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TRAINEE POSTER SESSION UNDERGRADUATE STUDENTS

Intersection Between Frailty, Sex, Duration of Antidepressant Medication Exposure, and the Development of Dementia

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Plain Language Summary: Antidepressants are common and taken for a long time. Our goal was to determine if antidepressants increase dementia risk. We included frailty, sex, and how long participants were taking antidepressants as potential factors in dementia risk. Our results suggest that antidepressants do not increase the risk of dementia, but that frailty, being male sex, and older age do in the population studied.

Background: In Canada, antidepressant medications (ADM) are the largest drug category in terms of prescription volume. Previous study of the relationship between ADM exposure and dementia is inconsistent. The objective of this secondary analysis was to investigate the relationship between frailty, sex, duration of ADM exposure, and the development of clinical dementia.

Method: This was a retrospective cohort study of the Religious Orders Study. Participants' health data was collected annually from enrollment to death. A 24-item frailty index was created. ADM use was defined as exposure to any antidepressant annually. Dementia was defined clinically as either Alzheimer's disease or another primary cause; excluding mild cognitive impairment. A general logistic regression model was used to assess the role of the variables: age, frailty, sex, ADM exposure, and duration of ADM exposure, on the outcome of dementia.

Result: There were 1828 participants, 26% were male. The mean age was 89.7±6.1. Preliminary results of a multivariable logistic regression model indicated that neither ADM exposure nor duration of ADM use was associated with an increased the risk of dementia. Three of the variables in the model revealed a statistically significant relationship to the development of dementia: age (OR: 1.09, 95%CI (1.03, 1.15)), sex (OR: 2.27, 95%CI (1.14, 4.47)), and frailty (OR: 9.08, 95%CI (1.99, 3983.37)).

Conclusion: Our findings conclude that neither ADM use nor increased duration of ADM use was associated with dementia. Future work will investigate if ADM exposure is related to the development of dementia related neuropathology.

The Effect of Multilingualism on the Executive Function of Older Adults With, or at Risk for, Dementia

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Plain Language Summary: This study examines whether speaking more than one language has a protective effect in older adults with, or at risk for, Alzheimer's disease (AD). Monolinguals and multilinguals suppressing distractions that involve managing and switching tasks. This allow us to identify if there is a benefit of multilingualism and, if so, the stage in AD development that has the greatest benefit.

Background: Compared to monolinguals, bilinguals may have greater executive function abilities and cognitive reserve. However, few studies have examined the relationship between bilingualism and executive function in individuals with neurodegenerative disease, when cognitive reserve is most likely to play a role. Among older adults with, or at risk, for Alzheimer's disease (AD), we examine whether being multilingual is associated with higher performance on executive function tests compared to being monolingual.

Methods: Participants include older adults who are cognitively unimpaired (CU; n = 196), have subjective cognitive decline (SCD; n = 292), mild cognitive impairment (MCI; n = 353), and AD (n = 119) from COMPASS-ND (Data Release 7) and CIMA-Q (Data Release 14). Approximately 60% of each diagnosis group is multilingual. Regression analyses will be used to examine the association between language status and performance on the Stroop Test and Trail Making Task, across the groups.

Results: We expect that multilinguals will outperform monolinguals on the Stroop Test and Trail Making Task across all groups. The difference in performance between language groups is expected to follow an inverted U-shaped curve as pathology increases, from CU and SCD to MCI to AD.

Conclusion: Our findings will inform the literature on multilingualism and executive function in the context of cognitive reserve by allowing us to identify the stage in AD development at which a multilingual benefit is most evident.

Beyond Involvement: Engaging and Empowering New Brunswick Older Adults in Brain Health Research (Winner of the Undergraduate trainee category competition)

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Plain Language Summary: Older adults living in the community are interested in learning about brain health and healthy aging, based on a bilingual survey done in New Brunswick. They want to hear about initiatives from trusted sources but would like to read about the details from online resources. Accessibility, social/peer support, costs, and location are important for success.

Background: The New Brunswick Preventing Alzheimer's by Lessening Modifiable Risk (NB-PALM) research study was designed to implement a feasibility study of remotely delivered exercise and cognitive interventions. Research team members and a community advisory group designed a sub-study to engage older adults in New Brunswick to learn about perceived barriers and supports to staying healthy as they age, and the best ways to learn about and participate in programs that support brain health/wellness.

Method: With a targeted sample size of 384, community-dwelling persons 60 years and older, were recruited to complete a bilingual survey online, by phone, or by mail. The survey asked participants for their definition of brain health, as well as their preferences in searching or receiving information, and their opinions on what makes it easier, or harder, to participate in health programs.

Results: Participants (n=245), mostly women (74%), lived in southern urban locations. They identified a need for a personal program connection as well as social/peer support to begin and maintain healthy habits. For information about programs and services, participants preferred to speak with others they trusted or seek information from online resources. The importance of ease of accessibility, including schedules that fit community needs, cost, location, and transportation was highlighted.

Conclusion: Older adults are interested in learning about brain health. Although the responses are not representative of all New Brunswick older adults, lessons learned provide a starting point to guide future planning for delivering brain health programs.

The Mental Health Impact of COVID-19 and Associated Risk Factors on Older Adults with or at Risk of Dementia from the COMPASS-ND Study

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Plain Language Summary: Research suggests that older adults with dementia experienced depression and anxiety during the COVID-19 pandemic. It also limited our abilities to engage in physical activity and social contact, which are risk factors for poor mental. This study explores how pandemic-related changes in mental health, physical activity and social contact have impacted older adults with or at risk for dementia.

Background: During the COVID-19 pandemic, increased levels of loneliness, low mental health and more cognitive symptoms were found in people with dementia. Physical inactivity and impaired social contact have been identified as risk factors for cognitive decline and low mental health. We aim to investigate changes in anxiety, depression, social contact, and physical activity in older adults with or at risk of dementia pre- and post-pandemic.

Method: Archival data from the COMPASS-ND study, LORIS data release 7, will be used. Beginning July 2020, questionnaires to assess experiences during the pandemic were sent to participants tested prior to the pandemic. 213 questionnaires are available for analysis (56 CU, 23 SCD, 68 MCD, 36 V-MCD, 30 AD). Responses will be analyzed using regression analysis to determine: if levels of anxiety, depression, social contact and physical activity changed from baseline to pandemic; if levels of social contact and physical activity predict levels of anxiety and depression during the pandemic.

Results: We expect depression and anxiety scores to increase, and levels of social contact and physical activity to decrease from baseline to pandemic. We expect lower levels of social contact and physical activity to predict higher depression and anxiety scores during the pandemic.

Conclusion: Findings will highlight the effect of pandemic experiences on mental health in older adults with or at risk of dementia. This can inform interventions on the modifiable risk factors (social contact and physical activity) to target in terms of their impact on mental health, especially during periods of isolation.

MASTER'S STUDENTS

Associations Between Polygenic Risk Score of Parkinson's Disease, Grey and White Matter Structure, and Behavioral Phenotypes

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Plain Language Summary: Brain's structure is affected in Parkinson's disease; however, the local associations among brain features and their links to behaviors are unknown. Here we looked at how genes related to Parkinson's disease affect brain structure and behavior. Our findings showed connections between brain structures, genetic risk of Parkinson's development, as well as behaviors such as addiction and alcohol use.

Background: Parkinson's disease (PD) is associated with brain tissue loss detectable by Magnetic Resonance Imaging (MRI) (Chan 2007). Here we test the relationship between genetic risk for PD and MRI-derived fractional anisotropy (FA), cortical surface area (SA), and subcortical volume. We then study the relation between these neuroanatomical measures and behavioral phenotypes.

Method: Demographics, behavioral, genomic and brain imaging data were obtained for 40,000 UK Biobank participants. The relationships between PD polygenic risk score and grey and white matter morphometry were assessed using linear regression. Partial least square (PLS) analysis was then used to investigate the behavioral phenotypes linked with brain features.

Result: PD polygenic risk score was positively associated with cortical SA, subcortical volume, and white matter FA across the brain. The PLS analysis revealed alcohol usage, education level, household income, fluid intelligence, and height as positively associated with these brain features and multiple deprivation index as negatively associated.

Conclusion: These results reveal a link between genetic susceptibility to PD and brain characteristics indicative of greater size of grey and white matter structures. This indicates that genes implicated in PD may also lead to increases in neuronal numbers and connections. These associations were in turn related to certain behavioral phenotypes. The findings are consistent with the view that an increase in neural density may make brains vulnerable to neurodegeneration.

Exploring Intranetwork and Internetwork Connectivity in the Olfactory Network and Default Mode Network Across the Alzheimer's Disease Spectrum: An Analysis of COMPASS-ND Data

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Plain Language Summary: Changes in one's sense of smell often precede the memory impairment symptoms of Alzheimer's disease. The brain connections underlying these changes are not well understood in those with or at-risk for the disease. As such, we will examine these changes and their relationships with one's ability to think and smell. These results may speak to the usefulness of smell as a predictor for disease.

Background: Olfactory dysfunction is a prevalent and early symptom of Alzheimer's disease (AD) and often precedes the core memory impairment features of the disorder. Previous work has suggested changes in functional connectivity related to olfaction across the AD spectrum, however few have examined these changes in those with subjective cognitive decline (SCD).

Method: Participants included individuals with SCD (n =131), mild cognitive impairment (MCI; n =352), AD (n =156), and cognitively unimpaired older adults (n =97) who served as controls from the 7th COMPASS-ND data release. Independent components analysis was used to identify the default mode (DMN) and olfactory network (ON). We compared intranetwork connectivity in the ON and internetwork connectivity between the ON and DMN between groups and related these findings to olfactory performance and measures of memory.

Results: We observed groupwise deficits in olfactory and cognitive function in MCI and AD groups relative to controls ($p < 0.01$), but not between the SCD and control groups. We expect to find stepwise alterations in functional connectivity within the ON and between the ON and DMN across the AD spectrum, with the greatest deficits in AD and subtle changes in SCD. Further, we expect these changes to relate to poorer olfaction and cognitive performance.

Conclusion: These expected findings would suggest early changes in the olfactory network underlying olfaction and cognition. These data contribute to the potential utility of measuring olfactory performance as a non-invasive and reliable biomarker in SCD for conversion to later stages of the AD continuum.

Cerebral Protective Effects of Sildenafil from Arterial Stiffness

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Plain Language Summary: Stiff arteries, a risk factor for dementia, worsen with age, smoking, and diabetes. This study explores if sildenafil (Viagra), known for dilating blood vessels, can protect the brain from arterial stiffness in mice. After 21 days of daily Viagra injections, results show reduced stress in brain arteries, offering hope for preventing brain damage in patients.

Background: Arterial stiffness is a key risk factor for dementia. The rigidity of large arteries leads to higher pulsatile blood flow in small vessels, increasing the risk of damage to end-organs such as the brain. This study investigates the potential of sildenafil, recognized for its cerebrovascular effects, to provide brain protection in a murine model of arterial stiffness.

Method: Daily intraperitoneal injections of sildenafil are administered for 21 days, with induced stiffness in the right carotid artery on the seventh day using a CaCl2 compress applied directly on the artery. Ultrasound imaging, autoradiography, and dihydroethidium (DHE) microfluorography are employed to evaluate pulsatility, cerebral blood flow, and oxidative stress. Carotid artery compliance is also measured.

Results: Following a dose/response study evaluating the effect on oxidative stress, a concentration of 7.5 mg/kg/day of sildenafil was chosen. This concentration demonstrates a decrease in DHE intensity in the hippocampus. Preliminary findings indicate an augmented compliance in calcified arteries and a reduction in DHE labeling in the hippocampus by sildenafil of mice with carotid calcification.

Conclusion: Given sildenafil's potent cerebrovascular dilating properties, it is anticipated to reduce pulsatility and pressure in cerebral blood vessels, preventing an upsurge in free radicals. Additionally, normalization of resting cerebral blood flow is expected. These results lay the groundwork for potential treatments in patients to avert brain damage.

Characterizing Cholinergic, Neuropathological, and Inflammatory Changes in Human Brain Nuclei Involved in the Sleep-Wake Cycle in Neurodegenerative Disorders

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Plain Language Summary: Persons with neurodegenerative disorders often exhibit sleep disturbances, likely due to changes in brain regions involved in sleep. Examination of these brain tissues showed changes to the cholinergic system and increased pathology and inflammation within sleep-related regions. Insights from this work may guide development of future treatments for these conditions.

Introduction: Neurodegenerative disorders (NDDs) like Alzheimer's disease (AD), dementia with Lewy bodies (DLB), and multiple sclerosis (MS), often manifest sleep disturbances in addition to cognitive symptoms. Sleep, wakefulness, memory, and cognition are, in part, modulated by the cholinergic system. Cholinergic dysregulation is common in NDD brains and appears to play a significant role in cognitive and sleep-wake dysfunction, neurodegeneration, and neuroinflammation. The aim of the present work was to investigate possible contributors to sleep disturbance in patients with NDDs.

Methods: Human tissue blocks containing nuclei related to the sleep-wake cycle in the basal forebrain (BF) and brainstem (BS) from AD, DLB, MS, and cognitively normal brains were examined. Tissues were stained for cholinergic, pathological, and inflammatory markers and analyzed quantitatively and semi-quantitatively.

Results: All AD and DLB cases showed loss of cholinergic neurons and increased microglial, astrocytic, and neuropathological load in BF and BS nuclei compared to normal controls. Most MS cases showed increased neuroinflammation in BF and BS nuclei compared to normal controls.

Conclusion: Results demonstrated that cholinergic, pathological, and inflammatory changes are observed in sleep nuclei in many NDD brains and may underlie sleep-wake disturbances. Investigating mechanisms and contributors of sleep dysfunction in NDDs could help facilitate our understanding of these conditions and provide a gateway for future disease-modifying therapies.

Arterial Territory-Specific White Matter Hyperintensity Burden and Cognitive Performance (Winner of the Master's trainee category competition)

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Plain Language Summary: In age-related dementias, MRI scans show abnormal bright areas called white matter hyperintensities (WMHs) that are often associated with brain blood vessel injury. Our prior research found disease-specific differences in the amount of WMHs in different brain vascular

regions. We show that these patterns correlate with cognition, particularly in mild cognitive impairment and Alzheimer disease.

Background: MRI-detected white matter hyperintensities (WMHs), a vascular brain injury marker, augment with age. WMH volume (WMHv) increase is linked to cognitive decline, and its anatomical distribution is thought to mediate its impact on cognition (Grey *et al*. 2022). Pathological remodeling of the major brain arteries can increase arterial territory (AT)-specific WMHs (Gutierrez *et al*. 2018). We explored the relationship between AT-specific WMHv and cognition in dementia.

Method: We investigated six COMPASS-ND clinical groups: cognitively unimpaired, subjective cognitive decline, mild cognitive impairment (MCI) and Alzheimer disease (AD) with and without high vascular brain injury (N=756). WMHs were segmented (Dadar *et al*. 2017) and AT-specific WMHv determined using the Schirmer atlas (2019). Cognitive performance was measured using psychometric tests (e.g., Montreal Cognitive Assessment). Statistical analyses consisted of a series of linear models adjusted for age, sex, and multiple comparisons.

Result: Poorer cognitive performance was only associated with greater WMHv in the posterior AT for MCI, and in all ATs for AD. Importantly, associations between cognitive performance and WMHv were generally detected in different ATs depending on the cognitive task performed.

Conclusion: AT-specific WMHv was associated with cognitive performance in MCI and AD patients. These categories share unique AT-specific WMH features (Housni *et al*. 2023), suggesting that disease-specific WMH signatures may have a variable impact on cognition. Finally, our results suggest a task-dependent cognitive impact of WMHs within different ATs.

Advancing Dementia Care: Memory Aid Technology and Data-Driven Insights for Autonomy at Home

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Plain Language Summary: This research involves the development of a home-based reminder system that uses electronic reminders to help PLWD manage their daily tasks. It can track their behavior to learn about their routines and detect any unusual changes. This system is being developed with insights from PLWD and family caregivers. The goal is to provide PLWD with more independence and to support their caregivers.

Background: Assistive technology (AT) can empower people living with dementia (PLWD), for example, by enabling them to complete tasks more independently. Following daily routines without the supervised help of caregivers increases the perception of autonomy and dignity in PLWD.

Method: This research focuses on creating a home-based reminder system, featuring electronic reminder units and a central base station, to facilitate dementia care and remote behavior monitoring. Reminders can be transmitted through the base station via a mobile application by the caregiver. The reminder units can detect when a reminder is acknowledged by the PLWD, enabling the collection and analysis of behavioral data. Machine learning models are employed to understand the PLWD's daily schedule and detect any deviations from their regular routines. We engage dyads of PLWD and their family caregivers, gathering information through interviews and usability testing.

Result: Preliminary development, data simulation, user interviews, and prototype demonstrations show that the reminder system has the potential to improve communication between PLWD and their caregivers and can be a useful aspect of their daily routine. The system can be further developed to monitor and analyze behavior, thereby providing valuable insights into the PLWD's daily life and enabling better support and intervention when necessary.

Conclusion: By developing and evaluating this innovative reminder system, we strive to improve the lives of PLWD, enhance their autonomy, and support caregivers in providing effective and personalized dementia care in a rapidly aging society.

DOCTORAL & MD STUDENTS

Fast and Robust Structural MRI Super-Resolution Using Voxel-Size Independent CNNs

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Plain Language Summary: Synthetically increasing brain MRI resolution is a relevant topic since it can improve the quality of the brain measurements used for studying different neurodegenerative diseases as well as normal aging. We are proposing a deep-learning based method that proposes a solution for fast, efficient, and robust brain MRI super-resolution that can be used in both in-vivo and post-mortem applications.

Background: Increasing MRI resolution is an active research field in neuroscience since it can potentially allow for improved brain morphometry without increasing acquisition times. We propose a voxel-size independent CNN that can robustly perform superresolution on in-vivo and ex-vivo MRIs.

Methods: We used 1045 randomly selected T1-weighted scans from ABIDE, ADNI, HCP, IXI, LA5c, MIRIAD, and HBA datasets. Low-resolution (LR) data was simulated by

downscaling by a factor of 2 the native-resolution (HR) data using average pooling. A super-resolution UNet++-like Generative Adversarial Network for brain MRI was trained until convergence using the described dataset. The goal was to approximate the network that maps back the LR to HR, recovering as much detail as possible from the brain MRIs.

Results: We tested on 10 independent images from the same cohorts, downsampling the brain volumes by a factor of 2 and upscaling them back to their original resolution. We compare our method versus cubic BSpline interpolation. Our results show that we managed to increase the image quality in terms of the metrics SSIM, LPIPS, and PSNR in 4 out of 6, 3 out of 6, and 1 out of 6 datasets respectively.

Conclusions: We have developed a super-resolution network capable of robustly upscaling in-vivo and ex-vivo brain MRIs in under 3 minutes, making it feasible for being used in large-cohort studies.

A Combined In-Vivo Ex-Vivo Approach to Assess Microstructural Differences in Neurodegeneration

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Plain Language Summary: The solutions used in brain banks to preserve donated brains lead to changes in their properties, making traditional tools ineffective. We examined these changes on the brains of those who suffered from Alzheimer's and Parkinson's diseases. We scanned them prior and post donation and found altered structures that could benefit our understanding of how these diseases develop.

Background: The Douglas-Bell Canada Brain Bank (DB-CBB) is the largest Canadian repository of donated human brains from various sources (e.g. CCNA, CIMA-Q), which spans various neurodegenerative conditions. The fixation of these brains changes their magnetic properties (Roebroeck *et al*., *Nmr in Biomedicine*, 2019), complicating post-mortem inference of pathology and preventing ante-mortem/post-mortem comparative mapping of the same microstructural characteristics.

Method: To do so, we acquired multimodal neuroimaging of a sample of post-mortem DBCBB specimens that have ante-mortem MRI and clinical data. We assessed fibre integrity and microstructure using diffusion MRI metrics (i.e. fractional anisotropy and mean diffusivity), and compared in-vivo to ex-vivo metrics across AD, PD, and ALS.

Results: We found altered integrity in white matter (WM) in AD and PD when accounting for sample fixation and post-mortem duration. Given that directional diffusivity (e.g. FA) in white matter is minimally affected by specimen fixation, our results point to a change in WM microstructure post-mortem. We were also able to delineate the same tracts in post- and ante-mortem scans, this comparing neurodegenerative effects on both levels.

Conclusion: Using this insight, invasive histological analysis on post-mortem samples can be extended retroactively to in-vivo progression of neurodegeneration by incorporating post-mortem expected microstructural changes.

Supporting Persons Living with Dementia and Their Caregiver with Knowledge Translation: An Ongoing Umbrella Review by the Vascular Training Platform Collaborative

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Plain Language Summary: Caring for a person with dementia requires making informed current and future decisions. We reviewed the existing knowledge available to people with dementia and their carers that help support their decision making. Information on end of life care and other decision making themes were identified. Given that we mostly identified small studies, we recommend larger studies for more reliable results.

Background: Navigating dementia care necessitates decision making on several topics, from daily activities to future care. Moreover, informal carers need additional support in their role (WHO, 2021). We conducted an umbrella review assessing knowledge translation (KT) interventions which support decision making of persons with dementia and their carers.

Method: We searched 4 databases to identify systematic reviews on KT interventions. Our search strategy included keyword combinations pertaining to KT, knowledge users, decision making, dementia, and literature reviews. Through a Vascular Training Platform collaborative, 9 reviewers participated in the screening process.

Result: 22 systematic reviews were included. The most common KT decision theme was advanced care planning such as advanced care directives, feeding options, and place of care. Other themes of KT decision focused on driving cessation and everyday decision making related to fall prevention and medication management. Some KT interventions addressed multiple decisions about current or future matters. Overall, interventions mainly targeted (a) dementia in general, with no studies devoted to specific dementia types, such as vascular cognitive impairment and dementia, and (b) carers without participation of the person with dementia.

Conclusion: KT being an emerging concept, our umbrella review offers insights on the current development of decision support tools for dementia. While a variety of KT interventions exists for persons with dementia and their carers, larger studies are needed since many interventions were tested in small pilot studies.

Disentangling the Effect of Brain Size from Sex Differentiated Aging Trajectories

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Plain Language Summary: The brain changes during aging at different structural levels with sex as a major differentiating factor. However, some brain related sex differences are heavily impacted by the brain size. We aim to separate the effects of sex and brain size in aging trajectories. Here we show regional differences for aging trajectories between sexes which were reduced or eliminated when corrected for brain size.

Background: The aging process leads to loss of cortical and subcortical gray and white matter volumes and these changes differ between females and males (Bethlehem *et al*., 2022). Although there are general aging trajectories, different factors, including sex, lead to distinct outcomes. Many volumetric sex differences found in the brain are induced by the brain size and present a different pattern once this is controlled for (Sanchis-Segura *et al*., 2020). We seek to disentangle the effects of sex from those derived from allometric differences in regional aging trajectories modeled with deformation based morphometry (DBM) and volumetric data from the UK Biobank (UKBB) sample.

Method: We extracted regional DBM values (Zeighami *et al*., 2015) and pre-computed freesurfer volumes from ~39,000 participants in the UKBB sample. We then created an age and total intracranial volume (TIV) matched sample of males and females (maximum one month of age difference at acquisition time and 0.2% difference in TIV) of ~15,000 participants, and another sample of the same size matched just by age. We then modeled the sex differentiated aging trajectories for regions that are commonly affected during neurodegenerative diseases (i.e. hippocampus) in each one of the samples.

Results: Bilateral hippocampi had sex differentiated non-overlapping trajectories in the non-tiv-matched samples, whereas the trajectories largely overlapped in the TIV matched sample. Similar patterns were observed for the substantia nigra and the pallidum, among others.

Conclusion: The differences observed in the modeled aging trajectories are highly influenced by brain size.

Integrating Data-Driven Polygenic Risk Scores, Vascular Health, and Sex in Dynamic Alzheimer's and Lewy Body Biomarker Networks: Precision Prediction of Cognitive Change and Clinical Status in the Victoria Longitudinal and COMPASS-ND Studies

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Plain Language Summary: We test a new technique for assessing genetic dementia risk in two Canadian datasets. First, with an unimpaired aging cohort followed over 42 years, we found that memory changes were predicted by genetic risk and vascular health but differently for women and men. Second, we apply a similar interactive approach to testing group differences in two sets of impairment and dementia cohorts in CCNA.

Background: A data-driven algorithmic approach to calculating polygenic risk scores (PRSs) can be applied for complex prediction in aging and neurodegeneration. In two studies, we calculate global, brain/cognitive aging (BCA), and mechanism-specific PRSs for Alzheimer's (AD) and Lewy body (LBD) disease. PRSs are interactively examined with vascular health (pulse pressure, PP) and sex as predictors of (1) memory change and (2) cohort membership.

Method: Study 1: Cognitively unimpaired (CU) adults (n=614; 53-95; 65.8% F) populated a 42-year distribution of memory trajectories. PRSice-2 software calculated three PRSs. Sex (binary) and PP (continuous) contributed to biomarker network analyses. Latent growth models tested biomarker predictions of memory change. Study 2: In COMPASS-ND, PRSice-2 is used to calculate two global (AD- and LBD-related) and selected mechanism-specific PRSs. For AD, we assess APOE+/- PRSs. Included cohorts: SCI, MCI, AD; PD, PD-MCI, LBD/PDD; with CU as common benchmark. Machine learning classifier models (random forest, SHAP) test the relative importance of PRSs, PP, sex and selected risk biomarkers in predicting cohort membership in the AD (eg., AD v CU; MCI v SCI) and LBD (e.g., LBD v CU; PD-MCI v PD) spectra.

Result: Study 1: PP predictions of memory trajectories were moderated interactively by each of the three PRSs and sex. Study 2 results are pending final data availability.

Conclusion: Study 1 results show that for CU adults, new data-driven PRSs interact with PP and sex to increase precision of memory change. Study 2 is expected to show data-driven PRSs among the leading predictors.

Validation d'un Catalogue de Vidéos à Valence Émotionnelle Positive pour Soutenir la Communication et l'Engagement auprès des Personnes Âgées

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Plain Language Summary: Pour lutter contre l'isolement social des aîné(e)s, nous étudions les effets du co-visionnement

de vidéos qui suscitent des émotions positives entre deux partenaires. Ainsi, 19 dyades de personnes âgées ont visionné 20 extraits vidéo. Nous avons mesuré la communication et les émotions. Nos premiers résultats suggèrent que le co-visionnement favorise la communication et les émotions positives.

Contexte : Au Canada, 30% des aînés vivent de l'isolement social, ce qui est associé au déclin cognitif. Des études suggèrent que le co-visionnement de vidéos à valence émotionnelle positive favorise la communication émotionnelle et l'engagement (Ansaldo *et al*., 2021). Les personnes âgées passent environ 4 heures par jour devant la télévision. Il est important d'explorer ces questions pour proposer un contenu favorisant leur engagement social.

Objectifs : Examiner les effets des vidéos sur le comportement des dyades et identifier les paramètres modulant les émotions positives, la communication et l'engagement.

Méthode : 19 dyades de personnes âgées ont visionné un catalogue de 20 vidéos à valence positive. Des données comportementales (expressions faciales, communication, etc.) et biophysiologiques (rythmes cardiaque et respiratoire) ont été collectées via des questionnaires, des bracelets connectés, des enregistrements audiovisuels et des entretiens semi-dirigés. Des analyses quantitatives avec des algorithmes d'apprentissage-machine et qualitatives sont en cours.

Résultats : Les données préliminaires montrent une corrélation entre le contenu d'écran et l'engagement des participant(e) s, reflétés par une dilatation pupillaire et la stabilisation du rythme respiratoire. Une corrélation positive entre le contenu d'écran et les paramètres liés aux mouvements de la bouche et des sourcils a été identifiée.

Conclusion : Ces résultats offrent des pistes méthodologiques pour l'étude des effets du co-visionnement sur la communication émotionnelle et l'engagement chez les personnes vivant avec des troubles neurocognitifs majeurs.

Brain Metabolite Level Differences Between Young and Middle-Aged Adults Assessed Using 7 Tesla Magnetic Resonance Spectroscopy

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Plain Language Summary: The chemical processes that sustain life, called metabolism, change with advancing age. Levels of metabolites (products of metabolism) can be measured in the brain using neuroimaging. We measured brain metabolite levels in young and middle-aged adults. Our results show alterations in brain metabolites in middle-age, an age where changes associated with dementia may appear.

Background: Magnetic resonance spectroscopy (MRS) can provide key insight into the neurochemical changes occurring with age. Our recent systematic review (Detcheverry *et al*. 2023) indicates that the study of brain metabolite changes in healthy aging is in its infancy, especially in middle-aged adults. Given that neurochemical changes associated with dementia start as early as middle-age, our study aims to characterize the differences in brain metabolite levels between young and middle-aged adults using MRS at 7 tesla (T), a magnet strength considered ideal for the detection of low-concentration, yet biologically relevant, metabolites.

Method: Included in our analysis were 23 adults (N=10 young, 20-29yrs; N=13 middle-aged, 40-59yrs) from our healthy adult cohort with 7T MRI/MRS and blood data. Metabolite levels were measured in posterior cingulate cortex (PCC) and centrum-semiovale white matter (CSWM). A series of linear models, adjusted for sex and multiple comparisons (p=0.05), was performed to assess group differences.

Result: In middle-aged compared to young adults, we found (a) higher levels of myo-inositol and total creatine in both PCC and CSWM, (b) higher levels of aspartate and phosphocreatine in PCC, and (c) lower glutamate levels in CSWM.

Conclusion: Overall, we demonstrate perturbations in brain metabolites in middle-aged adults, which may indicate alterations in the neuroglial glutamate cycle occurring in the mitochondria (Siegel *et al*. 1999). Our future directions are to investigate these pathways in older adults using (a) 7T MRS and (b) plasma metabolomics data from ours and the COMPASS-ND cohorts.

Oxidative Stress is Related to Vascular Brain Injury in Mild Cognitive Impairment of the Alzheimer's Type

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Plain Language Summary: Oxidative stress damages brain cells, and contributes to the pathology seen in Alzheimer's disease continuum. Glutathione is the most abundant antioxidant protecting the brain. We investigated the relationship between brain glutathione level and markers of vascular-brain injury. We demonstrated that oxidative stress is associated with markers of both neuronal and vascular injury in the brain.

Background: Oxidative stress (OS), an imbalance between reactive oxygen species production and neutralization, can damage brain cells and contribute to cognitive decline in Alzheimer disease (AD) (Mandal *et al*. 2015). Glutathione (GSH; most prevalent brain antioxidant) assessed with magnetic resonance spectroscopy (MRS), serves as a brain-OS index. Our systematic reviews (Detcheverry *et al*. 2023a,b) report that brain GSH decreases with age in most regions, with greater decrease in AD. Since the relationship between GSH and vascular-brain injury is unknown in the AD continuum, we address this gap in mild cognitive impairment (MCI).

Method: 3T MRI/MRS data from 31 MCI participants were obtained. GSH and total N-acetylaspartate (tNAA; neuroaxonal integrity marker) were measured in posterior cingulate cortex (PCC) and frontal white matter (FWM). Cerebrovascular injury was assessed using white matter hyperintensity (WMH) volume and Fazekas scores. Global and regional brain tissue integrity was assessed using normalized brain (NBV) and hippocampal (HCV) volumes, respectively. Cognition was assessed with the Montreal Cognitive Assessment (MoCA). MRS data were processed using FID-A and LCModel. Pearson correlations between GSH and other markers were performed.

Result: We found significant associations ($p<0.05$) in FWM between GSH/total creatine (tCr) and tNAA/tCr, and between GSH and (a) WMH volume, and (b) NBV; and no association with cognition.

Conclusion: In FWM, lower GSH was associated with higher cerebrovascular injury, and lower brain volume and axonal integrity, suggesting that OS in WM contributes to vascular-brain injury.

Advancing Inclusive Research: Exploring the Dynamics of Remote Research Using the Montreal Cognitive Assessment

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Plain Language Summary: The significance of remote research is growing due to its accessibility and cost-effectiveness. This study explored how participants and researchers perceive remote research, uncovering its pros and cons. The findings suggest that conducting research via phone is well-received and holds promise for underrepresented communities facing geographical, physical, or sensory limitations.

Rationale: Remote cognitive screening can be a pathway to inclusive research practices. Using tools such as the Montreal Cognitive Assessment (MoCA), serves to enhance accessibility, reduce logistical constraints, and can lead to cost-effective and efficient data collection. The transition from conventional (i.e., in-person) to remote test administration requires understanding of the remote process to effectively navigate challenges and develop best practices. We used the MoCA-Blind as a vehicle to examine the experience of delivering and participating in remotely delivered research.

Methods: Participants included research volunteers (n=10) and researcher assistants (n=4). The research interaction was framed by a tele-administration of the MoCA-Blind, followed by semi-structured debriefing interviews. Thematic analysis of the research interaction was conducted within each group.

Results: Participants emphasized the importance of measure brevity and convenience, as well as pre-session communication; barriers included session length, challenges with phone-based tasks, and potential participant dishonesty. Research assistants noted facilitators including measure brevity, rapport-building, and session preparation; concerns included tools with excessive response options, telephone-related issues, and communication challenges.

Conclusion: These findings suggest that a remotely administered cognitive test such as the MoCA-Blind could be a vehicle for feasible and acceptable data collection, with the potential to enhance the participation of underrepresented individuals, such as those with physical and/or sensory impairments.

A Computational Model of Cerebral Metabolism Bridging Nano, Micro, and Mesoscales

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Plain Language Summary: Alzheimer's disease patients unfortunately get diagnosed when it is far too late to intervene. Considering that its characteristics bear a striking resemblance to the normal aging brain, we are designing a mathematical model of the human brain. By simulating how a brain can move

from a healthy to a non-healthy state during normal aging, we may facilitate earlier diagnosis of Alzheimer's disease.

Abstract: Computational models enable us to better account for the abundance of causal candidate factors for AD, their parameters, as well as individual conditions. With a system of ordinary differential equations, we are developing a model to simulate how these factors interact through one's lifetime. This work describes our effort to model glucose hypometabolism, known to be one of the major changes associated with AD. We will structure our model 1) at the nanoscale, in terms of glucose and insulin concentrations; 2) the microscale, in terms of rates of uptake of glucose by neurons and neuronal populations; and 3) the mesoscale, with approximations of brain glucose uptake by cerebral structure. We will build the model through rounds of systematic and assumption-based adjustments, as well as sensitivity analyses during model validation where we correlate the expected outcomes of glucose uptake with real-life PET FDG data on well over 3,000 participants across the spectrum of normal cognition and AD, at the mesoscale. Using computational models can allow us to understand complex systems as they evolve through time, unearthing causal relationships, allowing for the formulation of numerical hypotheses, and providing information to tailor therapeutic approaches.

How People Living With Alzheimer's Disease Cope With It?

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Plain Language Summary: People newly diagnosed with Alzheimer's disease experience a wide range of undesired emotions leading them to adopt different individual coping strategies. In our research we found both adaptative and less adaptative coping, like hope and resilience versus withdrawal and avoidance. It appears obvious that individual accompaniment based on pleasant memories could be helpful to face the diagnosis.

Introduction: A diagnosis of a major cognitive disorder due to Alzheimer's (MCD-AD) represents a significant life change for aging people. To face the feelings accompanying this period, adaptative coping strategies are required. To better tailor interventions to their specific needs, it will be necessary to understand these processes.

Aims: An in-depth exploration of the coping strategies used by people with Alzheimer to face their recent diagnosis.

Method: An exploratory qualitative design was adopted. In-depth interviews were conducted with ten French-speaking individuals aged over 70 years, recently diagnosed with a mild MCD-AD. We applied an interpretative phenomenological analysis to transcribed data. Rigor was based on authenticity, reflexivity, and information power.

Results: Participants engaged in an oscillatory process between their positive past-life memories and their current experiences. This enabled them to cope with undesired emotions and maintain meaning in their life. Coping strategies helped to preserve their autonomy and quality of life. Some participants showed more adapted coping strategies reinforced by feelings of self-determination, hope, and resilience. On the contrary, less adaptive strategies were also observed, actualized by avoidance and withdrawal.

Conclusion: Our results a better understanding of individual differences in emotional experience and coping strategies used after a diagnosis of MCD-AD. This new understanding can be used to improve individual accompaniment during this period of change. An intervention based on nostalgic reminiscence would be helpful for improving adaptation.

A Bio-Cognitive Network Analysis of Alzheimer's Disease Using Neuroimaging and Neuropsychological Test Performance Data from the COMPASS-ND Dataset

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Plain Language Summary: The brain is incredibly complex. Given this, it can be difficult to capture all the factors involved in the decline of one's brain and mind when studying a disease like Alzheimer's. Our study used networks, which can better model this disease complexity, to study the interactions between brain structure and cognitive abilities (e.g., memory, attention) of older adults with or at risk for dementia.

Background: The brain-behavior relationship in the Alzheimer's disease (AD) spectrum involves interactions between numerous biopsychosocial factors. Network analysis can be utilized to capture the multiple associations between cognitive and biological factors in bio-cognitive networks[1]. Thus, the goals of this exploratory study were (1) to identify salient bio-cognitive relationships within different risk states for AD, and (2) to compare network structures generated by these relationships across different clinical groups.

Methods: Measures from the COMPASS-ND[2] cohort were used to construct mixed graphical models[3] for cognitively normal (CN, n = 90) aging, subjective cognitive decline (SCD, n = 127), mild cognitive impairment (MCI, n = 327), and AD (n = 134) groups. Neuroanatomical, cognitive, and sociodemographic variables were selected for group models. Analyses included determination of prominent within-group network structures and comparison of networks across clinical groups.

Results: Male sex was associated with decreased white matter burden (WMB) in clinical groups as well as poorer performance on verbal tasks. High WMB was strongly associated with age and female sex in SCD and MCI. Hippocampal volume

was positively associated with free recall tasks in MCI and AD groups.

Conclusion: Network analysis applied to bio-cognitive data is a promising method for researchers to harness multivariate complexity and clarify the brain-behavior associations expressed during earlier stages of AD risk.

References: [1] doi: 10.1016/j.neubiorev.2021.07.027; [2] doi: 10.1017/cjn.2019.27; [3] doi: 10.18637/JSS.V093.I08.

Sensory Profiles of Mild Behavioral Impairment in the COMPASS-ND Study

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Plain Language Summary: This research on 191 older adults from the COMPASS-ND study showed that better smell and vision are linked to a lower risk of mild behavioral impairment (MBI), which is an early warning sign for dementia. Different sensory changes were tied to specific MBI symptoms. The findings highlight the need for further research into sensory and behavioral warning signs for dementia.

Background: Later life emergent and persistent behavioral changes, known as mild behavioral impairment (MBI), can signal incipient dementia. Leveraging the Comprehensive Assessment of Neurodegeneration and Dementia (COMPASS-ND) study (release 7), we aimed to investigate the sensory profiles associated with MBI.

Method: Participants had normal cognition, subjective cognitive decline, or mild cognitive impairment. Olfactory, auditory, and visual functions were examined. MBI status was defined by an informant-reported MBI-Checklist score ≥5. We modelled associations between sensory measures (exposure) and MBI status (outcome) using logistic regression, adjusting for sensory aids, demographic factors, and cognitive diagnoses. A secondary analysis examined associations between sensory variables and specific MBI domains.

Result: In our sample (n=191, 55% female), 28.3% were MBI+ (mean MoCA=23.4±3.3) and 71.7% were MBI− (mean MoCA=25.1±3.0). Poorer olfaction (aOR=3.33, 95%CI [1.60−7.22]) and visual contrast sensitivity (aOR=2.47, 95%CI [1.14−5.49]) were associated with MBI+ status. For MBI domains, olfaction was linked to decreased motivation, affective dysregulation, and impulse dyscontrol. Hearing loss was specifically associated with affective dysregulation, and lower visual contrast sensitivity with impulse dyscontrol.

Conclusion: Sensory changes are linked to MBI in older adults without dementia and distinct sensory modalities are differentially related to MBI domains. These findings warrant further investigation into the interplay between sensory and behavioral dementia markers and potential shared etiology.

Validation of Accelerometry for the Identification/Monitoring of Neuropsychiatric Symptoms Correlated with Motor Activity in Persons Living with Dementia: Results from a Diagnostic Test Accuracy Systematic Review

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Plain Language Summary: We studied whether wearable devices that measure physical activity can recognize and track emotional responses in people with dementia. Our results show that these devices can reasonably detect 5 important symptoms. In future, these devices may be used to support caregivers with valuable emotional symptom information about the person(s) under their care.

Background/Objectives: Wearable sensor technology shows promise for neuropsychiatric symptoms (NPS) identification/monitoring in persons living with dementia (PLWD). Accelerometry measures acceleration of body segments and physical activity. This study explores the diagnostic test accuracy (DTA) of accelerometry to identify the following 5 NPS associated with motor activity: agitation, aggression, apathy, anxiety, and aberrant motor behavior (AMB).

Methods: As part of a larger systematic review, we conducted an extensive literature search in nine health science and engineering databases. Meta-analysis involved converting correlations to Fisher's Z scores, calculating 95% confidence intervals using the R Studio Metacor package, and assessing fixed effects, DerSimonian and Laird's random effects models, and heterogeneity.

Results: Out of 12,853 identified records, 84 reports were retained for analysis. Eight reports that provided 12 datasets assessed the DTA of accelerometry data for identifying/monitoring apathy (n=2), AMB (n=1), anxiety (n=2) agitation (n=5), and aggression (n=2). Studies included one single-blinded trial, one non-randomized trial, and six observational

studies. A random-effect meta-analysis yielded a pooled correlation across studies of r=0.54 (0.46; 0.61), heterogeneity I2=38%.

Conclusions: The findings suggest that accelerometry consistently provides moderate DTA for identifying/ monitoring apathy, AMB, anxiety, agitation, and aggression in PLWD. Future research should prioritize standardizing the reporting of measurement procedures, signal thresholds, outcome measures, devices, and reference stand.

Sociocultural (Re)Validation of the Cognitive Assessment Tools: Leveraging Expert Knowledge Using Bayesian Inference

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Plain Language Summary: Early detection of dementia is critical in improving the quality of life of persons with lived experience of dementia. There is little guidance available, however, on validating and adapting diagnostic tools for ethnically diverse populations. We propose an inferential statistics framework to formally integrate end-user expertise in validating and adapting dementia diagnostic tools.

Background: Early detection of dementia is a national research priority, aimed to improve interventional outcomes and quality of life of persons with lived experience of dementia. Nevertheless, there are mixed opinions on the accuracy and adaptability of cognitive assessment tools (CAT) used to initiate the diagnostic process. Cultural diversity can introduce disparities due to linguistic and cultural barriers. We propose the development of a novel Bayesian framework to formally consider sociocultural factors in the validation and adaptation of the Mini-Mental State Examination (MMSE) and Montreal Cognitive Assessment (MoCA).

Method: Our study is a Monte Carlo simulation study that assesses the sensitivity of construct validity measures of the MMSE and MoCA with respect to varying degrees of expert input (Bayesian prior distributions). Established construct validity metrics of the MMSE and MoCA from the literature will be aggregated with hypothetical expert prior input on the cultural appropriateness of questionnaire items.

Result: The location and width of posterior intervals (i.e., updated knowledge) for the item-domain correlations of CAT are sensitive to expert input, even if the number of experts included is low. That is, input from a small number of end-users can outweigh the results of large-scale studies to inform validation.

Conclusion: Bayesian instrument validation methods incorporating end-user expert input are effective in formally appraising the sociocultural appropriateness of CAT. They allow for a more equitable approach to the validation of CAT in the context of populations of diverse ethnic backgrounds.

Association Between DBM-Derived Atrophy Patterns and Cognition in Frontotemporal Dementia Variants

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Plain Language Summary: Frontotemporal Dementia (FTD) has different subtypes, each causing unique symptoms tied to specific brain changes. Using a sensitive machine learning method, we studied how these brain changes relate to FTD symptoms. Analyzing 136 patients, we found three key patterns linking cognition and atrophy. These patterns predicted FTD types with 76.70% accuracy, suggesting they could aid diagnosis of FTD.

Background: Frontotemporal Dementia (FTD) is a complex condition encompassing various subtypes which exhibit unique symptoms linked to distinct brain atrophy patterns. We used deformation-based morphometry (DBM), a sensitive method for analyzing structural brain differences, to study the relationship between atrophy patterns and clinical features across FTD variants.

Methods: We examined 136 FTD patients (70 behavioral variant FTD, 36 semantic variant primary progressive aphasia, 30 nonfluent variant PPA) from the frontotemporal lobar degeneration neuroimaging initiative (FTLDNI). Partial least squares (PLS) were used to correlate DBM-derived atrophy patterns with cognitive test scores. We then aimed to discern group differences in this relationship among FTD subtypes. We also explored whether combining PLS-derived neural and behavioral patterns could predict FTD subtypes.

Results: PLS analysis revealed 3 significant latent variables, explaining over 88% of shared variance between cognitive performance and brain atrophy patterns. These variables identified networks of primarily fronto-cortical and subcortical regions associated with global cognition and language function. Variations in latent variables II and III showed differing trends between FTD variants. These atrophy and behavioral patterns combined predicted FTD subtypes with 76.70% accuracy.

Conclusion: This study demonstrated a strong link between DBM-assessed neurodegeneration and cognitive symptoms in FTD. These findings highlight the potential use of DBM-based atrophy-cognition relationships as imaging biomarkers for assessing disease severity and subtyping FTD.

Exploring the Relationships Between Nutrition and Indices of Brain Health Among Indigenous Peoples in North America: A Systematic Review

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Plain Language Summary: Little is known about the relationship between consumption of Traditional foods and brain health among Indigenous populations. A review of the literature confirmed this gap in research and highlights existing research on the beneficial effects of polyunsaturated fatty acids in Traditional foods and the neurotoxic effects of environmental contaminants.

Abstract: Colonization has resulted in a loss of Traditional food systems (TFS) and a shift to increased consumption of Western diets, which has been associated with an increase in metabolic and cardiovascular diseases among Indigenous populations. The revitalization of TFS is thought to promote holistic indicators of wellness through the facilitation of self-determination, cultural reclamation, connection to ancestral knowledge, and access to nutritious foods. However, the variety and nutritional content of Traditional foods have been poorly described in scientific literature. Furthermore, despite the established connection between healthy dietary patterns and brain health, there is a paucity of research in this area in the context of Indigenous dietary patterns. This systematic review synthesizes extant literature that examines dietary or nutrient exposures and indices of brain health among Indigenous peoples in North America, and further assesses the extent to which Indigenous research paradigms and community engagement processes have been employed. Findings of this review highlight the neurotoxic effects of environmental contaminants, as well as the beneficial effects of omega-3 polyunsaturated fatty acids in traditional food sources on a range of brain health outcomes including visual processing, memory, and neurologic functioning. Findings also suggest a need for strength-based research that examines the positive effects of nutrients within Traditional foods on brain health, and highlights a lack of community-based research that employs Indigenous research paradigms and epistemologies.

Associations Between Canadian Brain Health Food Guide Adherence and Brain Volume in Older Adults

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Plain Language Summary: This study examined whether adherence to the Canadian Brain Health Food Guide is associated with brain volume among older adults in the Comprehensive Assessment of Neurodegeneration and Dementia Study. Results were not statistically significant and highlight the need to develop questionnaires that better quantify the consumption of specific foods that are associated with healthy brain aging.

Abstract: Research suggests that consuming a healthy diet is associated with better cognitive performance and lower risk of cognitive impairment in later adulthood. Through collaborative efforts of the Canadian Consortium on Neurodegeneration and Aging (CCNA), the Canadian Brain Health Food Guide (CBHFG) was developed to promote eating choices that support brain health, and emphasizes consumption of vegetables, fruits, nuts, fish, and legumes. The objective of this study was to examine whether CBHFG adherence is associated with biomarkers of neurodegeneration, specifically hippocampal volume (HV), and frontal and temporal lobe grey matter volumes (GMV). It was hypothesized that greater BHFG adherence would be associated with larger HV and frontal and temporal lobe GMV. Participants included 1010 older adults (>50 y) enrolled in the CCNA's Comprehensive Assessment of Neurodegeneration and Dementia Study (COMPASS-ND). Participants with different levels of cognitive functioning underwent magnetic resonance imaging and completed a short diet questionnaire (SDQ). Analyses revealed that adherence to the BHFG, as measured by a scale adapted for the COMPASS-ND SDQ, was not associated with volumetric brain data in older adults in unadjusted models or after adjusting for confounders like age and sex. Results did not differ in males and females when data were disaggregated by sex. Findings highlight limitations of the COMPASS-ND SDQ for this purpose and the importance of developing a tool assessing consumption of specific foods and nutrients associated with healthy brain aging.

Role of TREM2 in Amyloid Beta Clearance in the Alzheimer's Disease Eye and Brain

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Plain Language Summary: Plaque development in Alzheimer's disease (AD) disrupts neuronal function, leading to cognitive symptoms. Microglia are key immune cells that control plaque growth. By characterizing factors influencing microglia-plaque interactions, we sought to understand changes in pathological mechanisms with disease progression in the AD eye and brain to inform future early-stage diagnostic imaging.

Background: Triggering receptor expressed on myeloid cells 2 (TREM2) and its ligand apolipoprotein E (ApoE) facilitate microglial interactions with amyloid beta (A β) plaques in Alzheimer's disease (AD). This study assessed changes in TREM2 and A β in the eye and brain with AD progression, as well as the role of ApoE.

Method: Brain sagittal and retinal cross-sections from 3 different mouse models: transgenic APP-PS1, ApoE-knockout (ApoE-KO) and C57BL/6J wildtype (WT) mice were screened at 3 and 9 months using immunofluorescence staining with TREM2 and A β (6E10) antibodies. Images were captured using a Zeiss LSM 800 confocal microscope with ZEN3.7 software and immunoreactivity was quantified using ImageJ.

Result: Across timepoints, TREM2 increased in APP-PS1 ($p < 0.001$) and ApoE-KO ($p < 0.05$) mice retinas and decreased in WT ($p < 0.01$). This was also seen in the cerebrum (neocortex and hippocampus) (APP-PS1: $p < 0.001$; ApoE-KO and WT: $p < 0.05$). Retinal TREM2 and 6E10 were positively correlated in all models ($r = 0.434$-0.646; $p < 0.05$) and 6E10 showed a significant increase with age in both APP-PS1 ($p < 0.01$) and ApoE-KO ($p < 0.05$) mice. Retinal and cerebral TREM2 were positively correlated in APP-PS1 mice ($r = 0.799$, $p < 0.05$).

Conclusion: Our data shows an increase in TREM2 expression with aging in both pathological models, likely induced by A β build-up. A positive correlation between retinal TREM2 and 6E10 suggests a failure in TREM2-mediated A β clearance by microglia. Elucidating mechanistic similarities of AD progression in the retina and brain will help identify retinal biomarkers for future non-invasive imaging methods.

Molecular Cholinergic Dysfunction in the Presymptomatic Stages of Alzheimer's Disease

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[1]*Western University,* [2]*McGill University.*

Plain Language Summary: Cholinergic neurons are a type of cell in the brain. Research suggests that cholinergic dysfunction is an early sign of Alzheimer's disease. However, there is currently no method for measuring cholinergic function. This project evaluated a new tool for imaging cholinergic function. Using the tool, we found that individuals at high-risk for Alzheimer's disease exhibit cholinergic dysfunction.

Background: Alzheimer's disease (AD) staging models suggest that amyloid and tau pathologies do not emerge throughout the brain all at once. Rather, specific neurons exhibit early changes in function, which potentiate downstream pathophysiological events (Braak & Braak, 1991). The cholinergic neurons of the basal forebrain (BF) are among the first cell-types to exhibit pathology in AD (Schmitz *et al*., 2016). However, the lack of a cholinergic biomarker has prevented the evaluation of cholinergic function in early disease stages. PET imaging with [18F]FEOBV overcomes this obstacle (Mulholland *et al*., 1998). FEOBV targets VAChT, a protein found in cholinergic nerve terminals, making it well-suited for measuring changes in cholinergic function. Using FEOBV, we demonstrate the first molecular imaging evidence for cholinergic dysfunction in cognitively normal (CN) humans at-risk for AD.

Methods: We collected longitudinal MRI, cross-sectional FEOBV, and plasma ptau181 data in 64 CN older adults at-risk for AD.

Results: Individuals were clustered into risk groups according to their longitudinal decline in BF volume: normal, low, and high-risk groups. Using FEOBV, we found that high-risk individuals exhibited greater molecular cholinergic dysfunction compared to low and normal risk groups. Increased cholinergic degeneration and dysfunction was also found to be associated with increased levels of plasma ptau181.

Conclusions: We present the first evidence for molecular cholinergic dysfunction in CN humans at-risk for AD, highlighting the utility of FEOBV imaging for detecting at-risk individuals for preventative drug treatments.

Spatial Characterization of White Matter Hyperintensity Pathophysiology

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Plain Language Summary: White matter hyperintensities (WMHs) are radiological abnormalities indicative of small vessel disease often detected in elderly people. It is unclear if WMHs in different brain regions are due to similar causes and if they represent similar pathologies. Here, using advanced imaging sequences, we estimated WMH pathology and derived spatial regions of similar WMHs.

Background: White matter hyperintensities (WMHs) are age-related radiological abnormalities indicative of small vessel disease. It is unclear if WMHs in different regions represent WMHs with similar pathophysiology and etiology. Here, we

developed a framework to estimate WMH pathophysiological processes in vivo, which allowed us to precisely characterize spatial patterns of WMH tissue alterations.

Method: We used data from 32,014 UK Biobank participants. WMHs and normal-appearing white matter (NAWM) were automatically segmented. Diffusion-weighted and susceptibility-weighted images were used to derive fluid-sensitive, fiber-sensitive, and myelin- and iron-sensitive microstructural markers. We calculated voxel-wise normative models of NAWM microstructure using Bayesian linear regression. We then estimated WMH pathophysiology as the difference between WMH microstructure and expected NAWM microstructure.

Result: We used spectral clustering to derive spatial patterns of WMHs that share similar pathophysiological properties. The first cluster (periventricular) had low abnormality on all metrics. The second (posterior) and third (anterior) clusters both showed fluid accumulation, fiber alterations, and myelin and iron loss, but the anterior cluster had higher abnormality on most metrics.

Conclusion: Our results separating anterior and posterior WMHs are consistent with accumulating evidence showing that posterior WMHs could be linked to Alzheimer's pathology, whereas anterior WMHs could be caused by vascular pathologies (McAleese *et al*., 2017, *Acta Neuropathol*).

Exploring Stigmatizing Perceptions of Dementia Among Racialized Groups Living in the Anglosphere: A Scoping Review

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Plain Language Summary: Limited research exists on dementia-related stigma among racialized groups. Findings from this study provide insight in understanding the experiences and stigmatizing perceptions of dementia among racialized groups. Approaching awareness and education efforts with this knowledge can inform effective communication strategies and improve the well-being of persons with dementia and care partners.

Background: A prominent gap exists in understanding stigma among racialized persons living with dementia, care partners, and community. A scoping review was conducted to explore stigmatizing perceptions of dementia among racialized groups living in the Anglosphere.

Methods: Eligible studies focused on dementia and stigma, and reported data on racialized groups (i.e., Black, Hispanic, South Asian, East Asian, Middle Eastern) living in Anglosphere countries (i.e., Canada, United States, United Kingdom, Ireland, Australia, New Zealand). All publication dates were included. Eligible studies were published in English. Scopus, CINAHL, PubMed, PsycINFO, Medline(Ovid), EMBASE databases were searched. Data extraction and thematic analysis was performed on eligible studies using Corrigan's Model of Stigma. Themes were categorized into stereotypes, prejudice, and discrimination.

Results: Thirty-six studies were included. Themes aligning with stereotypes: derogatory and unpredictable labels, religious beliefs and mysticism toward dementia, and associating dementia with other diseases. Themes aligning with prejudices: shame or embarrassment of dementia. Themes aligning with discrimination: discouragement in help-seeking and isolation, and lack of social acceptance.

Conclusion: Dementia-related stigma among racialized groups delays diagnosis and the participation in support programs. Future studies will examine the communication of dementia-related stigma through conversations between racialized persons living with dementia and their care partners using conversational data from the Canadian Consortium on Neurodegeneration in Aging.

Multimodal Data Identification of Clusters in Alzheimer's and Vascular Dementia: A Sex Stratified Analysis

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Plain Language Summary: This study used machine learning to analyze health data from the UK Biobank, focusing on people with Alzheimer's disease and vascular dementia. The analysis revealed two distinct groups within each type of dementia, showing significant differences in genetic risk for heart disease, medication use, and frailty levels. However, these groups did not differ significantly in mortality rates.

Background: Inter-individual variability in frailty levels of people living with dementia motivates deeper investigation into dementia's typical presentations. Machine learning applied to large datasets can help identify disease phenotypes. We used unsupervised machine learning to discover clusters in AD and VaD and examine their association with mortality.

Methods: We used prescription medications, cardiovascular polygenic risk scores, frailty index, Townsend deprivation score, and physical activity data from the United Kingdom Biobank. K-means clustering was applied on each group of AD males (n=1588), AD females (n=1702), VaD males (n=1271), and VaD females (n=910). T-tests were used to compare features across clusters. Cox regression was used to determine the relationship between cluster assignment and mortality.

Results: Two clusters were identified for each subgroup. T-tests indicated significant differences ($p<0.05$) in cardiovascular polygenic risk scores, polypharmacy, and frailty index score between the two clusters across all subgroups. High frailty index clusters commonly paired with elevated genetic cardiovascular risk and greater deprivation. There were no significant associations between cluster membership and mortality ($p>0.05$).

Conclusions: Differences in frailty severity, cardiovascular genetic risk, and deprivation across clusters highlight variability in AD and VaD. Lack of association between clusters with mortality suggests that outcomes centered around patient well-being may be more relevant for evaluating disease impact and guiding individualized care.

Understanding Sensory-Psychosocial-Cognitive Relationships in Mild Cognitive Impairment: Does Psychosocial Function Mediate the Relationship Between Sensory Loss and Cognitive Function?

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Plain Language Summary: Our study explores how social functioning explains the link between hearing or vision difficulties and poor cognitive performance in older adults with mild cognitive impairment. Initial findings show that sensory loss has a direct relationship with cognitive performance, and this relationship is not explained by poor social function.

Background: Sensory and psychosocial factors are risk factors for Alzheimer's disease (AD). We explore whether sensory loss leads to communication and mobility difficulties, thereby reducing social engagement and contributing to cognitive decline. The interactive sensory-social-cognitive relationship remains unexplored in older adults with mild cognitive impairment (MCI), who are at-risk for AD.

Method: Using the COMPASS-ND dataset (Release 7), we assess sensory loss (e.g., pure-tone hearing, contrast sensitivity), cognitive test performance (e.g., memory, executive function, processing speed, verbal fluency), and psychosocial factors (e.g., anxiety, social support) in 351 individuals with MCI. Our objectives were to: 1) describe sensory-psychosocial function in this group and 2) determine if psychosocial function indirectly mediates the link between sensory loss and cognitive function.

Results: Individuals with MCI demonstrated mostly minimal scores on anxiety and depression questionnaires and reported adequate quality of life and social support. Psychosocial variables did not indirectly mediate pathways between sensory loss and cognitive performance. However, hearing loss was directly associated with phonemic fluency, whereas contrast sensitivity was directly associated with delayed recall and executive function. There were no significant relationships between sensory loss and psychosocial function. There were significant associations between quality of life and performance on delayed memory and processing speed.

Conclusion: Our findings suggest that psychosocial function may not mediate, but moderate, the relationship between sensory function and cognitive performance.

Preliminary Study on Developing an Indigenous Functional Assessment (IFA) Tool

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Plain Language Summary: There is an absence of appropriate culturally safe dementia assessment for the Indigenous population. With the adaptation of the Canadian Indigenous Cognitive Assessment, the community identified the need to develop an informant-based functional assessment tool. Thus, in partnership with Indigenous community organizations, we conducted a study on developing a functional assessment tool.

Abstract: Dementia prevalence is rising significantly among the Indigenous populations. Despite the significant rise in dementia prevalence, there is an absence of culturally safe, relevant, and appropriate dementia assessment and care services specifically for the Indigenous population. To address the need, the Canadian Indigenous Cognitive Assessment (CICA) was adapted and validated as a culturally safe and relevant tool for dementia assessment in Indigenous communities. While validating the tool, Indigenous communities and physicians involved in the process identified the need for an informant-based functional assessment tool. The functional assessment tool is supposed to assess the Instrumental Activities of Daily Living (IADLs) as they are the first to decline with cognitive impairment in an individual. Thus, we conducted community-engaged research in partnership with Maamwesying North Shore Community Health Services, an Indigenous health organization providing quality health care and dementia services to the Indigenous communities in Northeast Ontario. A Community Advisory Group (CAG) with an Elder was formed to guide the research process. Both the CAG and partner organizations were involved in every stage of the research process. Two focus groups were conducted with Indigenous and non-Indigenous health providers to understand their perspectives on the aspects of IADLs. Six themes and sub-themes were identified from the focus groups. This research lays a foundation for our community partner, Maamwesying, to develop an Indigenous Functional Assessment tool that is used along with CICA.

Neuropsychiatric Symptoms in Idiopathic REM Sleep Behaviour Disorder

Mariko Trépanier Maurais[1,2], Léa Bernier-Lalonger[2], Coline Zigrand[1,2], Ronald B. Postuma[1,3], Jacques Montplaisir[1,4], Isabelle Rouleau[2],Jean-François Gagnon[1,2].
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Plain Language Summary: Idiopathic REM sleep behaviour disorder (iRBD) is a prodromal stage of dementia with Lewy bodies (DLB). Mild cognitive impairment (MCI) and psychiatric symptoms are common in iRBD, but their association has been poorly studied in this population. Our results suggest that mild hallucinations are frequent in iRBD patients with MCI, evoking, even in a prodromal stage, the clinical profile of DLB.

Idiopathic REM sleep behaviour disorder (iRBD) is a parasomnia characterized by abnormal motor activity during REM sleep. iRBD is also recognized as a prodromal stage of dementia with Lewy bodies (DLB). Mild cognitive impairment (MCI) and psychiatric symptoms affect 30% of iRBD patients, but their association has been poorly studied. We aimed to evaluate the severity of psychiatric symptoms in iRBD in relation to cognitive status. We recruited 179 patients with iRBD, including 67 (37%) with MCI, and 99 controls matched for age, gender, and education. Questionnaires measuring symptoms of depression (BDI-II), anxiety (BAI-II), hallucinations (UPDRS-I), and apathy (UPDRS-I) were completed. Groups were compared using ANOVAs and chi-square tests, and correlations were performed to assess the relationship between cognitive performance and psychiatric symptoms.

Hallucinations were more frequent in patients with MCI compared to patients without MCI and controls (22% vs. 9% vs. 0%; $p<.05$). Depressive, anxiety, and apathy symptoms were more severe in both groups of patients than in controls ($p<.05$). Moreover, the presence of hallucinations was associated with poorer performance on tests measuring visuospatial abilities ($p=.009$). These results suggest that the presence of mild hallucinations in iRBD is associated with MCI and poorer visuospatial abilities. It is also consistent with the clinical profile of patients with clinical DLB. Longitudinal studies would provide a better understanding of the progression of psychiatric symptoms in relation to cognitive decline and the development of neurodegenerative diseases in iRBD.

Exploring Biomarkers in an Ongoing Phase 3 Clinical Trial of Nabilone for Agitation in Alzheimer's Disease (NAB-IT)

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Plain Language Summary: Agitation is a highly disruptive symptom in people with dementia. Current treatments have limited benefit and significant adverse effects. We previously showed that nabilone may reduce symptoms of agitation. We are now conducting a larger clinical trial to advance this finding to assess the efficacy of nabilone and whether a blood test can help determine which patients are likely to benefit most.

Background: Agitation is a highly prevalent and distressing neuropsychiatric symptom (NPS) of Alzheimer's disease (AD) with few treatments that have adverse effects. Our pilot study suggested that nabilone, a synthetic cannabinoid, may be a safe and efficacious treatment for agitation in AD. We are conducting a phase 3 trial across 5 centres of team 11 to advance this treatment and to explore biomarkers of mechanistic relevance.

Methods: Participants with AD and agitation will be randomized to receive either nabilone or placebo for 8 weeks. Agitation will be assessed with the Cohen-Mansfield Agitation Inventory (CMAI). As secondary outcomes, we will assess behaviour with the Neuropsychiatric Inventory Nursing Home Version (NPI-NH) and cognition with the standardized Mini Mental Status Exam (MMSE). The endocannabinoids 2-arachidonoylglycerol (2-AG) and N-arachidonoylethanolamine (AEA) will be assessed using liquid chromatography-mass spectrometry (LC-MS) as biomarkers of agitation and response to nabilone treatment.

Result: The mean age of the 44 participants that have enrolled thus far is 80.4±7.3, with 59% being female (n=26). Mean CMAI, NPI, and MMSE at baseline are 59±18 (n=43), 40±25 (n=43), and 9.5±7.0, respectively.

Conclusion: If positive, this clinical trial may advance a novel treatment for agitation in AD, and identify subgroups of agitated AD patients based on biomarkers who are most likely to benefit from treatment.

Interactive Associations of Age at Menopause and Vascular Risk with 3-Year Cognitive Change in The Canadian Longitudinal Study on Aging

Madeline Wood Alexander[1,2], Che-Yuan Wu[1,3], Gillian Coughlan[4], Tanvi Puri[5], Rachel F. Buckley[4,6,7], Priya Palta[8], Walter Swardfager[1,3], Mario Masellis[1,9], Liisa A. M. Galea[10,11], Gillian Einstein[12-14], Sandra E. Black[1,9], Jennifer S. Rabin[1,2,9,15].
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Plain Language Summary: This study investigated factors that increase women's risk for Alzheimer's disease. We analyzed data from postmenopausal women aged 45-85 in a Canadian observational study. We found that women with both younger age at menopause and greater cardiovascular risk had the most cognitive decline, suggesting that they may be at higher risk for Alzheimer's disease.

Background: Vascular and hormonal processes may together contribute to AD risk in women. We investigated whether age at menopause, vascular risk, and history of estrogens-containing hormone therapy (HT) together influence cognition over a 3-year follow-up period.

Methods: Participants were postmenopausal women in the Canadian Longitudinal Study on Aging. Vascular risk burden was quantified with a summary score. Cognition was measured with a global cognitive composite at baseline and 3-year follow-up. Linear models tested interactive associations of age at menopause, vascular risk, and history of HT with cognition at 3-year follow-up, adjusting for baseline cognition and relevant covariates.

Results: We included 8,360 postmenopausal women (mean age at baseline=65.0±8.53 years, mean age at menopause=50.1±4.62 years). There was an interaction between age at menopause and vascular risk, such that earlier menopause and higher vascular risk were synergistically associated with lower cognitive scores at follow-up (β=0.013, 95% CI: 0.001, 0.025, p=.03). In stratified analyses, vascular risk was significantly associated with lower cognitive scores in women with earlier menopause (menopausal ages 35-48), but not average (ages 49-52) or later menopause (ages 53-65). HT did not further modify the synergistic association of age at menopause and vascular risk with cognition (β=-0.005, 95% CI: -0.032, 0.021, p=.69).

Conclusion: Endocrine and vascular processes may together contribute to AD risk in women. These findings have implications for sex-specific dementia prevention and intervention strategies.

Best Practices of Information Transfer Between Hospital Geriatricians and Family Physicians: A Mixed Methods Study

Dimitri Yang[1], Carolyn Pavoni[1], Aigul Zaripova[1], Sandrine Couture[1], Sabrina Lessard[2], Claire Godard-Sebillotte[1].
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Plain Language Summary: Geriatricians often diagnose cognitive disorders in older patients during hospital stays. There lacks a systematic way of transferring geriatric notes to family doctors. This harms the care of the patient since crucial information about their health is lost. Geriatricians believe that having a system to do so is important, and using an electronic medical record can help.

Background: In Canada, many major neurocognitive disorders are diagnosed during an acute illness, in hospitals by geriatricians. However, there is no systematic process for transferring geriatrician notes to primary care physicians (PCPs), causing a loss of information. The objectives of this study are to describe the transmission of geriatrician plans to outpatient providers, identify barriers and facilitators to implementing best practices, and generate evidence-based recommendations to improve this transmission.

Methods: First, we developed a survey sent to geriatricians about the transmission of their notes to the patient's PCP. A descriptive analysis was performed. Second, we conducted 20-minute semi-structured interviews with geriatricians. Thematic content analysis was performed.

Results: Key survey results indicated that although geriatricians believe that consult notes should be sent to PCPs and lacking a systematic procedure negatively impacts quality of care, only 2% say that such a procedure exists. Thematic content analysis of our interviews revealed that there is no systematic way of transmitting geriatrician recommendations to PCPs, which disrupts the communication of diagnoses and medication changes; a unified EMR can help; and confidentiality considerations are vital.

Conclusion: Lacking a systematic process for information transfer to PCPs hinders safe and high-quality healthcare to frail older adults, and persons with dementia may be

disproportionately impacted. We hope to generate and disseminate actionable recommendations on effective strategies.

The Novel Amyloid-Interacting Peptide D-AIP Modulates Alzheimer Disease Pathology in a Transgenic Mice Model (Winner of the PhD/MD category trainee category competition)

Hedi Zhou[1], Adeola Shobo[2], Pei You Wu[2], Louis-Charles Masson[2], R Anne McKinney[1,2], Gerhard Multhaup[1,2].
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Plain Language Summary: Alzheimer disease (AD) is the most common dementia, mainly driven by toxic forms of amyloid protein. Our long-term efforts have proven that D-AIP is a therapeutic candidate as it prevented amyloid-related toxicity in test tubes, cells and animals. The recent beneficial effects of D-AIP shown in this mouse study fully support D-AIP to be tested in a clinical study as a prevention measure for AD.

Abstract: Alzheimer disease (AD) is the most prevalent neurodegenerative disease, characterized by progressive cognitive and memory impairment. Neurotoxic amyloid-β42 (Aβ42) oligomers are considered as a key player in AD pathogenesis. The Multhaup lab has developed and tested the Aβ42-oligomer Interacting Peptide (D-AIP) as preventative drug candidate. Previously, we showed that D-AIP possesses favorable biostability, pharmacokinetics, and brain region distribution without observable side effects during wildtype mice treatment. Here we report results from 3βyTg transgenic mouse model treated with D-AIP, proving D-AIP's potential in modulating AD pathology. 3βyTg mice were orally treated with D-AIP for 8 weeks and longitudinal behaviour tests evaluated memory and cognition during treatment. Mice were sacrificed and D-AIP was localized and detected by mass spectrometry (MS) in 3βyTg brains. Effects on amyloid pathology, microglia and astrocyte reactivity were evaluated by immunofluorescence. Ultrasensitive Meso Scale Discovery immunoassays were used to quantify Aβ species. MS analyses revealed that D-AIP had passed the blood-brain barrier and formed complexes with Aβ oligomers in specific brain regions of 3βyTg mice. D-AIP treated 3βyTg mice showed a significant reduction in amyloid-positive neurons, microglia activation, and astrocyte gliosis, indicating that D-AIP could ameliorate amyloid pathology. Our in vivo findings showed that D-AIP specifically targets the earliest amyloid pathology in AD pathogenesis, emphasizing the utility of D-AIP as a drug candidate and the importance of testing D-AIP in a clinical study for AD prevention.

Semantic Memory Deficit in Patients with Isolated Rapid Eye Movement Sleep Behavior Disorder

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Plain Language Summary: Isolated rapid eye movement (REM) sleep behavior disorder (iRBD) is characterized by abnormal sleep behaviors during REM sleep and is considered a prodromal stage of Parkinson's disease or Lewy body dementia. Semantic memory has received little attention in iRBD, and its predictive value for identifying iRBD patients at risk of Lewy body dementia needs further investigation.

Abstract: Isolated rapid eye movement (REM) sleep behavior disorder (iRBD) is characterized by abnormal sleep behaviors during REM sleep and is a prodromal stage of synucleinopathies (i.e. Parkinson's disease and dementia with Lewy bodies). iRBD patients exhibit cognitive decline and about 30% had mild cognitive impairment (MCI). Semantic memory (SM) refers to our ability to store and access to our general knowledge and has received little attention in iRBD. We aimed to evaluate SM performance in iRBD and determine the specific profile of SM deficits according to the presence of MCI. Participants with iRBD (n=107) underwent polysomnography, neurological exam, and neuropsychological assessment. MCI was identified according to published criteria. Two tasks measuring SM were administered, the POP-10 assessing famous person knowledge, and the PUB-12 assessing nonautobiographical retrograde SM. Non-parametric Mann-Whitney and chi-square tests were performed (patients with MCI versus without MCI). Thirty-nine patients (36%) had MCI. For the whole group, 33% and 28% of the patients had impaired performance on the PUB-12 and POP-10, respectively. A higher proportion of patients with MCI had impaired performance compared to patients without MCI on the two SM tasks (POP-10, 43% versus 19%, $p<0.001$; PUB-12, 49% versus 24%, $p<0.001$). Patients with MCI performed worse than those without MCI on both SM tasks ($p=0.02$). SM impairments are frequent in iRBD, particularly in patients with concomitant MCI. Further studies are needed to evaluate the predictive value of SM deficit for identifying iRBD patients at risk of dementia with Lewy bodies.

POSTDOCTORAL FELLOWS

The Role of Bilingualism and Biological Sex as Risk and Resilience Factors in the COMPASS-ND Cohort

Noelia Calvo[1], Natalie Phillips[2], Gillian Einstein[3-6].
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Plain Language Summary: Alzheimer's disease (AD) may disproportionately affect some populations (e.g. women are

more affected by AD than men). Bilingualism has been suggested as a source of Cognitive Reserve- brain's ability to withstand aging and AD. The aim of the present study was to evaluate the individual and potentially interacting effects of biological sex and bilingualism in the COMPASS-ND cohort.

Background: Women are more affected by AD than men (World Health Organization, 2021) and bilinguals show the first symptoms of AD 5 years later than monolinguals (Bialystok *et al*., 2007). Cognitive reserve (CR) can explain these individual differences in cognitive impairment (Stern *et al*., 2023). The aim of the present study was to evaluate the effects of biological sex and bilingualism on CR.

Method: This study used neuropsychology data from 270 MCI participants from the COMPASS-ND cohort, data release 6. Bilingualism was determined through a self-report questionnaire in which participants rated their second language proficiency in reading, writing, speaking and listening. A bilingualism score was calculated with the averages of these components (n=148 bilinguals, 124 monolinguals). Biological sex was a categorical variable with 2 levels (116 women and 156 men). Path analysis was conducted to test whether differences in verbal memory and the MOCA mediated the association between biological sex and bilingualism. Structural equation modelling (SEM) was used to create a CR index that included the following indicators: MOCA scores, RAVLT, bilingualism and biological sex. Simple regressions estimated cognitive performance in relation to the CR indexes.

Results: Preliminary findings showed that bilingualism was related to increased MOCA scores and women had better performance on the RAVLT than men. The CR index predicted better performance in visuospatial memory, and attention.

Conclusion: Higher CR as indexed by bilingualism and biological sex is associated with increased cognitive performance even in the presence of MCI.

A Protocol for Evaluating of the Efficacy of a Community-Based Personalized Dementia Risk Reduction Program for Middle-Aged and Older Adults

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Plain Language Summary: This poster will present the plan for a personalized program designed to reduce dementia risk and promote good cognitive function (memory, problem-solving, thinking speed) in adults ages 50+ without dementia at the Kimel Family Centre for Brain Health and Wellness in Toronto, a new research-driven community centre. This work will help to support healthy brain aging and reduce cases of dementia.

Background: With no effective treatment or cure for dementia, risk reduction is key for preserving cognitive health with aging. Precision risk reduction, which tailors an individual's risk reduction plan to their unique risk profile, is promising, yet limited research has evaluated the feasibility and efficacy of such a program. This poster will present the research protocol for the Kimel Family Centre for Brain Health and Wellness, a first-of-its-kind research-driven community centre built to evaluate personalized dementia risk reduction programs by tracking members' dementia risk and brain health over time.

Method: At baseline, members ages 50+ without dementia will provide a blood and saliva sample, undergo a clinical assessment including cognitive tasks, and complete a series of questionnaires. This information will be used to determine 1) members' polygenic risk scores for dementia, and 2) which lifestyle domains (physical activity, brain-healthy eating, cognitive engagement, mental wellbeing, and social connections) should be addressed. Members will then work with program specialists to address their personalized program strategy tailored to their unique set of risk factors. Dementia risk domains and cognition will be re-evaluated every 6 months and the full assessment of modifiable risk factors will be re-assessed every year to determine change in dementia risk and cognitive function as a function of program adherence.

Conclusion: The findings from this study will provide foundational knowledge about precision risk reduction for dementia to cultivate healthy brain aging and, ultimately, reduce dementia incidence.

Specific Regional Gene Expression Patterns Underlie Cortical Thinning in Dementia with Lewy Bodies

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Plain Language Summary: Mechanisms underlying cortical changes in Dementia with Lewy bodies (DLB) are not fully understood yet. We aimed to study cortical alterations and associated genetics in DLB using brain MRI. We found that DLB was associated with widespread thinning of the cerebral cortex. Regions showing cortical thinning in DLB were enriched for genes related to mitochondrial function and synaptic transmission.

Objectives: Previous studies showed diffuse cortical thinning in Dementia with Lewy bodies (DLB), but mechanistic underpinnings of cortical changes are not elucidated yet. This study aimed to assess cortical alterations and associated transcriptomics in DLB.

Methods: 83 patients with DLB and 86 age- and sex-matched healthy controls were included. T1-weighted MRI scans were processed using FreeSurfer to generate thickness, surface area, and volume cortical maps and parcellated into Desikan-Killiany atlas. Cortical measures were compared between DLB and controls using vertex-based general linear modeling and region-based analysis, correcting for scan site, age & sex. Regional gene expression data from Allen Human Brain Atlas were extracted from 6 healthy post-mortem brains. Partial least squares (PLS) regression was used to identify transcriptomic patterns predicting cortical thinning in DLB followed by gene set enrichment analysis (GSEA) to assess patterns of enrichment in terms of biological processes.

Results: Vertex-based analysis showed significant clusters of frontotemporal cortical thinning in DLB. PLS regression revealed one latent variable of gene expression that significantly predicted cortical thinning in DLB (35.3% of covariance explained). GSEA revealed that atrophy in DLB occurred in regions with higher expression of genes related to synaptic transmission or vesicle processing, and mitochondrial or metabolic factors.

Conclusions: DLB was associated with widespread cortical thinning. Regions showing cortical thinning in DLB were enriched for genes involved in synaptic signaling & mitochondrial function.

Education Protects People at Risk of Alzheimer's Disease from Hippocampal-Related Declines in Episodic Memory

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Plain Language Summary: 62 people above age 65 who were at risk for dementia were measured with brain imaging and a face-and-name memory test. We found that having a smaller hippocampus (a brain region critical for learning and remembering our past experiences) was associated with more memory decline, but only in people with low educational attainment. Over 14 years of education protected against memory decline.

Abstract: A brain region called the hippocampus is recruited when remembering events (episodic memory). Reductions in hippocampal volume occur due to age or Alzheimer's disease (AD), and are associated with greater episodic memory decline. We examine whether educational attainment moderates the impact of hippocampal volume on episodic memory decline. We used an existing database of 62 older adults at risk of AD (diagnosed with subjective cognitive decline or mild cognitive impairment. Participants were enrolled in the Consortium for Early Identification of Alzheimer's Disease-Quebec (CIMA-Q) and Canadian Consortium on Neurodegeneration in Aging (CCNA). At baseline, participants reported the years of education completed, and received structural MRIs examinations to measure hippocampal volume. They completed a Face-Name associative memory task to measure memory decline at baseline, 2 years later, and 4 years later. Education significantly moderated the effect of hippocampal volume on episodic memory decline, β=-1.97 (SE=0.93, 95% CI -3.83, -0.11), p=.04. Lower hippocampal volume was associated with greater memory decline at low education levels (-1 SD below the mean), but not at moderate (mean) or high (+1 SD above the mean) education levels. A Johnson-Neyman analysis indicated that over 14 years of education was needed for a protective effect. Analyses disaggregating by sex did not reveal any sex differences. Findings show educational attainment is neuroprotective against hippocampal-related memory decline, which supports the cognitive reserve hypothesis that lifestyle factors can shield cognition from neurodegeneration.

Patterns of Cognitive Deficits and Brain Atrophy in Mild Cognitive Impairment

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Plain Language Summary: We tested if individuals with MCI would show differences in cognitive deficits and brain atrophy. Damage to the medial temporal lobe has been linked to memory deficits, while damage in cortical areas have been associated with deficits in executive function. We found three different groups of MCI whose cognitive deficits matched the brain atrophy in MRI.

Background: Mild cognitive impairment (MCI) due to typical Alzheimer's disease (AD) is characterized by memory decline and medial temporal lobe atrophy, but atypical cognitive and atrophy patterns in AD have been described in the literature.

Method: We hypothesised that atypical patterns might be observable in individuals with MCI. We used COMPASS-ND data from individuals with MCI to examine 25 scores from the neuropsychological battery, including tests of memory, language, attention, and visuospatial and executive functions. Latent profile analysis was used to cluster the cognitive scores into subgroups. The profiles were then matched with measures of brain atrophy obtained via magnetic resonance imaging (MRI) also from the COMPASS-ND dataset.

Result: Three clusters were identified as the best fit for the data. Cluster 1 performed worse in measures of executive function, naming and reading. Cluster 2 performed worse in measures of memory, visuospatial function and attention. Cluster 3 performed better than the other clusters in almost every measure. These cognitive profiles were compatible with the patterns of brain atrophy. In Cluster 1, the pattern of more executive impairment was accompanied by more prominent

cortical changes, while in Cluster 2 the pattern of memory impairment was accompanied by more prominent atrophy in the hippocampus and entorhinal cortex.

Conclusion: These results suggest that different patterns of cognitive decline and brain atrophy are discernible in individuals with MCI. Further investigation of these differences can aid in the development of clinical tools to diagnose and treat subgroups.

Towards the Understanding of Unsuccessful Beta-Secretase Inhibitor Trials in Alzheimer Disease (Winner of the Postdoctoral trainee category competition)

Irem Ulku[1], Rocher Leung[1], Fritz Herre[1], Lina Walther[1], Gerhard Multhaup[1].
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Plain Language Summary: A particular focus of Alzheimer disease (AD) research has been on amyloid-β (Aβ) that causes plaque pathology. The enzyme BACE1 exerts the initial step in Aβ production but inhibitors so far have failed to show any beneficial effects. We investigated the molecular details of BACE1's functions and proposed a novel approach considering the role of BACE1 in Aβ clearance in addition to Aβ production.

Abstract: Alzheimer Disease (AD) is a chronic neurodegenerative disorder that is clinically characterized by a progressive decline in cognitive functioning. Neuropathologically, one of the characteristic hallmarks of AD is the buildup of plaques mainly consisting of amyloid-β42 (Aβ42). We recently showed that the beta-site amyloid precursor protein cleaving enzyme-1 (BACE1) has a major role in Aβ degradation in addition to its role in Aβ production. BACE1 cleaves Aβ42 into shorter non-toxic Aβ34. In our new study, we dissected the effects of BACE1 inhibition on Aβ-producing versus Aβ-degrading activity. We assessed inhibition of BACE1 in dependence of substrate and enzyme expression levels. Respective proteins and cleavage products were analyzed by Western blots, mass spectrometry and digital ELISA. When BACE1 is in cellular abundance, BACE1 inhibition elevated Aβ40 and Aβ42 levels while the degradation product Aβ34 was found diminished. Since the amount of newly produced Aβ34 was dramatically and primarily reduced, we concluded that enzyme inhibition targeted Aβ-degrading rather than Aβ-producing activity. Thus, BACE1 inhibitors that were unsuccessful in clinical studies may have failed because of a preferentially impaired BACE1-mediated Aβ-clearance activity in contrast to Aβ-producing activity. Given that BACE1levels have been found 2-folds higher in AD, clinical studies with BACE1 inhibitors could have failed due to attenuated amyloid clearance and concomitantly unaffected Aβ production. Thus, inhibitors preferentially targeting Aβ-producing activity while leaving BACE1's Aβ-degrading activity unimpaired are desperately needed.

Apolipoprotein E Absence Affects Glia Homoeostasis in the Alzheimer's Disease Pathogenesis

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Plain Language Summary: Apolipoprotein E (ApoE) is the strongest genetic risk factor in Alzheimer's disease (AD). Patients carrying APOE4 gene and ApoE null mice show similar features: impaired lipid metabolism and fatty deposits in vessels. In our work, the brain tissues of older ApoE null mice showed defective glia functions. This suggests that inflammatory neurodegeneration may play a role in patients with APOE4 gene.

Background: Apolipoprotein E (ApoE) regulates lipid homeostasis. In the central nervous system, astrocytes express the most ApoE, followed by microglia. This study aims to see the role of ApoE in the pathogenesis of Alzheimer's disease (AD).

Method: ApoE-knockout (ApoE-ko) mice and C57BL/6J wildtype (WT) controls (n=16, 4 per group, females) at two different ages (3-4 and 9-10 months) were studied. Expression levels of 8 microRNAs (miRNAs -101a/-125b/-140/-146a/-15a/-342/-34a/-374c) were determined in 4 brain regions: neocortex-hippocampus, olfactory bulb, brainstem and cerebellum. Next, expression levels of 20 messenger RNAs (mRNAs) which are direct or indirect biological targets of the above miRNAs, and 4 protein markers associated with amyloid beta (Aβ) and neuroinflammation were determined in the neocortex-hippocampus.

Result: Across the brain regions, miRNA levels were low in the younger, and their levels were high in the older ApoE-ko mice. In contrast, expression levels of the majority of the mRNAs were high in the younger, and their levels were low in the older ApoE-ko mice. Importantly, glia (astrocytes and microglia) mRNAs and proteins showed a significant increase or trend of increase in the neocortex-hippocampus of ApoE-ko mice with ageing. However, intraneuronal or extracellular accumulations of Aβ was not detected.

Conclusion: Overall, the expression levels of miRNAs and mRNAs involved in AD pathogenesis showed an opposite relationship in ApoE-ko mice. Impaired glia homeostasis observed with ageing suggests that it could have resulted from impaired lipid metabolism mediated via ApoE.

INVESTIGATORS AND RESEARCH STAFF POSTER SESSION

Awareness of Actions to Reduce Dementia Risk Among First Nations People in File Hills Qu'Appelle Tribal Council: An Adaptation of the Brain Health PRO Platform

Nicole Akan[1], Letebrhan Ferrow[2], Joyla A. Furlano[2], Sylvie Belleville[3], Walter Wittich[3], Laura Middleton[4], Amanda Froehlich Chow[5], Nicole Anderson[6], Natalie Phillips[7], Gail Boehme[1], Connie Ashdoehonk[1], Bonnie Peigan[1], Natalie Jack[1], Rozella McKay[1], Marita Crant[1], Robert Bellegarde[1], Glenda Goodpipe[1], Roberta Agecoutay[1], Margaret Keewatin[1], Tim Poitras[1], Danna Henderson[1], Jennifer D. Walker[2].
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Plain Language Summary: Educational modules designed for older adults in Canada often do not consider whether the materials produced will be relevant to Indigenous communities. This community-based research project highlights the challenges and perspectives from First Nations community members that arose when reviewing the educational online platform, Brain Health PRO.

Background: The Brain Health PRO Platform aims to reduce cognitive decline through online modules designed to educate older adults on preventative health measures for modifiable risk factors. The platform has not included First Nations perspectives in its program development, and therefore does not reflect the needs of First Nations communities. Together with First Nations community partners in File Hills Qu'Appelle Tribal Council, we reviewed Brain Health PRO content and approach. Based on this, we aim to improve the existing Brain Health PRO Platform and develop a guideline on creating a First Nations adaptation of the content and approach.

Method: Ten sequential focus groups were held with eleven community members to review Brain Health PRO content and approach, and to identify areas for improved cultural and contextual relevancy.

Results: Community members highlighted the lack of relevancy of the content presented, such as the exclusion of Indigenous Traditional Knowledge and medicines, land-based teachings, and spirituality. Online program delivery was not the preferred method of sharing information for community members; instead, tangible educational materials and opportunities for in-person gatherings were recommended.

Conclusion: Meaningful improvements to the existing Brain Health PRO Platform cannot be done with minor revisions; instead, larger foundational changes that reflect the interests, concerns and worldviews of First Nations communities are required.

Changes in Ambulatory Physician Visits Among Community-Dwelling Persons Living with Dementia During the First Two Waves of the COVID-19 Pandemic in Three Canadian Provinces

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Plain Language Summary: We investigated the impact of the first two pandemic waves on persons living with dementia using Alberta, Ontario, and Quebec administrative databases. Family physician visits were stable during the two waves compared to the pre-pandemic periods. Specialist visits were lower during the first wave. Among all types of visits, virtual ones were significantly higher while in person visits were lower.

Background: We measured the impact of the first two COVID-19 pandemic waves on physician visits among persons living with dementia (PLwD) in 3 Canadian provinces.

Method: Using Alberta, Ontario, and Quebec administrative databases, we identified retrospective cohorts of PLwD in the community on March 3, 2019 (non-pandemic) and March 1, 2020 (pandemic). We measured rates of overall family physician (FP) visits, cognitive specialists (neurologist, geriatrician, psychiatrist), and other specialists in 3 periods: 1st wave; interim period; and 2nd wave. We estimated incident rate ratios [IRR (95%CI)] with a Generalized Estimating Equation negative binomial model (2020 vs. 2019) and performed random-effects meta-analysis. Virtual and in person visit rates were reported for Alberta and Ontario.

Result: Pre-pandemic cohort (n=167,095) and pandemic (n=173,240) cohort had similar characteristics. Although not statistically significant, up to 12% higher FP visits rates were observed throughout the pandemic periods. Cognitive specialist visits were 15% lower (IRR 0.85, CI 0.8–0.9) in

the 1st wave. Other specialist visits were 29% lower in the 1st wave (IRR 0.71, 0.56–0.9) and 15% lower in the interim period (IRR 0.85, CI 0.78–0.93). For all types of physician visits, virtual visits were higher and in person visits were lower throughout the pandemic periods.

Conclusion: While overall FP visits remained stable during the first two pandemic waves, lower cognitive and other specialist visits during the first wave suggest opportunities for enhancement. The characteristics and outcomes of virtual and in person visits need to be investigated.

Considering Inequities in National Dementia Strategies: Breadth, Depth, and Scope

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Plain Language Summary: Countries are developing national strategies to address dementia. Our study assessed whether OECD countries' dementia strategies considered inequities as a target of concern. We found that most mentioned inequities but very few specified actionable targets to mitigate them in dementia outcomes and care. Countries must engage more deeply with inequity concerns to improve dementia outcomes for all.

Background: In response to global increases in prevalence, countries are developing national strategies to address dementia as a public health priority. These plans aim to improve dementia care to meet the needs of people living with dementia and their care partners. Social determinants of health (SDH) give rise to inequities that impact care and health outcomes in dementia: despite their impact on outcomes, it is unclear whether dementia plans address SDH. This study described whether national dementia strategies considered inequities and identified them as targets of concern.

Methods: We conducted an environmental scan: we screened strategies for eligibility and synthesised information through thematic analysis. We included accessible national-level strategies in English and French from countries that are part of the OECD.

Results: Of the 15 dementia strategies included, 13 mentioned at least one inequity related to: Race/Ethnicity; Religion; Age; Disability; Sexual Orientation/Gender Identity; Social Class; or Rurality. Age was the most, and religion the least, frequently mentioned. 11 strategies included general inequity-focused objectives, while only 5 had specific objectives (tangible goals, deadlines, or budgets) for achieving equity-related targets.

Conclusion: Even though most countries' dementia strategies mentioned inequities, only few had specific inequity-focused objectives. To reduce inequities in the care of persons with dementia, countries must not only consider inequities at a surface-level; rather, they must put forth actionable objectives that intend to lessen the impact of inequities in dementia care.

Deprivation, Dementia, and Disparities in Care and Health Service Use: A Population-wide Study of Community-Dwelling People with Dementia from Quebec (2000–2017)

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Plain Language Summary: We assessed if indicators of care and service use varied according to socioeconomic status (SES) in people newly diagnosed with dementia in Quebec between 2000-17. We found consistent differences across the majority of indicators: e.g., lower SES was associated with higher hospitalisations and deaths. Such disparities in outcomes across SES may indicate inequities in dementia care and service use.

Background: Socioeconomic status (SES) is associated with higher dementia risk and lower cognitive performance: new evidence suggests it is also associated with disparities in care and service use. To ensure equity in dementia care across SES, the association between SES, care received, and health service use in people with dementia must be studied. We described population-level trends of care and health service use in dementia in Quebec.

Methods: We conducted a repeated yearly cohort study of community-dwelling people with incident dementia using the Quebec health administrative database (2000-2017). SES was assessed through material deprivation, a composite measure of the level of education, employment, and income of a census dissemination area. We described age standardised rates per 100 person-year of 23 indicators of care and health service use

during the year following diagnosis across 5 levels of material deprivation based on the area of residence.

Results: Among the 193,834 community-dwelling people with a new diagnosis of dementia between 2000 and 2017, those living in the most versus the least deprived areas had higher rates of hospitalisations, ED visits, and potentially inappropriate medication prescriptions, whereas rates of anti-dementia medication prescription and primary care visits were comparable across SES.

Conclusion: Such differences across SES may signal inequities in the care received by people with dementia. Future research should investigate these associations to better understand their underlying causes and mitigating strategies, in order to offer equitable care to Canadians living with dementia.

Barriers and Facilitators to the Inclusion of Sex- and Gender-Based Analyses in CCNA Research

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Plain Language Summary: Sex- and gender-based analyses (SGBA) are underutilized in research and not well understood. The lack of analysis can result in negative consequences to research rigor and applicability. A survey conducted to assess SGBA uptake in the CCNA identified barriers such as lack of understanding and resources, and facilitators such as personal/local belief of SGBA's importance.

Background: The effects of sex and gender in research are not well understood, leading to consequences such as incomplete analyses and underdevelopment of appropriate interventions. Widespread recognition of the importance of sex- and gender-based analyses (SGBA) by large funders have highlighted the need for SGBA. By understanding the barriers and facilitators to SGBA uptake in the CCNA, we can develop needed next steps to ensure high quality SGBA.

Method: Using an online survey based on the theoretical domains framework, we evaluated all CCNA faculty, staff, and students to understand the barriers and facilitators to the use of SGBA. Quantitative and qualitative analyses were done.

Result: Fifty-seven participants submitted complete responses. Most participants were health services research faculty, who are female, identified as women, and from Canada. There were few respondents from cells, tissues, or animal model groups or Theme 1. Overall, there was a high degree of comfort with SGBA with 94.7% feeling it is part of their role and 84.2% including it in their work. Common barriers to doing SGBA include lack of resources and understanding around how to complete SGBA. Additionally, sex and gender data are inconsistently collected, and clinical tools tend not to capture gender. Common facilitators include having a sex/gender champion on the team and/or personal and local interest and belief in the importance of SGBA.

Conclusion: While there are barriers, we need to continue to work to improve upon SGBA in the CCNA. There has been significant progress in the inclusion of SGBA and faculty comfort with these analyses.

Overcoming Obstacles: Transitioning to Remote Delivery of Activity Assessments with Older Adults at Home

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Plain Language Summary: The SYNERGIC@Home study adapted to remote delivery due to COVID-19. Using Zoom, older adults completed mobility tests. Results: 97% of assessments were completed, 4% required adaptation, and 20% needed troubleshooting. Obstacles, including environmental and technological, were identified. Conclusion: Remote mobility assessments are feasible with planning, supporting future home-based research.

Background: Mobility assessments in brain health research such as dual-task gait and sit-to-stand are traditionally performed in a research lab or clinic setting. The COVID-19 pandemic necessitated a transition to remote assessment. The SYNERGIC@Home study explored the feasibility of delivering brain health interventions and assessments to older adults in their homes. To determine the success of mobility assessments delivered remotely, the percent of completed assessment components, adaptations, and troubleshooting were analyzed.

Method: SYNERGIC@Home recruited older adults with two or more risk factors for dementia. Mobility assessments were done over Zoom and involved a dual-task gait test, a 60-second sit-to-stand test, and several questionnaires. The research team devised materials, instructions, and type of environment participants required at home. Completed assessments were reviewed to determine the percent completed, the adaptions, and troubleshooting required.

Results: There were 157 mobility assessments completed. Of these, 97% of assessments were fully completed, 4% required adaptation, and 20% involved the assessor troubleshooting during delivery or scoring. There were obstacles met during the assessments study which can be categorized into environmental, technological, or performance.

Conclusion: SYNERGIC@Home demonstrated that mobility assessments consisting of mobility tests and questionnaires can be done successfully using a remote delivery model. These results suggest that future research focusing on mobility assessments in the home can be done with appropriate planning and adaptations.

Development and Validation of a New Prediction Tool for Worsening Cognitive Performance Among Home Care Clients

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Plain Language Summary: We set out to create a new tool to give people an idea about their risk for their cognitive performance getting worse over six months. This new tool was created using data on about 40,000 people getting home care. The new tool gives home care staff information about someone's risk. This will help them as they make key choices in providing care to older people living at home and getting home care.

Background: To develop and validate a prediction tool for the risk of a decline on the interRAI Cognitive Performance Scale (CPS).

Method: Retrospective cohort study using interRAI data, collected between 2010 and 2018, in five provinces and one territory. Eligible home care clients had at least two assessments and remained as home care recipients for the six-month observation window. They were selected randomly for model derivation (75%) and validation (25%). All clients had a CPS score of zero (intact) or one (borderline intact) at baseline, out of a possible score of six. The main outcome was any degree of worsening (i.e., increase) on the CPS score within six months. The derivation cohort was used to develop a multivariable logistic regression model to predict the risk of a deterioration in the CPS score. Model performance was assessed on the validation cohort using discrimination and calibration plots.

Results: We identified 39,292 eligible clients, with a median age of 79.0 years, 62.3% were female, 38.8% were married and 38.6% lived alone. On average, 30.3% experienced a worsening on the CPS score within the six-month window. The final model had a good ability to discriminate between those who did and did not deteriorate on the CPS (c-statistic of 0.65), with excellent calibration.

Conclusion: The model accurately predicted the risk of deterioration on the CPS score over six months among home care clients. This type of predictive model may provide useful information to support decisions for home care clinicians who use interRAI assessments across Canada.

Comparing Subjective and Objective Approaches to Evaluating Sleep Quality in Older Adults

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Plain Language Summary: Older adults often struggle with sleep, and this can impact cognitive function. Assessing sleep quality is challenging. Our study on dementia risk involved a 16-week exercise and cognitive intervention and used two tools to measure sleep quality. Comparing both tools revealed weak or no associations between sleep quality measures. This shows the importance of using multiple tools to measure sleep.

Background: Older adults frequently experience sleep difficulties. Adequate sleep is an important contributor to preserving cognitive function. However, assessing sleep quality is a challenging task. Previous research recommends including subjective and objective sleep measures when evaluating sleep quality in older adults, as evidence suggests that perceived sleep measures differ from objective sleep measures.

Methods: This contribution describes a secondary analysis of data from the SYNERGIC@Home/SYNERGIE~Chez soi randomized controlled trial. This was a home-based feasibility study that targeted older adults at risk for dementia to evaluate if they will adhere to a 16-week in-home, multidomain, supervised exercise and cognitive intervention. Baseline sleep measures included a subjective (Pittsburgh Sleep Quality Index (PSQI)) and an objective measure (wGT3X-BT, Actigraph). Partial Pearson correlations were calculated for the three sleep measures: sleep efficiency, sleep disturbance and sleep duration, while adjusting for covariates age and cognitive status (MOCA).

Results: For all comparisons between the subjective and objective measure of sleep, for each of the three sleep measures, the correlation values ranged from $r(59) = -0.19$ to 0.17 (N=60) and no significant correlations were found ($p \geq 0.05$).

Conclusion: These data provide further evidence that objective and subjective measures of sleep differ in older adults. This suggests that when assessing sleep quality in older adults, it is necessary to use subjective and objective measures, as these indicators do not seem to capture the same aspects of sleep quality.

Participant Experiences with a Patient Navigation Program for People with Dementia, Their Care Partners, and Members of the Care Team

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Plain Language Summary: The project Navigating Dementia NB embedded 6 patient navigators in primary care settings, to help persons with dementia and their family navigate health and social care systems in NB. The needs of the 150 participants included: social services, dementia information, advance care planning, community resources, and home health care. Evaluation results showed general satisfaction with the program.

Background: Navigating Dementia NB/ Naviguer la démence NB was a research project that piloted a patient navigation (PN) program in New Brunswick (NB) for people with dementia (PWD) and their care partners. This program aimed to increase the knowledge of, and access to, health and social services and resources related to dementia care.

Method: This program was piloted for 12 months (July 2022-July 2023). Six patient navigators (4 anglophone and 2 francophone) were embedded in preexisting primary care clinics and health centres across NB. We conducted a mixed-methods evaluation of the program, using data collected from patient navigator charts, self-report surveys, and semi-structured interviews with participants.

Results: Across sites, 150 participants (PWD and their care partner) took part in the study. Reasons for contacting the navigators included: connecting with social services, dementia specific information and resources, advance care planning, community resources, and home health care. Thirty-seven participants completed interviews about their experiences with the program, and qualitative content analysis of this data is underway. Preliminary analysis identified general satisfaction with the program, supportive patient navigator activities, existing systemic barriers, and recommendations for program improvement.

Conclusion: Preliminary findings indicate the PN program, integrated into existing clinics, benefits PWD and caregivers, enhancing their interaction with health and social care systems and emphasizing the importance of care integration.

Implementing a User-Friendly Electronic Informed Consent Process for the CAN-THUMBS UP Brain Health Support Program

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Plain Language Summary: The CAN-THUMBS UP Brain Health Support Program is a fully remote study that has created a user-friendly and interactive electronic informed consent process (e-consent). 6 out of 7 study sites used the interactive e-consent online system. 88% of participants completed the e-consent process to join the study. This supports the use of this e-consent process in future studies.

Background: The CAN-THUMBS UP Brain Health Support Program is a fully remote study that has enrolled participants with increased risk of dementia from all regions of Canada. To support remote enrollment, a user-friendly and interactive electronic informed consent process (e-consent) has been implemented with the goal of developing an online tool that is engaging and enhances participants' understanding of the study.

Method: The e-consent has been developed within the Longitudinal Online Research and Imaging System (LORIS). Participants are e-mailed a unique link to log into the online platform. The platform contains an e-consent landing page containing "doors" that the participant must enter to complete that section of the consent. Once a section is complete, the participant answers a short quiz to confirm comprehension. After successful completion of each section, the participant is given the option to voluntarily consent. A date and time stamp is stored as record of consent within LORIS and a PDF version of the consent is available to download and save.

Result: 6 out of 7 study sites implemented the e-consent process and received ethics approval from their local REBs. Among the 6 sites, 88% (n=322) completed the interactive

e-consent process. 10% did not complete the e-consent and declined participation. Only 2% (n=6) required an alternate version of consent.

Conclusion: Participants were able to self-navigate the platform and electronically provide consent with minimal issues. The adoption and uptake of this e-consent process was highly successful and supports its continued use in future remote clinical trials.

Exploring the Helpfulness and Feasibility of Recommendations to Diversify Dementia Research Through the Experiences and Attitudes of Minorities— DREAM Survey

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Plain Language Summary: People from minority groups are often left out of research studies about dementia. Advice is available to help researchers be more inclusive, but we don't know what people from minority groups think about it. We developed a survey to ask people from minority groups for their feedback on the advice for researchers. We present results of the survey and show people's opinions on the advice.

Background: Minority communities are disproportionally impacted by dementia yet remain underserved in research, leading to health disparities and complex ethical and social issues. The need to enhance participation in dementia research is urgent, and it is unclear whether existing guidelines to promote engagement have been developed in consultation with minority communities. This study aims to capture perspectives of individuals from or working with under-served communities about the feasibility and helpfulness of existing recommendations to improve representation in dementia research.

Method: Recommendations from dementia organizations in North America were collected and streamlined to develop a nationwide survey. The survey is delivered in five languages to increase accessibility and diversity among the target audience. People from underserved groups and those working in dementia research or services are invited to take part. Survey rating responses will be analyzed quantitively. Free-text responses will be analyzed by content analysis.

Results: Five publications were reviewed and a resulting 82 recommendations were developed into 28 survey questions across three themes: research design and planning, recruitment, and retention/research experience. Participants are invited to rate each recommendation for feasibility and helpfulness. We aim for a sample size of N=130. We reveal current findings from the survey.

Conclusion: Results will inform the development of participant-centred strategies for enhancing diversity in dementia research and serve as a step toward improved health outcomes and equity in dementia care.

Does Adherence to Interventions Depend on Pre-Allocation Preference?

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Plain Language Summary: In research comparing treatment combinations, people often receive treatment not matching their preference which could impact adherence. In a novel home-based online brain health intervention for older adults at risk of dementia, we found that preferences formed during, not before, the intervention. Regardless of treatment received, older adults will adhere to novel brain health interventions.

Background: Interventions using double-blind RCT can be difficult to mask, especially in multi-domain interventions where preference for one type of intervention may also influence adherence.

Methods: SYNERGIC@Home targeted older adults at risk for dementia and was powered to detect a relationship between adherence and pre-allocation preference for either exercise (E) or cognitive (C) training. Participants completed a preference questionnaire (IPQ) then were randomized to different combinations of C and E active and control treatments. Adherence over 16 weeks (3 βy per wk) was scored from intervention logs. Analyses included correlation between adherence and whether or not allocated to their preferred arm at baseline. The IPQ was completed after the intervention and they were asked which treatment arm they thought they completed.

Results: Overall adherence was high (>85%, n=52) with no significant correlation between adherence and pre-allocation preference for either E or C interventions. Pre-intervention, there was clear preference for C interventions but post- intervention preference shifted to E. Only 29% of participants guessed their intervention arm correctly.

Conclusion: No relationship was found between preference and adherence to the interventions. A greater interest level in cognitive training was found at the start of the trial but it shifted to exercise at the end, suggesting their preferences formed during the trial and not before. Many control group participants thought they were receiving an active intervention, suggesting the high adherence may be due to the novelty of home-based online interventions.

The Suspected Under-Diagnosis of Dementia in Materially Deprived People in Quebec (2000-2017)

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Plain Language Summary: Our study assessed the association between socioeconomic status (SES) and dementia under-diagnosis. We found that of the people who received a new dementia diagnosis in Quebec (2000-17), there was no difference in the proportion of people who belonged to 5 SES categories. Since lower SES confers higher dementia risk, this suggests that under-diagnosis is especially rampant in lower SES.

Background: Under-diagnosis of dementia is rampant in healthcare settings, with up to ⅔rds of people with dementia going undiagnosed. Evidence consistently demonstrates that lower socioeconomic status (SES) confers greater dementia risk. However, few studies investigate whether lower SES is associated with greater missed diagnoses: large-scale research is required to understand the association between under-diagnosis and SES.

Methods: We conducted a province-wide repeated yearly cohort study (2000-17) of community-dwelling people with incident dementia in Quebec. Data were sourced from the Quebec health administrative database and SES was assessed through an ecological material deprivation index, which provided a composite measure of the level of income, employment and education of one's residential area. People were assigned to 5 material deprivation categories, from least to most deprived. We described incident dementia diagnosis cases across each of these 5 categories.

Results: Among the 193,834 community-dwelling people with a new diagnosis of dementia between 2000 and 2017, the proportion of individuals diagnosed with dementia was similar across each material deprivation category: between 18-20% on average.

Conclusion: Despite the association between higher dementia incidence and lower SES, we found similar incidence rates across SES. These findings indicate that there is likely severe under-diagnosis of dementia in more materially deprived people. Improving access to diagnostic for all can improve quality of life and care, and paint a more accurate portrayal of SES-related disparities in dementia incidence in Quebec.

VRx@Home: A Virtual Reality At-Home Intervention for Persons Living with Dementia and Their Care Partners

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Plain Language Summary: VRx@Home is a virtual reality (VR) at-home intervention aimed at facilitating communication between persons living with dementia and their family care partners. Families watched videos together either using VR (paired with tablet) or tablet only (two weeks each). Both VR and tablet conditions elicited conversations and reminiscence but there was great variability in device and content preferences.

Background: Recent years have seen a notable increase in the popularity of head-mounted virtual reality (VR) systems for evoking reminiscence and improving the quality of life for people living with dementia (PLwD). However, comparatively less is known about the use of VR to facilitate communication between PLwD and their care partners (CP), which is the main goal of the current study. We also aim to explore whether an immersive VR experience would elicit conversations more than the traditional tablet-based technology.

Method: Fifteen families participated in the VR at-home intervention study (VRx@Home) and were presented first with either VR (paired with tablet) or tablet only conditions (two weeks per condition). PLwD and CP watched 360-degree videos together across four themes of entertainment, animals, travel, and sports.

Results: Our preliminary analyses of semi-structured interviews and survey data revealed that both VR and tablet facilitated communication (e.g., more natural, frequent, engaging, and longer in duration) between PLwD and CP as long as the content was stimulating. PLwD and CP both preferred entertainment videos the most, but there was great variability in content preferences overall with the same content eliciting different reactions within and across families. Further, we observed variability in the final preferences for the devices with VR being the preferred system for CP and PLwD being split on their preferences for VR and tablet.

Conclusion: Together, the outcomes of our study reveal that VR and tablet systems are feasible tools for enhancing communication and improving PLwD-CP interactions.

A Profile of Conversations Between Caregivers and Persons with Mild Cognitive Impairment, Alzheimer's Disease and Parkinson's Disease

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Plain Language Summary: A trouble-source-repair analysis of conversations between individuals living with mild cognitive impairment (MCI), Alzheimer's Disease (AD), Parkinson's Disease (PD), and family caregivers revealed significantly more trouble sources for AD and PD groups than MCI. However, caregivers notably created more trouble sources with AD groups. AD groups signaled notably more often misunderstandings.

Background: The purpose of this study was to describe the profiles of conversations between persons living with mild cognitive impairment (MCI), Alzheimer's Disease (AD), Parkinson's Disease (PD) and their family caregivers.

Method: The data includes conversations (N=130) between the study participant (60% male) and a family caregiver (75% female and spouses) and are part of the COMPASS-ND platform. All conversations were transcribed verbatim, segmented into communication units (c-units), and analyzed using the trouble-source repair (TSR) paradigm. A TSR paradigm includes communication breakdowns (or trouble sources), repair initiators (which signal a misunderstanding), and repair strategies (which resolve a misunderstanding).

Results: A one-way analysis of variance was conducted to evaluate between-group differences among communication variables. The MCI group used significantly more c-units than the AD and PD groups. The mean proportion of the TSR sequences was 13% across all groups but with significantly more sequences in the PD and AD groups than in the MCI group. The proportion of trouble sources created by caregivers was significantly greater in conversations with persons living with AD than with persons living with MCI and PD. The proportion of repair initiators used by persons with AD was significantly greater than persons living with MCI or PD.

Conclusion: The findings highlight the active participation of persons living with AD in signalling misunderstandings created by caregivers. They underscore the need for caregivers to be mindful about using language that creates misunderstandings in everyday conversations.

Sociodemographic and Risk Factor Profile of Participants Randomized to a Dementia Prevention Trial Based on Location of Residence and Language

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Plain Language Summary: Recent studies have identified physical and cognitive interventions that may delay the onset of dementia. Less is known about the people who participate. This describes the characteristics of participants randomized to a dementia prevention study by location of residence and preferred language. The groups were similar except the dementia risk factors were fewer in the French participants.

Background: Interventions combining cognitive and physical exercises may delay the onset of dementia. Less is known about individuals choosing to participate in such interventions. This paper reports characteristics of participants that were randomized to a home-based clinical trial for older adults at risk for dementia SYNERGIC@Home/SYNERGIE~Chez soi.

Methods: Age, sex, preferred language, location of residence, education, health literacy, income, and risk factors for dementia were analyzed for 60 participants. They were stratified by location of residence (urban/suburban vs. rural) and preferred language (English=EN vs. French=FR).

Results: Almost half (41.7%) lived in rural locations in New Brunswick. The average age, sex, level of health literacy, language, and number of risk factors were not statistically different between the urban and rural dwellers. In addition, the educational level and income bracket were not significantly different ($p>0.05$). For preferred language, the majority (78.3%) were EN, 46.8% living in rural communities in the province. There were no significant differences between age, sex, location of residence, education, income, or health literacy. However, the FR group had significantly fewer dementia risk factors (3.7 vs. 4.9, $p=0.012$) reporting better sleep quality and being more physically active on risk factor assessment.

Conclusion: Participants in this study are similar in these respects except for the mean number of risk factors for dementia. This suggests that the study sample was homogeneous for location of residence, but more study is needed into the difference in risk factors by language.

Comparing the Sensitivity of Cognitive Tests Delivered Remotely in Older Adults at Risk for Dementia

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Plain Language Summary: The Montreal Cognitive Assessment (MoCA) and Cognitive Function Composite 2 (CFC2) are tools that assess cognition; remote use of these tools is uncommon. This research examined the remote delivery of exercise and cognitive interventions with older adults at risk for dementia. Cognitive tests can be done successfully remotely. The CFC2 seems to be more sensitive to change in this population.

Background: Physical exercise and cognitive training may be beneficial in slowing cognitive decline in older adults at risk of dementia. There is no consensus on how to evaluate cognition remotely and which instruments are sensitive to change in this population. This research compared the sensitivity of the Montreal Cognitive Assessment (MoCA) and Cognitive Function Composite 2 (CFC2) when used remotely to assess cognition of older adults.

Methods: SYNERGIC@Home/SYNERGIE~Chez soi (NCT04997681) is a home-based clinical trial targeting older adults at risk for dementia. Participants were randomized to one of 4 physical exercise and cognitive training arms for 16 weeks. Cognitive tests were completed remotely via Zoom™. A descriptive approach was used to analyze the sensitivity of the MoCA and CFC2 by quantifying the interquartile range (IQR) and measuring ceiling and floor affects.

Results: Sixty participants were consented, 71.7% female, mean age of 69.5 (SD=6.5) years. The IQR for the MoCA was 4 points compared to 7.5 points for the CFC2. Almost 10.5% of the sample had the best possible score on the MoCA, while 5.3 % achieved the best score in the sample on the CFC2, though no one achieved a perfect score. Neither the MoCA ($p=0.076$) nor the CFC2 ($p=0.052$) showed statistically significant changes in scores post-intervention.

Conclusion: The findings suggest that this testing, which is usually done in person, can be adapted and completed remotely via videoconferencing. Although the MoCA is more commonly used clinically, the CFC2 seems to be a more sensitive measure of cognition in this population.

Web-Based Training Module Development to Improve Communication Between Providers and Deafblind Long-Term Care Residents Under Their Care

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Plain Language Summary: Long-term care (LTC) residents who are deafblind often find it difficult to communicate their needs to the people who care for them. We aim to create three web-based, bilingual communication training modules for staff and others who care for deafblind LTC residents. We expect that our training modules under development will improve the quality of care in this setting.

Introduction: Communication challenges between older adult long-term care (LTC) residents with dual sensory impairment (DSI) and their care providers impede care delivery and affect quality of care. Recent evidence has reported positive associations between sensory impairment and both the number and severity of neuropsychiatric symptoms experienced. The goals of our study are to develop and evaluate web-based, bilingual DSI-specific communication support training modules for both regulated and non-regulated LTC providers.

Methods: In Phase 1 of this mixed-methods study, our intersectoral expert team, in collaboration with a purposefully selected co-creation group of knowledge users, developed the content of three 10-min online bilingual video training modules using an online survey, focus groups and member checking.

Results: Survey participants included 12 non-regulated and 17 regulated caregivers; only 14% had received any formal DSI communication strategies training. All participants agreed that training on sensory disabilities and communication strategies is a high priority. Education priorities for both groups included adapting communication behaviours and the use and maintenance of assistive technologies. Non-regulated care providers prioritized the need for training on how to detect sensory difficulties through behavioural observations.

Conclusion: Ultimately, we expect that our training modules under development will improve communication, facilitate relationship-building and enrich the care experience for LTC residents, reduce caregiver burden, and improve overall quality of care in this setting.