not possible to predict which patients, actions or situations present the highest risks of such incidents occurring.

Methods

This mixed methods study includes quantitative analyses on demographic and medical data and information related to OV incidents and a backwards logistic regression to identify which variables are risk factors for OV. Qualitative analyses will be carried out on the incident reports of OV completed by hospital staff. All data are drawn from five metropolitan hospitals over a five-year period (2018-2022) in Brisbane, Australia. Data were extracted by hospital staff and deidentified prior to analyses.

Results

The data includes over 20,000 cases examining all OV incidents across the hospitals with a specific focus on people over the age of 65 and those with cognitive impairment. Variables easily extractable from medical records are risk factors for OV occurring. Several themes were identified from incident reports which further highlight situations which may increase the risk of OV occurring.

Discussion

In total numbers, OV incidents involving people with cognitive impairment are relatively low, but occur in a higher proportion of patients. Identifying high risk factors and situations allows the development of interventions and changes in practice to reduce the incidence of OV occurring.

Drawing on Lived Experience to Design a Tailored, Multimodal Sleep Intervention for Dyads of People Living with Dementia and Their Caregivers

Prerna Varma [1], Marina G. Cavuoto [1, 2], Michael Woodward [3], Rosemary Gibson [4], Bei Bei [1], Tom Valenta [5], Ann Piestch [5], Susan M. McCurry [6], Aimee D. Brown [1], Sumedha Verma [1], Melinda L. Jackson [1], Jasmine Dowling [1]

[1] Turner Institute for Brain and Mental Health, School of Psychological Science, Monash University, Clayton, Victoria, Australia, [2] National Ageing Research Institute, Parkville, Australia, [3] Aged and Continuing Care Services, Austin Health, Heidelberg, Victoria, Australia, [4] Health and Ageing Research Team, School of Psychology, Massey University, Palmerston North, New Zealand, [5] Independent Researcher, Australia, [6] School of Nursing, University of Washington, Washington, US

Introduction

Sleep disturbances are prevalent and challenging for people living with dementia and their primary caregivers and can have a significant impact on their health and well-being. Few sleep interventions exist that are designed to support the needs of both caregivers and people living with dementia simultaneously, nor are they based on lived experience. This study aimed to understand the sleep challenges faced by caregivers, and to codesign a multimodal intervention targeting sleep disturbances and supporting wellbeing within dyads of people living with dementia and caregivers.

Methods

Two focus groups and five semi-structured interviews were conducted (n=4 people with dementia, n=6 caregivers). Community advisors were actively involved during the design, development, and facilitation phases of the study. Reflexive thematic analysis taking an interpretivist approach was employed to analyse lived experiences of sleep disturbance and receive feedback to design the sleep intervention.

Results

People living with dementia described disruptions in their sleep and circadian rhythms, leading to consequential effects of fatigue and mental fog throughout the day. Caregivers encountered sleep difficulties including insomnia, hypervigilance, and daytime impairment. Both people living with dementia and caregivers responded positively to the proposed sleep intervention and the virtual group delivery format. The importance of a flexible and multimodal 'toolkit' approach to the intervention was highly recommended, emphasising adaption across different stages of dementia, with a particular focus on developing the intervention toward caregivers.

Discussion/Conclusion

Findings from this study demonstrate that multimodal sleep and well-being interventions may meaningfully improve sleep and daytime functioning for people living with dementia and their caregivers. Adopting a toolkit approach, using a group-based format, and disseminating the strategies to caregivers can increase the applicability of sleep interventions across various stages of types of dementia. Additionally, this approach may help to support the enduring sleep health concerns faced by caregivers.

Recruiting People with Mild Cognitive Impairment into a Falls Prevention Trial

Rachael Moorin [1], Anne-Marie Hill [2], Kathryn Ellis [3], Sarah Bernard [4], Nicola Lautenschlager [3], Melanie Clark [5], Keith Hill [6], Kirk Erickson [7], Angela Jacques [8], Carolyn Orr [9], Elissa Burton [10], Luke Bongiascia [11], Joanne McVeigh [12], Joel Tate [13], Meggen Lowry [14]

[1] Curtin School of Population Health, Curtin University, [2] School of Allied Health, Western Australian Centre for Health and Ageing, The University of Western Australia, [3]The Academic Unit for Psychiatry of Old Age, Department of Psychiatry, University of Melbourne, [4] Geriatric Acute and Rehabilitation Medicine, Sir Charles Gairdner Osborne Park Healthcare Group, [5] Neurosciences Unit, North Metropolitan Health Service Mental Health, [6] Rehabilitation, Ageing and Independent Living (RAIL) Research Centre, School of Primary and Allied Health Care, Monash University, [7] AdventHealth Research Institute, Orlando, Florida, [8] Institute for Health Research, University of Notre Dame Australia, [9] Cognitive Clinic, Royal Perth Hospital, [10] School of Allied Health & enAble Institute, Curtin University, [11] Physiotherapy Department, Adult Community and Allied Health Directorate, Rockingham Peel Group, [12] Curtin School of Allied Health, Curtin University, [13] Department of Rehabilitation and Aged Care, Armadale Health Service, [14] Next Step Health

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Background

People living with mild cognitive impairment (MCI) fall more frequently than older adults without cognitive impairment. However, it is unclear if balance training reduces falls in people with MCI. Balance on the Brain is a randomised controlled trial aimed at reducing falls and improving balance for people with MCI. Recruitment began in 2020 concurrently with the commencement of the COVID-19 pandemic. This presentation will describe the avenues used to recruit participants into Balance on the Brain and the lessons learnt.

Methods

Inclusion criteria included living in Perth or Rockingham areas, 50 years and older, diagnosis of MCI, consistent with the Petersen criteria (including self-report memory issues, Clinical Dementia Rating Scale Score of 0.5, and Standardised Mini Mental State Examination score of 24 or above), not meeting physical activity guidelines (<150 minutes of physical activity weekly) and not participating in regular balance training.

Results

To date, 576 participants have completed pre-screening, 258 full-screening and 128 participants have been recruited. Recruitment has occurred from six memory clinics around Perth (including the neuroscience unit), Facebook adverts, radio adverts on CurtinFM radio and flyers displayed in 20+ GP clinics, Step Up for Dementia research database, advertisements in multiple newspapers, balance on the brain website and word of mouth. Forty percent of participants recruited had fallen in the previous year. Recruitment stopped for 8 weeks due to Covid-19 lockdowns and 7 weeks for staff isolation requirements.

Discussion/Conclusion

Recruiting people with MCI is difficult. It is essential to have numerous opportunities when recruiting specific target audiences, such as this. Building relationships with health care professionals working with people with MCI is essential. Recruiting participants during a pandemic has created additional issues, such as time lost due to lockdowns and staff isolating with Covid-19, as well as older people being hesitant to participate.

Evaluating a Novel Training Course about Dementia-Friendly Eyecare for Optometrists

Bao Nguyen [1, 2], Marianne Piano [1, 3], Lynette Joubert [4], Ambhruni Padhye [3], Allison McKendrick [5, 6], Kwang Cham [1]

[1] Department of Optometry and Vision Sciences, University of Melbourne, [2] Department of Biomedical Engineering, University of Melbourne, [3] National Vision Research Institute, Australian College of Optometry, [4] Department of Social Work, University of Melbourne, [5] Optometry, School of Allied Health, University of Western Australia, [6] Lions Eye Institute, University of Western Australia

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Introduction/Background

Global reports highlight the importance of access to eyecare for older adults living with dementia in communities, to help maintain their independence. However, people living with dementia experience barriers to accessing routine eyecare and are less likely to see an optometrist than people without dementia. Optometrists experience challenges assessing people living with dementia, which could be addressed with evidence-based education/training to break down these barriers.

Research Aims:

1) Explore the impact of completing an evidence-based education intervention upon knowledge, attitudes and practice of optometrists regarding older adults living with dementia in the community.

2) Identify barriers and facilitators impacting translation of knowledge gained from the course into changes in practice.

Methods

This mixed method evaluation study will utilise knowledge, attitudes and practice surveys and qualitative semi-structured interviews with learners completing the course. The Dementia Knowledge Assessment Scale (DKAS), Dementia Attitudes Scale (DAS), Confidence in Dementia Scale (CODES) will be completed pre-course, post-course, and one year post-course. A practice pattern survey completed pre- and one year post-course will explore practice changes. Interviews post-course and one year post-course will explore motivations for/experiences of completing the course, and practicalities in applying learning within place of practice.

Results/Evaluation

58 optometrists have enrolled to date. We will present learner demographics and preliminary short-term outcomes data post-course, including mean change in self-reported knowledge and attitudes about dementia (DKAS and DAS scores), confidence in working with people with dementia (CODES score), and emerging themes around barriers and facilitators to translation of learning to practice.

Discussion

The course attracted considerable interest, demonstrating a role in addressing unmet education/training needs identified from our research. Increasing optometrist capacity to provide dementia-friendly eyecare through an accessible, online course makes it easier for people living with dementia and family carers to find an optometrist who knows dementia, supporting access to eyecare.

Sustainable Personalised Interventions for Cognition, Care, and Engagement (SPICE): Update of a Twelve-Week Multicomponent Intervention for People with Dementia and Care Partners

Diane Gibson PhD [1], Sam Kosari PhD [1], Nathan D'Cunha PhD [1], Michelle Bennett [1, 2], Kathleen Rutherford [2], Julie Griffin [2], Sanduni De Silva [2], Stephen Isbel PhD [1], Kasia Bail PhD [1], Louise Barrett PhD [1, 2], Helen Holloway PhD [1], Ian Walker [2], Sarah Whitting [2], Rachael Mitterfellner [1, 2], Lara Wiseman [1]

[1] Centre for Ageing Research and Translation, University of Canberra, Bruce, ACT 2617, [2] Canberra Health Services, Bruce, ACT 2617

Background

The SPICE program addresses an identified gap in access to integrated post-diagnostic rehabilitation for people with dementia and care partners in Canberra, Australia. The multicomponent intervention aims to maximise quality of life (QoL) by increasing engagement in everyday activities and promoting physical and mental well-being.

Methods

The SPICE program is a waiting-list study design delivered by a multidisciplinary allied health team over twelve weeks consisting of: 1) cognitive stimulation therapy; 2) carer support and capacity building; 3) physical activity; 4) Care of People with dementia in their Environments (COPE) program; and 5) dietary advice. Each group of up to seven dyads engage in group activities twice weekly and receive the COPE program and dietary advice as a dyad. Outcome measures include QoL, neuropsychiatric symptoms, cognitive and physical function, and carer well-being. Early results contributed to expansion of the study. Here, we report on the first six completed groups.

Results

Thirty-eight people with dementia and 38 care partners attended group activities with 92% and 91% attendance, respectively. Pre- to post-program improvements were observed in proxy-reported QoL ($p=0.02$), reduced neuropsychiatric symptoms ($p<0.001$) and carer distress related to these symptoms ($p=0.04$), and reduced caregiving challenges ($p<0.001$). Both people with dementia and care partners improved in the Alternating Step Test (AST) (both; $p<0.001$), as did care partners in Timed Up and Go (TUG) ($p=0.04$). Twenty-six people with dementia and 26 care partners completed follow-up, improving from baseline to 24 weeks in self-reported QoL of the person with dementia ($p=0.03$), and reduced neuropsychiatric symptoms ($p<0.01$) and carer distress related to these symptoms ($p=0.02$). Care partners maintained improvements in the AST ($p<0.01$) and TUG ($p=0.05$).

Conclusions

Results to date suggest the SPICE program benefits people with dementia and their care partners. Further results are required to support the continuation and expansion of the program.

Learning through Adapting: Reflections on Co-designing Solutions with People Living with Dementia

Dr. Natasha Layton [1, 2], A/Prof Michele L Callisaya [1, 3, 4], Ms. Catherine Devanny [1, 3]

[1] National Centre for Healthy Ageing, Melbourne, Australia, [2] Rehabilitation Ageing and Independent Living (RAIL) Research Centre, Monash University, Melbourne, Australia, [3] Peninsula Clinical School, Monash University, Melbourne, Australia, [4] Menzies Institute for Medical Research, Hobart, Tasmania, Australia

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Background

People living with dementia have the right to be actively involved in designing the services and projects that affect them. Co-design approaches are increasingly used to support this involvement, but knowledge gaps remain regarding key principles and practices of co-design, particularly with people living with dementia.

This work aims to share practical learnings and critical reflections on working in a co-design project focused on improving rehabilitation access for people living with dementia.

Methods

Co-designers, including people living with dementia, care partners, and professionals, engaged in experience-based co-design over three virtual workshops. Throughout the co-design process, records were kept of activities, interactions and learnings, including practical adjustments made, and insights from conversations with co-designers in and outside of workshops. A critical self-reflection process was used to reflect on these records.

Results

Self-reflection learnings were grouped to form three key themes. Theme 1, 'Adapting and Adjusting,' highlights the ongoing importance of adapting to meet the person with dementia's needs, and recognises the adaptability of people living with dementia, who actively engaged when offered reasonable adjustments. Theme 2, 'Values,' emphasises that co-design is a values- and rights- based approach, and that we need to deeply value people with dementia's time, relationships, and expertise. Theme 3, 'Challenging Assumptions,' underscores the central role of reflexivity within co-design, as a way to interrogate assumptions about knowledge, expertise and power.

Discussion

Co-design approaches require ongoing reflexivity, to learn from people's living expertise and to learn more about the process of co-design itself. Practical adjustments, a values-based approach, and a learning mindset can assist in improving co-design approaches when working with people with dementia.

Improving Genome-Wide Association-By-Proxy Studies of Alzheimer's Disease with Machine Learning Derived Phenotypes

Benjamin Goudey [1, 2], Martin Saint-Jalmes [1, 2], Colin L. Masters [1], Simon M. Laws [3, 4, 5], Shu Liu [1, 2]

[1] Florey Institute, The University of Melbourne, Parkville, Victoria, Australia, [2] ARC Training Centre in Cognitive Computing for Medical Technologies, University of Melbourne, Carlton, Victoria, Australia, [3] Centre for Precision Health, Edith Cowan University, Joondalup, Western Australia, Australia, 4 Collaborative Genomics and Translation Group, Edith Cowan University, Joondalup, Western Australia, Australia, [4] School of Medical and Health Sciences, Edith Cowan University, Joondalup, Western Australia, Australia, [5] Curtin Medical School, Curtin University, Bentley, Western Australia, Australia

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Background

For genomic studies of middle-aged individuals, the prevalence of Alzheimer's disease (AD) is extremely low, making it difficult to conduct genomic analysis. One approach to bypass this issue, called Genome-wide association by proxy (GWAX), uses family history of disease as a proxy for disease status. In this work, we view the development of such proxy AD labels as equivalent to accurately predicting the lifetime risk of AD. As such, we develop and evaluate ML-derived proxy phenotypes of AD for downstream GWAX based on survival models of conversion to AD.

Methods

Using cognitively normal (CN) and mild cognitive impaired (MCI) individuals with at least 2 timepoints in AIBL (n=426), ADNI (n=283) and UK Biobank (n=56,105), we derived two proxy phenotypes of AD: i) an ML-derived boosting model with age, sex, years of education and AD family history, i.e. number of parents with a history of AD and ii) family history alone. Model performance was measured using concordance index (C-index) in 10-fold cross-validation. The two models were applied to the UK Biobank (n=408,165) and a GWAX was conducted on the predicted labels. From this GWAX, PRS was derived and evaluated using area under the ROC curve (AUC).

Results

ML-derived phenotypes were more predictive of conversion to AD than family history alone (median C-index: 0.7 vs 0.5, Mann Whitney p-value <0.001). GWAX of UKB from these proxy phenotypes shows the multivariate model detects a higher number of significant regions compared to family history alone. PRS from these ML-derived phenotypes improve the separation of true AD case/control labels when externally validated on ADNI.

Conclusion

Preliminary analysis of ML-derived proxy phenotypes of AD shows it may be a promising approach to improve AD genomic studies in middle-aged cohorts. Further analysis of potential biases are needed to fully characterise this method.

Motoric Cognitive Risk Syndrome and Car Collisions in Older Drivers in Japan

Takehiko Doi [1], Chiharu Nishijima [1], Hiroyuki Shimada [1], Kenji Harada [1], Ryo Yamaguchi [1], Kazuya Fujii [1], Yuka Misu [1], Daisuke Kakita [1], Masanori Morikawa [1], Satoshi Kurita [1], von Fingerhut Georg [1], Osamu Katayama [1]

[1] National Center for Geriatrics and Gerontology

Background

To prevent car collisions in older drivers, the increased risk of collisions should be considered early. Motoric cognitive risk syndrome (MCR), characterized by the presence of subjective cognitive concerns and slow gait, can be assessed conveniently and is useful for assessing the risk of dementia. This study aimed to examine the association between MCR assessment findings and car collisions among older drivers in Japan.

Methods

This cross-sectional study used data from a community-based cohort study in Japan from 2015 to 2018. Participants were community-dwelling older adults aged 65 years or older. Participants were asked about their experience of car collisions during the last 2 years through face-to-face interviews. MCR was defined as having subjective memory concerns (SMC) and slow gait. Participants were classified into 4 groups: no SMC or slow gait, only SMC, only slow gait, and MCR. The odds of experiencing a collision were assessed using a logistic regression model.

Results

Among a total of 12 475 participants, the mean (SD) age was 72.6 (5.2) years, and 7093 (56.9%) were male. The group with only SMC and the group with MCR showed a higher proportion of both car collisions than the other groups (adjusted standardized residuals > 1.96; P < .001). Logistic regression analysis showed the only SMC and MCR groups had increased odds of car collisions (only SMC group: odds ratio [OR], 1.48; 95% CI, 1.27-1.72; MCR group: OR, 1.73; 95% CI, 1.39-2.16) after adjusting for confounding factors. After stratifying MCR assessments by objective cognitive impairment, significant associations were still observed.

Discussion

In this cross-sectional study of community-dwelling older drivers in Japan, SMC and MCR were associated with car collisions independent from objective cognitive impairment. Future studies should examine the mechanism of these associations in more detail.

Investigating Genetic Overlap Between Alzheimer's Disease, Lipids and Coronary Artery Disease

Tenielle Porter (PhD, BSc.(Hons.)) [1], Emmanuel O. Adewuyi (PhD, MPH (Applied Epid and Biostat), BPharm) [1], Simon M. Laws (PhD, BSc.(Med Sci) (Hons.)) [2], Artika Kirby (MBI, BSc.(Med Sci)) [3]

[1] Doctor, [2] Professor, [3] Student

Background

Alzheimer's disease (AD) is a prevalent neurodegenerative disorder characterised by cognitive impairment and memory loss. While lipid disorders are established risk factors for coronary artery disease (CAD), there is consistent evidence linking abnormal lipid metabolism to the risk of AD. Notably, observational studies have associated CAD with an increased risk of AD, suggesting a potential comorbid relationship. However, AD's underlying biological mechanisms and association with lipids and CAD traits remain poorly understood.

Methods

We leveraged large scale genome-wide association studies summary statistics to comprehensively assess cross-trait genetic overlap of AD with 13 representative lipids (from eight major lipid classes) and seven CAD traits. We utilised 'linkage disequilibrium score regression' analysis to assess genome-wide (global) genetic correlation and LAVA (local analysis of [co]Variant association) for insights into the local genetic correlation of AD with lipids and CAD traits. Lastly, we used gene-based analysis to investigate the gene-level overlap of AD with lipids and CAD traits.

Results

We found a significant positive global genetic correlation between AD and one lipid (triglycerides). In contrast, AD demonstrated a significant positive global genetic correlation with all seven CAD traits - angina pectoris, cardiac dysrhythmias, coronary arteriosclerosis, ischemic heart disease, myocardial infarction, non-specific chest pain, and coronary artery disease. The gene-level analysis largely reinforced these findings and highlighted the genetic overlap between AD and three additional lipids, including high-density lipoproteins, low-density lipoproteins, and total cholesterol. Local genetic correlation analysis identified several loci (local pleiotropic hotspots) contributing disproportionately to the positive relationship of AD with lipids and CAD traits across chromosomes 6, 8, 17, and 19.

Discussion

Current findings provide evidence of genetic overlap between AD, specific lipids, and CAD traits, implicating shared genetic susceptibility. The identified pleiotropic hotspots serve as valuable targets for further investigation in AD and, potentially, its comorbidity with CAD traits.

Crossing Paths? Assessing Genetic Overlap of Alzheimer's Disease with Type 2 Diabetes

Simon Laws [1], Giuseppe Verdile [2], Tenielle Porter [1], Emmanuel Adewuyi [1]

[1] Edith Cowan University, [2] Curtin University

Background

Whilst numerous studies have explored the relationship between Alzheimer's disease (AD) and diabetes, there remains conflicting evidence and possible mechanisms underlying their association are unclear. Some studies suggest an increased likelihood of developing AD, especially in individuals with type 2 diabetes (T2D). In contrast, other evidence indicates no significant correlation between the two disorders. Understanding the genetic relationship between these potentially comorbid conditions could offer insights into AD's poorly understood biological mechanisms. Here, we utilised two complementary methods to evaluate the genetic relationship between AD and T2D.

Methods

We conducted an extensive analysis of large-scale genome-wide association summary data using the 'linkage disequilibrium score regression' analysis (for genome-wide correlation estimates) and 'single nucleotide polymorphism (SNP) effect concordance analysis' (SECA, for genetic overlap assessment). We performed several analyses testing our findings' potential (partial) replications, using several GWAS data for AD (with and without the APOE region) and T2D.

Results

We found a highly significant positive genome-wide genetic correlation between AD (combining clinically diagnosed with proxy cases) and all T2D GWAS assessed, with or without the APOE region. We replicated the positive and significant results using clinically diagnosed AD cases. Utilising SECA, we found robust SNP overlap and strong effect concordance with low permutation p-value and significant Fisher's exact test—underscoring the strong association between SNP sets (and association in effect direction) for both disorders. Our SECA results were consistently significant whether AD or T2D was dataset 1 or dataset 2. We replicated SECA's results across clinically diagnosed AD and other T2D GWAS data.

Conclusion

Our analyses reveal a replicable positive genetic correlation and SNP-level overlap between AD and T2D, implicating shared genetics and biological pathways in their susceptibility. These findings provide an impetus for further characterising putative causal genes shared by the disorders towards identifying novel therapeutic targets for AD.

Understanding the Relevance of Genetic Variants on DNA Methylation Changes in Alzheimer's Disease Pathogenesis

Dr Michael Vacher [1, 2], Prof. Simon Laws [2], Dr James Doecke [3], Ishika Mahajan [1]

[1] The Australian eHealth Research Centre, CSIRO Health and Biosecurity, Kensington 6151, Western, Australia, Australia, [2] Centre for Precision Health, School of Medical and Health Sciences, Edith Cowan University, Joondalup, 6027, Western Australia, Australia. , [3] The Australian eHealth Research Centre, CSIRO Health and Biosecurity, Herston 4029, Queensland, Australia

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Background

The complex relationship between single-nucleotide polymorphisms (SNPs) and epigenetic (CpG) regulation, remains unexplored and poorly understood. In this study, we investigated the potential effect of genetic variants on shifts in methylation levels of surrounding genes and its relevance to Alzheimer's disease (AD).

Methods

The study cohort comprises 688 participants (434 males and 253 females; mean age 85.17 ± 5.53), from the Religious Orders Study and Memory and Aging Project (ROSMAP). Participants were dichotomised based on CERAD score (>2), reflecting the neuropathologic diagnosis of AD (cases = 434, control = 253). To elucidate the regulatory relationships between SNP (N=121409) and CpG (N=363305), specific to each subgroup, we used linear regression models, integrating age and sex as covariates. Analyses were restricted to cis-effect, limiting SNP-CpG combination within 50kb and the results were adjusted for multiple comparisons.

Results

We identified 1209 significant SNP-CpG interactions, located in 226 unique genes. Most of the interactions exhibited a strong additive effect, where the number of minor alleles was directly proportional to the magnitude of change in methylation levels. None of the identified interactions were specific to the case or control subgroup.

Conclusions

The findings underscore the profound influence of some genetic variants on epigenetic alterations. While the study did not reveal any significant SNP-CpG interactions specific to AD, this could be due to its limited number of samples. Future research, with a larger cohort, could offer deeper insights into the interplay between genetics and epigenetics in the context of AD.

Developing 3D iPSC Patient Derived Neurovascular Unit (NVU) Models of Motor Neuron Disease (MND)

Anthony White [1], Lotta Oikari [1], Juliana Chaves [1], Ian Peall [1], Stephani Viljoen [1]

[1] QIMRB

Background

Motor Neuron Disease (MND) is a progressive neurodegenerative condition leading to loss of motor function. Existing treatments focus on alleviating symptoms rather than providing a cure. The neurovascular unit, comprising the central nervous system (CNS) and blood-brain-barrier (BBB), is vital to maintaining brain integrity. The BBB is a selective barrier formed by brain endothelial cells (BECs), whose Tight Junctions (TJs) restrict passage across the barrier. This barrier is a major impediment in the successful delivery of therapeutics.

Methods

MND patient derived induced pluripotent stem cells (iPSCs) underwent neural progenitor cell (NPC) differentiation, after which cells were seeded into a hydrogel mix. Cells were maintained in NPC growth media for 3 days after which cells were spontaneously differentiated to mixed cultures of neurons and astrocytes. Patient-derived iPSCs underwent induced BEC (iBEC) differentiation, these cells were then seeded onto the spontaneously differentiated NPC cultures to form the NVU.

Results

2D spontaneous differentiation data indicated the formation of a heterogenous neural culture from MND derived cells, wherein neural networks emerged and were encompassed by astrocytes. Initial findings from 3D data suggest robust neural network formation within the 3D microenvironment. In the context of 2D iPSC-derived iBEC differentiation, the data revealed the development of an endothelial layer from patient-derived cells characterized by well-defined TJs Preliminary 3D results demonstrated the establishment of an iBEC layer overlaying the 3D neural network, with discernible TJs, suggesting the formation of an NVU.

Discussion

The development of accurate 3D human based cell models that recreate the complexity of the NVU is key in the development and screening of viable therapeutics for neurodegenerative disorders. Here we provide a viable, reproducible model for the study of the interaction between the CNS and the BBB, which has the potential to be applied to other models of neurodegenerative disorders such as Dementia.

Exploring AD-Related Protein Kinase Genes in Healthy Human Mesenchymal Stem Cells

Rachel Okolicsanyi [1, 2], Sofia Petersen [1], Larisa Haupt [1, 2, 3], Lyn Griffiths [4]

[1] Stem Cell and Neurogenesis Group, Genomics Research Centre, Centre for Genomics and Personalised Health, School of Biomedical Sciences, Queensland University of Technology (QUT), [2] Max Planck Queensland Centre for the Materials Sciences of Extracellular Matrices, [3]ARC Training Centre for Cell and Tissue Engineering Technologies, Queensland University of Technology (QUT), Australia, [4]Genomics Research Centre, Centre for Genomics and Personalised Health, School of Biomedical Sciences, Queensland University of Technology (QUT), 60 Musk Ave., Kelvin Grove, Queensland 4059, Australia

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Background

Alzheimer's disease (AD) affects over 38 million individuals worldwide, presenting a significant health challenge, with the apolipoprotein E (APOE) gene a significant genetic risk factor. Current treatments lack targeted approaches to limit AD neural cell death. Human mesenchymal stem cells (hMSCs) hold promise for AD stem cell therapy due to their ease of isolation and expansion potential, neural lineage capacity and extracellular matrix (ECM) component production. Heparan sulfate proteoglycans (HSPGs), including the syndecans (SDCs1-4), are ubiquitous within ECM, interacting with proteins and ligands. The Protein kinase C (PRKC) family of genes influence cellular proliferation and dysregulation with PRKC genes linked to AD pathogenesis.

Methods

We examined the gene expression of 84 AD-related genes using the Qiagen RT2 Profiler PCR Array. HSPG ligand heparin treated (+HEP; 10µg/mL) were compared to basal cultures of previously genotyped high-risk and no-risk APOE hMSC cell populations (n=2). RT2 Profiling was conducted according to the manufacturer's instructions.

Results

Our study revealed distinctive gene expression profiles in varying APOE hMSCs. PRKCB and PRKCZ expression was significantly upregulated in +HEP high-risk APOE hMSCs compared to basal cells, while PRKCD, PRKCE, PRKCI and PRKCQ expression was significantly downregulated. Interestingly, we also detected SDC1, SDC3 and SDC4 downregulation and SDC3 upregulation in +HEP hMSCs. Contrasting expression of PRKCs (PRKCD and PRKCI) in +HEP high-risk and no-risk populations was observed.

Discussion

SDC4 activates PRKC signalling. In this study, SDC4 downregulation correlated with PRKCD, PRKCE, PRKCI and PRKCQ expression changes in high-risk hMSCs. Additionally, SDC2 interacts with PRKCB protein products, with both genes upregulated in +HEP cultures. Our data suggest that these SDCs interact with PRKCs, known drivers in AD pathology. Further investigation into these connections in the context of APOE risk may provide valuable information regarding the use of hMSCs and SDC-PRKC mechanisms and their contribution to AD development.

Napping Wisely According to Genetic Risk for Dementia

Renate Thienel [1], Caroline Faucher [1, 2], Jurgen Fripp [2], Michael Breakspear [1], Michelle K. Lupton [3], Nicholas G. Martin [3], Lina Gomez [3]

[1] The University of Newcastle, [2] Australian eHealth Research Centre, CSIRO, [3] QIMR Berghofer Medical Research Institute

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Background

Evidence points to an interplay between genetics and sleep in the trajectory to Alzheimer's Disease (AD). Considerable research has focused on the relationship between overnight sleep parameters and APOE ε4, a genetic risk factor for late-onset AD. The influence of napping and other AD genetic risk factors on cognitive function is poorly understood. This study investigates the interaction of napping with APOE ε4 and polygenic risk scores (PRS) for dementia on the cognitive performance of healthy older adults.

Method

We studied 1629 adults aged between 42–75 years (M=61.0, ±6.7) from the Prospective Imaging Study of Ageing (PISA). Principal Component Analysis reduced neuropsychological data to three cognitive components: visuospatial abilities, memory, executive functions. We used ANCOVA to study the effects and interactions of napping and AD genetic risk on cognition, with age, education, sex and reported sleep apnoea as covariates.

Results

APOE ε4 positive participants who reported habitual long naps (>1 hour) had higher memory scores than APOE ε4 negative participants ((1,1619)=9.68, p=.002). Napping had a positive effect on memory for APOE ε4 positive participants (F(2,1619)=3.31, p=.037), with longer naps (>1 hour) associated with better performance.

A significant interaction of PRS (top versus bottom quintiles, n=663) and napping duration on the memory component was observed (F(2,640)=3.25, p=.040). Without napping, high risk participants performed worse than low risk participants (F(1,640)=6.47, p=.011). The later performed better without napping than they did with short naps (<1 hour; (F(2,640)=3.12, p=.045).

Conclusion

These findings suggest that napping interacts with genetic risk factors for dementia, influencing memory performance. Understanding this relationship could guide preventive personalised sleep strategies for adults at risk of dementia.

Advancing Dementia Prevention: Creating a Framework for Evaluating Self-Directed Goal Setting in Risk Reduction Interventions

Kaarin J. Anstey [1], Jessica G. Amos [1], Sophie Andrews [2], Lidan Zheng [1]

[1] UNSW School of Psychology, The University of New South Wales, Sydney, NSW, Australia, [2] Thompson Institute, University of the Sunshine Coast, Birtinya, QLD, Australia

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Background

Behaviour change techniques, such as goal setting, are considered key components of interventions designed to alter behaviours. However, their evaluation in the context of dementia risk reduction interventions is limited and, to our knowledge, absent for self-directed goals which increasingly feature within digital interventions.

Methods

Within the online dementia risk reduction intervention MyCOACH (Amos et al., 2023) self-directed goal setting was featured in the multi-chapter e-learning course (chapters included: memory strategies, physical activity, diet, social and cognitive engagement, and stress). Adapted from Bowman and colleagues' SMART-Goal Evaluation Method, the Dementia Risk Reduction-Goal Evaluation (DRR-GE) framework was created. The DRR-GE offers the first standardised framework to assess quality of self-directed SMART goals within the dementia prevention domain. Scores range from 1-8, indicating goal quality (≤5 = poor, 6 = average, 7 = good, 8 = excellent).

Results

Using the DRR-GE framework, 501 self-directed goals from 148 participants (61.5% women, age: 65-93 years, M=74.47, SD=6.20) were assessed by two independent researchers, showing strong interrater reliability (weighted Kappa 0.87, 95% CI [0.84, 0.90]). Most goals were rated 'good' (164/501, 32.73%), followed by 'average' (117/501, 23.35%), 'poor' (111/501, 22.16%) then 'excellent' (109/501, 21.76%). Results indicated that younger adults (65-74) scored significantly higher in physical activity goals compared to older adults (75+) (U=1254.00, p =.041), and women outperformed men in social and cognitive engagement goals (U=643.50, p =.024). No other significant differences were found.

Discussion/Conclusions

Age-related and gender differences in goal quality may reflect declining physical health and varying socialisation patterns, respectively. This underscores the importance of additional support for self-directed goal setting for less familiar or comfortable behaviours. The DRR-GE framework facilitates detailed sub-component analysis, often overlooked for dementia risk reduction trials, aiding both the design and analysis of interventions and their broader implementation.

Predicting Frailty and Associated Outcomes with Genetic Information

Tobias K Karakach [1], John D Fisk [2, 3], Isabelle F Foote [4, 5], Kenneth Rockwood [2, 3], Jonny P Flint [6, 7, 8, 9, 10,] Michelle K Lupton [10], Andrew Rutenberg [11], Simon R Cox [6, 7], Michelle Luciano [6, 7], Andrew D Grotzinger [4, 12], Nicholas G Martin [10]

[1] Department of Pharmacology, Dalhousie University, Halifax, Nova Scotia, Canada, [2] Department of Psychiatry, Dalhousie University, Nova Scotia Health, Halifax, Nova Scotia, Canada, [3] Division of Geriatric Medicine, Dalhousie University, Halifax, Nova Scotia, Canada, [4] Institute for Behavioral Genetics, University of Colorado Boulder, Boulder, Colorado, USA, [5] Centre for Preventive Neurology, Wolfson Institute of Population Health, Queen Mary University of London, London, UK, [6] Lothian Birth Cohorts, Department of Psychology, University of Edinburgh, Edinburgh, UK, [7] Department of Psychology, University of Edinburgh, Edinburgh, UK, [8] Advanced Care Research Centre School of Engineering, College of Science and Engineering, The University of Edinburgh, Edinburgh, UK, [9] Alzheimer Scotland Dementia Research Centre, University of Edinburgh, Edinburgh, UK, [10] Department of Mental Health and Neuroscience, QIMR Berghofer Medical Research Institute, Brisbane, Queensland, Australia, [11] Department of Physics and Atmospheric Science, Dalhousie University, Halifax, Nova Scotia, Canada , [12] Department of Psychology and Neuroscience, University of Colorado Boulder, Boulder, Colorado, USA

Background

Frailty is a clinical state associated with adverse outcomes and a heightened risk of dementia. Genome-wide association studies (GWAS) have demonstrated a strong genetic basis of frailty. These studies measured frailty using aggregate measures. However differing pathways of frailty are likely to have diverse effects which may dilute GWAS signal and miss important subtypes.

Methods

We utilised summary statistics from a multivariate GWAS, which modelled frailty using a general frailty factor and 6 residual latent factors (social isolation, unhealthy lifestyle, multimorbidity, metabolic/respiratory status, cognition, and disability) reflecting genetic variance unexplained by the general factor. We calculated polygenic risk scores (PRS) for each frailty factor to examine how well they predict frailty and associated outcomes in three cohorts: 1005 adults in the Lothian Birth Cohort 1936 (LBC1936) measured longitudinally age ~70 - ~83, 5956 adults age 65+ in the English Longitudinal Study of Ageing (ELSA) and 1646 adults age 65+ in the Prospective Imaging Study of Ageing.

Results

Preliminary findings from LBC1936 and ELSA show a combined PRS of the general factor and 6 latent factors explain 3.8% and 2.2% of the variance in frailty. The most predictive PRS' were the general-factor PRS (β = 0.10, 95%CI, 0.023-0.18), p < 0.01; (β = 0.10, 95%CI, 0.072-0.12), p < 0.001, multimorbidity PRS (β = 0.12, 95%CI, 0.048-0.20), p < 0.01; (β = 0.046, 95%CI, 0.02-0.07), p < 0.001) and cognition PRS (β = 0.10, 95%CI, 0.014-0.17), p < 0.05; (β = 0.07, 95%CI, 0.05-0.09), p < 0.001 in LBC1936 and ELSA respectively. Whereas a single-aggregate-frailty PRS explained 1.4% of variance (β = 0.10, 95%CI, 0.030-0.18) and (β = 0.11, 95%CI, 0.093-0.14), ps < 0.01. PRSs for multimorbidity and cognition were also significantly associated with dementia risk and cognitive ability in LBC1936.

Conclusion

Our findings demonstrate that genetic pathways linked to multimorbidity and cognition represent important subgroups for predicting frailty, dementia risk, and cognitive ability in older adults.

Diversity and Inclusivity in Australian Dementia Prevention Research: A Comprehensive Mapping Study

Dr Paul Gardiner [1], Assoc. Prof. Ashleigh Smith [2], Dr Diana Karamacoska [3], Dr Maddison Mellow [2], Olivia Giameos [2]

[1] University of Queensland, [2] University of South Australia, [3] Western Sydney University

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Background

Twelve modifiable risk factors have been identified which may prevent or delay up to 40% of dementia cases. Several barriers to their 'modifiability' have been identified, including disparities in access to science and healthcare and other social inequities. Many dementia risk factors disproportionately impact culturally and linguistically diverse groups, remote/rural residents, LGBTQIA+ individuals, and other priority populations. Most of the evidence in the dementia prevention space emerges from high-income, well-educated or non-marginalised populations. There is a need to analyse and map the characteristics of dementia prevention research cohorts in Australia to determine the generalisability of current evidence, and encourage future inclusive and representative sample recruitment. This data is imperative to identify risk factors which disproportionately impact certain groups and to design personalised interventions for our diverse Australian population.

Methods

A scoping review of the literature was conducted, including a systematic literature search of OVID and EBSCO databases, clinical trials registries, and released outcomes of funded grants. A five-question survey was distributed to the wider dementia research-community for identification of additional studies/grants, and to obtain de-identified demographic data of both published and unpublished research cohorts and randomised controlled trials (including age, gender, education level, sexuality, ethnicity, nationality, Aboriginal and Torres Strait Islander status, socioeconomic status, geographic location/postcode, first language, and country of birth). Included studies were focused on dementia risk reduction (non-pharmacological) with an Australian sample.

Results

The systematic literature search identified 351 articles for title and abstract screening, resulting in 79 studies following full-text screening. Seventy-two grants were identified, following screening of 259. Thirteen clinical trials resulted from screening of 70.

Discussion/Conclusion

The demographic characteristics of the identified cohorts will be analysed to highlight the need for careful consideration and design of recruitment strategies to include more diverse and representative samples in future dementia prevention studies.

Supporting Primary Care Practitioners to Promote Dementia Risk Reduction in Australian General Practice: Outcomes of a Non-Randomised Implementation Pilot Study

Dr Kali Godbee [1, 2], Prof Nicola T Lautenschlager [1, 3], Prof Victoria J Palmer [1], Prof Jill J Francis [1, 4], Prof Jane Gunn [1]

[1] The University of Melbourne, [2] Monash University, [3] Royal Melbourne Hospital Mental Health Service, [4] Ottawa Hospital Research Institute

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Background

Primary care practitioners (PCPs) worldwide are being called on to promote dementia risk reduction (DRR) as part of delivering preventive care. To support practice change of Australian PCPs in promoting DRR, we developed an intervention that combined a waiting room survey with patient information cards for PCPs to use in consultations (the Umbrella intervention). We also developed a targeted implementation approach that combined educational and relational strategies to support PCPs to use the Umbrella intervention.

Methods

This was a non-randomised implementation study. Practices were recruited from the South East Melbourne Primary Health Network catchment. The mixed-methods approach to outcome evaluation triangulated outcome data from multiple sources. We evaluated antecedent outcomes (acceptability, appropriateness, and feasibility) and actual outcomes (adoption, penetration, and fidelity) for both the intervention and targeted implementation approach. We considered the perspective of both PCPs and patients affected by the change in practice.

Results

Five practices agreed to pilot the intervention and targeted implementation approach. Sixteen PCPs promoted DRR with 159 patients. Sixteen of these patients completed a telephone interview. PCPs and patients found the Umbrella intervention to be acceptable, appropriate, and feasible. However, penetration (or 'reach') of the Umbrella intervention was low. Approximately half of eligible PCPs engaged with at least one component of the targeted implementation approach and promoted DRR using the Umbrella intervention at least once. The targeted implementation approach was seen to be acceptable, appropriate, and feasible, although PCPs wanted a simpler platform for online peer discussions and for reception staff to be better prepared for the change in practice.

Conclusions

The Umbrella intervention is an acceptable, appropriate, and feasible intervention to support the promotion of DRR in Australian general practice. Combining educational and relational strategies is an acceptable and appropriate approach to support implementation. However, research into improving uptake is needed.

Medication Optimisation for Dementia Risk Reduction

A/Prof Johnson George [1], Prof Parker Magin [2], Prof Vincent Versace [3], Prof Elizabeth Manias [1], Dr Kali Godbee [1, 4], Prof Billie Bonevski [5], A/Prof Sharleen O'Reilly [3, 6], Ms Mary Tullipan [1, 2], Dr Andrea Hernan [3], Dr Marlien Varnfield [7], Mr Gopisankar Mohanannair Geethadevi [1], Dr Dennis Thomas [2], Dr Cik Lee [1, 4], A/Prof Rohan Elliott [1], Prof Simon Bell [1], A/Prof Kevin Mc Namara [1, 3], Ms Denise van den Bosch [1], Dr Stephanie Ward [1, 8], Dr Amanda Cross [1], Dr Rajiv Jayasena [7], Prof Kaarin Anstey [8], Prof Ajay Mahal [4], Prof Amanda Baker [2]

[1] Monash University, [2] University of Newcastle, [3] Deakin University, [4] University of Melbourne, [5] Flinders University, [6] University College Dublin, [7] Australian eHealth Research Centre, [8] University of New South Wales

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Background

Some modifiable risk factors for dementia (e.g., diabetes, dyslipidaemia, hypertension) can be managed using medications. This study aimed to explore the potential for medication optimisation in patients at increased risk of dementia in primary care.

Methods

We analysed baseline data from the HAPPI MIND dementia risk reduction trial. The trial recruited 403 middle-aged adults (median age 57 years, 63% female) with ≥2 dementia risk factors from 40 Australian general practices. This analysis examined the co-occurrence of self-reported cardiometabolic conditions (diabetes, dyslipidaemia, hypertension), lifestyle risk factors (smoking, obesity, excessive alcohol intake, physical inactivity), suboptimal management of cardiometabolic conditions (as indicated by clinical observations or pathology results), self-reported medication nonadherence (forgetting or skipping prescribed medication in the past week), polypharmacy (>5 regular, prescribed medications), and history of a Home Medicines Review (HMR).

Results

Three-quarters of participants (299/403, 74%) reported having either diabetes, dyslipidaemia, or hypertension. Of these, 93% (277/299) showed suboptimal management of one or more cardiometabolic conditions. Of the participants with suboptimal management, 27% (76/277) reported medication nonadherence in the past week. Therefore, 19% of the entire cohort (76/403) had poorly managed cardiometabolic conditions and medication nonadherence. Only ten participants (10/39, 26%) with polypharmacy and medication nonadherence had received an HMR. In this cohort, 17% (68/403) of participants had poorly managed cardiometabolic condition(s), medication nonadherence, and lifestyle risk factors for dementia.

Discussion

Among middle-aged patients at risk of dementia, there is room for lifestyle changes and medication optimisation to improve health. Patients may benefit from holistic support (e.g., HMR, motivational interviewing, self-monitoring apps) to better manage their dementia risk factors.

Informing Timely Dementia Diagnosis: Dementia-Related Concerns, Literacy, Knowledge, Stigma and Motivation for Behaviour Change in a Large Sample of Older Australians

Dr. Terence Chong [1], Prof. Sharon Naismith [2], Prof. Alison Hutchinson [3], Prof. Kon Mouzakis [3], Adj. Prof. Bernice Redley [3], Dr. Loren Mowszowski [2], Prof. Tracey Bucknall [3], Prof. Liliana Orellana [3], Prof. Rajesh Vasa [3], Dr. Tanita Botha [3], Dr. Helen Macpherson [3], Dr. Eva Yuen [3], Ms. Kelly Burns [4], Mr. Andrew Vouliotis [3], Ms. Justine Lomas [3], Dr. Stephanie Daly [5], Dr. Lidia Engel [6], Dr. Tanya Petrovich [4], Dr. Jessica Rivera Villicana [7]

[1] University of Melbourne, [2] University of Sydney, [3] Deakin University, [4] Dementia Australia, [5] General Practitioner, [6] Monash University, [7] RMIT University

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Background

Research and guidelines highlight the importance of a timely dementia diagnosis. To be effective, interventions to delay cognitive decline need to be implemented in the early stages of disease. However, recent Australian research indicated that at the time of diagnosis, 76% of people had advanced beyond the early stage, and 20% were in moderate to severe stages of disease. BrainTrack is a mobile app designed for self-assessment of cognition to promote conversations with health professionals about brain health and enable timely dementia diagnosis. We aimed to investigate dementia-related concerns, literacy, knowledge, stigma and motivation for behaviour change and explore associations with demographic characteristics in a sample of BrainTrack users.

Methods

We conducted a cross-sectional survey in 2022-2023. Demographics measured: postcode, gender, age, English proficiency, primary language spoken, Aboriginal and/or Torres Strait Islander status, and education level. Outcomes measured: Subjective concerns about memory, dementia-related literacy, knowledge and stigma, and motivation to change behaviours for dementia risk reduction were measured using: Subjective Memory Complaints Questionnaire; Consumer Access, Appraisal, and Application of Services and Information for Dementia instrument; Dementia Knowledge Assessment Scale; Motivation to Change Lifestyle and Health Behaviours for Dementia Risk Reduction Scale; and the Dementia Public Stigma Scale.

Results

Nationwide, over 7,000 Australian residents ≥50 years of age, without a dementia diagnosis, mild cognitive impairment or stroke, participated. We report the demographic characteristics of participants, summarise the outcome scales across the whole sample, and explore associations between each outcome and participants' demographic characteristics.

Discussion

This research provides valuable knowledge from a large sample of Australians to inform strategies, such as BrainTrack, to promote timely dementia diagnosis. Strategies to improve dementia literacy and knowledge and help overcome stigma may assist in achieving timely dementia diagnosis and enable the uptake of strategies to promote lifestyle and health behaviour risk reduction.

Hearing Loss and Expectations Regarding Cognitive Ageing: Insights From an App-Based Research Study and Implications for Dementia Prevention

Jana Koch [1, 2, 3], Kaarin J. Anstey [1, 2, 3], Brooke Brady [1, 2, 3]

[1] University of New South Wales, School of Psychology, Sydney, Australia, [2] UNSW Ageing Futures Institute, Sydney, Australia , [3] Neuroscience Research Australia, Sydney, Australia

Background

Positive age expectations, particularly those related to maintaining strong cognitive function, can drive healthy ageing and promote preventative health behaviours crucial for reducing dementia risk. This might be particularly important for people with hearing loss who may experience shifts in age expectations due to sensory changes. We investigate whether people with hearing loss hold less positive expectations regarding cognitive ageing compared to those without hearing loss.

Methods

Participants were selected from the app-based, longitudinal 'Labs without Walls' study. An online hearing task was administered to participants via the study app, and a pure-tone average was calculated in the better-hearing ear on frequencies 0.5, 1, 2, and 4 kHz. Hearing loss was defined as pure tone average above 20 dBHL. Expectations regarding cognitive ageing was measured using the cognitive function subscale of the expectations regarding ageing scale. An analysis of covariance (ANCOVA) was used to test whether people with hearing loss had worse expectations regarding cognitive ageing compared to those without hearing loss while controlling for sex.

Results

The total sample for this study included 184 participants with a mean age of 55.6 (17.1 SD). Hearing loss was detected in 34.5% of participants. Females reported more positive expectations regarding cognitive ageing than males ($F(1.2961)=6.43$, $p=.01$). After controlling for the effect of sex, people with hearing loss had significantly worse expectations regarding cognitive ageing ($M=37$ vs $M=44.6$) compared to those without hearing loss ($F(1.1695)=3.91$, $p=.05$).

Discussion/Conclusion

The results indicate that people with hearing loss may have concerns about cognitive decline as they age, possibly due to a heightened awareness of the ageing process. Future research will explore whether this awareness can be utilised as a motivational factor for increased dementia risk reduction activities among this population while considering the possible influence of sex on these ageing expectations.

Implementing a Dementia Risk Reduction Strategy (Educational Intervention) in Non-English Speaking Communities

Kathleen Doherty [1], Yashi Koirala [2], Claire Eccleston [1], James Vickers [3]

[1] Secondary Supervisor, [2] Presenter, [3] Primary Supervisor

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Background

The Preventing Dementia Massive Open Online Course (PD MOOC) has been shown to improve dementia risk reduction knowledge and encourage positive behavioural changes related to risk factors. To enhance the accessibility of this health promotion initiative in non-English speaking community, it has been translated and adapted into the Nepali language and piloted online.

Methods

The PD MOOC was translated into Nepali by following five steps, including split translation, group editing, second revision, final revision, and audit by a healthcare professional. Online survey tools, translated into Nepali were used to achieve the aim of our project which is to measure the effect of the course on participants' knowledge and risk profile and to explore the enablers and barriers in accessing the Nepali PD MOOC course by the targeted population. Research participants completed feedback surveys at the end of the PD MOOC. Research participants were recruited through social media marketing including Facebook, YouTube and LinkedIn, through health care organisations internationally, word of mouth and community gatherings.

Results

Currently, 142 people from 28 different countries who speak Nepali have enrolled in the Nepali PD MOOC. This includes 45 from Australia, 20 from Nepal and 13 from India. 62% of these participants are female and 35% of them are male. 19 participants have completed a feedback survey post-course completion on the quality of the contents, translation, language used and enablers and barriers in accessing course material. Enablers and barriers in accessing course material will be further explored using interviews to understand ways to enhance participation in dementia risk reduction initiatives by people from non-English speaking groups.

Conclusion

Uptake of the pilot Nepali PD MOOC extended across Australia as well as Nepal and neighboring countries. Translation enables Nepali speakers to engage in learning about dementia, its risk factors and evidence-based dementia risk reduction strategies.

Older Adults' Awareness, Interest, and Preferences for Cognitive Interventions

Shirly Sareyka [1], Kerryn Pike [1]

[1] Griffith University

Background

Cognitive interventions are a viable option to maintain, improve, and support the lifestyle of those with dementia, and are even more effective for those at risk of dementia and healthy older adults. Starting interventions as early as possible is the key to mitigating cognitive decline, but awareness of available interventions is limited and often not pursued until memory or cognition issues are advanced. This research investigated whether community dwelling older Australians were aware of and interested in cognitive interventions. Additionally, the research explored older adult's preferences, barriers, and facilitators for these interventions.

Methods

392 participants 50+ completed an online survey, and 17 semi-structured interviews were conducted in this mixed methods study. Hierarchical multiple regressions analysed predictors of awareness and interest and reflexive thematic analysis was used for the qualitative interviews, which discussed cognitive intervention knowledge, awareness, interest, preferences, barriers, and facilitators.

Results

Levels of awareness were high, and higher stress levels, greater memory satisfaction, and lower depression were related to increased awareness. Interest in cognitive interventions was high and positively associated with dementia anxiety. The study found wide ranging preferences for cognitive intervention delivery methods, styles, content, facilitators, and barriers. Seven themes were generated from the interviews: (1) Knowledge of modifiable risk factors, (2) Diverse channels for accessing health information, (3) Understanding of memory and cognition, (4) Reflections on self, including changing memory, ability, and the ageing process, (5) Self-efficacy in relation to memory and cognition, (6) Opposite-based preferences and motivations for intervention engagement, and (7) Strong preference for a fun, engaging experience with cognitive interventions.

Conclusion

Despite high awareness and high interest in cognitive interventions, individual differences highlight the need for intervention designs which are tailored to meet the requirements of older adults. Additionally, an education campaign promoting the benefits of interventions and early intervention would encourage participation.

The Automsted Elecsys Measurement of the Fluid Biomarkers Provides Support for the Diagnosis of Alzheimers Disease

Christopher Rowe [1], Shiji Varghese [2], Colin Masters (AO) [2], Rodrigo Canovas [3], Ralph Martin [4], Steven Collins (AO) [5], Christopher Fowler [6], Kevin Taddei [4], Qiao-Xin Li [2], James Doecke [3], Stephanie Rainey-Smith [4]

[1] Molecular Imaging & Therapy, Austin Health, Heidelberg, VIC, Australia, [2] National Dementia Diagnostics Laboratory, The Florey Institute, The University of Melbourne, Victoria, Australia 3010., [3] Australian e-Health Research Centre, CSIRO, Brisbane, QLD, 4029, Australia. , [4] Edith Cowan University WA, [5] National Dementia Diagnostics Laboratory, The Florey Institute, Department of Medicine (RMH), The University of Melbourne, [6] The Florey Institute, The University of Melbourne, Victoria, Australia 3010

Background

Alzheimer's disease (AD) treatment at an early stage with monoclonal antibody treatment is approved by the Food and Drug Administration (FDA) and has brought hope for millions of people afflicted by this malady. Measurement with the Generation II Elecsys® platform of Aβ42, P-tau181 and T-tau in fresh cerebrospinal fluid (CSF) is approved by the FDA to confirm underlying AD neuropathology and thereby enable access to the disease-modifying therapies. This study reports AD biomarkers in a community setting using the Elecsys® and the concordance of the CSF biomarkers with PET amyloid imaging.

Methods

CSF samples were from Australian Imaging Biomarker and Lifestyle (AIBL) and from referred local hospitals/clinics. ALL CSF samples were collected into low-bind tubes.

Results

Of the 1388 referred CSF samples, 66% had low Ab42 and 26% had a profile supporting the AD diagnosis. In the 78 AIBL samples (mean age 72±), 50 had normal PET amyloid of Centiloid (CL) <15, of which 44 (88%) had normal CSF biomarkers, four had abnormal CSF Ab42, one had AD profile (the PET was 5 yr early), and one had normal Ab42 but abnormal Tau (SNAP, Suspected non-Alzheimer's disease pathophysiology). Of 9 subjects with a CL between 75-146, 7 had an AD CSF profile, one with abnormal Ab42 only, and one with borderline normal Ab42 and positive P-tau. A mixture of CSF profiles was observed for those with CL values of 16-74. The CSF test is able to detect those with normal Ab but abnormal Tau (SNAP).

Discussion

The automated Elecsys® II platform is accessible for further evaluating a diagnosis of AD and offers high throughput and excellent precision. It minimises pre-analytical sample handling, which increases the reliability of results. Our study supports the use of Elecsys® II for AD diagnostics in routine clinical practice.

Developing a Novel Computerised Assessment of Functional Ability for Older Adults

Katya Numbers [1], Brian Draper [1], Jacqueline Wesson [2], Julian Trollor [1], Lindy Clemson [2], Jeewani Anupama Ginige [3], Henry Brodaty [1], Kim Delbaere [4], Ping-hsiu Lin [1], Simone Reppermund [1]

[1] University of New South Wales, [2] The University of Sydney, [3] Western Sydney University, [4] Neuroscience Research Australia

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Background

Functional impairment in daily activities is a diagnostic criterion of dementia and distinguishes it from mild cognitive impairment (MCI). Subjective measures of functional decline such as self-reports or informant-reports are commonly used to assess functional ability. However, these methods are prone to bias and therefore might not truly reflect an individual's functional ability. Performance-based measures of daily function are considered more objective, but the equipment, training and scoring required for these can be costly. This study aims to develop and validate a new performance-based computerised diagnostic tool (Computerised-Sydney Test of Activities of daily living in Memory disorders, C-STAM) for older adults with and without cognitive decline.

Methods

The C-STAM is being developed by a multidisciplinary team of researchers, psychologists, neuropsychiatrists, psychogeriatricians, occupational therapists, physiotherapists, and computer scientists. We conducted an international Delphi study to select and refine suitable tasks and implemented feedback from an advisory group of older adults with and without cognitive impairment and caregivers. A pilot study comprising 30 participants with and without cognitive impairment is underway to examine feasibility and user experience.

Results

The pilot version of the C-STAM included nine tasks across seven subdomains: communication, shopping, dressing, community mobility, financial affairs, medication management and memory. The total C-STAM score is the sum of scores for each of the nine tasks (maximum total = 36). The pilot study aims to recruit 30 participants by May. To date, 13 participants have completed the pilot study. Subsequently, we will validate and determine cut-off scores for the C-STAM in a larger sample of people with normal cognition, MCI, and dementia.

Discussion

The validated C-STAM will provide clinicians and researchers a cost-efficient, remotely accessible and accurate way to measure functional abilities in older adults with normal cognition or cognitive decline to improve early diagnosis of dementia and facilitate monitoring disease progression.

Evaluating Patients' and Carers' Experiences of Memory and Cognition Services: Two and a Half Years' Findings from the Australian Dementia Network Registry

Henry Brodaty [1], Scott Cooper [2], Sharon Naismith [3], Jane Alty [4], Kerrie McAloney [5], Lee-Fay Low [3], Jenny Fitzpatrick [2], Stephanie Ward [1, 6, 7], Xiaoping Lin [7], Sally Lambourne [8], Lyn Phillipson [9], Kasey Wallis [7], Barbara Kain [2], Yun-Hee Jeon [3]

[1] University of New South Wales, [2] Consumer Representative, [3] University of Sydney, [4] University of Tasmania, [5] QIMR Berghofer Medical Research Institute, [6] The Prince of Wales Hospital, [7] Monash University, [8] Dementia Australia, [9] University of Wollongong

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Background

The Australian Dementia Network (ADNeT) is a Clinical Quality Registry that provides data on diagnosis and early management of people with dementia or mild cognitive impairment (MCI). It also collects data on patients' and carers' experience of memory and cognition diagnostic clinics with the aim to inform patient-centred care.

Methods

After a patient is recruited into the registry, the patient and their carer receive a survey which includes eight questions on their experience of memory and cognition diagnostic clinics. These surveys were developed through expert consensus by a working group comprising people living with dementia, carers, peak bodies, clinicians and researchers.

Results

Between March 2021 and September 2023, 1,196 patients and 958 carers returned surveys (50% response rate for both surveys). Patients who were female, had primary school or lower education, or lived alone were less likely to return the patient survey or have the carer survey returned. Patients who were older, were diagnosed with dementia or lived in residential aged care were less likely to return the patient survey. Most patients and carers (both 89%) reported "Good/Very good' experience and the aspect most positively reported was "treated with dignity and respect' (agreed by 97% patients and carers). The aspect showing least positive experience was "given advice about how and where to get more information or help' (agreed by 80% patients and 85% carers). The biggest discrepancy between patients' and carers' experience was "being involved in decision making about treatment and care' (agreed by 81% patients and 91% carers).

Discussion

The ADNeT Registry provides valuable data on patients' and carers' experience of memory and cognition diagnostic clinics. Early findings suggest that although most report positive experience, provision of support information and ensuring patient involvement in decision-making are areas for improvement to further enhance their experience.

‘Infographing’ Dementia Prevention: A Co-Design Approach

Kathleen Doherty [1], Ignacio Martinez Escobedo [1], Claire Eccleston [1]

[1] Wicking Dementia Research and Education Centre, University of Tasmania, Hobart, Australia

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Background

Designing effective public health messages is challenging, particularly when communicating complex and unfamiliar health messages such as dementia risk prevention. These messages need to be accessible broadly, and inclusive of individuals who speak English as an additional language. Visual tools are a key strategy to enhance the communication of evidence-based information. Our aim was to identify key design principles which underpin the creation of effective infographics relaying dementia risk reduction health messages.

Methods

Participants were recruited from the May 2022 iteration of the Preventing Dementia Massive Open Online Course (PDMOOC). Those who resided in Australia, spoke English as an additional language, and were over 18 years of age were invited to participate in the study. Co-design sessions were conducted in September and December 2022. In addition, participants were invited to complete a survey about the co-designed infographics.

Results

Six participants were involved in the co-design process. Qualitative data from four co-design sessions were coded using an inductive, data driven, reflexive thematic analysis with production of latent themes. Multiple investigators reviewed candidate themes to ensure meaningful interpretation of patterns in the data. Three themes were generated from active engagement with the data analysis. These themes reflect the visual message design preferences of participants: ‘all hands on deck’; ‘charting the course’; and ‘get on board’. Data from twenty-two survey responses suggested that the co-designed infographics appealed to respondents.

Discussion

This work explores the key elements to consider when designing effective visual messages, and the role of co-design to help create meaningful and accessible health educational tools that will resonate with the intended audience. Doing so may help health communicators navigate the creation of visual messages across diverse health domains and populations.

Should we Work Smarter or Harder for our Health? A Cross-Sectional Comparative Analysis of Domain- and Intensity-Based Time-Use Compositions, and Their Associations with Cognitive and Cardiometabolic Health in Older Adults.

Dr Maddison Mellow [1], A/Prof. Ashleigh Smith [1], Prof. Timothy Olds [1], Prof. Frini Karayanidis [2], Dr Dorothea Dumuid [1], Dr. Ty Stanford [1], Dr Alexandra Wade [3], Prof. Hannah Keage [4]

[1] Alliance for Research in Exercise, Nutrition and Activity (ARENA), Allied Health and Human Performance, University of South Australia, [2] Functional Neuroimaging Laboratory, School of Psychological Sciences, College of Engineering, Science and the Environment, University of Newcastle, [3] College of Education, Psychology and Social Work, Flinders University, [4] Behaviour-Brain-Body Research Centre, Justice and Society, University of South Australia

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Background

Daily time-use behaviours that make up the 24-hour day can be classified by their intensity (e.g., sedentary behaviour (SB), sleep, light and moderate-vigorous PA) or domain (e.g., sleep, sport/exercise, chores), and the balance (or composition) of these behaviours in the 24-hour day has important implications for cardiometabolic and cognitive health. Typically, older adults are encouraged to 'move more and sit less' for their health, despite evidence that some SBs are beneficial for cognition (e.g., reading, puzzles). We investigated whether cognitive and cardiometabolic outcomes relate differently to intensity- and domain-based time-use compositions.

Methods

Participants recalled their past 2 days of activities using the Multimedia Activity Recall for Children and Adults. Each activity was classified into one of 8 domains (chores, quiet time, screen time, self-care, sleep, social, household administration, sport/exercise), and one of 4 intensities (sleep, SB, LPA, MVPA) to create two time-use compositions (8-part and 4-part, respectively). Cognition was measured using the Addenbrooke's Cognitive Examination III, whilst cardiometabolic outcomes included waist circumference (WC), systolic and diastolic blood pressure, and total cholesterol. Compositional data analysis was used to investigate whether domain and intensity compositions were related to each outcome, and we explored significant associations further using isotemporal substitution analyses.

Results

397 participants from the ACTIVate study were included (65 ± 3.0 years, 69% female). WC was associated with both compositions, whilst cognition was only associated with the domain composition. Spending more time in quiet time (e.g., reading) was beneficial for cognition but not WC, whilst spending more time in sport/exercise was strongly related to WC and less so with cognition. In intensity models, spending more time in MVPA was strongly associated with WC.

Conclusions

Findings suggest that the impact of daily activities on cognition may differ depending on their context, whilst physical activity appears beneficial for WC regardless of context.

Risk of Mild Behavioral Impairment: Examining the Role of Gender and APOE Allele Carrier Status

Kaarin Anstey [1, 2, 3], Corinne Fischer [4], Kim Kiely [1, 2, 3, 5], Moyra Mortby [1, 2, 3], Zahinoor Ismail [6]

[1] University of New South Wales, [2] Neuroscience Research Australia, [3] UNSW Ageing Futures Institute, [4] Keenan Research Centre for Biomedical Science, [5] University of Wollongong , [6] University of Calgary

Background

Gender differences in dementia and neuropsychiatric symptoms are well described. Similarly, the Apolipoprotein E (APOE) ε4 allele is a well-known predictor of Alzheimer's disease. However, their impact on the clinical manifestation of Mild Behavioral Impairment (MBI) remains unclear. Using data from the PATH Through Life Study we examined associations between gender and APOE-ε4 carrier status with MBI.

Methods

1316 dementia-free participants (48% female; aged 72-79). Gender was self-reported (female/male). Participants were classified as APOE ε4+ if they carried at least one ε4 allele (APOE ε4/ε4, ε2/ε4, ε3/ε4). MBI and its five domains (decreased motivation, affect dysregulation, impulse dyscontrol, social inappropriateness, abnormal perception/thought content) were approximated using a previously published transformation algorithm utilising the Neuropsychiatric Inventory. Binomial logistic regression, controlling for years of education, examined gender, APOE ε4 carrier status and their interaction as a predictor of MBI status.

Results

Of the 1316 participants, 339 (25.8%) were APOE ε4+ and 445 (34%) had MBI. A higher proportion of APOE ε4+ carriers ($\chi2(1)=5.99$, p=.014) and men ($\chi2(1)=4.59$, p=.032) had MBI. APOE ε4 carrier status (OR=1.58, 95%CI: 1.063-2.344) and male gender (OR=1.45, 95%CI: 1.093-1.925) were associated with a greater likelihood of MBI. Male gender was associated with a 2-fold greater likelihood of decreased motivation (OR=2.08, 95%CI: 1.13-3.86) and impulse dyscontrol (OR=2.16, 95%CI: 1.54-3.03). No significant interaction effects were found between gender and APOE ε4 carrier status for MBI or any of its domains.

Discussion

In dementia-free older adults, both male gender and APOE ε4+ status increased the risk of MBI. However, no cumulative/interaction effect between gender and APOE ε4 carrier status was found, suggesting that being both male and APOE ε4+ does not further increase the risk of MBI. These results provide novel and valuable insight into the connection between gender, APOE ε4 carrier status and MBI.

Pre-Hypertension and Antihypertensive Medication Use in a Healthy Brain Ageing Memory and Cognition Clinic

Craig Anderson [1, 2], Cheryl Carcel [1, 2], Ruth Peters [1, 2], Catriona Ireland [3], Johannes Michaelian [3, 4, 5], Shawn Kong [3, 4, 5], Sharon Naismith [3, 4, 5], Simone Simonetti [3, 4, 5], Sultana Shajahan [1, 2]

[1] University of New South Wales, [2] The George Institute for Global Health, [3] Brain and Mind Centre, [4] Charles Perkins Centre, [5] School of Psychology, University of Sydney

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Background

Hypertension in mid-life has emerged as a risk factor for dementia. Antihypertensive treatment may optimise brain health at all ages. We aimed to determine the frequency of pre-hypertension and hypertension, and associated treatment, in a memory and cognition clinic.

Methods

Consecutive older adults (aged >50 years) with cognitive concerns underwent neuropsychological, mental health and specialist geriatrician assessments. Global cognition (MMSE) and age corrected z-scores on composites of learning, memory, executive function, and processing speed, were compared between groups classified as normotensive (SBP ≤120 mmHg), pre-hypertensive (SBP 121-140 mmHg) and hypertensive (SBP >140 mmHg)

Results

Of 763 participants (mean age 67.5 years, female 60.1%), 80% were able to be classified according to SBP level with 17.7%, 43.6% and 38.7% defined as normotensive, pre-hypertensive and hypertensive, respectively. Only 34.1% of the sample were on antihypertensive treatment. Of those with a formal diagnosis of hypertension (38.2%), less than one-fifth (18.8%) were on antihypertensive treatment. The hypertensive group was significantly older and had higher medical burden than the pre-hypertensive and normotensive groups; the hypertensive group also had higher body mass index. Both the hypertensive and pre-hypertensive group had lower verbal learning scores than the normotensive group.

Conclusion

Overall, hypertension and pre-hypertension rates are high and antihypertensive medication use is low in a memory and cognition clinic setting. Efforts to monitor and treat blood pressure in such clinics appears to be justified. More research is required to understand the significance of early cognitive deficits in those with pre-hypertension.

Differential Diagnosis of Progressive Supranuclear Palsy Compared from Lewy Body Diseases using MRI

Peter Nestor [1, 2], Amir Fazlollahi [1, 3], John O'Sullivan [4, 5]

[1] Queensland Brain Institute, The University of Queensland, Brisbane, Queensland, Australia, [2] Mater Hospital, Brisbane, Queensland, Australia, [3] Department of Radiology, Royal Melbourne Hospital, The University of Melbourne, Melbourne, Victoria, Australia, [4] UQ Centre for Clinical Research, Faculty of Medicine, The University of Queensland, Herston, Queensland, Australia, [5]Department of Neurology, Royal Brisbane & Women's Hospital, Herston, Queensland, Australia

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Background

The overlapping motor and non-motor features of progressive supranuclear palsy (PSP) with Lewy body disorders (LBD comprising Parkinson's disease±dementia, and, dementia with Lewy bodies) may lead to misdiagnosis. Previous studies have suggested that white-matter changes and iron accumulation measured by MRI are prominent in PSP. We aimed to assess the usefulness of diffusion and susceptibility metrics to discriminate PSP from LBD. We focused on the corpus callosum with the least partial volume effects and crossing fibres, and globus pallidus (GP) and substantia nigra (SN) with distinct iron susceptibility.

Method

Forty healthy controls, 29 LBD and 14 PSP patients underwent 3.0T MRI. Two-shell diffusion-weighted images were acquired with 96 directions: fractional anisotropy (FA), mean diffusivity (MD), axial diffusivity (AD), and radial diffusivity (RD) were estimated using MRTrix toolbox. Subcortical iron deposition measures were derived from quantitative susceptibility mapping (QSM, STI Suite-v3). Regions-of-interest were manually placed on the centre of the genu of corpus callosum (GCC), GP and SN. Differences between groups were assessed using two-tailed unpaired Wilcoxon-rank sum tests. Classification between PSP and LBD was performed using a support vector machine (SVM) with a leave-one-patient-out approach.

Results

FA, MD and RD were significantly different in PSP compared to controls in GCC ($p=0.007$, $p=0.02$ and $p=0.008$). FA and RD were significantly different between PSP and PD in GCC ($p=0.04$ and $p=0.03$). QSM values in GP and SN were significantly different in PSP vs LBD and PSP vs Control ($p<0.005$). To differentiate between PSP and LBD patients, the SVM performance had a sensitivity of 96% and a specificity of 92%.

Discussion

Differences in white-matter integrity within the rostral CC and variations in iron-susceptibility within subcortical regions were discovered to distinguish patients with PSP from those with LBD. This could be integrated as part of a multimodal diagnostic imaging algorithm in clinical settings.

Exploring Relationships among Neuropsychiatric Symptoms, Subjective Cognitive Complaints, Cognitive Performance, and Incident Dementia: Findings from the Sydney Memory and Ageing Study

Nicole A Kochan [1], Perminder S Sachdev [1], Katya Numbers [1], Russell J Chander [1], Henry Brodaty [1], Jason Chen [1]

[1] Centre for Healthy Brain Ageing (CHeBA), Discipline of Psychiatry & Mental Health, School of Clinical Medicine, University of New South Wales

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Background

Subjective cognitive complaints (SCCs) and neuropsychiatric symptoms (NPS) are increasingly considered early indicators of dementia pathology. SCCs are self-perceived decline in cognition without objective impairment, while NPS are neuropsychiatric symptoms in later life that precede or co-occur with cognitive decline. We explore the association between SCCs, NPS, global cognition, and incident dementia using data from the Sydney Memory and Ageing Study (MAS).

Methods

Participants were 754 older adults (M age = 78.76, SD = 4.71) with normal cognition at baseline. SCC was defined as a yes response to “Have you noticed difficulties with your memory?’. NPS was defined as a score >1 on the Neuropsychiatric Inventory. Participants were categorised based on the presence of SCC and/or NPS. Outcomes were global cognition composite z-scores and clinical consensus diagnoses of dementia according to DSM-IV criteria.

Results

Of the 754 participants included, 217 (28.8%) had neither SCC nor NPS (SCC-NPS-), 350 (46.4%) had SCC only (SCC+NPS-), 52 (6.9%) had NPS only (SCC-NPS+), and 236 had both SCC and NPS (NPS+SCC+). At baseline, SCC-NPS+ had significantly poorer global cognition than SCC-NPS- or SCC+ NPS-. At wave 4 (6-year follow-up), SCC-NPS+ showed a steeper decline in global cognition compared to other groups. A greater proportion of SCC+NPS+ had developed dementia by wave 6 compared to SCC-NPS-. Multivariable logistic regression, with age as the only covariate surviving stepwise elimination, showed SCC-NPS+ (OR=3.70; SE=2.15; p=.025) and SCC+NPS+ (OR=3.18; SE=1.25; p=.003) had increased odds over SCC- NPS- in developing dementia by Wave 6.

Discussion

NPS is associated with poorer global cognition and, with or without SCC, is a significant long-term risk factor for dementia. The findings highlight the potential importance of considering NPS alongside cognitive features and suggest that assessing both neurobehavioral and neurocognitive dimensions could offer a more comprehensive risk assessment in cognitively normal individuals.

What is the Current Approach to Reablement for Community-Dwelling People Living with Dementia? Practitioner-Led Goals and Targets for Practice Change: Preliminary Outcomes

Susan Kurrle [1], Christopher Poulos [2, 3], Claire O'Connor [2, 3, 4, 5], Kaarin Anstey [3, 4, 5]

[1] University of Sydney, [2] HammondCare, [3] University of New South Wales, [4] Ageing Futures Institute, UNSW, [5] Neuroscience Research Australia

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Background

Reablement (and/or 'rehabilitation') for people living with dementia, involves multidisciplinary approaches such as occupational therapy and exercise to address a variety of functional, physical, cognitive, and behaviour needs. While community aged care teams are receiving referrals for everyday living support for people with dementia, evidence informed reablement is still not routinely available. This project aims to explore the current approach to reablement for people with dementia in the community, and identify practitioner-led goals and targets for practice change. The preliminary outcomes presented here form part of a broader project that seeks to understand how to implement evidence informed reablement for people with dementia in Australia.

Methods

A retrospective file audit was conducted with two community aged care providers in NSW to explore how reablement is currently provided for people with dementia. The providers had not yet used the evidence-informed reablement handbook (www.hammond.com.au/reablement) in practice. Clinical file notes from each provider were compared against the reablement handbook, then presented back to the respective allied health teams from each provider via focus groups, to identify practitioner-led goals and targets for practice change.

Results

The audit included data from n=10 clients with cognitive impairment or dementia. Interventions partially aligned with the reablement handbook (e.g. personally prescribed multicomponent exercises; provision of compensatory strategies), with some discrepancies (e.g. very few written support plans provided to clients). Focus groups included 12 allied health professionals (occupational therapy, physiotherapy, social work, dietetics). Participants identified potential for more structured functional cognition assessment, and better tailored information for clients' cognitive/physical functioning.

Discussion

While there was some alignment with the reablement handbook, there was room for improvement in provision of reablement for people living with dementia. To achieve this change on a national scale, broad consultation with a range of stakeholders is needed to determine the best implementation approach.

The Co-Design of a Sensory Support Intervention for People with Dementia in Residential Aged Care Facilities

Assoc Prof Melanie Ferguson [1], Dr. Najwan El-Saifi [2], Assoc Prof Iracema Leroi [3], Prof. Piers Dawes [4], Ms Naomi Rose [5], Emma Scanlan [6], Assoc Pro John Newall [7], Assoc Prof Reema Harrison [8], Dr. Carly Meyer [9], Assoc Prof Gerald Liew [10], Ms Cassandra Clarke [5], Mr Tim England [11], Prof Kasia Bail [12], Assoc Prof Yuanyuan Gu [13], Prof Hamid Sohrabi [14], Assoc Prof Angelita Martini [15], Prof Lisa Keay [16], Prof Johanna Westbrook [8], Prof Chyrisse Heine [17], Prof Ralph Martins [8], Prof Colette Browning [18], Dr, Smriti Raichand [13], Melinda Toomey [2]

[1] Curtin University, Perth, Australia, [2] Centre for Hearing Research, The University of Queensland, Brisbane, QLD 4072, [3] Trinity College, Dublin, Ireland, [4] Centre for Hearing Research, The University of Queensland, Brisbane, QLD 4072 2. School of Health and Rehabilitation Sciences, The University of Queensland, Brisbane, QLD 4072, Australia., [5] Centre for Healthy Ageing, Murdoch University, Perth, Australia, [6] Hearing Australia, Sydney, Australia, [7] Macquarie University Centre for Language Sciences, Sydney, Australia, [8] Australian Institute of Health Innovation, Macquarie University, Sydney, Australia, [9] 1. Bolton Clarke Research Institute, Bolton Clarke, Brisbane, Australia 2. School of Health and Rehabilitation Sciences, The University of Queensland, Brisbane, QLD 4072, Australia, [10] University of Sydney, Sydney, Australia, [11] Freelance consultant, Sydney, Australia, [12] University of Canberra, Canberra, Australia, [13] Macquarie University Centre for the Health Economy, Sydney, Australia, [14] Centre for Healthy Ageing, Murdoch University, Perth,Australia , [15] Brightwater Research Centre, Perth, Australia, [16] University of New South Walws, Sydney, Australia, [17] Federation University Australia, Ballarat and Gippsland, Australia, [18] Federation University Australia, Mt Helen, Australia

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Background

Hearing and vision impairments are common comorbidities of people with dementia (PwD) living in residential aged care facilities (RACFs). These impairments exacerbate the impact of dementia on the quality of life and psychological symptoms of residents, leading to increased medication and restraint use and higher care costs.

Methods

A mixed methods, two-step sequential design using a behavioural science approach to intervention refinement. Step 1 comprised a cross sectional survey to identify priority behaviours for a sensory support intervention for PwD in RACFs from the perspectives of residents, family carers, hearing and vision professionals, and aged care staff. Step 2 included interviews and workshops to explore the adaptation of an individualised sensory support intervention for PwD in RACFs. This involved understanding implementation barriers and facilitators, as well as assessing the acceptability and feasibility of theory-informed strategies.

Results

Sixty-nine participants were surveyed, and three key behaviours were identified: supporting device use, effective communication, and environmental adjustments. Informed by insights from interviews (n=22) and three workshops (n=11), a comprehensive sensory support intervention was developed with four components: 1) Mastering Sensory Support through staff training; 2) Sensory Support Goal Setting by integrating sensory support into staff daily tasks: 3) Sensory Support Station as a designated area in residents' rooms equipped with hearing and visual aids and maintenance kit; and 4) Sensory Support Prompts whereby visual cues are used for sensory support. The consensus among participants underscores agreement on the intervention's structure and content, affirming its appropriateness and practicality in RACFs.

Discussion

This study resulted in the co-design of a multicomponent intervention to support people with dementia and hearing and vision impairment living in RACFs. The intervention is practical and acceptable according to aged care staff. The effectiveness and feasibility of the intervention will next be assessed via a field trial.

Exploring the Social Value and Design Preferences for a Jome-Based Dementia Community Program in Australia

Brenda Gannon [1], Richard Norman [2], Laura Gitlin [3], Sally Bennett [1], Sabrina Lenzen [1], Lindy Clemsen [4]

[1] The University of Queensland, [2] Curtin University, [3] Drexel University, [4] University of Sydney

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Background

We study the monetary value and the relative importance of several program characteristics for an evidence-based intervention provided at home for people living with dementia and their carers in Australia.

Methods

Using a discrete choice experiment, advised through an expert and consumer co-design approach, we consider the total number of sessions, the delivery mode, the primary outcome and focus of the program as well as its costs as attributes.

Results

Results from a representative sample of the Australian adult population show a high willingness to pay for the program overall, even greater than the actual costs. Choice data from 940 respondents show preferences for in-person sessions over telehealth options and respondents place a high value on improving mood and dementia-related behaviour as well as independence in daily activities. Preference heterogeneity shows that people who have experience with home care services place an even highermonetary value on the program, compared to the rest of the sample.

Discussion

In light of the increased emphasis of governments on expanding home care options over residential care, these results contribute towards the design and implementation of a home-based community program for people with dementia and their carers and highlight its social value.

Dementia Friendly Communities, is it Friendly if People Living with Dementia are Not Included or Heard?

Dr. Caroline Grogan [1]

[1] Wesley Research Institute

Background

People living with dementia (PLWD) have voiced a desire to age-in-place in their own homes for as long as possible. The global Dementia-Friendly Communities (DFC) movement has grown since the early 2000s to support this aim. Processes to incorporate the needs of PLWD are paramount in fostering an effective DFC. However, in practice barriers prevent PLWD from even attending, let alone authentically participating in DFC Committee Meetings. PLWD therefore do not have the opportunity to lead or contribute to their DFCs. Understanding and navigating these barriers is necessary.

Methods

Two DFC committees in Queensland were observed between September 2019 and January 2020. Semi-structured interviews were coupled with participant observations and fieldnotes. Purposeful and snowballing sampling, and thematic analysis, were used.

Results

20 participants were interviewed, n=4 PLWD, n=7 family carers, n=9 workers. Involvement of PLWD in DFC initiatives was observed to be limited or non-existent. Tensions arose in DFC development around power-sharing between PLWD and other stakeholders. For instance, aged care workers and facilities tended to position PLWD as passive recipients of care, as opposed to experts in their own needs, meaning they did not prioritise authentic inclusion of PLWD in DFC meetings. Microprocesses are critical to navigating known barriers to actively participating in meetings, e.g.: · Develop concise agendas, shared well in advance· Democratic nomination of chair with training/ skillset to facilitate dementia-friendly meetings· Consideration of time of day, number of attendees, and length of meeting · Accessible location or facilitated transport.

Discussion

Although inclusion of PLWD is central to the aims of DFCs, this is not currently happening in practice. Addressing existing shortfalls in microprocesses for DFCs mean their aspirational goals can be actively implemented locally, improving the quality of life and social connectedness of PLWD. This activates Recommendations 2.biii and 3.a.ii of the Royal Commission into Aged Care.

Understanding the Perspectives and Wishes of Family Carers and People Living with Dementia to Inform the Dementia In-Home Respite Service

Dr. Caroline Grogan [1], Dr Olivia Fisher [1, 2], Lyndsey Hawthorne [3], Rebecca Waite [3], Dr Elizabeth Martin [1, 4], Sarah Harriman [1]

[1] Wesley Research Institute, [2] Charles Darwin University , [3] BlueCare, [4] UQ

Background

Family carers provide pivotal support to enable people living with dementia (PLWD) to live at home. Breaks, through respite, are needed to sustain the caring relationship. However, respite options are not meeting family carers needs. BlueCare Community, a large aged care and community services provider, engaged Wesley Research Institute to conduct an explorative, interpretivist research project to understand the perspectives of family carers and PLWD. The aim was to inform implementation of a dementia In-home respite service.

Methods

Three locations across Queensland were engaged. Purposeful and snowballing sampling were used. Interviews and focus groups with PLWD and family carers, field notes and participant observations were used.

Results

Eleven family carers and four clients participated. Five themes were inductively derived.

1. Give me a break: Family carers need a break, they are exhausted, socially isolated and have emotional, physical, and psychological needs which go unmet because of prioritising their caring role.
2. Enabling and hearing their voice: family carers want to be heard and have input into the service.
3. Family carers need safety, rapport, and trust: both at an individual level and organisational level.
4. Family carers want to understand administration and costs: there was confusion about service costings and an expressed need for transparency about costs of the respite service.
5. Service model specifics: related to staffing preferences and consistency of care.

Discussion

These findings can guide service adaptation to appropriately meet family carers' and PLWD's needs. Addressing these needs fosters implementation of the Royal Commission into Aged Care Quality and Safety's recommendations: "1.3.c. Enable people entitled to aged care to exercise choice and control in the planning and delivery of their care and 3.a.ii Putting older people first so that their preferences and needs drive the delivery of care' (1.).

A Multimodal Dyadic Sleep Intervention for Care Partners and Individuals Living with Dementia: A Pilot Feasibility Study

Susan McCurry [1], Ann Piestch [2], Prerna Varma [3], Rosemary Gibson [4], Melinda Jackson [3], Marina Cavuoto [5], Tom Valenta [2], Jingling Huang [3], Michael Woodward [6], Aimee Brown [3], Sumedha Verma [7], Bei Bei [3]

[1] University of Washington, [2] Independent researcher, [3] Monash University, [4] Massey University, [5] National Ageing Research Institute, [6] Austin Health, [7] Eating Disorders Victoria

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Background

Sleep disturbances are commonly associated with dementia and frequently impact the sleep of caregivers. Currently, there are limited interventions specifically designed to address sleep disturbances and improve wellbeing within the intricate dynamics of caregiver and person living with dementia dyads. This research examined the feasibility of a tailored, multi-component sleep intervention program for dyads of primary caregivers and people living with dementia.

Methods

Using a single-arm feasibility approach with a repeated measures design, the study delivered a six-week virtual sleep intervention. The intervention combined Cognitive Behavioural Therapy for Insomnia with mindfulness and physical activity interventions, and light therapy. Feasibility was assessed via program adherence rates and satisfaction levels, measured by the Client Satisfaction Questionnaire and a post-intervention evaluation survey. Sleep disturbance and psychological wellbeing were measured using the Insomnia Severity Index and the Depression Anxiety Stress Scale-21, respectively. Feasibility outcomes were evaluated descriptively and qualitatively, and secondary outcomes were analysed using linear mixed effects models.

Results

Eighteen dyads (n=36 participants) successfully completed the program. Four dyads withdrew prior to the intervention, and one dyad withdrew after commencement. Seven caregivers attended all sessions, while 7 missed one session. Dyads expressed high satisfaction with the program, particularly commending the quality of training and most willing to recommend the program to others. Post intervention revealed significant improvements in insomnia severity for caregivers (p=.008) and both insomnia severity (p=.006) and depressive symptoms (p=.008) for people living with dementia.

Discussion

This study provides promising initial support for a virtually delivered, multi-component sleep intervention designed for dyads caregivers and people living with dementia. There were high levels of engagement and satisfaction, alongside preliminary evidence of improved sleep and psychological wellbeing. These findings highlight the importance of a holistic approach to supporting sleep and wellbeing of both caregivers and people living with dementia.

Genetic Variation within the Aquaporin-4 Gene Alters the Relationship Between Sleep and Cortical Amyloid Beta Levels.

Dr. Vincent Dore [1, 2, 3], Prof. Christopher Rowe [3, 4], Prof. Simon. M. Laws [1, 5, 6], Ayeisha Milligan Armstrong [5, 6], Dr. Pierrick Bourgeat [2], Dr. Eleanor O'Brien [1, 5], Dr. Tenielle Porter [1, 5, 6], Prof. Victor. L. Villemagne [1, 3, 7], A/Prof. Stephanie Rainey-Smith [8], Prof. Paul Maruff [4, 9]

[1] Centre for Precision Health, Edith Cowan University, WA, Australia, [2] Australian E-Health Research Centre, CSIRO, Australia, [3] Department of Molecular Imaging and Therapy and Centre for PET, Austin Health, VIC, Australia, [4] Florey Institute of Neuroscience and Mental Health, The University of Melbourne, VIC, Australia, [5] Collaborative Genomics and Translation Group, School of Medical and Health Sciences, Edith Cowan University, WA, Australia, [6] Curtin Medical School, Curtin University, WA, Australia, [7] Department of Psychiatry, University of Pittsburgh, PA, USA, [8] Centre for Healthy Ageing, Murdoch University, WA, Australia, [9] Cogstate Ltd, VIC, Australia

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Background

The glymphatic system has been suggested as an important clearance mechanism for amyloid-β (Aβ) during sleep. Animal and cellular models have suggested this clearance mechanism involves the water-channel protein, Aquaporin-4 (encoded by the AQP4 gene), located primarily in the astrocytic end-feet. We have previously reported on the interaction between genetic variants within AQP4, sleep and cross-sectional cortical amyloid-β (Aβ) burden. This study investigated the relationship between AQP4 genetic variants, sleep, and changes in cortical Aβ levels.

Methods

This study assessed cognitively unimpaired individuals enrolled in the Australian Imaging, Biomarker and Lifestyle (AIBL) Study of Ageing, who were Aβ accumulators (n=319). Aβ accumulators were defined as those who had a high baseline cortical Aβ (centiloid ^{3}20), or a positive rate of change in cortical Aβ, calculated using a minimum of 3 study time-points. 13 AQP4 gene variants were selected for analysis, and sleep was assessed using measures calculated from the Pittsburgh Sleep Quality Index (PSQI) questionnaire. The relationship between AQP4 gene variants and rate of Aβ accumulation was investigated using linear regressions. Additional linear regression models with AQP4 variant x sleep measure interaction terms and post-hoc simple slopes were analysed to assess how these relationships may influence Aβ accumulation.

Results

AQP4-rs68006382 was associated with Aβ accumulation, where minor allele carriers/homozygotes were observed to have a higher rate of accumulation when compared to major allele homozygotes. Linear regressions with AQP4 variant x sleep measure interaction terms revealed that it in AQP4-rs68006382 minor allele carriers there was a significant relationship between Aβ accumulation and sleep quality. Additionally, interaction analysis revealed a relationship between Aβ accumulation and sleep latency in AQP4-rs3875089 minor allele carriers.

Conclusion

The results of this study confirm our previous findings and suggests that interactions between AQP4 genotypes and sleep measures are also associated with the rate of Aβ accumulation.

Genetic Variation within the Melanopsin Gene is Associated with Cognition and Moderates the Relationship of Sleep with Cognition in a Cohort of Older Adults.

Dr. Tenielle Porter [1, 2, 3], Dr. Vincent Dore [1, 4, 5], Assoc. Prof. Stephanie Rainey-Smith [6], Dr. Eleanor O'Brien [1, 2], Ayeisha Milligan Armstrong [1, 2, 3], Prof. Victor L. Villemagne [5, 7], Dr. Pierrick Bourgeat [4], Prof. Simon M. Laws [1, 2, 3], Prof. Paul Maruff [8, 9], Prof. Christopher Rowe [5, 8]

[1] Centre for Precision Health, Edith Cowan University, WA, Australia, [2] Collaborative Genomics and Translation Group, School of Medical and Health Sciences, Edith Cowan University, WA, Australia, [3] Curtin Medical School, Curtin University, WA, Australia, [4] Australian E-Health Research Centre, CSIRO, Australia, [5] Department of Molecular Imaging and Therapy and Centre for PET, Austin Health, VIC, Australia, [6] Centre for Healthy Ageing, Murdoch University, WA, Australia, [7] Department of Psychiatry, University of Pittsburgh, PA, USA, [8] Florey Institute of Neuroscience and Mental Health, The University of Melbourne, VIC, Australia, [9] Cogstate Ltd, VIC, Australia

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Background

Melanopsin is a photopigment which mediates physiological processes including circadian rhythm, pupillary light response, endocrine regulation, and sleep-wake cycles. Animal studies show that melanopsin is at least in part responsible for mediating the association of light with cognition, long-term potentiation, neonatal cortical synaptogenesis, learning and sleep homeostasis. Disruptions to sleep cycles and circadian rhythms are often observed in people living with Alzheimer's disease (AD), and poor sleep has been associated with amyloid-β (Aβ) burden and reduced cognitive performance. Given the role of melanopsin in processes that are often disrupted in AD, such as sleep cycles, and its role in mediating the effects of light on cognition, the aim of this study was to investigate the role of melanopsin genetic variants on cross-sectional AD-related phenotypes; cognition, brain volumes and Aβ.

Methods

This study included data from cognitively unimpaired participants of the Australian Imaging, Biomarker and Lifestyle Study of Ageing. Six single nucleotide polymorphisms (SNPs) within the melanopsin gene (OPN4) were selected for analysis. Linear regression analyses were undertaken to investigate the relationship of these OPN4 SNPs, with Aβ, cognition, brain volumes and sleep traits measured by the Pittsburgh Sleep Quality Index (PSQI). To investigate whether sleep traits moderate the relationship of OPN4 SNPs with AD-related phenotypes, analyses were also run with a SNP x sleep trait interaction term.

Results

OPN4 SNPs rs2355009 and rs3740334 were associated with attention and processing speed, and with ventricular volume and language performance respectively. No significant associations were observed between OPN4 SNPs and Aβ or sleep traits. However, two SNPs (rs3740334 and rs1079610) showed significant interactions with multiple sleep traits in association with language performance.

Discussion

This is the first study to reveal associations of OPN4 genetic variants with AD-related phenotypes, and suggests these variants interact with sleep to exacerbate effects on cognition.

The Efficacy of Facial Emotion Recognition Task Performance in Predicting Risk and Early Stage Dementia

Michelle Lupton [1], Michael Breakspear [2], Renate Thienel [2], Jessica Adsett [1], Nicholas Martin [1], Caroline Faucher [2], Lina Gomez [1], Kerrie McAloney [1], Niklas Schultze [1]

[1] QIMR Berghofer Medical Research Institute, Brisbane, Queensland, Australia, [2] The University of Newcastle, Newcastle, Australia

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Background

Facial emotion recognition (FER), defined as recognising and interpreting emotions through facial expressions, is facilitated by the prefrontal and temporal cortical regions, including visual perception, attention modulation, and memory integration. FER impairment has been demonstrated in those living with different types of dementia and mild cognitive impairment (MCI). However, there has not yet been a comprehensive investigation of how an FER task could perform as a prodromal marker of Alzheimer's disease.

Methods

As part of the Prospective Imaging Study of Ageing (PISA), 967 adults aged 43-77 completed a self-administered online Emotion Recognition Task. During the task, dynamically morphed facial expressions of the six basic emotions (surprise, happiness, sadness, fear, disgust and anger) are presented at different levels of intensity using morphed video clips (Kessels et al. 2014). This sample has a large phenotypic data set available including genome-wide genetic SNP chip data, self-report survey data and cognitive testing.

Results

Preliminary analyses demonstrated significant associations of FER with higher levels of education, younger age, and female sex, as seen in previous literature. Further results will be presented following analysis of the association of FER with genetic risk of Alzheimer's disease (APOE ε4 status, and polygenic risk scores (PRS)), and prodromal AD phenotypes including measures of cognition and functional decline. Sex, age, level of education and socioeconomic status will be taken into account.

Discussion

Using our large sample size we will determine whether a deficit in FER is associated with both genetic risk of AD and early stage, prodromal phenotypes. This will give insight into the earliest cognitive changes in AD, and test whether an easy to administer computerized FER task could be used as an affordable screening tool in the identification of those at the earliest stages of AD.

Clinical Pharmacology and Development of Xanamem, A Tissue-Specific Inhibitor of 11β-HSD1

Prof. Paul Maruff [1, 2], Prof. Paul Rolan [3], A/Prof. Christopher Chen [4], Dr. Colin Farrell [5], Prof. Jonathan Seckl [6], Prof. John Harrison [7, 8, 9,] A/Prof. Michael Woodward [10], Dr. Jack Taylor [3]

[1] Cogstate Ltd., Melbourne, VIC, Australia, [2] Florey Institute of Neuroscience and Mental Health, Parkville, VIC, Australia, [3] Actinogen Medical, Sydney, Australia, [4] Memory Ageing and Cognition Centre, National University Health System, Singapore, Singapore, [5] ICON Inc., Dublin, Ireland, [6] University of Edinburgh, Edinburgh, United Kingdom, [7] Scottish Brain Sciences, Edinburgh, United Kingdom, [8] King's College, London, United Kingdom, [9] Alzheimercentrum, AUmc, Amsterdam, The Netherlands, [10] Austin Health, Melbourne, VIC, Australia

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Background

Selecting the optimal dose for clinical development is especially problematic for drugs directed at CNS-specific targets. We describe the approach to dose selection and clinical pharmacology of Xanamem, a tissue-specific inhibitor of 11β-HSD1, which is under clinical development as a pro-cognitive and disease modifying drug for Alzheimer's disease.

Method

Plasma pharmacokinetics (PK), endocrine, PET imaging, and cognitive data were evaluated over a daily dose range of 5mg to 70mg in 6 clinical trials. PK was summarized by a population PK model using data from 4 clinical trials. A PET imaging trial used the displacement of 11C-TARACT tracer to measure target occupancy in the brain after 7 days of Xanamem therapy with doses of 5mg to 30mg daily. Detailed hormonal assessment of the hypothalamic-pituitary-adrenal (HPA) axis was conducted with doses of 10mg to 70mg daily and computerized cognitive testing with doses of 5mg to 20mg daily

Results

PK were consistent across subgroups with only one covariate relationship between V/F and body weight. Plasma cortisol decreased slightly 3-5hrs after a first dose of 10mg but not at later timepoints. ACTH levels were consistently elevated by 2-fold without a dose-response relationship. While testosterone concentration did not increase with 10mg, DHEAS and androstenedione levels were increased by approximately 50%. PET imaging showed a relatively flat dose response relationship ≥5mg with median 11β-HSD1 occupancies >60% in all regions at ≥10mg mane. Two trials observed improved attention and working memory with Xanamem compared to placebo. The magnitude of cognitive improvement from baseline was similar for the 5mg, 10mg and 20mg dose levels.

Conclusion

Computerized cognitive testing provided central pharmacodynamic confirmation of the target and ≤10mg daily dose range suggested by PET imaging and HPA hormonal measurements. There is a high degree of confidence that Xanamem ≤10mg daily will be pharmacologically active in the brain.

Role of Lauric Acid in Alzheimer's Disease Brain

R.M Uththara S. Senarath [1, 2], Lotta E. Oikari [3], Prashant Bharadwaj [1, 2], Vijay Jayasena4, Ralph N. Martins [1, 2, 5, 6], W.M.A.D. Binosha Fernando [1, 2]

[1] School of Medical and Health Sciences, Edith Cowan University, Western Australia, Australia, [2] Australian Alzheimer's Research Foundation, Ralph and Patricia Sarich Neuroscience Research Institute, Nedlands, Western Australia, Australia, [3] Cellular and Molecular Neurodegeneration, QIMR Berghofer Medical Research Institute, [4] Nutrition and Food Science, School of Science, Western Sydney University, Australia, [5] Lions Alzheimer's Foundation, Nedlands, Western Australia, Australia, [6] Department of Biomedical Sciences, Macquarie University, Sydney, New South Wales, Australia

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Background

Numerous neurodegenerative disorders, including Alzheimer's disease (AD), have been linked with activation of inflammatory pathways, oxidative stress and mitochondrial dysfunctions. Lauric acid present with neuroprotective effects which are due to its ability to provide an alternative source of energy for neurons through the production of ketone bodies by astrocytes. A substantial amount of direct evidence as well as comprehensive studies has been conducted, but little has been done to specifically investigate the effects of lauric acid on the brain. However, the mechanism involving lauric acids neuroprotection is still unclear. By combating inflammation and oxidative stress, lauric acid is an excellent antioxidant, which helps to reduce the aetiology of AD. In this study, we seek to further understand the influence of lauric acid on astrocytes and neurons derived from Induced pluripotent stem cells (iPSCs).

Method

Lauric acid were administered to cultures of astrocytes, neurons derived from iPSCs obtained from a healthy human control subject. Inflammatory responses of astrocytes and neurons were measured under synthetic amyloid beta stimulating conditions similar to AD.

Results

Lauric acid had modulatory effects on pro- and anti-inflammatory cytokines following amyloid-beta exposure, suggesting its immunomodulatory effects.

Conclusions

The findings indicate that lauric acid inhibit inflammation in Alzheimer's-induced astrocytes and neurons.

Longitudinal Changes in Cognitive Function are Associated with Changes in Fasting Plasma Insulin, Fasting Plasma Glucose and Insulin Resistance in the Australian Imaging, Biomarker and Lifestyle (AIBL) Study of Ageing.

Simon M Laws [1, 2, 3], Amy Woodfield [1, 4], Giuseppe Verdile [1, 4, 5], The AIBL Research Group [6], Tenielle Porter [1, 2, 3], David Groth [1, 4]

[1] Curtin Medical School, Curtin University, Bentley, Australia, 6102, [2] Centre for Precision Health, School of Health and Medical Sciences, Edith Cowan University, Joondalup, Australia, 6027, [3] Collaborative Genomics and Translation Group, School of Health and Medical Sciences, Edith Cowan University, Joondalup, Australia, 6027, [4] Curtin Health Innovation Research Institute, Curtin University, Bentley, Australia, 6102, [5] School of Health and Medical Sciences, Edith Cowan University, Joondalup, Australia, 6027, [6] The Australian Imaging, Biomarker and Lifestyle Study of Ageing

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Background

Insulin resistance has been associated with cognitive impairment and may contribute to the development of Alzheimer's Disease (AD). However, at what stage of AD progression insulin resistance has the greatest impact remains unclear. Our previous analyses in AIBL reported cross-sectional associations between insulin resistance, cognition, and AD biomarkers. In this longitudinal study, the relationship between insulin resistance (HOMA-IR), fasting plasma insulin (FPI), fasting plasma glucose (FPG) and cognitive change was explored.

Methods

Linear mixed modelling was used to assess if baseline FPI, FPG or HOMA-IR predict cognitive change, whilst associations between longitudinal FPI, FPG or HOMA-IR and cognitive change were explored using linear regression analyses. Contributions of sex, brain amyloid-B (AB) burden and APOE-e4 status were also explored.

Results

Baseline FPI, FPG and HOMA-IR were not independent predictors for cognitive change. However, in the context of sex and brain AB burden, significant associations were observed. Lower baseline FPI was associated with executive function decline in males and a decline in both visual recognition and language processing in participants with high brain AB burden. High brain AB burden and APOE-e4 status also influenced the relationship between FPG and cognition. In participants with high brain AB burden, increasing FPG was associated with a decline in verbal episodic, visual recognition, and global cognition. In APOE-e4 carriers, increasing FPG was associated with verbal episodic memory decline. Longitudinal increases in FPI and HOMA-IR were associated with a decline in visual recognition and increases in FPG were associated with executive function decline.

Discussion

Our findings indicate that baseline FPI, FPG or insulin resistance aren't independently associated with cognitive change. Rather, a relationship was only observed assessing change in these indices. The study provides insight into the relationship between glucose homeostasis measures and decline in specific cognitive domains, which has implications for interventions targeting such measures.

Associations of C-reactive Protein and Homocysteine with Neuropsychological Outcomes in Older Adults at Risk of Dementia

Kimberley Bassett (MClinNeuroPsy) [1], Catriona Ireland (MBBS FRACP) [1], Johannes Michaelian (PhD) [1], Shawn Kong (PhD) [1], Sharon Naismith (DPsych) [1], Rachael Yu [1]

[1] The University of Sydney

Background

Inflammation is becoming increasingly recognised as a core feature of dementia and neurodegenerative processes. High-sensitivity C-reactive protein (hs-CRP) and homocysteine are blood-based markers of non-specific inflammation used in clinical settings. This study aimed to 1) investigate the associations of hs-CRP and homocysteine on neuropsychological performance (i.e. verbal memory, executive function, processing speed) in older adults attending a memory clinic; and 2) examine whether these associations differed for individuals at varying risk stages of dementia, i.e. with subjective cognitive decline (SCD) vs. mild cognitive impairment (MCI).

Methods

We recruited older adults aged ≥ 50 years with new-onset cognitive concerns without dementia. A fasting blood sample was used to obtain concentrations of serum hs-CRP (mg/L) and plasma homocysteine (µmol/L). Hs-CRP levels were grouped into low <1.0mg/L, moderate 1.0-3.0mg/L, and high >3.0-10.0 mg/L. Composite scores for each neuropsychological outcome were calculated as an average of z-scores of all tests within the same domain. Multiple regression analyses were conducted, adjusting for relevant demographic and clinical factors.

Result

The final sample consisted of 423 participants (Mean age = 67.37 years [SD = 8.15], 63.1% female, mean MMSE = 28.95 [SD = 1.35]), who were classified as either having SCD (n = 158) or MCI (n = 265). Hs-CRP and homocysteine concentrations did not differ between SCD and MCI groups. In participants with SCD, high-risk CRP concentrations were significantly associated with poorer executive function (β = -.226, 95% CI = [-0.692, -0.059], p = .020) and processing speed (β = -.212, 95% CI = [-0.584, -0.025], p = .033). There were no significant associations between CRP and neuropsychological outcomes in those with MCI, or in the total sample. Homocysteine was not associated with cognitive outcomes.

Conclusion

CRP may be involved in early disruptions to cerebral frontal-subcortical pathways. Targeting inflammation in the earliest stages of cognitive decline, where subjective complains are paramount, may be a viable strategy for prevention.

Cross-Sectional and Longitudinal Associations Between Cognitive Domains and Attitudes to Ageing in Older Australians

Serena Sabatini [1], Perminder S Sachdev [2], Henry Brodaty [2], Katya Numbers [2], Nichole A Kochan [2]

[1] School of Psychology, Faculty of Health and Medical Sciences, University of Surrey, Guildford, UK, [2] Centre for Healthy Brain Ageing (CHeBA), Discipline of Psychiatry & Mental Health, School of Clinical Medicine, University of New South Wales, Sydney, AU

Background

Age-related changes in cognition can impact self-perceptions of ageing (SPAs), which in turn influences attitudes towards the ageing process. Positive SPAs are associated with a better physical and mental health, while negative SPAs are related to worse health and quality of life. We examine the association between SPAs, cognitive performance, and cognitive decline, in a sample of older Memory and Ageing Study (MAS) participants.

Methods

Participants were 258 older adults (M=87.43; SD=3.60; 60% women) from (MAS) with complete wave 7 (14-year follow-up) data. Comprehensive neuropsychological testing resulted in z-scores for domains of attention/processing speed, language, executive functions, visuospatial abilities, and memory; these were averaged to form a composite global cognition z-score. SPAs were scores from the Attitudes to Ageing Questionnaire (AAQ), which is comprised of three subscales: psychological growth, psychosocial loss, and perceived physical change. Multiple linear regression models were run to determine the association between domain and global cognition scores, and the three AAQ subscales scores, cross-sectionally (baseline) and longitudinally (wave 7), adjusting for covariates.

Results

Cross-sectionally, higher executive functions (B=0.75; 95% CI: 0.19,1.31), visuospatial abilities (B=0.59; 95% CI: 0.01,1.16), memory (B=1.00; 95% CI: 0.26,1.74), verbal memory (B=1.01; 95% CI: 0.29,1.73), and global cognition (B=0.81; 95% CI: 0.02,1.61) scores were associated with subjective physical change. Longitudinally, decline in executive function (B=-0.78; 95% CI: -1.43,-0.12) and global cognition (B=-1.06; 95% CI:-2.04,-0.08) score were associated with subjective physical change. No significant associations were found for psychological growth or psychosocial loss cross-sectionally or longitudinally.

Discussion

Current cognitive ability was associated with perceived physical change, suggesting an immediate influence of cognitive functioning on perceptions of ageing. Longitudinal associations indicate a more nuanced relationship between actual cognitive decline and perceived physical change. Further research is required to understand the complex relationship between cognitive decline and SPAs over time.

Community Informed Development of, and Recruitment to Validate, a New Measure for Use in the Cognitive Assessment of Culturally and Linguistically Diverse Older Adults, the Characterising Language Experience and Acculturation Questionnaire (CLEAr-Q)

Zara Page [1], Dr. Nicole Kochan [1], Dr. Karen Croot [1], Prof. Henry Brodaty (AO) [1]

1Centre for Healthy Brain Ageing (CHeBA), UNSW Sydney

Background

Older adults from culturally and linguistically diverse (CALD) backgrounds are underrepresented in, and often excluded from, dementia research. A new measure, the Characterising Language Experience and Acculturation Questionnaire (CLEAr-Q) was developed with community consultation to provide a brief measure of language and cultural factors known to influence performance on cognitive tests used in mild cognitive impairment and dementia assessments. We introduced a Community Working Group as an ongoing, small-scale approach to community consultation via an adapted participatory research framework. The aim of the Working Group was to involve and engage older CALD community members in the design and implementation of an online survey validation of the CLEAr-Q.

Methods

Purposive sampling was used to recruit Working Group members (four individuals aged 60+ who reported speaking a language other than English [LOTE] and volunteered from the CogSCAN Study). Working group members provided input on research priorities, design, and recruitment strategies in response to structured questions during Stage One (Online Focus Group). Key themes were summarised and circulated for further feedback during Stage Two (Preliminary Report and Feedback). Stage Three (Face-to-face Workshop) will follow analysis of validation data.

Results

Key recommendations included highlighting that survey responses were anonymous and clearly describing the purpose and motivations of the research in culturally informed lay terms. Recruitment of validation sample proved challenging, requiring multiple nationwide approaches including StepUp for Dementia Research platform, community events, social and traditional media. The validation sample consists of 244 participants aged 60-90 who were born in over 50 overseas countries and speak on average more than two languages. Data analysis is in progress.

Conclusion

Participatory research approaches are especially important to achieve culturally appropriate study designs and representative samples, and to address health disparities in dementia research by improving community engagement and awareness of the research process in its entirety.

Temporal Patterns of Eating and Their Associations with Cognitive Performance in Older Australian Adults: An Exploratory Cross-sectional Study

Dan Ping (Jaslie) Wu [1], Dr. DorotheaDumuid [1], Dr. Maddison Mellow [1], Emeritus Prof Timothy Olds [1], Prof Jillian Dorrian [2], Prof Alison Coates [1], Prof Frini Karayanidis [3], A/Prof Ashleigh Smith [1]

[1] Alliance for Research in Exercise, Nutrition and Activity, Allied Health and Human Performance, University of South Australia, [2] UniSA Justice and Society, University of South Australia, [3] Functional Neuroimaging Laboratory, School of Psychological Sciences, College of Engineering, Science and the Environment, University of Newcastle

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Background

How people use their time and what they eat have been associated with cognitive performance. Most studies to date have focused on what activities people engage in (e.g., how much physical activity and sleep) and what/how much they eat (healthy diet), with few studies considering if the timing of activities such as eating, sleeping and physical activity are important for cognition. This study aimed first to describe the temporal patterns of eating in a cohort of older adults (ACTIVate) and then explore associations of these temporal patterns of eating with cognition.

Methods

Four hundred forty-eight community-dwelling adults aged 60-70 were recruited as part of the ACTIVate study in Adelaide and Newcastle, Australia. To explore the type and timing of daily activities, all participants recalled their past two days of activities in minimum 5-minute intervals using the Multimedia Activity Recall for Children and Adults (MARCA). Cognition was measured by a series of cognitive tests, including ACE-III.

Results

The first part of the analysis is primarily descriptive and summarised the demographics for temporal eating patterns in the ACTIVate study's baseline data. The second step used linear regression models to explore the associations between temporal eating and cognitive outcomes, with covariates including age, sex, BMI, and years of education.

Discussion

There were no associations between eating window or eating occasions and ACE after adjusting for covaries. Age moderated the relationship between the length of the eating window and the ACE score; with older age, a longer eating window was associated with higher ACE scores, whilst with younger age, a longer eating window was associated with lower ACE scores.

Neuropsychological Predictors of Cognitive Decline in Parkinson's Disease: A Systematic Review (PDCogniCare)

Daniel Bailey [1], Kumareshan Sivakumaran [1], Jihyun Yang [1], Deborah Brooks [1], Dana Pourzinal [1], Leander Mitchell [1], Nadeeka Dissanayaka [1]

[1] University of Queensland Centre for Clinical Research

Background

Variability in neuropsychological measures used to assess cognition in Parkinson's disease (PD) attributes to heterogeneity of observed cognitive function in PD in clinical and research settings. We aimed to systematically review current literature evaluating neuropsychological predictors of cognitive decline in PD.

Methods

Systematic searches for cognitive predictors of longitudinal cognitive decline and dementia in PD were performed following PRISMA guidelines. Articles published up to July 2023 from PubMed, SCOPUS, Medline, PyscINFO and CINAHL databases were included. Risk of bias was assessed using the Newcastle-Ottawa scale for individual studies and recommendations for each cognitive outcome were made using the GRADE system.

Results

Twenty-eight relevant articles with moderate to low risk of bias were included. Category verbal fluency, Symbol Digit Modalities Test, Trail-making A, and immediate verbal memory were highly recommended and produced the strongest evidence base. The Stroop test, Letter Number Sequencing, pentagon copying, Trail-making B and delayed verbal and visual memory were recommended. Letter fluency and digit span measures produced consistent evidence against their predictive utility and were not recommended. Montreal Cognitive Assessment was recommended as a measure of global cognition, while the Mini Mental State Examination produced mixed evidence.

Conclusions

The present review summarised key evidence for the predictive utility of neuropsychological measures for cognitive decline in PD. Ultimately, the review will inform recommendations for an evidence-based cognitive toolkit for the evaluation of cognitive impairment in PD (PDCogniCare).

Possibility of Delaying Alzheimer's Disease (AD): Altering Gut Microbiota Composition through Lifestyle Modifications

Dr. Samantha Ramachandra [1], Dr. WMAD Binosha Fernando [2], Professor Hamid Sorhabi [3], Professor Ralph Martins [4]

[1] PhD Reader, Centre of Excellence for Alzheimer's Disease Research and Care, School of Medical and health Sciences, Edith Cowan University, [2] Research Fellow, Centre of Excellence for Alzheimer's Disease Research and Care, School of Medical and health Sciences, Edith Cowan University & Alzheimer's Research Australia, Ralph and Patricia Sarich Neuroscience Research Institute, Nedlands, WA 6009, [3] Professor in Psychology and Clinical Neuroscience, Director, Murdoch University Centre for Healthy Ageing, Murdoch University & Alzheimer's Research Australia, Ralph and Patricia Sarich Neuroscience Research Institute, Nedlands, WA 6009, [4] Professor, Centre of Excellence for Alzheimer's Disease Research and Care, School of Medical and health Sciences, Edith Cowan University, Chair in Alzheimer's Research Australia, Ralph and Patricia Sarich Neuroscience Research Institute, Nedlands, WA 6009 & Professor, Department of Biomedical Sciences, Faculty of Medicine, Health and Human Sciences, Macquarie University, Sydney, NSW 2109, Australia

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Background

Traditionally, the role of gut microbiota in human health was focused on aspects like immunity, appetite, and energy metabolism. However, recent research has unveiled the impact of changes in gut microbiota on brain function and behavior. This influence operates through diverse mechanisms, including heightened amyloid deposits, tau phosphorylation, neuroinflammation, metabolic dysfunctions, and chronic oxidative stress, which are pathological pathways of Alzheimer's disease (AD). Findings are particularly important in opening new avenues to explore disease prevention strategies. Research indicates that diet and physical activity exert powerful, modifiable, bidirectional influences on gut microbiota composition.

Methods

The proposed project aims to investigate the impact of gut dysbiosis, physical activity, and dietary patterns on cognitive functions in Alzheimer's disease (AD). Participants are categorized into four subgroups: cognitively normal without Aβ deposition, cognitively normal with Aβ deposition, mild cognitive impairment, and AD. Single-point fecal samples will be collected for microbiota composition analysis using shotgun metagenomic methods. Cognitive performance data (Neurological battery test), dietary patterns (Cancer Council of Victoria Food Frequency Questionnaire), and physical activity levels (International Physical Activity Questionnaire) will be extracted from existing data of a large cohort study. Multiple regression analysis will be used to assess the effects of these factors on both gut dysbiosis and cognition.

Results

The research is at the data collection stage and preliminary results might be available by the time of presentation.

Discussion

This study aims to investigate the impact of diet and physical activity on gut microbiota composition in cognitively normal individuals (Aβ +ve/-ve), those with Mild Cognitive Impairment (MCI), and AD patients. Time series analysis will reveal the connection between diet, physical activity, and cognitive decline, independent of gut microbiota changes. Integrating these findings with existing evidence will provide a solid foundation for developing interventions aimed at delaying the onset and progression of AD.

Baseline Demographic, Risk and Cognitive Characteristics of the Final Randomised Sample Enrolled in a Decentralised Multi-Domain Lifestyle Intervention Trial (BetterBrains) to Delay Cognitive Decline

Matthew P. Pase [1], Maya Norfolk [1], Gabrielle Da Costa [1], Darshini Ayton [2], Leonid Churilov [3], Yen Ying Lim [1], Paul Maruff [1, 4], Amy Brodtmann [5], Ashley I. Bush [6], Hannah Cummins [1], Chris Barton [7], Emily Rosenich [1], Nawaf Yassi [1], Richard O. Sinnott [8], Stephanie Pirotta [2]

[1] Turner Institute for Brain and Mental Health, Monash University, [2] School of Public Health and Preventive Medicine, Monash University, [3] Melbourne Medicial School, University of Melbourne, [4] Cogstate Ltd., [5] Department of Neuroscience, Central Clinical School, Monash University, [6] Florey Institute of Neuroscience and Mental Health , [7] Department of General Practice, Monash University, [8] School of Computing and Information Systems, Melbourne School of Engineering, University of Melbourne

Background

BetterBrains is a prospective behaviour-modification blinded endpoint randomised controlled trial to delay cognitive decline in middle-aged adults (aged 40-70) with a family history of dementia. The primary outcome is absence of decline on at-least one out of four cognitive tests at 24-months. We present trial recruitment and current participant completion statistics and baseline demographic, modifiable dementia risk factor (MDRF) and cognitive characteristics of the randomised sample, blinded to intervention arm.

Methods

Participants completed online assessments (betterbrains.org.au), including assessment of vascular, sleep, mood, and social/cognitive engagement MDRFs. Participants with ≥1 MDRF were eligible. Participants completed assessments of cognition, general health, medical history, and lifestyle factors at baseline, 12- and 24-months. Unsupervised cognitive testing was conducted using the Cogstate Brief Battery. Subjective cognition was assessed using a modified Cognitive Function Instrument.

Results

From August 2021 to July 2023, 1830 participants enrolled and 1053 (57%) were randomised. Randomised participants were, on average, 59.7 (±6.8) years, 83% women, 90% highly educated (< or =12 years of education), 93% White, and 86% reported a first-degree dementia family history. Importantly, 27% resided in regional or rural Australia. Participants showed a mean Cardiovascular Risk Factors, Ageing and Incidence of Dementia risk score (without APOE) of 6.3 (max=15). Baseline cognitive performance scores will be presented. To date, 61% and 70% of randomised participants have completed the 12- and 24-month assessments (respectively), with study attrition at 3%.

Conclusion

Participants exhibit some increased dementia risk, indicated by high prevalence of first-degree family history, female gender, and prevalent MDRFs. Participant characteristics are similar to those observed within other lifestyle intervention trials. The finding that 27% of the sample resides in regional or rural Australia highlights that the BetterBrains methodology facilitates inclusion of hard-to-reach populations. Low attrition and high follow-up rates suggest that the BetterBrains program is acceptable and feasible.

Demographic, Clinical and Alzheimer's Disease Risk Characteristics Associated with Interest in APOE Disclosure Amongst Middle-Aged Australian Adults

Yen Ying Lim [1], Emily Rosenich [1], Tamar Foreman [1], Hannah Olver [1], Stephanie Perin [1], Jason Karlawish [2, 3], Ruby Haeusler [1]

[1] Turner Institute for Brain and Mental Health, Monash University, [2] Penn Healthy Brain Research Center, University of Pennsylvania, [3] Penn Memory Center, University of Pennsylvania

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Background

Clinical guidelines in Australia discourage disclosure of apolipoprotein E (APOE) genotypes but therapeutic advances will likely change this. Limited work has assessed interest in APOE disclosure in Australian adults, and it remains unclear which characteristics are associated with interest within this sample. This study aimed to describe interest in APOE disclosure and investigate differences in demographic/clinical characteristics and AD risk perceptions among adults with varying interest in disclosure.

Methods

Cognitively unimpaired middle-aged adults aged 40-70 (N=460) enrolled in the Healthy Brain Project or BetterBrains Trial completed the Knowledge, Interest and Preferences for APOE Testing and Disclosure questionnaire. Online assessments measured demographics, anxiety and depressive symptoms, subjective cognition, perceived AD risk, and knowledge of AD. Participants were categorised into groups based on interest in disclosure (interested/want more information/not interested). Frequencies described interest in APOE disclosure and perceived benefits and concerns. Kruskal-Wallis and chi-square tests assessed whether characteristics and AD risk perceptions differed between groups.

Results

Only 6% of participants were not interested, with most either interested (51%) or wanting more information about APOE (43%). Compared to those not interested, interested participants were younger, more knowledgeable about AD, more likely to report any dementia family history, had stronger beliefs in negative ageing stereotypes and about the benefits of engaging in protective health behaviours, had greater hope for an AD cure, and greater perceived risk of AD-related mortality. Amongst interested participants, motivation to change behaviours to reduce AD risk was the most common perceived benefit of disclosure (82%), whereas worry about attributing subtle memory changes to impending AD dementia was the most common concern (23%).

Conclusion

Most middle-aged adults sampled expressed interest in APOE disclosure in a research setting. Contrary to previous findings, subjective cognition did not influence interest. Results highlight that an array of biopsychosocial factors influence interest in APOE disclosure.

Digital Dementia Risk Screening Tools: A Scoping Review

Professor Kate Laver [1], A/Professor. Ashleigh E. Smith [2], Ms. Zandile Rwodzi [2], Ms. Dan Ping Wu [2], Dr. Dorothea Dumuid [2]

[1] Allied Health and Active Ageing, Department of Rehabilitation, Flinders University, SA, AU, [2] Alliance for Research In Exercise, Nutrition and Activity (ARENA), Allied Health and Human Performance, University of South Australia, SA, AUS.

Background

Digital dementia risk screening tools offer a promising avenue for conveying information about dementia and its risk factors. There is little information on currently available screening tools, their targeted audience, and the risk factors they include. This scoping review aims to provide an overview of existing tools, platforms of administration, inclusion of dementia risk factors, psychometric properties, target population, and settings of implementation.

Methods

A Population, Concept, Context framework was used to develop a search strategy. Four databases Embase, MEDLINE (Ovid), PsycINFO, and Google Scholar (grey literature) were searched. Studies conducted in adults aged over 18 years, published in English, focussed on risk of cognitive decline, mild cognitive impairment (MCI) and/or dementia risk screening were eligible for inclusion. Data extracted from eligible studies included study characteristics, target population and digital test features such as administration platforms, location settings and psychometric properties.

Results

11,152 articles identified in initial searches, with 11 studies (6 screening tools) meeting inclusion criteria. Studies included tools such as CogDrisk, ANU ADRI, Alzhe Alert, CAIDE, DRA and the deep learning algorithm of CAIDE. Of the 12 modifiable risk factors from the Livingston Lancet Report (2020), only 10 were identified in digital tools with hearing loss and air pollution notably absent. Tools were administered independently by individuals (8 studies) or clinicians (2 studies) in home or healthcare settings. Psychometric properties were only reported in two tools.

Conclusions

Evaluation of dementia risk screening tools reveals a focus on modifiable risk factors, yet two risk factors from the 2020 Lancet Report are absent in all tools. Despite ongoing research, no consensus on the most optimal tool has emerged, highlighting the need to consider additional risk factors beyond those conventionally assessed. Further investigation is warranted to ascertain the specific impact of various risk factors on dementia risk.

Genetic and Environmental Contributions to the Social Connections of Older Adults: the Older Australian Twins Study

Perminder S. Sachdev [1], Suraj Samtani [1], Anne-Nicole Casey [1], Ben C.P. Lam [1, 2], Henry Brodaty [1], Anbupalam Thalamuthu [1], Vibeke S. Catts [1]

[1] Centre for Healthy Brain Ageing (CHeBA), UNSW Sydney, [2] La Trobe University

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Background

Social connections are associated with cognitive health, but genetic and environmental influences on social connections in older age remains unclear. We explored the heritability of social connections and the influence of social connections on cognition using longitudinal twin data. We expected that social connections would be influenced by genetics and unique environment and associated with cognitive performance.

Methods

Data from 333 monozygotic and 266 dizygotic twins 65 years of age or older in the Older Australian Twins Study were collected at baseline, wave 2 and wave 3 follow-up. Target variables were social activity items and neuropsychological subtest scores for attention, memory, language, visuospatial function, and executive function. Analyses included exploratory structural equation modelling, univariate and multivariate twin modelling, and linear mixed-effects modelling. Covariates were age, sex, education, APOE4 status, hypertension, diabetes, smoking, alcohol use, history of depression, BMI, exercise, and hearing loss.

Results

Of three social connection dimensions identified – interacting with friends/neighbours/community, family interactions and childcare, and involvement in religious groups and caregiving, the first two had weak heritability and the third demonstrated none. Small-to-moderate genetic correlations revealed overlapping genetic influences for interactions with friends/neighbours/community with cognitive domains (range r=0.07-0.31). Small-to-moderate unique environmental correlations between cognitive domains and friend/neighbour/community interactions (range r= -0.18-0.03) and family/childcare interactions (range r= -0.17-0.07) were observed. Social connections were not associated with cognition longitudinally.

Conclusion

Interactions with friends/neighbours/community, and interactions with family and childcare were weakly heritable. There was moderate genetic and unique environmental influences affecting social connections and performance in individual cognitive domains. Social connections were not associated with cognitive change over 4 years among older adults in this study. Our findings highlight that social connections are largely environmentally driven, raising the possibility that they may be potentially improved via interventions.

Effect of Body Scanning and Walking Mindfullness on the Spatial Memory of Persons with Dementia

Mr. Gayan Karunarathna [1], Dr. Kanthi Hettigoda [2], Mr. Kumaranayake [1]

[1] University of Kelaniya, [2] University of Peradeniya

Background

As a non-pharmacological approach, mindfulness has become increasingly popular for people with dementia. Research has presented mixed results, which may partly relate to the different forms of mindfulness. This study aimed to compare the effect of two types of mindfulness (body scanning; walking) on spatial memory of people with dementia.

Methods

Sixty persons diagnosed with dementia based on the Sinhala version of the Mini Mental State Examination were recruited from residential aged care centers and community councils for elders in Sri Lanka (age range 55-80; 45% male; 65% >5 years education).

Adopting a pre/post design, participants were randomized into two experimental groups (body scanning meditation and walking meditation). Each intervention occurred for 15-minute group sessions for 3 days per week over 8 weeks. Spatial memory was assessed using the Rey-Osterrieth Complex figure.

Results

Mixed methods ANOVA, using Greenhouse-Geisser correction demonstrated a significant main effect of mindfulness practice where F (1, 58) =140.745, where P=0.000 which is less than 0.05 level and large effect size (partial eta squared = 0.708). The group effect and groupXmindfulness effect were not statistically significant. Although we ignore the type of mindfulness practice, there is an improvement of spatial memory score after practicing mindfulness in general.

Discussion

As participants underwent only one of the interventions, it can be noted that both appeared equally effective according to the findings. This study can be considered as a good endeavor of a pilot study on dementia research activity in Sri Lanka with the possibility of extending it into a highly controlled clinical trial in the future with an adequate sample size, with minimized effects of extraneous factors such as potential practice effects due to the same version of the Rey Osterrieth Complex Figure being used for both pre and post testing and, absence of a control group.

Incidence of Dementia Following Entry into Residential Aged Care: A National Retrospective Cohort Study

Tracy Air [1], Stephanie Harrison [1], Geraint Rogers [1], Tesfahun Eshetie [1], Andrew Shoubridge [1], Steven Taylor [1], Maria Inacio [1]

[1] South Australian Health and Medical Research Institute

Background

Dementia is Australia's second-leading cause of death and affects over half of those in residential aged care. As no effective treatments exist, prevention or delay of dementia onset is critical. While risk factors contribute to more than half of dementia cases globally, their contribution to outcomes within the Australian population specifically is poorly understood. Our goal was to relate risk profiles to the cumulative incidence of dementia diagnosis in an Australian residential aged care cohort.

Methods

A retrospective cohort study was conducted using the National ROSA Historical Cohort (N~3.5 million participants). Criteria for study inclusion were: 1) entry to residential aged care between 2009-2018, 2) age ≥65 years, 3) accessible hospital data, 4) no dementia diagnosis, 5) cognitive evaluation at entry into care. Individuals were characterised by demographics, healthcare, medications, and facility, and followed-up until end of 2019. Dementia diagnosis was ascertained from care assessments, and medication/hospital/mortality records.

Results

The cohort (n=96,865 individuals) had a median (interquartile range) age of 84 (79-88) years and was 64.3% (n=62,281) female. Of those included, 22.9% (n=22,218) had no/minimal cognitive impairment, 51.4% (n=49,740) had mild cognitive impairment, and 25.7% (n=24,907) had moderate-severe cognitive impairment at entry into aged care. During follow-up, n=23,876 (24.6%) received a dementia diagnosis with a median (interquartile range) time to diagnosis of 430 (184-814) days, with n=10,706 (44.8%) diagnosed at subsequent care assessment.

Conclusion

We have established a cohort of 96,865 older Australians who entered residential aged care between 2009-2018 that will provide the basis to understand the relationships between risk factors and dementia onset. Within our cohort, 24.6% received a dementia diagnosis, which could be because of risk factors, such as health or medication history. Understanding the contributions of risk factors to dementia progression in this cohort could inform opportunities to prevent/delay dementia onset in Australians entering care.

A Smell Clinic for Early Detection of Alzheimer's Disease

Ali Delbaz [1], James St John [1], Brent McMonagle [2]

[1] Griffith University, 2Gold Coast University Hospital

Background

Loss of the sense of smell is one of the earliest symptoms in Alzheimer's disease and can occur 10-20 years before cognitive decline is diagnosed. However, routine diagnostic testing for the sense of smell is not conducted in Australia. Our research has identified that some species of microorganisms within the nose can use the olfactory nerve to enter the brain where they induce a range of pathologies consistent with Alzheimer's disease. Therefore, assessing sense of smell in conjunction with detection of microorganisms, gene expression and protein changes may provide an early indication of the onset of Alzheimer's disease.

Methods

A pilot Smell Clinic was established. Volunteers underwent smell testing using the Sensonics Snap & Sniff identification, threshold and discrimination tests. Nasal swabs were used to obtain samples for next generation sequencing for identification of microorganisms, and for RNA and protein analysis.

Results

Healthy volunteers aged 20-60 underwent the smell testing to help develop the pipeline. There was a considerable range in the ability to detect odours across the healthy population. Nasal swab analysis for taxonomic composition derived from metagenomics 16S rRNA gene amplicon sequencing identified numerous microorganisms including Staphylococcus, Corynebacterium, Propionibacterium, Streptococcus, and Haemophilus. Nanostring RNA expression analyses detected differences in gene expression across the healthy samples.

Discussion/Conclusion

A pipeline for the Smell Clinic has been established using rapid assessment of odour detection, combined with intranasal sampling for next generation sequencing, RNA sequencing and proteomics. The Smell Clinic will now be expanded to test people (1) aged below 40 years, (2) 40-49 years, (3) 50-64 years, (4) 65+ years including people diagnosed with mild cognitive impairment. These rapid analyses will enable identification of individuals with heightened risk of developing Alzheimer's disease. Earlier diagnosis will enable earlier intervention which may reduce onset and progression of neurodegeneration.

Associations between BDNF Val66Met and Tau-PET and Episodic Memory Performance in Sporadic AD

Paul Maruff [1], Emily Rosenich [2], Diny Thomson [2], Yen Ying Lim [2]

[1] Cogstate Ltd, Melbourne, VIC, Australia, [2] Turner Institute for Brain and Mental Health, School of Psychological Sciences, Monash University, Clayton, VIC, Australia

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Background

In the presence of abnormally high amyloid (Aβ+), carriage of the brain-derived neurotrophic factor (BDNF) Val66Met polymorphism Met allele (Met66) is associated with faster clinical disease progression, greater neuronal loss and faster increases in CSF total-tau and p-tau181 compared to matched Val66 Aβ+ homozygotes. Aβ levels are unaffected by Met66 carriage. This suggests reduced neurotrophic support may accelerate Aβ-related neuronal dysfunction and cognitive decline. We aimed to clarify the role of BDNF Val66Met in moderating region-specific neurofibrillary tangle (NFT) formation in the brain in sporadic Alzheimer's disease. (AD).

Methods

Aβ+ older adult Met66 carriers (n=26) and Val66 homozygotes (n=68) enrolled in the Alzheimer's Disease Neuroimaging Initiative (ADNI) were included in the analysis if they had at least one tau-PET scan, Aβ-PET scan, and neuropsychological assessment available. Participants were not excluded based on disease stage. ANCOVAs were conducted to determine, cross-sectionally, whether Met66 carriers and Val66 homozygotes differed in levels of tau-PET tracer retention at each Braak stage and the ADNI memory composite at the time of first tau-PET scan.

Results

Aβ+ Met66 carriers showed significantly greater tracer retention in the entorhinal cortex (i.e., Braak 1) compared to Val66 homozygotes (p=.03), with the magnitude of this difference moderate (d=0.39). There were no significant differences between groups in tracer retention across all other Braak stages, episodic memory performance or Aβ levels.

Conclusion

The greater tau-PET tracer retention in the entorhinal cortex in Met66 carriers may reflect their greater NFT pathology relative to Val66 homozygotes during early stages of AD. This is consistent with previous observations of higher levels of CSF tau biomarkers in Aβ+ Met66 carriers, both in sporadic AD and autosomal dominant AD. Together, these findings support the hypothesis that loss of neurotrophic support, associated with Met66 carriage, may confer greater vulnerability to Aβ-related neurodegeneration compared to Val66 homozygosity.

Preclinical Frailty Trajectories and Dementia Risk in the United States

Marco Canevelli [1], Isabelle Foote [2], Janice Ranson [3], Jonny Flint [4], Thomas Littlejohns [5], David Llewellyn [3], David Ward [6], Lindsay Wallace [7], Emily Gordon [6], Erwin Stolz [8]

[1] Department of Human Neuroscience, Sapienza University of Rome, [2] Institute for Behavioral Genetics, University of Colorado Boulder, [3] University of Exeter Medical School, [4] College of Medicine and Veterinary Medicine, The University of Edinburgh, [5] Translational Epidemiology Unit, University of Oxford, [6] Centre for Health Services Research, The University of Queensland, [7] Cambridge Public Health, University of Cambridge, [8] Medical University of Graz

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Background

It is uncertain whether frailty is a modifiable dementia risk factor due to the unresolved possibility of reverse causation. We aimed to clarify the temporal relationship between frailty and incident dementia using two cohort studies from the United States.

Methods

Samples included individuals aged 60 years and over without cognitive impairment from the National Alzheimer's Coordinating Center (NACC, N = 6,918) and Rush Memory and Aging Project (MAP, N = 1,345). Frailty was measured using a frailty index over repeated annual assessments. We used Bayesian non-linear multilevel models to determine when frailty accumulation accelerates before incident dementia and Cox proportional hazards models to estimate the association of frailty with incident dementia after controlling for that period. All models included age, sex and education as covariates.

Results

Overall, 67% of individuals were women and 1,172 cases of incident dementia were detected across 62,819 person-years of follow up. When modelling frailty index scores over time, the inclusion of an interaction between time x event group (incident dementia or censored) improved model fit in both MAP and NACC (expected log pointwise predictive density, difference = 39.2 [95% CI = 21.4, 57.0] and 221.9 [95% CI = 173.9, 269.9], respectively). Compared with the censored group, expected frailty scores in the incident dementia group accelerated and were consistently higher ($P < 0.05$) five (MAP) and seven (NACC) years before dementia diagnosis. Even among individuals whose time between frailty measurement and incident dementia or censor was greater than that period, frailty remained associated with dementia risk in both datasets (MAP, HR = 1.25 [95% CI = 1.06, 1.47]; NACC, HR = 1.61 [95% CI = 1.32, 1.95]). These associations were robust to multiple tests of sensitivity.

Conclusion

Frailty may represent a useful upstream target for behavioural and societal approaches to dementia prevention.

Associations of Social Determinants with Non-Participation in a Multi-Domain Lifestyle Intervention Trial in Cognitively Healthy Older Adults to Prevent Cognitive Decline

Lisa Bransby [1], Wiesje van der Flier [2], Lisa Waterink [2], Emily Rosenich [3], Sietske Sikkes [2], Yen Ying Lim [1], Marissa Zwan [2]

[1] Turner Institute for Brain and Mental Health, School of Psychological Sciences, Monash University, Clayton, VIC, Australia, [2] Alzheimer Center Amsterdam, Neurology, Vrije Universiteit Amsterdam, Amsterdam UMC location VUmc, Amsterdam, The Netherlands, [3] Turner Institute for Brain and Mental Health, School of Psychological Sciences, Monash University, Clayton, VIC, Australia

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Background

Including a representative sample in dementia research is challenging, despite the increased risk for dementia in socially disadvantaged groups. In two large multi-domain lifestyle intervention trials to prevent cognitive decline - BetterBrains (online) and FINGER-NL (in-person) - this study aimed to investigate differences in social determinants of health between non-responders, non-participants, and participants recruited via online registries.

Method

5,375 adults (69% female) aged 60-79 years enrolled in the Dutch Brain Research Registry (DBRR), and 6,900 adults (72% female) aged 40-70 from the Healthy Brain Project (HBP), were eligible and received an open-invitation to participate. Individuals were categorized into three groups: 1) non-responders (did not respond to invitation), 2) non-participants (responded but were not interested; or screen failed), and 3) participants (randomized). Data regarding social determinants was collected via the baseline assessments of the online registries. Associations of social determinants with not participating were tested with multinomial logistic regression models, using participants as reference group.

Results

For FINGER-NL, non-responders were more often individuals with a migrant background (OR[95%CI] = 1.59[1.11-2.28]) or ≤12 years of education (1.50[1.21-1.87]), and non-participants also more often had ≤12 years of education (1.53[1.26-1.85]) and were older (1.03[1.01-1.05]). For BetterBrains, non-responders were more often males (1.63[1.23-2.16]) and younger (0.97[0.95-0.98]). No associations with non-participants were found.

Conclusion

Our results suggest that individuals with a migrant background or with ≤12 years of education from an online recruitment registry are less likely to participate when invited for an in-person multi-domain lifestyle intervention trial to prevent cognitive decline. For an online multi-domain intervention trial, individuals that were younger and male were less likely to respond. Focus-groups will be conducted to explore the differences in results and reasons underlying non-participation to gain deeper insights that will inform strategies to minimise non-participation in future research and improve generalisability of results.

"It Does Feel a Bit, Sort of, Infantilising": Lived Experiences of Neuropsychological Testing for Dementia Diagnosis

Monica Cations [1, 2], Michelle Kelly [3], Alexandra Wade [2], Stephanie Wong [2]

[1] Australian Institute of Health and Welfare, [2] Flinders University, [3] University of Newcastle

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Background

Latest figures indicate that the average time to receiving a dementia diagnosis is 2.8 years. Such diagnostic delays can impede access to support services and interventions, which can improve quality of life for people living with dementia and their carers. Novel neuropsychological screening tests have the potential to reduce the time to diagnosis, but maximising their use requires a better understanding of how commonly used tests are experienced by people with cognitive concerns and their carers.

Methods

Focus groups were conducted with people with lived experience of dementia (n=1) and care partners (n=4). Using a semi-structured protocol, participants were asked to describe their experiences of the dementia diagnosis process, including their experience of being assessed with neuropsychological tests. Data were analysed using thematic analysis.

Results

Participants expressed negative perceptions of neuropsychological tests currently used in the dementia diagnostic process. This was due to 1) limited communication and understanding of the rationale for tests; 2) patients feeling test questions were inappropriate and demeaning; and 3) tests not being sensitive to detect cognitive decline, which increased time to diagnosis. Participants also questioned whether tests accounted for demographic differences between patients, such as age, gender, level of education and ethnicity.

Discussion

As identified by people living with dementia and their care partners, the purpose of commonly used neuropsychological tests is not currently understood by people with cognitive concerns, leading to negative experiences of the assessment process. Clinicians should prioritise explaining the rationale and importance of neuropsychological tests to increase patient understanding and alleviate stress. Participants also identified the failure of current tests to detect cognitive decline, which prolonged the diagnostic process and had negative impacts on patients and their families. The development and validation of newer, more sensitive and inclusive tests capable of reducing time to diagnosis is therefore a priority.

Association of Basal Forebrain Atrophy with Cognitive Decline in early Alzheimer's Disease

Jurgen Fripp [1], Simon M. Laws [2, 3, 4], Paul Maruff [5, 6], Vincent Doré [1, 7], Christopher Fowler [6], Stephanie R. Rainey-Smith [8, 9, 10, 11], Ying Xia [12], Christopher C. Rowe [6, 7], Elizabeth J. Coulson [13, 14], Colin L. Masters [6], Pierrick Bourgeat [1], Ralph N. Martins [9, 11, 15]

[1] The Australian e-Health Research Centre, CSIRO Health and Biosecurity, [2] Centre for Precision Health, Edith Cowan University, [3] Collaborative Genomics and Translation Group, School of Medical and Health Sciences, Edith Cowan University, [4] Curtin Medical School, Curtin University, [5] Cogstate Ltd., [6] The Florey Institute of Neuroscience and Mental Health, The University of Melbourne, [7] Austin Health, [8] Centre for Healthy Ageing, Health Futures Institute, Murdoch University, [9] Australian Alzheimer's Research Foundation, Sarich Neuroscience Research Institute, [10] School of Psychological Science, University of Western Australia, [11] School of Medical and Health Sciences, Edith Cowan University, [12] The Australian e-Health Research Centre, CSIRO Health and Biosecurity, [13] Queensland Brain Institute, The University of Queensland, [14] School of Biomedical Sciences, The University of Queensland, [15] Department of Biomedical Sciences, Macquarie University

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Background

In early Alzheimer's disease (AD), amyloid-β (Aβ) accumulation is associated with volume loss in the basal forebrain (BF) and cognitive decline. However, the extent to which Aβ-related BF atrophy manifests as cognitive decline is not understood. This study sought to characterize the relationship between BF atrophy and the decline in memory and attention in individuals without dementia.

Methods

The 476 participants (72.6±5.9 years, 55.0% female) from the Australian Imaging, Biomarker and Lifestyle (AIBL) study who completed Aβ-PET imaging and repeated MRI and cognitive assessments were included. At baseline, participants were classified based on their clinical dementia stage and Aβ status, which were cognitively unimpaired (CU) Aβ-, CU Aβ+, and mild cognitive impairment (MCI) Aβ+. Linear mixed-effects models assessed atrophy in BF subregions (including Ch4p - posterior segment of the nucleus basalis of Meynert) and hippocampus as well as changes in their AIBL memory and attention composite scores. Associations between baseline Aβ burden, brain atrophy, and cognitive decline were evaluated and explored using mediation analyses.

Results

Compared to CU Aβ-, CU Aβ+ and MCI Aβ+ adults both showed faster decline in BF and hippocampal volumes as well as in memory and attention. While rates of atrophy across all regions correlated with cognitive decline, baseline Ch4p volume was associated moderately with rates of memory and attention decline. Furthermore, single-mediator models demonstrated that rates of atrophy in all regions of interest significantly influenced the effects of Aβ burden on memory and attention decline. When considering all three mediators simultaneously, hippocampal atrophy primarily mediated the effects of Aβ burden on memory decline, whereas Ch4p and hippocampal atrophy play unique mediating roles in Aβ-related attention decline.

Conclusion

These findings underscore the important role of BF atrophy, especially in Ch4p, in the complex pathway linking Aβ to cognitive impairment in early AD.

Verbal Fluency Correlates with Medial Temporal Lobe Volumes in Parkinson's Disease with Memory Impairment

Dana Pourzinal [1], Nadeeka Dissanayaka [1, 2, 3], Jihyun Yang [1]

[1] UQ Centre for Clinical Research, Faculty of Medicine, The University of Queensland, Royal Brisbane & Women's Hospital, Brisbane, [2] Department of Neurology, Royal Brisbane & Women's Hospital, Brisbane, [3] School of Psychology, The University of Queensland, Brisbane

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Background

Mild memory impairment, termed amnestic Mild Cognitive Impairment (aMCI), and impairment on verbal fluency tasks are associated with rapid progression toward dementia in Parkinson's Disease (PD). The medial temporal lobe (MTL) plays crucial role for memory processes, but its specific involvement in PD-aMCI and verbal fluency in PD remains unclear. This study aimed to investigate MTL volumes and their association with PD-aMCI and verbal fluency tasks.

Methods

41 participants (10 PD-aMCI, 21 PD with normal cognition (PD-NC) and 20 healthy controls) underwent structural MRI (Siemens 3T Scanner). Volumes of MTL structures including hippocampus, entorhinal cortex, parahippocampal cortex, and perirhinal cortex (Brodmann area 35 and 36) were measured using automatic segmentation of hippocampal subfields (ASHS) and compared across groups. Correlation analyses were conducted to explore relationships between MTL volumes and category, letter, and category-switching fluency measures.

Results

PD-aMCI exhibited significantly smaller bilateral posterior hippocampi compared to PD-NC and HC . Additionally, bilateral Brodmann area 35 volumes were reduced in PD-aMCI compared to two other groups. Both PD groups (aMCI and NC) showed reduced volumes in bilateral Brodmann area 36 compared to HC. While no significant correlations were found between MTL volume and category fluency in PD, the bilateral entorhinal cortex (left: $R = 0.64$, $p = 0.046$; right: $R = 0.79$, $p = 0.0063$) correlated positively with letter fluency in PD-aMCI and the left entorhinal cortex ($R = 0.68$, $p = 0.031$) positively correlated with category switching in PD-aMCI.

Discussions

Our findings suggest MTL atrophy in the hippocampus and perirhinal cortex in PD-aMCI. While category fluency was independent of MTL volume, letter fluency and category switching performance improved with increased hippocampal and entorhinal volumes in PD-aMCI. These results highlight MTL subregions as potential structural markers of dementia risk in PD.

SHAPE-ing the Future of Post-Diagnostic Support for People Living with Dementia: An International, Randomised, Controlled Trial

Kaarin J. Anstey [1, 2, 3], Linda Clare [4], Ingelin Testad [5], Jana Koch [1, 2, 3]

[1] University of New South Wales, School of Psychology, Sydney, Australia, [2] UNSW Ageing Futures Institute, Sydney, Australia, [3] Neuroscience Research Australia, Sydney, Australia, [4] University of Exeter, Exeter, UK, [5] Stravanger University Hospital, Norway

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Background

Evidence-based programs providing post-diagnostic support for people living with dementia are needed to ensure effective and replicable outcomes. SHAPE is an international (Norway, England, Australia) multi-site, single-blind, controlled trial to develop self-management skills among people in the early stages of dementia. Drawing on multi-domain expertise in dementia care (self-management, health promotion, and e-learning), we developed an innovative online program to support people living with early-stage dementia and their carers. Here, we describe preliminary data demonstrating response to the program.

Methods

Participants were randomised into treatment-as-usual or the intervention group (2:1 in favour of the intervention). The 10-week intervention was conducted in groups of four participants via Zoom (due to COVID-19) by trained psychologists and nurses. Assessments included baseline, 6- and 12-month follow-up. Total scores on the General Self-Efficacy Scale were used as the primary outcome and quality of life, neuropsychiatric symptoms, cognition, and health behaviour were included as secondary outcomes.

Results

A total of 210 participants with a formal diagnosis of dementia (aged 65+) were recruited between May 2020 and October 2023 (Australia n=30, UK n=90, Norway n=90). The mean age of Australian participants was 75 years (range: 65-84), with majority being male (66.7%). Most of the participants lived in metropolitan areas (67%), followed by rural towns (22%) and regional centers (11%). Australian participants were recruited via Facebook advertisement (30%), referral from a health professional (27%), online newsletters/advertisements (26%), and volunteer websites (17%). The total study drop-out rate is 21% (44/210) and there was 92% attendance at all intervention sessions in Australia. The last follow-up assessments will be completed in 2024.

Discussion

The pivot to online delivery has been successful, demonstrating feasibility of post-diagnostic support using digital health tools. If demonstrated to be effective, this trial will provide world-first findings for evidence-based diagnostic support for people living with dementia.

Community Implementation and National Scale-Up of a Healthy Brain Ageing Cognitive Intervention Program: A Partnership with Dementia Australia

Loren Mowszowski [1, 2], Sharon Naismith [1, 2], Vincent Poisson [3], Alessandra Lee [1, 2]

[1] The University of Sydney, [2] The Brain and Mind Centre, [3] Dementia Australia

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Background

Despite compelling research evidence for the effectiveness of neuropsychological interventions for people with mild cognitive impairment (MCI), such interventions are not readily available in the community. In partnership with Dementia Australia, this ongoing project represents a tailored adaption and national scale-up of the evidence-based, multi-faceted Healthy Brain Ageing (HBA) cognitive intervention program to facilitate broader community access. Here, we report outcomes from initial staff training to deliver the five-week program.

Methods

Our team adapted the existing program, now the MCI: Thinking Ahead program, to suit the logistical priorities of Dementia Australia. Participants' feedback captured during the pilot phase informed the development of a customised training package for Dementia Australia staff including a detailed facilitator manual and half-day, online workshop. Ongoing, structured mentoring was offered via optional, fortnightly online meetings. Facilitators completed surveys at baseline, immediately post-training and after approximately 9-months of program delivery. Surveys covered current practice, clinician knowledge and confidence relating to delivering cognitive intervention, work satisfaction, organisational readiness for implementing change, as well as barriers and facilitators to implementation.

Results

To-date, 24 Dementia Australia staff members from 6 Australian states and 2 territories have completed training and commenced facilitation of the MCI: Thinking Ahead program. We will report on clinician changes in knowledge, confidence, and work satisfaction, as well as changes in organisational readiness for change, and perceived barriers and facilitators to implementation.

Discussion

This project demonstrates the capacity for partnership between research and community organisations to adapt and implement evidence-based interventions for people with MCI, and the importance of structured training for staff rollout. Learnings from this study will inform sustainability of the intervention in this setting and can be used to inform further implementation efforts in community contexts.

Title Case: Learning Pathways - the Destination for Discovering Dementia Training

Isabelle Meyer [1]

[1] Dementia Training Australia

Background

Quality Care for those living with Dementia depends on quality training. Dementia Training Australia(DTA) has been tasked by the Commonwealth Government to lead the provision of quality dementia training; setting standards for learning and skills development via its Learning Standards Framework. Learning Pathways is DTA's new and innovative learning resource tool, designed to assist learners and workers at any level of dementia care with personalised training that best suits the needs of individuals and organisations.

Methods

Learning Pathways, is a web-based tool designed to support workers, health professionals and others in the dementia care space; identifying courses and other resources which support training endeavours, improve quality of care, and provide a secure path from learned skills to best practice. Learning Pathways is connected to a database of valuable content from education and training providers like DTA, the Wicking Institute and other training providers including Dementia Australia (DA). The tool is suitable for support workers, health professionals and other care staff including volunteers, whatever their care setting.

Results

Learning Pathways was developed in alignment with Aged Care Quality Standards, as well as DTA's own National Dementia Education and Training Standards Framework, release July 2024. This resource tool can be a guide for those undertaking dementia training for the first time, or those wanting to upskill their existing knowledge for not only dementia support workers, but those receiving care. All courses listed in the pathways tool have been assessed against the Quality Framework, ensuring the courses are relevant, timely and comprehensive.

Discussion

Learning Pathways has been created with the goal of revolutionising the way we train dementia care workers, creating a nexus between learning opportunities and quality improvement, based on the National Dementia Education and Standards Framework commissioned by the Commonwealth Government as part of its National Aged Care Workforce Strategy.

Technology Assisted and Remotely Delivered Anxiety Psychotherapy Intervention for People living with Dementia and Their Care Partners: TechCBT Project

Tiffany Au [1], Peter Worthy [1], Gerard Byrne [1], Gabriela Pacas Fronza [1], Mark Chatfield [1], Nancy Pachana [1], Annette Broome [2], Nadeeka Dissanayaka [1], Alexander Lehn [2], Joanne Oram [2], Syed Afroz Keramat [1], Tracy Comans [1], Kimberley Welsh [1], Sally Bennett [1], Ray Guy [3], Teagan King [1], Elizabeth Beattie [4], Deborah Brooks [1], Joseph Tan [5], Ann Pietsch [6], Jacki Liddle [1], John O'Sullivan [1], Leander Mitchell [1]

[1] The University of Queensland , [2] Metro South Health, [3] TalkVia AI, [4] Queensland University of Technology, [5] Metro North Health, [6] Dementia Australia

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Background

The prevalence of anxiety is four times higher in people living with dementia than older people. Despite this, anxiety treatment is absent in most usual clinical care models for this vulnerable group. Anxiety has far reaching impacts, resulting in accelerated cognitive decline, increased aggressive behaviours, and an increased risk of suicide in people living with dementia, as well as increased carer burden. Anxiety negatively influences the quality of life of the person with dementia and their carer, and amplifies economic burden. Technology assisted Cognitive Behaviour Therapy (Tech-CBT) is a holistic tool that can deliver a customised, scalable, technologically advanced solution to manage anxiety in people with dementia, and their carers.

Methods

Tech-CBT utilises a tailored digital platform (My Anxiety Care) for delivery of psychotherapy via video-conferencing guided by a personalised digital assistant voice App (Quiet Mind) enabling home practice. The efficacy of the Tech-CBT is evaluated involving 70 dyads of people with dementia and their carers nationwide. Using a randomised controlled trial design, the TechCBT intervention is compared with usual care in a Hybrid-II effectiveness-implementation trial. An economic evaluation and a process evaluation are undertaken to assess future implementation in community and health services. To facilitate digital development, testing, and rapid translation, our multidisciplinary research team is partnered with software industry to develop the digital technology, consumers, and community organisations, and health services.

Results

Co-design and development of the TechCBT intervention and results to date will be discussed.

Discussion

This project will deliver a robust evidence-base for a new remotely delivered Tech-CBT to reduce anxiety in people living with dementia, and improve wellbeing in their carers. Simultaneously it will provide (i) a strategic plan for future implementation in health services, (ii) a program to upskill the psychological workforce for dementia care, and (iii) mental health economics in dementia.

Identifying Priorites for Medication Management Resources for People Living with Dementia and Their Carers Through Community Action

Dr Jacqeline Wesson [1], Dr Mouna Sawan [2], Joanne Lo [2], Dr Karen Watson [3], Dr Amanda Cross [4], Dr Natali Jokanovic [5], A/Prof Danijela Gnjidic [2]

[1] School of Health Sciences, University of Sydney, [2] Sydney Pharmacy School, University of Sydney, [3] Sydney Nursing School, The University of Sydney, [4] Centre for Medicine Use and Safety, Monash University, [5] The Alfred Hospital and Monash University

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Background

People with dementia and their carers are provided limited guidance in medication management, potentially contributing to medication-related harm. Importantly, there are no resources that provide comprehensive medication management guidance across care settings. To ensure that resources are co-designed, genuine involvement of people with dementia, their carers and the community in identifying the priorities for medication management guidance resources is needed. We explored community-centred priorities for medication management guidance resources for people with dementia and their carers.

Methods

We established a 23-member consortium partnership with people living with dementia, carers, healthcare professionals, and national consumer and professional organisations using a community-based participatory research approach. A qualitative descriptive design, using four focus groups and two interviews with key informants was conducted between September to December 2023 to explore partners' priorities for medication management resources across care settings. Content analysis was performed to generate a list of priorities.

Results

The key priorities for inclusion in the medication resource were to: 1) empower the person with dementia and their carers to make informed choices; 2) provide pragmatic and accessible information to meet their needs and promote key questions to engage health providers in shared decision-making; and 3) inclusion of strategies to address medication challenges.

Conclusion

This is the first time a community action approach has been adopted to co-design resources to support people with dementia and carers in medication management challenges. The community-centred priorities will be used to generate an inventory of consumer-tailored communication strategies for people with dementia and their carers.

How Can We Improve Hearing and Vision Loss Support in Home Care Settings? Exploring Sensory Support Care Needs of Home Care Recipients with Self-reported Dementia Diagnosis or Memory Difficulties

Dr John Newall, PhD [1], Prof Lisa Keay, PhD [2], Prof Piers Dawes, PhD [3], Dr Marianne Piano, PhD [4], Dr Sheela Kumaran, PhD [2], Dr Helen Gurteen, PhD [3], Dr Chyrisse Heine, PhD [5], Prof Hamid Sohrabi, PhD [6], A/Prof Melanie Ferguson [7], Dr Sabrina Lenzen, PhD [8], Prof Nancy A Pachana, PhD [9], Dr Carly Meyer [10], Prof Judy Lowthian, PhD [10], A/Prof Angelita Martini, PhD [11], Dr Melinda Toomey, PhD [3], A/Prof Yuanyuan Gu, PhD [12]

[1] Department of Linguistics, Faculty of Medicine, Health and Human Sciences, The Australian Hearing Hub, Macquarie University, [2] School of Optometry and Vision Science, University of New South Wales, [3] School of Health and Rehabilitation Sciences. University of Queensland, [4] Department of Optometry and Vision Sciences, Melbourne School of Health Sciences, University of Melbourne, [5] Institute of Health and Wellbeing, Federation University Australia, [6] Centre for Healthy Ageing, Murdoch University, [7] Shcool of Allied Health, Curtin University, [8] Centre for the Business and Economics of Health, The University of Queensland, [9] Healthy Ageing Initiative, University of Queensland, [10] Bolton Clarke Research Institute, [11] The University of Western Australia, [12] Macquarie University Centre for the Health Economy, Macquarie Business School & Australian Institute of Health Innovation, Macquarie University

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Background

Sensory impairment (vision and/or hearing) can significantly impact people living with dementia, affecting wellbeing, social participation, independence, communication and increasing risk of falls. Looking after sensory health is an important aspect of post-diagnosis dementia care. Over 70% of people receiving home care are affected by sensory impairment. This study aimed to identify the sensory care needs of people receiving home care services in Australia, and how they are met, or unmet, in the context of the home care services they receive.

Methods

Semi-structured interviews with home care recipients with vision and/or hearing loss and supporting family members explored sensory care needs at home. Topic guide was derived from the Adapted Support Care Needs survey covering five areas: psychological/emotional, health information about condition, physical/daily living, care and support, interpersonal relationships. Preliminary thematic analysis was undertaken.

Results

Interviews were completed with twelve home care recipients (mean age 81.3 ± 7 years, 8 with self-reported memory problems, 2 with self-reported dementia diagnosis) and 3 family members. Of home care recipients, 6 had dual sensory impairment, 2 had hearing impairment, 4 had vision impairment. Emerging themes were “Navigating the sensory support network – the need for information’, “Challenges in access, finances and care suitability’, “Challenges of daily living and the functional support that promotes independence’, “Communication challenges, needs and supports’, and “Emotional and social well-being in sensory loss, nurturing positivity and support’.

Discussion

Older adults living with sensory impairment in Australia experience unique practical and psychosocial support needs, compounded by barriers to accessing sensory care and costs of assistive devices, such as hearing aids and low vision aids. These needs are not consistently identified and responded to through an appropriately tailored home care service, with far-reaching impacts and frustrations. A sensory care navigator role could facilitate interprofessional information sharing and service access.

Barriers to and Facilitators for CBT Interventions for People Living with MCI/Dementia: A Systematic Review of Technology and Non-Technology Assisted Approaches

Dr. Deborah Brooks [1], Kimberley Welsh [1], Dr Leander Mitchell [2], Associate Professor Nadeeka Dissanayaka [1]

[1] UQ CCR, 2UQ School of Psychology

Background

Cognitive behavioural therapy (CBT) is an evidence-based approach that has been utilised with people living with mild cognitive impairment (MCI) and dementia to improve quality of life and reduce symptomology for a range of concerns such as anxiety, depression, and sleep difficulties. Evidence has also shown that technology assisted approaches can increase access to mental health support. This systematic review aims to critically synthesise the existing evidence for the barriers and facilitators to the delivery of and engagement with CBT interventions, using both technology and non-technology assisted approaches, for people living with dementia/MCI.

Methods

A systematic search was conducted in multiple databases. We searched for CBT and modified CBT interventions within the last 20 years (2002-2022) targeting people living with MCI/dementia. Studies were restricted to those available in English. We included all empirical research studies that reported any information on barriers and facilitators to the delivery or engagement of CBT interventions for people living with MCI/dementia, such as randomized controlled trials (RCTs), case reports, mixed-methods, and qualitative studies.

Results

Factors were grouped relating to user levels (individual, carers, providers, services, system) and stages (access, implementation, participation, maintenance). Some common barriers included memory and motivation difficulties, and technology specific difficulties with dexterity and fine motor skills and connectivity issues. Some common facilitators included reminder cues, having a support person in attendance during therapy sessions, and MCI/dementia specific adaptations.

Conclusion

The identification and application of barriers and facilitators are integral to the effective delivery of any intervention. The factors identified in this review can provide guidance for both the users and providers of CBT interventions for people living with MCI/dementia. As well as this, these factors can help explain user engagement and delivery outcomes and further inform the design, development, and implementation of future interventions, both technology and non-technology assisted.

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Page	Presentation Type	Theme	First Name	Last Name	Email
02	Keynote		Christopher	Chen	cplhchen@yahoo.com.sg
03	Keynote		Gary	Cheung	g.cheung@auckland.ac.nz
04	Keynote		Karen	Duff	k.duff@ucl.ac.uk
05	Keynote		Heidi	Jacobs	hjacobs@mgh.harvard.edu
06	Keynote		Peter	Nestor	p.nestor@uq.edu.au
07	Keynote		Stephen	Salloway	Stephen_Salloway@brown.edu
08	Keynote		Ashleigh	Smith	Ashleigh.Smith@unisa.edu.au
09	Symposia	ADNeT Initatives	Susannah	Ahern	Susannah.ahern@monash.edu
10	Symposia	ADNeT Initatives	Kerryn	Pike	k.pike@griffith.edu.au
11	Symposia	ADNeT Initatives	Sharon	Naismith	Sharon.naismith@sydney.edu.au
12	Symposia	ADNeT Initatives	Christopher	Rowe	christopher.rowe@austin.org.au
13	Symposia	Anti-amyloid	Amy	Brodtmann	Amy.Brodtmann@monash.edu
14	Symposia	Anti-amyloid	Gideon	Caplan	g.caplan@unsw.edu.au
15	Symposia	Anti-amyloid	Michael	Woodward	Michael.WOODWARD@austin.org.au
16	Symposia	ASAD	Ming Ann	Sim	mingann.sim@gmail.com
17	Symposia	ASAD	Allen	Lee	allenlee@cuhk.edu.hk
18	Symposia	ASAD	Xin	Xu	xuxinsummer@zju.edu.cn
19	Symposia	ASAD	Yuan-Han	Yang	endlessyhy@gmail.com
20	Symposia	Data Landscape	Melanie	Dunford	melanie.dunford@aihw.gov.au
21	Symposia	Data Landscape	Megan	Fraser	megan.fraser@aihw.gov.au
22	Symposia	Data Landscape	Sarang	Kim	sarang.kim@aihw.gov.au
23	Symposia	Data Landscape	Velandai	Srikanth	velandai.srikanth@monash.edu
24	Symposia	Biomarkers	Benjamin	Heng	benjamin.heng@Mq.edu.au
25	Symposia	Biomarkers	Kevin	Huynh	kevin.huynh@baker.edu.au
26	Symposia	Biomarkers	Mourad	Tayebi	m.tayebi@westernsydney.edu.au
27	Symposia	Biomarkers	Joanna	Williams	joanna.williams@otago.ac.nz
28	Symposia	Diverse Pop.	Bianca	Brijnath	b.brijnath@nari.edu.au
29	Symposia	Diverse Pop.	Diana	Karamacoska	d.karamacoska@westernsydney.edu.au
30	Symposia	Diverse Pop.	Joyce	Siette	joyce.siette@westernsydney.edu.au
31	Symposia	Diverse Pop.	Lily	Xiao	lily.xiao@flinders.edu.au
32	Symposia	Aged Care	Darshini	Ayton	Darshini.Ayton@monash.edu

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Page	Presentation Type	Theme	First Name	Last Name	Email
33	Symposia	Aged Care	Dongjun	Wu	dongjun.wu@griffithuni.edu.au
34	Symposia	Aged Care	Jacqueline	Wesson	jacqueline.wesson@sydney.edu.au
35	Symposia	Aged Care	Robyn	Lewis	robyn.lewis@canberra.edu.au
36	Symposia	Post Care	Scott	Cooper	Scooper1957@gmail.com
36	Symposia	Post Care	Dana	Haywood	dana.haywood@dementia.org.au
36	Symposia	Post Care	Kaele	Stokes	Kaele.Stokes@dementia.org.au
36	Symposia	Post Care	Kerrie	Tuite	kerrietuite@bigpond.com
37	Orals	Discovery	Pierrick	Bourgeat	pierrick.bourgeat@csiro.au
38	Orals	Discovery	Juan	Carlos Polanco	j.polanco@uq.edu.au
39	Orals	Discovery	Esteban	Cruz	e.cruz@uq.edu.au
40	Orals	Discovery	Vincent	Dore	vincent.dore@csiro.au
41	Orals	Discovery	Eleanor	Drummond	eleanor.drummond@sydney.edu.au
42	Orals	Discovery	Lou	Fourriere-Chea	lou.fourriere@unimelb.edu.au
43	Orals	Discovery	Joseph	Giorgio	jgiorgio@berkeley.edu
44	Orals	Discovery	Eleanor	O'Brien	e.obrien@ecu.edu.au
45	Orals	Prevention	Hilal	Al Shamsi	hilala@our.ecu.edu.au
46	Orals	Prevention	Jane	Alty	jane.alty@utas.edu.au
47	Orals	Prevention	Lyndsey	Collins-Praino	lyndsey.collins-praino@adelaide.edu.au
48	Orals	Prevention	Hannah	Fair	hannah.fair@utas.edu.au
49	Orals	Prevention	Md Hamidul	Huque	MdHamidul.Huque@unsw.edu.au
50	Orals	Prevention	Blossom	Stephan	blossom.stephan@curtin.edu.au
51	Orals	Prevention	Jamie	Tait	j.tait@deakin.edu.au
52	Orals	Prevention	Thao	Vu	thao.vu@aihw.gov.au
53	Orals	Post Diagnostic	Alinka	Fisher	alinka.fisher@flinders.edu.au
54	Orals	Post Diagnostic	Megan	Freund	megan.freund@newcastle.edu.au
55	Orals	Post Diagnostic	Stephanie	Harrison	stephanie.harrison@sahmri.com
56	Orals	Post Diagnostic	Linda	Koria	linda.koria@health.nsw.gov.au
57	Orals	Post Diagnostic	Tom	Morris	tmorris@dementia.com.au
58	Orals	Post Diagnostic	Kerryn	Pike	k.pike@griffith.edu.au
59	Orals	Post Diagnostic	Christine	Sender-Ivanov	christine.senderivanov@health.nsw.gov.au
60	Orals	Post Diagnostic	Edwin	Tan	edwin.tan@sydney.edu.au

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61	Poster Blitz	Discovery	Olasunkanmi	Bamidele	obamidel@our.ecu.edu.au
62	Poster Blitz	Discovery	Prashant	Bharadwaj	p.bharadwaj@ecu.edu.au
63	Poster Blitz	Discovery	Azadeh	Feizpour	azadeh.feizpour@florey.edu.au
64	Poster Blitz	Discovery	Laura	Rantanen	laura.rantanen@qimrberghofer.edu.au
65	Poster Blitz	Prevention	Hannah	Fair	eddy.roccati@utas.edu.au
66	Poster Blitz	Prevention	Mohammad Shoaib	Hamrah	mohammad.hamrah@utas.edu.au
67	Poster Blitz	Prevention	Xiaoping	Lin	xiaoping.lin@monash.edu
68	Poster Blitz	Post Diagnostic	Deborah	Brooks	deborah.brooks@uq.edu.au
69	Poster Blitz	Post Diagnostic	Michele	Callisaya	michele.callisaya@monash.edu
70	Poster Blitz	Post Diagnostic	Diana	Matovic	diana.matovic@mq.edu.au
71	Poster	Discovery	Eunice	Cheng	z3528525@ad.unsw.edu.au
72	Poster	Discovery	Anthony	Cook	anthony.cook@utas.edu.au
73	Poster	Discovery	Juliana	Cristina da Silva Chaves	juliana.dasilvachaves@qimrberghofer.edu.au
74	Poster	Discovery	Sithara	Dissanayaka	sitharad@our.ecu.edu.au
75	Poster	Discovery	Lina	Gomez	lina.gomez@qimrberghofer.edu.au
76	Poster	Discovery	Jane	Alty	jane.alty@utas.edu.au
77	Poster	Prevention	Jane	Alty	jane.alty@utas.edu.au
78	Poster	Prevention	Jane	Alty	jane.alty@utas.edu.au
79	Poster	Prevention	Maha	Alshahrani	m.alshahrani12@postgrad.curtin.edu.au
80	Poster	Prevention	Malika	Fernando	malika.fernando@mq.edu.au
81	Poster	Prevention	Sophie	Andrews	sandrews1@usc.edu.au
82	Poster	Prevention	Kaarin	Anstey	k.anstey@unsw.edu.au
83	Poster	Prevention	Kaarin	Anstey	k.anstey@unsw.edu.au
84	Poster	Prevention	Carolina	Blagojevic Castro	carolina.castro@murdoch.edu.au
85	Poster	Prevention	Deborah	Brooks	deborah.brooks@uq.edu.au
86	Poster	Prevention	Michele	Callisaya	michele.callisaya@utas.edu.au
87	Poster	Prevention	Rodrigo	Canovas	rodrigo.canovas@csiro.au
88	Poster	Prevention	Ivana	Chan	ivana.chan@monash.edu
89	Poster	Prevention	Nadeeka	Dissanayaka	n.dissanayaka@uq.edu.au
90	Poster	Prevention	Annette	Dobson	a.dobson@sph.uq.edu.au
91	Poster	Prevention	Laura	Dodds	l.dodds@westernsydney.edu.au

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92	Poster	Prevention	Vincent	Dore	vincent.dore@csiro.au
93	Poster	Prevention	Shaun	Eslick	shaun.eslick@mq.edu.au
94	Poster	Prevention	Nicole	Espinosa	nicole.espinosa@sydney.edu.au
95	Poster	Prevention	Hannah	Fair	hannah.fair@utas.edu.au
96	Poster	Prevention	Daniel	Bailey	daniel.bailey@uq.edu.au
97	Poster	Post Diagnostic	Daniel	Bailey	daniel.bailey@uq.edu.au
98	Poster	Post Diagnostic	Aimee	Brown	aimee.brown@monash.edu
99	Poster	Post Diagnostic	Elissa	Burton	E.Burton@curtin.edu.au
100	Poster	Post Diagnostic	Marianne	Coleman	marianne.coleman@unimelb.edu.au
101	Poster	Post Diagnostic	Nathan M	D'Cunha	nathan.dcunha@canberra.edu.au
102	Poster	Post Diagnostic	Catherine	Devanny	Catherine.Devanny@monash.edu
103	Poster	Discovery	Benjamin	Goudey	ben.goudey@unimelb.edu.au
104	Poster	Discovery	Satoshi	Kurita	kuritoshi@unsw.edu.au
105	Poster	Discovery	Simon	Laws	s.laws@ecu.edu.au
106	Poster	Discovery	Simon	Laws	s.laws@ecu.edu.au
107	Poster	Discovery	Ishika	Mahajan	ishikamahajan7824@gmail.com
108	Poster	Discovery	Ian	Peall	ian.peall@qimrberghofer.edu.au
109	Poster	Discovery	Sofia	Petersen	sofia.petersen@hdr.qut.edu.au
110	Poster	Prevention	Caroline	Faucher	caroline.faucher@uon.edu.au
111	Poster	Prevention	Jess	Amos	j.amos@unsw.edu.au
112	Poster	Prevention	Jonny	Flint	jonny.flint@ed.ac.uk
113	Poster	Prevention	Olivia	Giameos	olivia.giameos@unisa.edu.au
114	Poster	Prevention	Kali	Godbee	kali.godbee@monash.edu
115	Poster	Prevention	Kali	Godbee	godbeek@student.unimelb.edu.au
116	Poster	Prevention	Alison	Hutchinson	alison.hutchinson@deakin.edu.au
117	Poster	Prevention	Jana	Koch	jana.koch@unsw.edu.au
118	Poster	Prevention	Yashi	Koirala	yashi.koirala@utas.edu.au
119	Poster	Prevention	Shirly	Sareyka	shirly.sareyka@griffithuni.edu.au
120	Poster	Prevention	Qiao-Xin	Li	q.li@unimelb.edu.au
121	Poster	Prevention	Pinghsiu	Lin	pinghsiu.lin@unsw.edu.au
122	Poster	Prevention	Xiaoping	Lin	xiaoping.lin@monash.edu

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Page	Presentation Type	Theme	First Name	Last Name	Email
123	Poster	Prevention	Ignacio	Martinez Escobedo	ignacio.martinezescobedo@utas.edu.au
124	Poster	Prevention	Maddison	Mellow	maddison.mellow@unisa.edu.au
125	Poster	Prevention	Moyra	Mortby	m.mortby@unsw.edu.au
126	Poster	Prevention	Sharon	Naismith	dexiao.kong@sydney.edu.au
127	Poster	Prevention	Amir	Fazlollahi	fazlollahi@gmail.com
128	Poster	Prevention	Katya	Numbers	k.numbers@unsw.edu.au
129	Poster	Post Diagnostic	Claire	O'Connor	claire.oconnor@unsw.edu.au
130	Poster	Post Diagnostic	Najwan	El-Saifi	n.elsaifi@uq.edu.au
131	Poster	Post Diagnostic	Brenda	Gannon	brenda.gannon@uq.edu.au
132	Poster	Post Diagnostic	Caroline	Grogan	Caroline.Grogan@WesleyResearch.org.au
134	Poster	Post Diagnostic	Melinda	Jackson	melinda.jackson@monash.edu
135	Poster	Discovery	Tenielle	Porter	a.milliganarmstrong@ecu.edu.au
136	Poster	Discovery	Tenielle	Porter	t.porter@ecu.edu.au
137	Poster	Discovery	Niklas	Schultze	Niklas.Schultze@qimrberghofer.edu.au
138	Poster	Discovery	Jack	Taylor	jack.taylor@actinogen.com.au
139	Poster	Discovery	R.M. Uththara S.	Senarath	rsenarat@our.ecu.edu.au
140	Poster	Discovery	Amy	Woodfield	amy.woodfield@postgrad.curtin.edu.au
141	Poster	Discovery	Rachael	Yu	rachael.yu@sydney.edu.au
142	Poster	Prevention	Katya	Numbers	k.numbers@unsw.edu.au
143	Poster	Prevention	Zara	Page	z.page@unsw.edu.au
144	Poster	Prevention	Dan	Ping Wu	dan_ping.wu@mymail.unisa.edu.au
145	Poster	Prevention	Dana	Pourzinal	dana.pourzinal@gmail.com
146	Poster	Prevention	Samantha	Ramachandra	rbramach@our.ecu.edu.au
147	Poster	Prevention	Emily	Rosenich	emily.rosenich@monash.edu
149	Poster	Prevention	Zandile	Rwodzi	zandile.rwodzi@mymail.unisa.edu.au
150	Poster	Prevention	Suraj	Samtani	s.samtani@unsw.edu.au
151	Poster	Prevention	Ranil	Kumaranayake	rankuna82@gmail.com
152	Poster	Prevention	Andrew	Shoubridge	andrew.shoubridge@sahmri.com
153	Poster	Prevention	James	St John	j.stjohn@griffith.edu.au
154	Poster	Prevention	Diny	Thomson	diny.thomson@monash.edu
155	Poster	Prevention	David	Ward	david.ward@uq.edu.au

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Page	Presentation Type	Theme	First Name	Last Name	Email
156	Poster	Prevention	Lisa	Waterink	lisa.waterink@monash.edu
157	Poster	Prevention	Stephanie	Wong	stephanie.wong@flinders.edu.au
158	Poster	Prevention	Ying	Xia	ying.xia@csiro.au
159	Poster	Prevention	Jihyun	Yang	j.yang1@uq.edu.au
160	Poster	Post Diagnostic	Jana	Koch	jana.koch@unsw.edu.au
161	Poster	Post Diagnostic	Alessandra	Lee	alessandra.lee@sydney.edu.au
162	Poster	Post Diagnostic	Isabelle	Meyer	imeyer@uow.edu.au
163	Poster	Post Diagnostic	Nadeeka	Dissanayaka	n.dissanayaka@uq.edu.au
164	Poster	Post Diagnostic	Mouna	Sawan	mouna.sawan@sydney.edu.au
165	Poster	Post Diagnostic	Melinda	Toomey	m.toomey@uq.edu.au
166	Poster	Post Diagnostic	Kimberley	Welsh	kimberley.welsh@uq.edu.au