Toronto Dementia Research Alliance

Impact Report 2021

TDRA

www.tdra.utoronto.ca

Toronto Dementia Research Alliance
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Executive Summary

With the end of 2021, the Toronto Dementia Research Alliance (TDRA) reflects a challenging yet a successful year. Supported by a strong governance (**Appendix 1**), TDRA clinicians, educators, researchers, learners, patients, caregivers, and staff are committed to advance its mission. They are due a great deal of gratitude. Toward a vision of seamless collaboration among all stakeholders, TDRA has two strategic directions**: standardization of dementia care** and **dementia prevention**. Work along these directions is enabled by an **infrastructure** supported by TDRA's Coordinating Centre.

Projects that aim to standardize care benefit patients by reducing variation in care and providing clinicians with high-quality data. An example is the launch and successful uptake of a common clinical dementia MRI protocol, implemented in April at Sunnybrook Health Sciences Centre, University Health Network and Unity Health Toronto. Since April, nearly 400 scans have used this protocol, providing patients with one of the world's most comprehensive scans to assess dementia.

Towards dementia prevention, TDRA invested nearly $320,000 in **training** and grants including a Brain Medicine Fellowship and three seed grants for six PIs across all TDRA partner sites. In addition, two medical students were funded to conduct dementia research through the Graduate Diploma in Health Research and Comprehensive Research Experience for Medical Students. Lastly, one graduate student was awarded the first Sandra E. Black award for outstanding achievement in clinical dementia research.

Infrastructure projects led by TDRA aim to address key challenges faced by the researchers. To support recruitment, TDRA, along with its Patient and Family Advisory Council, partnered with the Alzheimer Society of Toronto to develop an innovative site that lists lay summaries of studies and allows for direct contact from the community with research teams. This unique approach to recruitment has 25 studies listed to date across the TDRA sites and started to yield successful recruitment. We also launched a new U of T website for TDRA designed to engage the scientific community and the general public.

In 2021, we welcomed Ontario Shores Centre for Mental Health Sciences as a new TDRA partner hospital. Ontario Shores scientists are already leading new TDRA initiatives focused on caregivers and neurotechnology. Projects emerging from TDRA Research Working Groups attracted $4.8 million in external funding in 2021. These projects span the areas of standardizing care in memory clinics and long-term care homes, to discovering novel biomarkers based AI approaches to diagnosing neurodegenerative diseases, combining electrical and ultrasound based interventions to enhance cognition in mild cognitive impairment, and medication re-purposing to delay the onset of dementia.

While the pandemic continues to have a tremendous toll on the people we serve, there is much to look forward to in 2022. TDRA will build on the achievements outlined in this report, and focus on more bench-to-bedside research, more knowledge translation and public education, and more infrastructure to facilitate research collaborations. The future is indeed bright. (For TDRA Governance See **Appendix 1**)

Standardization of Dementia Care

Working closely with stakeholders, TDRA is leading initiatives that aim to implement a set of standardized, evidence-informed approaches to care for dementia across multiple settings. By taking such an approach, the quality of care is improved, and those clinical data can later be leveraged for research.

1. **Standardized Clinical Dementia MRI Protocol:** A common clinical MRI protocol for dementia has been agreed upon and is in use at Sunnybrook, University Health Network (UHN), and Unity Health Toronto (UHT). This protocol will ensure that identifiable pathologies are equally detectable at each site, and ultimately enable these images to be leveraged for research. Since April 2021, 397 MRI scans have been completed (Sunnybrook: 279; UHT: 52; UHN: 160)
   Together with the Ontario Association of Radiologists, TDRA will develop a course accredited by the Royal College of Physicians and Surgeons to promote the protocol. It will provide an overview of the protocol, the pathologies it will detect, and introduce a standard form to interpret the images **(Appendix 2)**. Target audiences are radiologists, neurologists, and geriatric psychiatrists.
   Investigators: **Sandra Black** (Sunnybrook), **Corinne Fischer** (UHT), **Chinthaka Heyn** (Sunnybrook), **Sanjeev Kumar** (CAMH), **Paula Alcaide Leon** (UHN), **Amy Lin** (UHT), **Walter Montanera** (UHT), **Alan Moody** (Sunnybrook), **Christopher Scott** (Sunnybrook), **Carmela Tartaglia** (UHN).

2. **Memory Clinic Standardization:** The operation of this working group (*previously* the Dementia Clinical Research Database) is now led by TDRA, which is focusing on data quality and completeness, and making data from the over 2000 participants available for research. Since last December, five requests for data analysis have been fulfilled **(Appendix 3)**. TDRA is funding a co-op student to support data entry at each site that took part in the initial recruitment of participants. Ontario Shores has also joined this project, and is now able to access and contribute data. A pilot among clinicians of the standardized intake form has been completed. Feedback will be incorporated into a new release. This group was also successful in receiving external funding (~$2 million) to support ongoing work and incorporate AI into these memory clinic assessments and triaging.
   Investigators: **Sandra Black** (Sunnybrook), **Bradley Buchsbaum** (Baycrest), **Morris Freedman** (Baycrest), **Sean Hill** (CAMH), **Sanjeev Kumar** (CAMH), **Tyler Redublo** (PFAC), **Stephen Strother** (Baycrest), **David Tang-Wai** (UHN**), Carmela Tartaglia** (UHN)

3. **Long-Term Care Homes Standardization:** A new Research Working Group formed in 2021 and developed standards for neurology and geriatric psychiatry consultation to patients living with dementia in long-term care homes. The group also received external funding ($200,000) to develop a clinical intake took that captures these standards and allows embedding research into care with the long-term care sector.
   Investigators: **Amer Burhan** (Ontario Shores), **Corinne Fischer** (UHT), **Morris Freedman** (Baycrest), **Sean Hill** (CAMH), **Sanjeev Kumar** (CAMH**), Krista Lanctôt** (Sunnybrook), **Frank Palmer** (PFAC)

Dementia Prevention

A number of modifiable factors have been identified that contribute to the risk of dementia. TDRA's efforts to advance work in this area focus largely on building capacity in translational research, and on supporting the development of promising ideas through small, targeted grants.

1. **Temerty-Tanz-TDRA Initiative:** In partnership with the Temerty Faculty of Medicine and the Tanz Centre for Research in Neurodegenerative Diseases, TDRA launched a 3-year and $1.05 million initiative focused on exploring the link between dementia and depression. Depression has been identified as a key risk factor for dementia. There are three elements to this initiative:

   Temerty-Tanz-TDRA Research Fellowships:

   i) *Temerty-Tanz-TDRA Brain Medicine Research Fellowship in Dementia and Depression:* Eleven applications were received and reviewed by a Selection Committee with representatives from Baycrest, CAMH, Sunnybrook, UHN, and U of T. The Committee selected **Dr. Iryna Palamarchuk**. Dr. Palamarchuk will focus on combining transcranial alternating current stimulation and focused ultrasound to enhance prefrontal cortical function in older patients with depression or mild cognitive impairment.

   ii) *Temerty-Tanz-TDRA Post-Doc Research Fellowship in Dementia and Depression:* This fellowship call remains open to applicants with PhDs.

   Temerty-Tanz-TDRA Seed Funding: Awards valued at $70,000 to seed innovative research at the intersection of depression and dementia were launched in June. Submissions were to be multi-site, or collaborative among basic and clinical sciences. Nine applications were received and scored by a panel of four external reviewers and a member of the Patient and Family Advisory Committee (PFAC). All applications were of high quality and three were funded:

   i) *Impact of lipopolysaccharide on immune response and cerebral amyloid deposition in older adults with a history of major depressive disorder*
   Investigators: **Damien Gallagher** (Sunnybrook), **Ariel Graff-Guerrero** (CAMH)

   ii) *The contribution of cerebrovascular disease to depression in patients with and without Alzheimer's disease*
   Investigators: **Carmela Tartaglia** (UHN), **Angela Golas** (CAMH)

   iii) *Assessment of heart rate variability in older adults with lifetime history of depression or mild cognitive impairment*
   Investigators: **Linda Mah** (Baycrest), **Jean Chen** (Baycrest/U of T)

   Annual Workshop: To promote the work of the Fellows, Seed Fund awardees, and the community of researchers focusing on depression and dementia, an in-person workshop will be organized in November 2022.

2. **KCNI-Tanz-TDRA Project:** In a collaborative effort that brought together a team of scientists from across CAMH Krembil Centre for Neuroinformatics (KCNI), the Tanz Centre for Research in Neurodegenerative Diseases, and the TDRA, funding was secured ($600,000) to develop non-invasive diagnostic and prognostic algorithms - based on biomarkers and supported by AI - in older individuals presenting with cognitive complaints. The aim of this project is to better diagnose neurodegenerative diseases and ultimately enable targeted treatment in patients with specific underlying disease pathologies.
   Investigators: **Daniel Felsky** (CAMH/KCNI), **Morris Freedman** (Baycrest/TDRA), **Ekaterina Rogaeva** (UHN/Tanz), **David Tang-Wai** (UHN/TDRA), **Carmela Tartaglia** (UHN/Tanz)

3. **Focused Ultrasound (FUS) – transcranial Alternating Current Stimulation (tACS) Project:** : This other externally funded ($500,000) collaborative project will focus on the feasibility and preliminary effects of combining two non-invasive stimulation methods, FUS because of its ability to stimulate precisely deeper brain structures, e.g. hippocampus, with tACS delivered to the cortex has been shown to enhance working memory in older adults, and assess whether the combined stimulation with result in synergistic effects by activating together the prefrontal-hippocampus network.
   Investigators: **Kullervo Hynynen** (Sunnybrook), **Tarek Rajji** (CAMH)

Investing in Learners

In addition to the training opportunities secured by the above initiatives and projects, TDRA is supporting the following initiatives and learners:

1. **CREMS Summer Students**: This program provides medical students the opportunity to lead a summer research project. TDRA funded half of the stipend of **Daksh Datta**, who worked with **Krista Lanctôt** at Sunnybrook in 2021. Daksh examined data from the COMPASS-ND study for changes to the brain related to neuropsychiatric symptoms common across the dementias. TDRA plans to fund additional CREMS students in 2022.

2. **GDipHR Program:** Over 20 months, medical students in this program take graduate-level courses and lead a research project. TDRA will fund half the stipend of **Shreya Jha**, who will be working with **Sanjeev Kumar** at CAMH on abnormal cortical excitability in dementia and its association with brain metabolites and clinical symptoms using TMS-EEG and Magnetic Resonance spectroscopy.

3. **MITO2i-TDRA Fellowship***:* The Mitochondrial Innovation Initiative (MITO2i) and TDRA have partnered to co-fund a fellowship focusing on the role of the mitochondria in dementia. Two applications are currently under review with a decision anticipated in early 2022.

4. **Sandra E. Black Award in Clinical Dementia Research:** This year's recipient of the Sandra E. Black award was **Veronica Vuong**, a Ph.D. student in **Claude Alain**'s lab at Baycrest. Veronica's project focuses on how listening to music influences memory and neuroplasticity in people with MCI and early dementia, combining behavioural and cognitive measures and EEG.

Building Research Infrastructure

Administrative and operational hurdles in clinical and multi-site research initiatives can cause significant delays and they are often not unique. TDRA is working across sites to develop harmonized solutions to pressing issues, and build infrastructure to fill gaps that impact progress.

1. **Pre-negotiated legal agreements:** TDRA is working with legal teams across partner sites to create standardized, pre-negotiated agreements. A standardized licensing agreement for the Toronto Cognitive Assessment (TorCA) and a data-sharing agreement are nearing the final stages of review. The former enables TDRA to collaborate with groups to translate and validate the TorCA in different languages, and the latter facilitates access to data across studies within the TDRA network. A draft clinical research collaboration agreement for a new clinical trial will soon be circulated for review.

2. **Partnership with the Alzheimer Society of Toronto**: TDRA has partnered with the Alzheimer Society of Toronto (AST) to help connect the public with research through two new initiatives.

   Listing Research on the Toronto Dementia Network: The Toronto Dementia Network (TDN) is a site operated by the AST that lists services such as respite care, nursing, transportation and other forms of support. On June 29, 2021, a section was added that lists plain-language descriptions of research studies led by members of the TDRA community. Individuals can indicate their interest in a specific study and be connected to the research team. If they cannot find a study, they can choose to be triaged to a study through a defined process based on information they enter (ex., preferred location, intervention vs observations, age, etc.). A process to equitably triage these potential participants was developed with input from all TDRA sites.

   The site lists 25 studies (Baycrest: 4, CAMH: 5, Sunnybrook: 11, UHN: 5), and has received 18 inquiries (7 for a specific study, 11 wishing to be triaged). Of these, three are pending enrollment.

   *Webinar Series: Advances in Dementia Research***:** This new series called *Advances in Dementia Research* features bi-monthly plain-language webinars delivered by TDRA researchers. Researchers are encouraged to discuss a study that is actively recruiting and listed on the TDN. The webinars are open to anyone, allowing members of the public to engage directly with researchers. To date, two webinars have been hosted, with 45 and 70 attendees, respectively. Detail on the types of attendees is listed in **Appendix 4**.

3. **Collaborations with the MINT Memory Clinics:** TDRA is supporting the MINT Memory Clinics – a primary care group that specializes in diagnosing and managing dementia in the community – in their efforts to build a research referral service similar to the TDN. This could be another avenue to cross-promote studies led by researchers in the TDRA community.

4. **Supporting the Canadian Agency for Drugs and Technology in Health (CADTH)**: A working relationship has been established with CADTH, a federal agency that provides evidence-based reviews of new medications to groups like Health Canada. With the recent approval of aducanumab by the FDA, CADTH is preparing for its review in Canada and of similar drugs targeting amyloid. Members of the TDRA community – including members of the PFAC – will provide subject matter expertise on a range of topics for which CADTH is seeking input.

5. **Enriching Shareable Resources***:* Several studies led by TDRA investigators have collected samples and banked them for future use. TDRA proposes to catalogue these samples and create a virtual biobank that other investigators can browse and request for analysis. This approach aims to create mutually beneficial, collaborative relationships between the study investigators and researchers looking to access samples. When analyzed in a consistent manner, these data could be pooled with other common assessments (*i.e.,* TorCA, standardized imaging protocol) to create a growing collection of high-quality, research-ready data on dementia.

6. **Open Science:** To support the accessibility of data and to encourage its use, TDRA is collating a set of principles to support the practice of open science among its community of researchers. Researchers who adopt the common standards listed above will be encouraged to make their data available based on these principles, which will acknowledge the producers of the data. A preliminary review of these principles has been carried out by a member of the TDRA's Patient and Family Advisory Council (PFAC).

Knowledge Translation

TDRA aims to inform its broad range of stakeholders (*i.e.*, patients, researchers, learners, decision-makers, and donors) of ongoing progress through several knowledge products, as well as opportunities to share information. They include:

1. **TDRA Website:** TDRA's website is the main "source of truth", and with feedback from several stakeholders, was redesigned and launched on December 20th. In its present form, content is clearly organized for different audiences; the previous site has been embedded within the current site and will host tools for researchers, such as the TorCA. TDRA hosts two blogs: *Scientist Explains Series*, which offers plain-language summaries of key topics in dementia, and the *TDRA Spotlight Series*, which provides plain-language overviews of the work led by a TDRA researcher. Traffic to the website has been steadily increasing, as outlined in **Appendix 5**.

2. **Social Media:** TDRA operates Twitter and LinkedIn accounts that aim to extend the reach of knowledge products to broader audiences, provide platforms to promote upcoming opportunities/events, and drive traffic to the website. Overtime, TDRA's social media presence has been steadily growing. Key metrics for Twitter and LinkedIn are listed in **Appendix 6** and **Appendix 7**, respectively.

3. **An Engaged Patient and Family Advisory Council (PFAC):** TDRA is pleased and fortunate to have a very engaged PFAC that maintains the patient's and caregiver's perspectives across all initiatives. To ensure they have the opportunity to contribute, efforts are being made to have a member of the PFAC join each of the Research Working Groups (RWGs), as well as the Scientific Advisory Committee and the Research Operations Committee; 9 of 14 committees/groups have a representative. As noted earlier, a PFAC member joined the review of the Temerty-Tanz-TDRA Seed Funding competition, and a PFAC members have been co-Investigators in grant proposals. Other highlights of the PFAC's activity are in **Appendix 8**.

4. TDRA's Voice to the Canadian Dementia Research Community's Stance on Aducanumab – To ensure patients and their families have an accessible understanding of the implications of the FDA approving Aducanumab, a statement was co-developed with the Tanz Centre for Research in Neurodegenerative Disease. TDRA also provided significant feedback to a similar pan-Canadian statement led by the CCNA, and published in the Canadian Geriatrics Journal. Recently, this statement was linked to in an article by the New York Times.

Grants Secured and Submissions Under Review by TDRA Research Working Groups in 2021

TDRA has created theme-based working Research Working Groups and brought together researchers – many who had not worked together previously – to develop ideas into funding proposals or lead key initiatives. Several of these RWGs were successful in submitting joint grants together and many in securing external funding in 2021. Below is a list of funded projects and grant submissions currently under review. For a full list of the RWGs, see **Appendix 9.**

Philanthropic Funding Received

1. Amount: $1.5 million (USD)
   Title: Artificial Intelligence in the Memory Clinic
   Description: To develop artificial intelligence-based approaches to support the diagnosis of dementia. Will build on the work of the Memory Clinic Standardization RWG.
   Investigators: **M. Freedman** (lead, Baycrest), **Bradley Buchsbaum** (co-lead, Baycrest), **S. Black** (Sunnybrook), **D. Felsky** (CAMH), **S. Kumar** (CAMH), **S. Strother** (Baycrest), **D. Tang-Wai** (UHN), **C. Tartaglia** (UHN)

2. Amount: $600,000
   Title: Improving prognostic confidence in neurodegenerative diseases causing dementia using peripheral biomarkers and integrative modelling
   Description: To develop non-invasive diagnostic and prognostic algorithms in older individuals presenting with cognitive complaints, to ultimately enable targeted treatment in patients with specific underlying disease pathologies.
   Investigators: **D. Felsky** (CAMH/KCNI), **M. Freedman** (Baycrest/TDRA), **E. Rogaeva** (UHN/Tanz), **D. Tang-Wai** (UHN/TDRA), **C. Tartaglia** (UHN/Tanz)

3. Amount: $500,000
   Title: FUS and tACS to Improve Working Memory in Mild Cognitive Impairment
   Description: To study the feasibility and preliminary effects of combining two non-invasive stimulation methods to engage theta-gamma coupling, and in turn, enhance working memory in amnestic patients with mild cognitive impairment.
   Investigators: **K. Hynynen** (Sunnybook), **T. Rajji** (CAMH), **A. Datta** (Soterix Medical)

4. Amount: $200,000
   Title: Standardization of Specialty Care in Long-Term Care Homes
   Description: Implement framework to triage patients with dementia in long-term care experiencing neuropsychiatric symptoms, and test evidence-based approaches to managing those symptoms.
   Investigators: **A. Burhan** (OS), **C. Fischer** (UHT), **M. Freedman** (Baycrest), **S. Kumar** (CAMH), **K. Lanctôt** (Sunnybrook), **G. Strudwick** (CAMH)

Peer-Reviewed Grants Received:

1. Agency: Weston Brain Institute
   Amount: $1.4 million
   Title: Levetiracetam to modulate hippocampal hyperactivity in a population at risk for Alzheimer's disease
   Description: Excess activation of the hippocampus assessed via fMRI during pattern separation task present in prodromal Alzheimer's disease (AD), and thought to contribute to disease pathology. This study will test Levetiracetam's (LEV) ability to quell elevated activation, and potentially preserve hippocampal circuitry. This study will proceed in two phases; in the first the baseline levels of activation will be characterized in 30 persons not at risk for AD. In the second, 40 individuals showing activation above baseline will be randomized to placebo or LEV 125mg BID, and cross-over to treatment or placebo at 8 weeks. Outcome measure in Phases 1 and 2 is activation in DG/CA3 subfield of hippocampus in normal individuals, in the latter will be assessed pre/post treatment.
   Investigators: **S. Black** (lead applicant, Sunnybrook) **A. Bakker** (Johns Hopkins University), **H. Chertkow** (Baycrest), **M. Freedman** (Baycrest), **M. Goubran** (Sunnybrook), **N. Hermmann** (Sunnybrook), **A. Kiss** (Sunnybrook), **S. Kumar** (CAMH), **B. Lam** (Sunnybrook), **K. Lanctôt**

(Sunnybrook), **M. Masellis** (Sunnybrook), **M.P.McAndrews** (UHN), **S. Mitchell** (Sunnybrook), **L. Pisterzi** (CAMH), **J. Rabin** (Sunnybrook), **T. Rajji** (CAMH), **J. Ramirez** (Sunnybrook), **P. Rosa Neto** (Douglas Hospital Research Centre), **A. Strafella** (UHN), **D. Tang-Wai** (UHN), **C. Tartaglia** (UHN), **K. Uludag** (UHN), **N. Vasdev** (CAMH), **D. Weaver** (UHN), **R. Wennberg** (UHN), **K. Zukotynski** (McMaster University).

2. Agency: Alzheimer Society Research Program
   Amount: $99,932
   Title: Virtual assessment of praxis as a predictor of basic activities of daily living
   Description: Ideomotor limb praxis refers to ability to perform movements such as "pretending to hammer a nail". Research in individuals with stroke suggests that deficits in ideomotor praxis are associated with impaired activities of daily living (ADLs). These deficits can contribute to disability and admission to long-term care. The main questions addressed by the study are whether virtual assessment of praxis can serve as a novel predictor of impaired ADLs in dementia and if it is superior to virtually administered standard ADL questionnaires. We will assess praxis in people living with dementia using videoconferencing on computer or iPad. We will determine whether tests of praxis are better than usual questionnaires for identifying individuals with impaired ADLs, such as feeding, and who thus need a thorough ADL evaluation by an occupational therapist (OT). If successful, the research will improve resource utilization for home ADL assessments carried out by OTs due to better selection of people with dementia who require these evaluations. In addition, demonstrating that praxis can predict ADL deficits may lead to developing novel therapies based on improving praxis to enhance basic ADL function.
   Investigators: **M. Freedman** (lead applicant, Baycrest), **M. Binns,** (Baycrest), **S. Black** (Sunnybrook), **S. Kumar** (CAMH), **T. Rajji** (CAMH), **S. Rotenberg** (CAMH), **D. Tang-Wai** (UHN), **S. Strother** (Baycrest)

3. Agency: Baycrest Health Sciences. AFP Grant.
   Amount: $69,919 (*NOT ACCEPTED*)
   Title: Virtual assessment of praxis as a predictor of basic activities of daily living
   Description: See above
   Investigators: **M. Freedman** (lead applicant, Baycrest), **M. Binns, (**Baycrest), **S. Black** (Sunnybrook), **S. Kumar** (CAMH), **T. Rajji** (CAMH), **S. Rotenberg** (CAMH), **D. Tang-Wai** (UHN), **S. Strother** (Baycrest)

Peer-Reviewed Grants Pending

1. Agency: Alzheimer Society Research Program
   Title: Complexity in EEG: a dynamic indicator of functional integrity to advance research on dementia therapy
   Description: Although there are hundreds of studies per year using conventional techniques, computational EEG has been minimally employed in AD research. Dynamic functional measures such as we propose have been used in a handful of papers, typically focused on discriminating

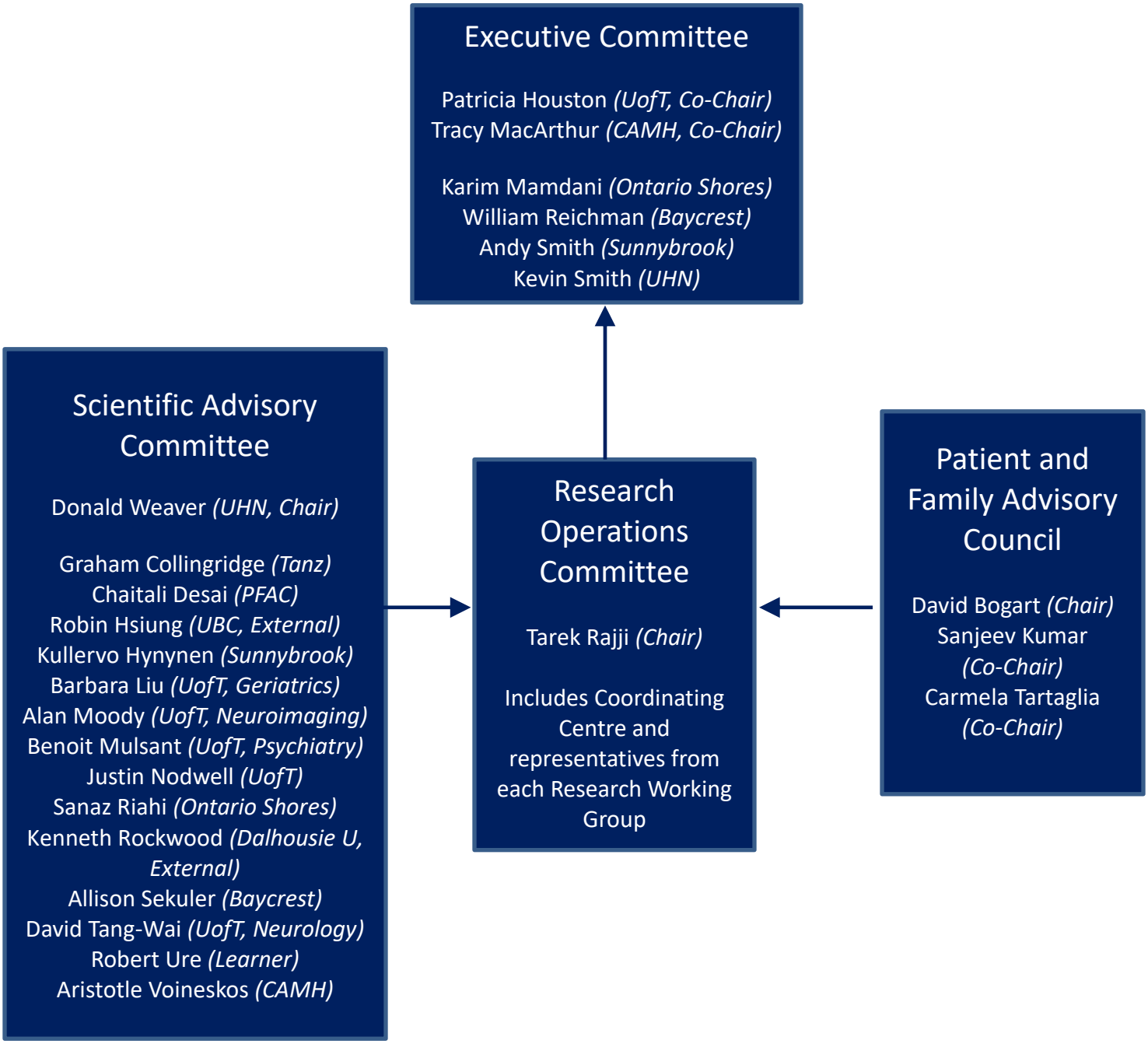
between AD or MCI and controls. However, these sensitive indicators link directly with neural states and thus are likely to afford unique insights into mechanisms. The first step toward exploring these possibilities involves implementing a set of entropy measures on a well-curated data set that includes several deeply phenotyped diagnostic cohorts and the possibility to derive associations with other key measures.
Investigators: **M.P. McAndrews** (lead applicant, UHN), **H. Azami** (CAMH), **S. Kumar** (CAMH), **R. MacIntosh** (Baycrest), **T. Rajji** (CAMH), **E. Roudaia** (Baycrest), **A. Sekuler** (Baycrest)

2. Agency: Brain Canada
   Title: Optimization of Prefrontal Theta-Burst Stimulation to Treat Depression: A Bench to First-in-Human Study
   Description: This project will be a true translational neuroscience project that will optimize the parameters of theta-beta stimulation (TBS), a novel treatment for depression, to induce neuroplasticity in preclinical animal models of depression and then apply these discoveries to compare the new TBS to the old form of TBS in inducing neuroplasticity in people with depression. Enhancing neuroplasticity in depression, a high risk condition for dementia, could not only improve depression outcomes but also reduce dementia risk.
   Investigators: **T. Rajji** (Overall PI, CAMH), **G. Collingridge** (Co-PI, Tanz), **E. Lambe** (Co-PI, U of T), **S. Sockalingam** (Co-PI, CAMH)

3. Agency: Canadian Institutes of Health Research (CIHR)
   Title: Transcranial direct current stimulation (tDCS) for agitation in dementia: a double blind randomized controlled trial
   Description: This study will evaluate the efficacy of tDCS in treating agitation in patients with AD in a randomized controlled trial in LTCH settings. This study will also explore the plasma biomarkers associated with agitation in AD and impact of treatment on these biomarkers.
   Investigators: **S. Kumar** (lead applicant, CAMH), **P Derkach** (West Park), **C. Fischer** (UHT), **G. Strudwick** (CAMH), **K. Lanctôt** (Sunnybrook), **M. Freedman** (Baycrest), **F. Palmer** (TDRA PFAC)

4. Agency: Canadian Institutes of Health Research (CIHR)
   Title: Dementia caregivers skills training through virtual reality
   Description: To build an immersive virtual reality (VR) training environment for caregivers to be directly in touch with the realities of caregiving, and safely practice communications and behavioural management of persons with dementia; and to conduct a quasi-experimental, non-randomized, comparison study to ascertain effectiveness of VR-based caregiver training in improving empathy, competence and caregiver resilience, and reducing depression and stress in dementia family caregivers.
   Investigators: **A. Burhan** (lead applicant, OS), **Mary Chiu** (co-lead applicant, OS), **R. Beleno** (AGE WELL), **K. Kokorelias** (UHN), **T. Rajji** (CAMH), **I. Rubinstein** (U of T), **J. Sadavoy** (Sinai), **A. Shnall** (Baycrest), **M. Smith** (NRC), **J. Zabukovec** (OS), **Lynn Zhu** (OS)

Appendix 1: TDRA Governance Structure



Appendix 2: Proposed Standard Scales for Common Clinical Dementia MRI Protocol

ATROPHY:
Global Cortical Atrophy Scale:
0: normal volume
1: opening of sulci
2: volume loss of gyri
3: 'knife blade' atrophy

Medial Temporal lobe atrophy Score (Scheltens' scale):
Left: Right:
< 75 years: score 2 or more is abnormal.
> 75 years: score 3 or more is abnormal.

Other focal atrophy:

VASCULAR DISEASE
Infarcts:

Microbleeds:

Fazekas scale for white matter lesions:
0 = absent
1 = punctate foci
2 = beginning confluence
3 = large confluent areas

OTHER:

CONCLUSION:

Appendix 3: Requests for Data from the TDRA Dementia Clinical Research Database Project

a. Analysis of whether the sequence in which the elements of the *Clock Drawing Test* are completed differs among the dementias. **Baycrest**; Lead Investigator: **M. Freedman**.

b. Assessing whether one's performance on a cognitive test is impacted by the season in which it is performed. **CAMH**; Lead Investigator: **S. Kumar**

c. An examination of the cognitive domains assessed by the TorCA in persons with Alzheimer's disease to identify subgoups and their neuropsychological markers. **Baycrest**; Lead Investigator: **H. Chertkow**.

d. Examining how the symptoms of Cerebral Amyloid Angiopathy manifest in the various domains assessed by the TorCA and Behavioural Neurology Assessment-Short Form. **Ontario Shores**; Lead Investigator: **A. Burhan**.

e. Using specific errors in the CDT to assess domain-specific cognitive impairments. **Baycrest;** Lead Investigator: **M. Freedman**.

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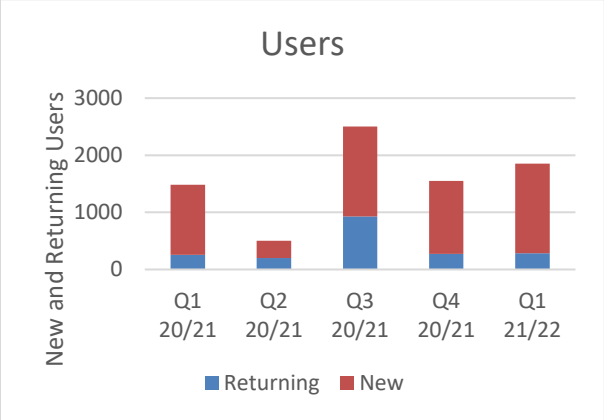
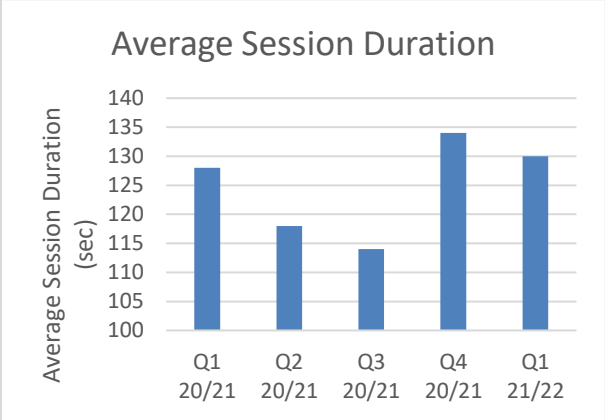
Appendix 4: Detailed Metrics for Advances in Dementia Research Webinars

Metrics	Sept 14 - Driving & Dementia	Nov 17 - Agitation & Dementia
# Attendees	**45**	**70**
Attendee breakdown	- Clinician/HCP- **2**(13%) - Community org- **5** (31%) - Researcher- **4** (25%) - Caregiver/family member-**2**(13%) - Patient- **2**(13%) - Other- **1**(6%) **only n=16 answered this poll*	- Clinician/HCP- **29**(41%) - Community org- **23**(33%) - Researcher- **7**(10%) - Caregiver/family member- **6**(9%) - Patient- **2**(3%) - Other- **3**(4%) **based on registration (not poll)*
Referrals	None yet	1 person connected to study team

Appendix 5: Key Metrics for the TDRA Website

New and Returning Users to the TDRA Website (left), and Average Session Duration (right) from Q1 20/21 – Q1 21/22





Comparison Website Metrics for Q4 (FY: 2020-2021) and Q1 (FY: 2021-2022)

Metric	Q4 2020-2021 (Jun 1- Aug 31, 2021)	Q1 2021-2022 (Sept 1- Nov 30, 2021)	% Change
Returning users	271	285	5.2
New users	1,277	1,567	22.7
Average session duration	2 minutes 14 seconds	2 minutes 10 seconds	-2.7

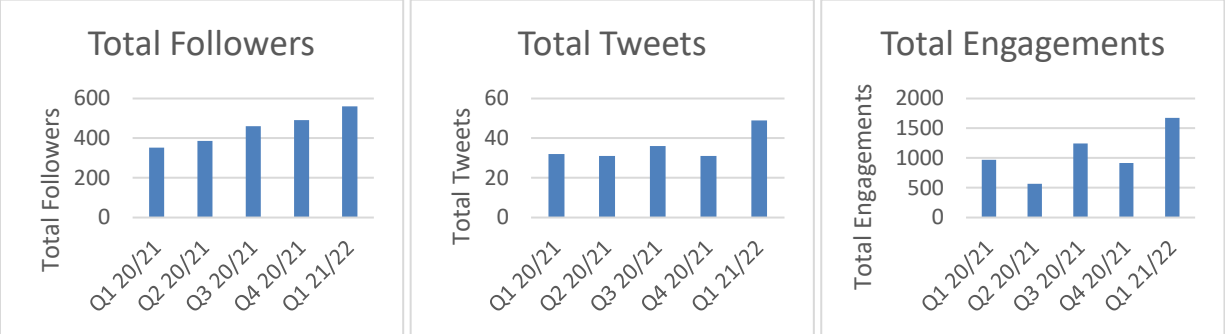
All analytics include CAMH's IP address (our internal traffic/use of the website)

Metric Glossary:

1. Returning users: Users who have visited the website before.
2. New users: Users visiting the website for the first time on a specific device (e.g., if you visit from your desktop and then again from mobile, you are recorded as two users).
3. Average session duration: Amount of time measured from the moment a user lands on the website until the session ends (i.e., user exits the website or is inactive for a predetermined amount of time). A session includes all the interactions a user has with the website (e.g., visiting pages, downloading pdfs, completing a form, etc.).

Appendix 6: Key Metrics for Twitter

Total Twitter Followers (left), Tweets (middle), and Engagements (right) from Q1 20/21 – Q1 21/22



Comparison of Twitter Metrics for Q4 (FY: 2020-2021) and Q1 (FY: 2021-2022)

Metric	Q4 2020-2021 (Jun 1- Aug 31, 2021)	Q1 2021-2022 (Sept 1- Nov 30, 2021)	% Change
Total followers	491	561	14.3
Total tweets (excluding retweets/ quote re-tweets)	31	49	58.1
Total engagements	917	1,673	82.4

Metric Glossary

1. Total followers: Total number of Twitter user accounts that follow the TDRA account.
2. Total Tweets: Number of times the TDRA has posted an original Tweet on the TDRA Twitter account (*i.e.,* excluding re-tweets).
3. Total engagements: Total number of times that Twitter user accounts interacted with TDRA Tweets. This includes clicks anywhere on the Tweet (e.g., Retweets, replies, follows, likes, links, cards, hashtags, embedded media, username, profile photo, Tweet expansion).

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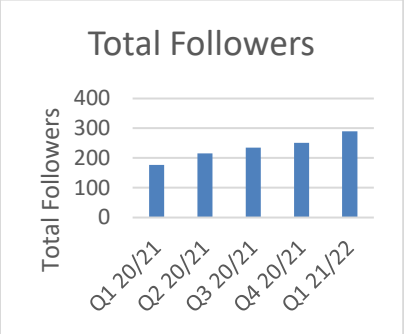
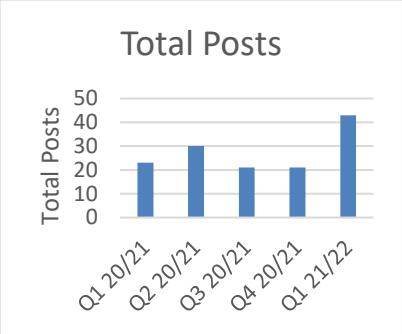
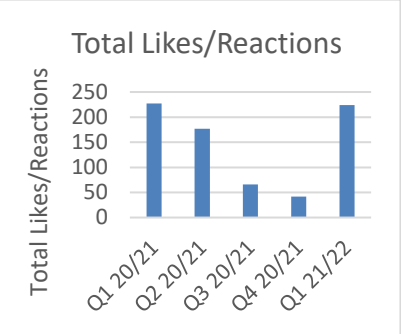
Appendix 7: Key Metrics for TDRA's LinkedIn Profile

Total LinkedIn Followers (left), Posts (middle), and Likes/Reactions (right) from Q1 20/21 – Q1 21/22







Comparison of LinkedIn Metrics for Q4 (FY: 2020-2021) and Q1 (FY: 2021-2022)

Metric	Q4 2020-2021 (Jun 1- Aug 31, 2021)	Q1 2021-2022 (Sept 1- Nov 30, 2021)	% Change
Total followers	251	290	15.5
Total posts	21	43	104.8
Total post likes/reactions	42	224	433.3

Metric Glossary:

1. Total followers: Total number of LinkedIn user accounts that follow the TDRA account.
2. Total posts: Number of times the TDRA made an original post on the TDRA LinkedIn page (i.e., excluding shares).
3. Total post likes/reactions: Total number of times LinkedIn user accounts liked or used an available LinkedIn reaction on TRDA posts.

Appendix 8: Notable Activity for TDRA's PFAC

- Addition of five new family care partners to the PFAC
- Lay summaries for TDRA studies- PFAC focus group (four members) met to discuss the benefit and format for producing lay summary information about TDRA-affiliated studies, these PFAC members will advise throughout the development process (for written materials and webinars)
- Increased collaboration with CAMH PFAC through development of a joint workshop focused on patient/family engagement in research, also through potentially having CAMH organization member sit on TDRA PFAC

Appendix 9: Research Working Group Members

Basic Science
- Graham Collingridge
- John Georgiou
- Evelyn Lambe
- Tarek Rajji

Caregiver Interventions
- *Mary Chiu*
- *Kristina Kokorelias*
- *Kari Quinn-Humphrey*
- *Joel Sadavoy*
- *Adriana Shnall*
- *Sophie Soklaridis*
- *Lynn Zhu*

EEG
- *Sanjeev Kumar*
- *Paul Lea*
- *Andrew Lim*
- *Mary McAndrews*
- *Tarek Rajji*
- *Eugenie Roudaia*
- *Allison Sekuler*
- *Richard Wennberg*

Fluid Biomarkers
- *Ana Andreazza*
- *Fang Liu*
- *Joanne McLaurin*
- *Walter Swardfager*
- *Carmela Tartaglia*
- *Erica Vieira*

Genetics
- *James Kennedy*
- *Mario Masellis*
- *Ekaterina Rogaeva*

Long-Term Care
- *Peter Derkach*
- *Corinne Fischer*
- *Morris Freedman*
- *Sanjeev Kumar*
- *Krista Lanctot*
- *Clement Ma*
- *Frank Palmer*
- *Gillian Strudwick*

Memory Clinics Standardization
- *Sandra Black*
- *Bradley Buchsbaum*
- *Howard Chertkow*
- *Morris Freedman*
- *Sean Hill*
- *Sanjeev Kumar*
- *Tarek Rajji*
- *Tyler Redublo*
- *Stephen Strother*
- *David Tang-Wai*

Neuroimaging
- *Sandra Black*
- *David Bogart*
- *Corinne Fischer*
- *Sanjeev Kumar*
- *Alan Moody*
- *Christopher Scott*
- *Carmela Tartaglia*

Neuropathology
- *Andrew Gao*
- *Julia Keith*
- *Gabor Kovacs*
- *David Munoz*

Neurostimulation

Howard Chertkow
Kullervo Hynynen
Suneil Kalia
Sanjeev Kumar
Nir Lipsman
Jed Meltzer
Tarek Rajji

Neurotechnology

Amer Burhan
Chaitali Desai
Andrea Iaboni
Andrew Lim
Abhishek Pratap
Allison Sekuler

Open Science

Bradley Buchsbaum
Sean Hill
Paul Lea
Randy McIntosh
Donna Rose-Addis