VAST
Vascular Training Platform | Plateforme de Formation Vasculaire

2023 Vascular Training (VAST) Conference

Program and Proceedings

May 17-18, 2023
In partnership with, and at the Centre de recherche de l'Institut universitaire de gériatrie de Montréal
Montreal, QC

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Dr. Louis Bherer, Professor, Université de Montréal
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Ellen Snowball, CCNA EPLED Coordinator

Abstract Reviewers:
Dr. Sarah Gagliano Taliun, Dr. Aravind Ganesh, Dr. Eric Smith, Dr. Sridar Narayanan

Presentation Judges:
Dr. Sandi Azab, Dr. Philip Barber, Dr. Jaspreet Bhangu, Dr. Steffany Bennett, Dr. Brandy Callahan, Dr. Simon Duchesne, Dr. Claudine Gauthier, Dr. Hélène Girouard, Dr. Edith Hamel, Wayne Hykaway, Paul Lea, Dr. Benjamin Le Gac, Emily McLellan, Dr. Eric Smith, Ellen Snowball, Christine Thelker

Award Categories:
- Participants choice
- Oral presentation award
- Poster awards
- People's voice knowledge translation award

Partners and Sponsors

We are grateful for the support from our partners and sponsors. Thank you!

Centre de recherche de l'Institut universitaire de gériatrie de Montréal (CRIUGM)

CRIUGM has graciously provided space and technical support for the 2023 VAST Conference, as well as sponsorship for Dr. Ludovica Griffanti to speak.

Canadian Institute of Health Research Institute of Aging

We thank the CIHR Institute of Aging (CIHR-IA) for its support of the VAST Conference, as well as its support for the participation of people with lived experience to attend the program.

Canadian Consortium on Neurodegeneration in Aging

We thank the CCNA for their in-kind support and facilitation of the KT workshop and involvement of people with lived experience.

Healthy Brains Healthy Lives

We thank Healthy Brains Healthy Lives and McGill University for their contributions as an event partner.

Rogue Research Inc.

We thank Rogue Research for their contributions as an event sponsor.

A special thanks to Dr. AmanPreet Badhwar for her donation of her mixed media art piece "The Big Bend" seen on the front cover of the program.

Wednesday, May 17 2023

8:00am – 8:45am	**Breakfast and registration**	CRIUGM Foyer
8:45am - 9:10am	**Welcome** **Oury Monchi**, *Scientific Director of CRIUGM* **Natalie Philips**, *Associate Scientific Director of CCNA* **AmanPreet Badhwar**, *VAST Co-Lead, Assistant Professor, Université de Montréal, CRIUGM*	CRIUGM Auditorium
9:10am - 10:00am	**Keynote speaker** Session chairs: AmanPreet Badhwar, Eric Smith **Danica Stanimirovic** *Director of the Translational Bioscience Department, Human Health Therapeutics Research Centre, National Research Council of Canada* Ins and Outs of the Blood Brain Barrier: From Molecular Physiology to New Therapies	CRIUGM Auditorium
10:00am - 11:05am	**Podium Presentations** Session chairs: Sarah Gagliano Taliun, Manpreet Singh	CRIUGM Auditorium
10:00am - 10:20am	**Invited Speaker:** **Haz-Edine Assemlal**, *Associate Director of Image Processing, NeuroRX* Leveraging AI for Improved Detection of White Matter Lesions in Neuroimaging	
10:20am - 11:00am	**Abstract Presentations:** **Benjamin Le Gac**, *Université de Montréal* Astrocytic nitric oxide in response to cholinergic stimulation in mouse somatosensory cortex **Jessica Youwakim**, *Université de Montréal* IL-17A Contributes to the Angiotensin II-induced Neurovascular Coupling impairment through Oxidative Stress **Ateyeh Soroush**, *University of Calgary* The impact of cortical microvasculature hypoxia on measures of brain function in people with Multiple Sclerosis **Sajeevan Sujanthan**, *University of Toronto* AcT-Cog: Cognitive outcomes in the Alteplase compared to Tenecteplase (AcT) trial	
11:00am - 11:05am	**Eric Smith**, *University of Calgary* Introducing the Vascular Cognitive Impairment Video Project	
11:05am - 11:30am	**Coffee Break**	CRIUGM Foyer
11:30am - 1:00pm	**Career Panel** Session chairs: William Betzner, Munira Sultana **Speakers:** **Haz-Edine Assemlal** *Associate Director of Image Processing, NeuroRX*	CRIUGM Auditorium

Wednesday, May 17 2023 – Continued

11:30am - 1:00pm	**Career Panel Speakers, continued:**	CRIUGM Auditorium
	Nouha Ben Gaied *Director of Research and Development, Quality of Services, Federation of Quebec Alzheimer Societies*	
	Adrienne Crampton *Business Development Manager, Healthy Brains, Healthy Lives*	
	Marc Cuesta *Chef de service, CRIUGM*	
	Danica Stanimirovic *Director of the Translational Bioscience Department, National Research Council of Canada*	
11:30am - 1:00pm	**Roundtable discussions for PIs (parallel to career panel)**	CRIUGM M6804
	Led by Eric Smith	
1:00pm - 2:00pm	**Lunch**	CRIUGM Foyer
	Optional mentorship group tables	
2:00pm - 3:00pm	**Podium Presentations**	CRIUGM Auditorium
	Session chairs: Hélène Girouard, Ateyeh Soroush	
2:00pm - 2:20pm	**Invited Speaker:**	
	Adrienne Crampton, *Healthy Brains, Healthy Lives* NeuroHub… A one-stop-shop for data management, analysis and collaboration	
2:20pm – 3:00pm	**Abstract Presentations:**	
	Ahmadreza Attarpour, *University of Toronto* A deep learning network for 3D segmentation of neurons in tera-voxel light sheet fluorescence microscopy data	
	Munira Sultana, *Western University* A Novel Phenotype of Older Adults with Dual Decline in Gait and Cognition at Higher Risk of Dementia. A Metabolomics Analysis	
	Flavie Detcheverry, *Université de Montréal* Level variations in brain and blood of the antioxidant glutathione in healthy aging, Alzheimer's disease and vascular dementia: A systematic review	
	Manpreet Singh, *Université de Montréal* Heritability enrichment identifies systemic tissue-specific signatures for white matter hyperintensities and other brain-MRI-derived complex phenotypic traits	
3:00pm - 5:00pm	**Poster Session and Refreshments**	CRIUGM Foyer
7:00pm - 9:00pm	**Dinner**	Gibby's, Old Montreal
	298 Pl. d'Youville, Montréal, QC H2Y 2B6 – 17 min walk from Hotel Bonaventure	

Thursday, May 18 2023

8:30am - 9:00am	**Breakfast**	CRIUGM Foyer
9:00am - 9:50am	**Keynote speaker**	CRIUGM Auditorium
	Session chairs: Sridar Narayanan	
	Ludovica Griffanti *Research Scientist, Wellcome Centre for Integrative Neuroimaging (WIN), University of Oxford* Harnessing the Power of Advanced Magnetic Resonance Imaging and Big Data to Study Brain Vascular Changes	
9:50am - 11:00am	**Panel - Engaging People with Lived Experience in Research**	CRIUGM Auditorium
	Session chairs: Eric Smith, Ellen Snowball (Inbal Itzhak)	
	Speakers:	
	Nouha Ben Gaied *Federation of Quebec Alzheimer Societies*	
	Paul Lea *Person living with vascular dementia, advocate, and EPLED advisory member*	
	Wayne Hykaway *Care partner, dementia advocate, and EPLED advisory member*	
	JoAnne McLaurin *Director and Senior Scientist, Sunnybrook Research Institute*	
	Emily McLellan *Care partner, dementia advocate, and EPLED advisory member*	
	Christine Thelker *Person living with vascular dementia, advocate, and EPLED advisory member*	
11:00am - 11:30am	**Coffee Break and Conversations**	CRIUGM Meeting Rooms
	EPLED members and facilitators will be available in meeting rooms if you would like to follow up on any conversations.	
	Emily McLellan, Paul Lea, JoAnne McLaurin, Inbal Itzhak	Room E1902
	Christine Thelker, Wayne Hykaway, Ellen Snowball, Nouha Ben Gaeid	Room E1904
11:30am - 12:30pm	**Podium Presentations**	CRIUGM Auditorium
	Session chairs: Louis Bherer, Sara Becker	
11:30am - 11:50am	**Invited Speaker:**	
	Patrice Lindsay, *Heart and Stroke Foundation* The Lived Experience Journey with VCI	

Thursday, May 18 2023 – Continued

11:50am - 12:30pm	**Abstract Presentations:**	CRIUGM Auditorium
	Caroline Dallaire-Theroux, *Université Laval* Clinical predictors of post-mortem cerebral small vessel disease in middle-aged to older adults	
	George Tadros, *University of Calgary* The PREVENT VCI Study: Application of Rich-Club Behavior in the Human Brain Connectome as a Potential Novel Early Biomarker of Cognitive Decline	
	Fariba Sharmin, *University of Ottawa* The plasma sphingolipid and glycerophosphocholine lipidome identifies metabolic correlates of depression in a clinical population with Coronary Artery Disease	
	Sandi Azab, *McMaster University* Air Pollution and Cognitive Function in the Canadian Alliance for Healthy Hearts and Minds Study	
12:30pm - 1:30pm	**Lunch**	CRIUGM Foyer
1:30pm - 3:00pm	**Knowledge Translation Workshop**	CRIUGM Foyer
	Inbal Itzhak *Knowledge Translation Specialist, CCNA*	
3:00pm – 3:30pm	**Awards and Goodbyes from the VAST Executive Team**	CRIUGM Auditorium
	Eric Smith, *University of Calgary*	
	AmanPreet Badhwar, *Université de Montréal*	
	Steffany Bennett, *University of Ottawa*	

Keynote Speakers

Dr. Danica Stanimirovic

Danica Stanimirovic, MD, PhD is the Director of the Translational Bioscience Department, Human Health Therapeutics Research Centre, National Research Council of Canada. Her research focuses on brain vascular physiology and pathology and developing innovations and technologies to support clinical and commercial translational research in the field of neuroscience and therapeutic delivery to the central nervous system.

Ins and Outs of the Blood Brain Barrier: From Molecular Physiology to New Therapies

The talk will introduce cellular anatomy, molecular composition and physiology of the blood-brain barrier and its role in neurological diseases. It will then lay out a path for developing blood-brain barrier (BBB) crossing therapies anchored in molecular physiology of brain vessels. The talk will cover development of translational (human) BBB models and tools and drug delivery strategies from pre-clinical to clinical studies.

Dr. Ludovica Griffanti

Dr. Ludovica Griffanti is an Alzheimer's Association Research Fellow at the Wellcome Centre for Integrative Neuroimaging, University of Oxford. Previously she completed a MSc and PhD in Biomedical Engineering at Politecnico di Milano, Italy. Her research focuses on brain MRI analysis in ageing, dementia and neurodegeneration with the ultimate aim to make research translational and applicable in clinical settings. She is involved in the development and support of the FSL analysis software package, used by > 1000 laboratories worldwide as well as in big data projects like the UK Biobank imaging study.

Harnessing the Power of Advanced Magnetic Resonance Imaging and Big Data to Study Brain Vascular Changes

Magnetic Resonance Imaging (MRI) has emerged as an invaluable tool in the diagnostic evaluation of vascular cognitive impairment (VCI), by enabling the detection of structural and microstructural changes in the brain. This talk will give examples of how image analysis tools can help in quantifying and characterising vascular changes and how we can study their impact on cognition in healthy and diseased populations; how big datasets like the UK Biobank represent a powerful resource to study other aspects of vascular changes, for example their link with genetics; and how the Oxford Brain Health Clinic is translating advanced brain MRI into clinical practice for people with memory problems.

Partner Presentations

Haz-Edine Assemlal, PhD
Associate Director of Image Processing, NeuroRX

Dr. Haz-Edine Assemlal, PhD, is the Associate Director of Image Processing at NeuroRx, an advanced imaging analysis company located in Montreal. He holds an academic appointment in the Magnetic Resonance Studies Lab at the Montreal Neurological Institute, McGill University. His work focuses on using artificial intelligence and machine learning to develop image analysis techniques that facilitate clinical trials for new drugs intended to treat multiple sclerosis and other neurological disorders.

Leveraging AI for improved detection of White Matter Lesions in NeuroImaging

This talk will explore the potential applications of artificial intelligence in segmenting white matter lesions, seen as hyperintense foci on T2-weighted and fluid-attenuated inversion recovery (FLAIR) magnetic resonance imaging (MRI). Focal white matter lesions on MRI are observed in several neurodegenerative diseases of aging, where they represent part of the spectrum of small vessel disease. Similar-looking white matter lesions of different (inflammatory) origin are also prominent in multiple sclerosis, a field with a long history for developing and applying white matter lesion segmentation techniques. Identification of white matter lesions is important for diagnosis and staging of disease, and quantitative measures of their number and volume are useful metrics for assessing drug efficacy in clinical trials. This talk will discuss how the latest advances in AI technology can help to improve the detection and quantification of these lesions, which could lead to improved patient monitoring in the clinic.

Partner Presentations Continued

Dr. Adrienne Crampton
Business Development Manager, Healthy Brains, Healthy Lives Program

Adrienne Crampton graduated in 2021 from McGill University with a PhD in Rehabilitation Science (focusing on mild traumatic brain injury). Prior to this, she completed her Master's degree in Sports Management from the University of Ottawa ('17) and her BSc in Kinesiology at McGill University ('15) while competing as a varsity athlete for the latter. Adrienne has worked for both non-profit and for-profit organizations spanning various fields, such as kinesiology, human performance, neuroscience and brain health. Throughout her PhD, she developed a passion for innovation and entrepreneurship, as well as for creating conduits between research and industry. At HBHL, Adrienne's efforts are directed towards supporting various innovative projects in their journey towards commercialization and/or sustainability.

NeuroHub… A one-stop-shop for data management, analysis and collaboration

This presentation will explain what the NeuroHub platform is and how it could be helpful to researchers in the VAST community. NeuroHub is a platform which solves researchers' data management needs. It allows one to collect, store and share data with colleagues or the community. NeuroHub's services provide turn-key solutions to address data management requirements from funders and high impact journals. NeuroHub also makes data analysis easier, faster and reproducible. Using our platform one can run complex tools and pipelines on high performance computing with a click of a button saving time and resources. Using our sharing systems one can collaborate easily with collaborators around the world by having one platform where one can perform collection, analysis and dissemination.

Partner Presentations Continued

Dr. Patrice Lindsay, RN, PhD, FWSO
Director of Health Systems at the Heart and Stroke Foundation, Canada

Patrice Lindsay RN, PhD is currently the Director of Health Systems at the Heart and Stroke Foundation, Canada. She leads strategic directions for evidence informed systems change in planning and delivering health services across the care continuum for individuals with a range of heart conditions, stroke and vascular cognitive impairment. She is senior editor of the Canadian Stroke Best Practice Recommendations leading clinical guideline development and quality monitoring initiatives. She is a leader and innovator in approaches to the active and meaningful inclusion of people with lived experience in all Heart & Stroke and partnership activities. Dr. Lindsay is a recipient of the Queen Elizabeth II Diamond Jubilee medal for her efforts to improve stroke care and outcomes in Canada and internationally and has recently been recognized as one of the World Stroke organization's leading Women in Stroke. She sits on several national and international advisory committees and research collaborations.

The lived Experience Journey with VCI

Vascular cognitive impairment (VCI) is a devastating condition that is both a risk factor for and a sequelae of stroke. The experiences of people with VCI and their caregivers across the continuum of care are not well defined, is complex and can be overwhelming. In collaboration with People with Lived Experience (PWLE), a VCI journey map was created to capture the lived experiences and critical needs from symptom onset to pre-diagnosis, to diagnosis, to management and living with VCI. Several qualitative approaches were utilized including an environmental scan, structured literature review, review of existing journey maps, focus groups and consultations with PWLE experiencing VCI and caregivers. Qualitative theme analysis and validation with PWLE and health professionals were conducted to create the journey map.

Conference Panel Speakers

An opportunity to hear from and interact with professionals in a variety of career areas.

Dr. Nouha Ben Gaied
Director of Research and Development, Quality of Services, Federation of Quebec Alzheimer Societies

Dr. Nouha Ben Gaied holds a Ph.D. in organic chemistry from the University of Strasbourg, which she completed with a postdoctoral fellowship at the University of Southampton. In 2013, Dr. Ben Gaied joined the Federation of Quebec Alzheimer Societies as Director of Communication before becoming Director of Research and Development, Quality of Services in 2016. Her role is to promote the Alzheimer Society Research Program, develop and manage KT&E activities while supporting the recruitment process for several studies conducted by Quebec researchers working in the field of neurodegenerative diseases. She also leads the implementation of programs and services within Alzheimer Societies in Quebec, including the referrals program and the education program for healthcare professionals. Actively engaged in scientific projects as co-investigator, Dr. Ben Gaied is the author of several scientific articles and sits on several ministerial committees or provincial initiatives dedicated to Alzheimer's disease and other forms of dementia.

Dr. Marc Cuesta
Chef de service, Centre de recherche de l'Institut universitaire en gériatrie de Montréal

Dr. Marc Cuesta holds a Ph.D. in neurosciences from the University of Strasbourg and worked in the field of circadian rhythms for 12 years as a postdoctoral fellow and research associate at the University of Cambridge and McGill University. In 2016, Marc left the academic world to become Manager of Programs and Science at the Brain Canada Foundation and participate in the management and administration of a $240M research funding program. In 2018, Marc decided to come back to the research field. He spent four years as a project manager at the IUGM research center before becoming its administrative director in 2022.

Dr. Haz-Edine Assemlal
See previous biography on page 8.

Dr. Adrienne Crampton
See previous biography on page 9.

Dr. Danica Stanimirovic
See previous biography on page 7.

Engaging People with Lived Experience Panel Speakers

Hear from a panel of patient and care partners to better understand their needs and challenges in research. We will be aiming to answer the question, “How can we better engage people with lived experience throughout the research process”.

Wayne Hykaway

Wayne Hykaway currently resides in Calgary, Alberta, and has a background as a University and College educator, designing and teaching computer, business and web courses. Wayne’s wife was diagnosed with dementia. At that time, Wayne became a full-time care partner and moved into the same long-term care facility as his wife until her passing in 2021. As a passionate advocate, Wayne actively contributes to over 25 projects focusing on dementia, long-term care and seniors’ health. He serves on the Health Services Organization Long-Term Care Technical Committee, Dementia Advocacy Canada Advisory Group, PRIUS 4 project (AHS), and the Canadian Consortium on Neurodegeneration in Aging’s (CCNA) Engagement of People with Lived Experience of Dementia (EPLED) Advisory Group, Caregivers Alberta, Caregiver Canada, Dementia Network Calgary, Alzheimer's Disease International, various Alzheimer's societies, to name a few. Wayne collaborates on research projects with 6 Canadian universities and has co-authored 4 published papers. Wayne’s research interests include, but are not limited to, Dementia, long-term care and caregiving.

Paul Lea

Paul is a person living with vascular dementia, living alone in Etobicoke, which is part of Toronto. He is a dementia advocate and is 70 years young.

Paul suffered a massive stroke in 2008 and was diagnosed with vascular dementia in 2009. In 2015, he found the Alzheimer Society Toronto, which represented the beginning of his advocacy for those living with dementia. In 2016, he joined a group that participated in the Youth Dementia Awareness Symposium, led by Dr. Kristine Newman and her research team. Since then, he has worked with several research organizations, including being a member of the Canadian Consortium on Neurodegeneration in Aging’s (CCNA) Engagement of People with Lived Experience of Dementia (EPLED) Advisory Group. Paul is excited to have been exposed me to many opportunities and introduced to so many people who are trying to find cures and trying to make life more bearable.

Engaging People with Lived Experience Panel Speakers, Continued

Dr. JoAnne McLaurin

Dr. McLaurin is a Director and Senior Scientist within Biological Sciences Platform at Sunnybrook Research Institute, CRC Tier 1 in Alzheimer's disease Therapeutics, Lead Theme 1 Preclinical Research in Dementia for the Canadian Consortium on Neurodegeneration and Aging and a Professor in the Department of Laboratory Medicine and Pathobiology at the University of Toronto. She is recognized for a body of work on the detrimental effects of Ab accumulation and benefit of reduction of Ab using small molecules. Dr. McLaurin's present focus is translational research to understand factors impacting risk and progression of age-related cognitive decline. Specifically, the discovery of much-needed treatments for Alzheimer's disease and dementia.

Dr. McLaurin's laboratory identified a family of naturally occurring compounds that inhibit the formation of toxic soluble aggregates in AD, which resulted in 3 worldwide patents, and collaborations with small cap biotechnology (Ellipsis Neurotherapeutics, Transition Therapeutics) and large pharmaceutical industry (Elan Inc, OPKO Health). Preclinical studies in Dr. McLaurin's laboratory demonstrated efficacy, subsequent early clinical trials in AD patients were initiated, and are presently under development by OPKO Health Inc (Miami, USA). This successful research program demonstrates Dr. McLaurin's ability to identify target molecules, to develop lead compounds through preclinical development and to translate this knowledge to appropriate international stakeholders.

To further impact patient experience, Dr. McLaurin has first-hand knowledge of the benefit of engaging with people with lived experience in dementia and how this leads to refined experimental approaches, novel avenues of research and understanding of disease outcomes at multiple levels. The engagement of people with lived experience in early discovery and preclinical phases of research is in its infancy, is dependent on meaningfully and actively collaborations in the governance, priority setting, and conduct of research, as well as in summarizing, distributing, sharing, and applying its resulting knowledge and is important for future advances.

Dr. Nouha Ben Gaied

See previous biography on page 11.

Engaging People with Lived Experience Panel Speakers, Continued

Emily McLellan

Emily McLellan currently resides in Vancouver, British Columbia. She holds a BSc in Psychology and was pursuing an MSc in neuroscience when her father was diagnosed with young-onset Alzheimer's disease in 2017. Emily put her academic research on hold to care for her father during the daytime while she worked evenings as a clerk at a nearby hospital. Although Emily had learned a great deal about the science of dementia in classrooms, she did not find that it equipped her to handle the practical realities of caregiving. She did find that her understanding of the brain made it easier for her to cope with her father's rapid declines. At the time she was disappointed to find that there was not much in the literature about young-onset dementia, nor were there many resources available to assist patients. While her father was still in the community, they participated in the COMPASS-ND study as well as a few other studies. In early May of 2019, her father was hospitalized and he died in late January 2020: he was never a candidate for long term care because of his physical size, agitation, and intrusive behaviour. Emily joined the CCNA's EPLED advisory team in June 2020 and is interested in research that investigates young-onset dementia, the role of sleep disorders in dementia, language and visual deficits in dementia, and the neuropsychiatric symptoms of dementia.

Christine Thelker

Christine is from Vernon, BC, and describes herself as bright, fun, and adventurous. At 63, her sense of humour has grown since her diagnosis of vascular dementia and cerebrovascular disease at 56. Christine believes that having been diagnosed with dementia has given her the ability to truly enjoy and appreciate life in the simplest form, and dislikes hearing that people with dementia are suffering, when in fact many are living well with dementia. Her motto since being diagnosed is "I'm not done yet".

Christine worked for Interior Health Authority for 13 years in various sites. Her most loved work was in dementia care, where she advocated for families, patients, and for better training of workers. Christine is still advocating and using her voice to try to help others and to try to end the stigma around the illness. She loves working with the Dementia Alliance International and believes whole heartedly that is what helps keep her living well with her dementia. Christine has presented at various venues including the Alzheimer's Disease International Conference, and the United Nations Convention of State Parties on Rights of People with Disabilities. She has also been involved with several publications, writes a blog called Chrissy's Journey, and is currently working on her second book.

Knowledge Translation Workshop

Learn to better translate the impact of your research to public and patient audiences. Led by CCNA knowledge translation specialist, Dr. Inbal Itzhak. We will be going through a short exercise to extract the meaning/significance from your research, where you will work in small groups encompassing other trainees, people with lived experience, faculty, and facilitators from community and research organizations.

There is one important homework item for trainees. Please bring to the KT workshop a figure of data (a graph, a plot, a neuroimaging figure etc.) from one of your past or current research projects. The figure should be printed on a full page (or be ready to show it on a laptop such that the figure fills the screen). The figure should be:

1. One that you know well.
2. A figure that you think shows interesting / important findings.
3. It does NOT have to be published work, it can be a draft.
4. If you are not sure, you can bring more than one.

Dr. Inbal Itzhak

Dr. Inbal Itzhak is a certified Knowledge Translation (KT) Specialist with a PhD in Communication Sciences and Disorders from McGill University. Inbal is the Knowledge Translation and Exchange Specialist at the Canadian Consortium on Neurodegeneration in Aging (CCNA). She is experienced in knowledge translation capacity building, project planning, and impact evaluation, as well as stakeholder engagement and partnership development. Her training in both research and knowledge translation reflect her passion for creating meaningful links between science and the world outside of academia. She believes this gap is best bridged by creating boundary-crossing relationships where people with lived experience, scientists, and professionals collaborate and learn together.

Poster Session – May 17th 3:00pm - 5:00pm

P01	Ayden Hansen, Damilola Adingupu, **Ateyeh Soroush**, Jeff F. Dunn *University of Calgary* Investigating brain hypoxia and functional connectivity in individuals who have had COVID-19
P02	Damilola Adingupu, **Ateyeh Soroush**, Ayden Hansen, Jeff F. Dunn *University of Calgary* Reduced cortical oxygen, hemoglobin, and impaired cognitive function in post COVID-19 sequalae
P03	**Luis Ángel Albarrán-Ponce**, Thao T. Nguyen, Sneha Gupta, Victoria Hamilton, Evan Bushnik, Graeme P. Taylor, David Dyment, Miroslava Cuperlovic-Cult, Steffany A.L. Bennett *University of Ottawa* Behavioural and biochemical validation of a novel acid ceramidase disorder mouse model for preclinical research
P04	**Qassim Alkassir**, Miroslava Cuperlovic-Culf, Steffany A.L. Bennett *University of Ottawa* Advancing bioinformatic technologies for lipidomic discovery: pathway and network analysis for interpretation of metabolic changes in vascular dementia
P05	**Jasmine R. Aziz**, Teagan Milligan, Paula M. McLaughlin, Gail A. Eskes *Dalhousie University* Using the attention-motor task to measure subtypes of spatial neglect after stroke
P06	**Sara Becker**, Daniel Cunningham, Brandy L. Callahan *University of Calgary* Do vascular risk factors contribute to increased dementia risk in adults with attention-deficit hyperactivity disorder?
P07	**William Betzner**, Aravind Ganesh *University of Calgary* A qualitative study of physician approaches to the management of people living with dementia who experience a stroke
P08	**William Betzner**, Aravind Ganesh *University of Calgary* Comparison of cortical and subcortical brain atrophy as well as white matter disease and lacune assessments on NCCT and MRI in ischemic stroke
P09	**Marie Biard**, Flavie Detcheverry, Sandi Azab, Sara Becker, William Betzner, Patrick F. Bloniasz, Karl Grewal, Jolene Phelps, Erin Mazerolle, Eric Smith, AmanPreet Badhwar *Université de Montréal* Supporting persons living with dementia and their caregiver with knowledge translation: an ongoing umbrella review by the VAST collaborative

Poster Session – May 17th 3:00pm - 5:00pm Continued

P10	**Karl Grewal**, Eric E. Smith, Megan E. O'Connell *University of Saskatchewan* Do group differences in cardiovascular risk profiles impact the effect of lifestyle interventions on cognition? A project outline
P11	**Quinton Hake-Volling**, Julianna Tomlinson, Thao T. Nguyen, Victoria Hamilton, Graeme P. Taylor, Miroslava Cuperlovic-Culf, Michael G. Schlossmacher, Steffany A.L. Bennett *University of Ottawa* Age, sex, and lipid metabolism intersect to elicit cognitive decline in two mouse models of GBA1-Parkinson's disease
P12	**Victoria Hamilton**, Quinton Hake-Volling, Steffany Bennett *University of Ottawa* Phenotyping a mouse model of Parkinson's disease with dementia
P13	**Sotaro Hirai**, Milene Vandal, Aidan Pagador, Grant Gordon, Minh Dang Nguyen *University of Calgary* The role of ApoER2 signaling in cerebrovascular function
P14	**Ikrame Housni**, Manpreet Singh, Mahsa Dadar, Flavie Detcheverry, Chloe Anastassiadis, Ali Filali-Mouhim, Mario Masellis, Zahinoor Ismail, Simon Duchesne, Carmela Tartaglia, Eric E. Smith, Sridar Narayanan, AmanPreet Badhwar *Université de Montréal* The distribution of white matter hyperintensity across arterial territories in the age-related dementia
P15	**Remi Lamontagne-Caron**, Simon Duchesne *Université Laval* Synthesis of perfusion maps using U-Net for the retrospective study of the cerebrovascular system
P16	**Osama Mahdi**, Subash Sad, Steffany A. L. Bennett *University of Ottawa* Impact of Pseudomonas aeruginosa ExoU on host inflammatory response
P17	**Graeme McDowell**, Danielle T. Robinson, Irina Alecu, Mark Akins, Graeme P. Taylor, Samantha Sherman, Greg O. Cron, Kym Boycott, David A. Dyment, Steffany A.L. Bennett *University of Ottawa* Gain of function mutations in ANO6/TMEM16F cause a variant form of Neonatal Progeroid Syndrome
P18	**Hanieh Mohammadi**, Frédéric Lesage, Yves Joanette *Université de Montréal* Cerebral pulsatility and the neurofunctional reorganization allowing for preservation of cognitive abilities in ageing: An MRI and NIRS study

Poster Session – May 17th 3:00pm - 5:00pm Continued

P19	**Thao T. Nguyen**, Miroslava Cuperlovic-Culf, Eric E. Smith, Steffany A.L. Bennett *University of Ottawa* An analytical and bioinformatic pipeline for profiling glycosphingolipids and phospholipids in plasma of patients with cerebral small vessel diseases (cSVD) subjected to remote ischemic conditioning (RCI)
P20	**Chloe Oleksiuk**, Ioana Diana Abalasei, Marie Biard, Ikrame Housni, AmanPreet Badhwar, Erin L. Mazerolle *St. Francis Xavier University* Systematically evaluating VCID-related YouTube videos – English version
P21	**Benjamin Peckham**, Brandy L. Callahan *University of Calgary* Do cardiovascular risk factors mediate the relationship between bipolar disorder and incident dementia?
P22	**Louise Reveret**, V. Emond, A. Loiselle, P. Bourassa, C. Tremblay, D. Benett, S. Hebert, F. Calon *Université Laval* Brain levels of ACE2 are associated with a neuropathological diagnosis of Alzheimer's disease, cognitive decline and cerebral amyloid angiopathy
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P24	**Matthew Rozak**, J.R. Mester, A. Dorr, Maged Goubran, Bojana Stefanovic *University of Toronto* Deep-Learning Insights into Cerebrovascular Networks Coordination in Moderate Traumatic Brain Injury
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P27	**Jolene Phelps**, Wayne Hykaway, Chloe Oleksiuk, AmanPreet Badhwar, Eric E. Smith, Erin Mazerolle *Vascular Training Platform* Vascular cognitive impairment knowledge translation video project

Abstracts

Abstracts for podium presentations are presented on the following pages in alphabetical order.

A deep learning network for 3D segmentation of neurons in tera-voxel light sheet fluorescence microscopy data

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Background: Mapping neuronal structural connectivity and brain vasculature is critical to understand the progression of pathophysiology and develop targeted interventions for neurodegenerative diseases such as Alzheimer's[1]. Advances in tissue clearing and microscopy techniques provide high-resolution, whole-brain, and tera-voxel scale images of neurons and vasculature. However, current computational pipelines either rely on 2D-based techniques or conventional algorithms which require human intervention, limiting their abilities to automatically and quantitatively assess brain-wide 3D volumetric changes.

Methods: We developed 3D deep learning (DL) models to segment neuronal somas in whole-brain light-sheet fluorescence microscopy (LSFM) data using the U-Net[2] and UNETR[3] architectures. The models were trained on LSFM data of tissue-cleared brains from 18 healthy transgenic mice (TRAP2-Ai9) with the cFos promoter (20,000 patches in total of size 128^3 and 10/3/5 subjects for train/validation/test splits). A series of semi-automatic image processing steps with the expert intervention were used to generate ground truth (GT) data. Each model's output was obtained by averaging 50 models' predictions using the Monto-Carlo dropout technique[4]. Using this technique, a voxel-wise uncertainty map was also generated to estimate the model's uncertainty/confidence. A final mapping of neurons was generated using an ensemble of both models (ensemble of ensembles). The trained models were evaluated using different evaluation metrics (including Dice coefficient, Precision, and Sensitivity). The segmentation outputs were compared with the state-of-the-art (SOTA) cell-detection algorithm (CellFinder[5]).

Results: Table 1 and Fig1 demonstrate quantitative and qualitative comparisons of the predicted segmentation maps to GT. The Monto-Carlo dropout and ensembling technique improved the performance of the models over baseline performance, resulting in a Dice coefficient of 0.769±0.08. Our proposed pipeline outperformed CellFinder on all evaluation metrics ($p_{value} < 0.0001$) (Fig. 2), resulting in an F1-score of 0.745±0.08, compared to 0.546±0.15 for CellFinder.

Conclusions: We present a novel robust 3D DL ensemble network to segment neuronal somas in whole-brain LSFM data, outperforming the SOTA detection algorithm. Future work will include validation of our results across brain regions and an unseen test dataset.

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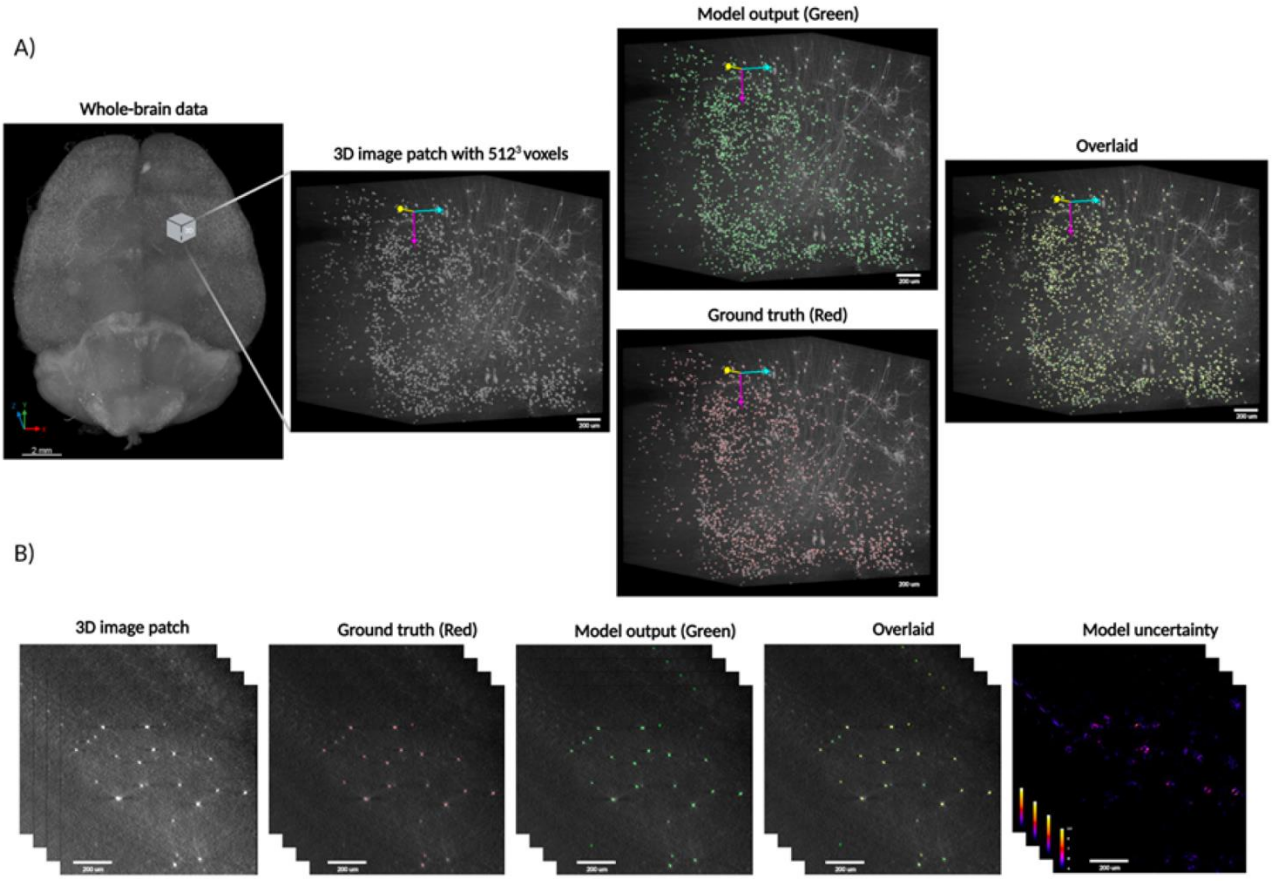

Fig 1. Performance of the proposed segmentation model. A) 3D whole-brain LSFM data will be divided into smaller 3D image patches. For each image, the model predicts a binary map (green) with averaging the U-Net and UNETR outputs after MC-dropout. Model output (green) and ground truth (red) are overlaid on raw image in the last column. B) Model output (green) is compared with ground truth (red). Model uncertainty is shown in last column. The areas of high uncertainties were mostly localized in the boundary of neurons.

Table1. Performance of the developed segmentation model on the test set.

Model	Baseline Performance	MC-dropout	Ensemble
U-Net	Dice= 0.765±0.07 Sensitivity = 0.824±0.09 Precision = 0.721±0.07 F1-score = 0.769±0.071	Dice-score = 0.764±0.08 Sensitivity = 0.794±0.11 Precision = 0.749±0.06 F1-score = 0.770±0.08	Dice-score = 0.769±0.08 Sensitivity = 0.803±0.11 Precision = 0.750±0.06 F1-score = 0.775±0.08
UNETR	Dice-score = 0.762±0.07 Sensitivity = 0.830±0.10 Precision = 0.714±0.07 F1-score = 0.767±0.07	Dice-score = 0.761±0.08 Sensitivity = 0.809±0.10 Precision = 0.729±0.07 F1-score = 0.767±0.08	

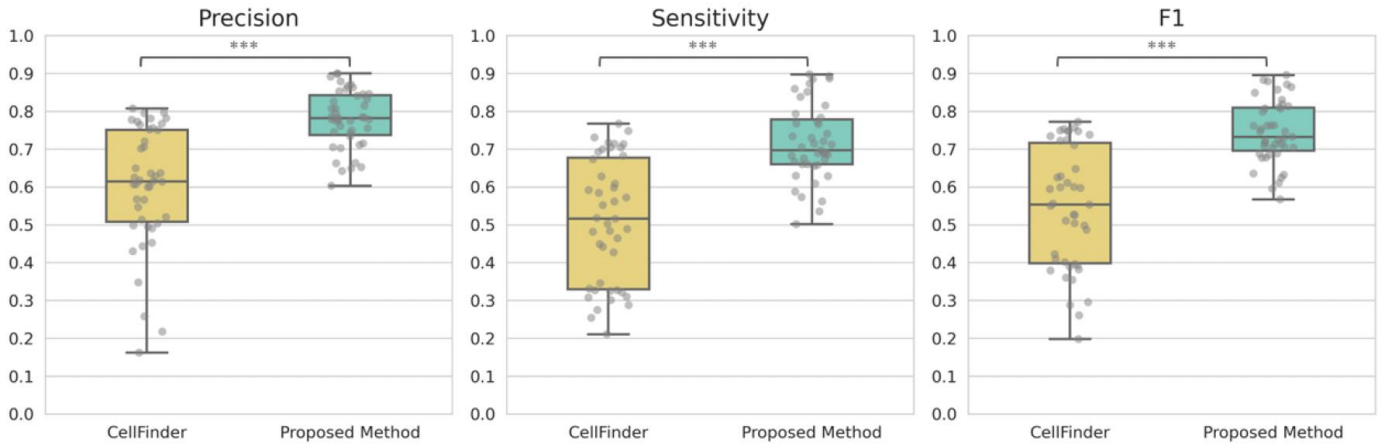

Fig 2. Comparison of the performance of the proposed method with CellFinder. The segmentation outputs are transformed to detection maps by finding the center of mass of each neuron. *** $p_{value} < 0.0001$ obtained using Mann-Whitney U test.

Air Pollution and Cognitive Function in the Canadian Alliance for Healthy Hearts and Minds Study

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Background: Air pollution is proposed to be a risk factor for cognitive impairment and dementia[1]; however, the mechanisms underpinning this association are not fully resolved. We investigated the association of low-level exposure to key air pollutants with cognitive function and silent brain infarction in adults without known clinical cardiovascular disease.

Methods: The Canadian Alliance for Healthy Hearts and Minds Cohort Study (CAHHM)[2] is a cohort of 6878 Canadian adults recruited between 2014-2018 from the provinces of British Columbia, Alberta, Ontario, Quebec, and Nova Scotia, for whom averages of long-term exposures to nitrogen dioxide (NO2) and fine particulate matter ($PM_{2.5}$) were estimated for five years prior to the start of CAHHM recruitment.[3] Participants underwent brain magnetic resonance imaging (MRI) to assess silent brain injury and took cognitive function metric tests at baseline.

The associations of air pollutants with silent brain infarction as detected by MRI, and with cognitive function scores on 1) The Montréal Cognitive Assessment (MoCA) and 2) Digit Symbol Substitution Test (DSST) were assessed using generalized linear mixed models adjusting for age, sex, ethnicity, individual-level cardiovascular risk factors (captured in the INTERHEART risk score) and education as fixed effects,[4] with a random intercept representing the effect of recruitment centre.

Results: Each 5 µg/m^3 higher PM2.5 concentration was associated with 0.46-points lower MoCA (95% confidence intervals (CI) -0.65, -0.27; p<0.0001) and 1.61 lower DSST (95% CI -2.73,-0.50; p=0.0045) scores. A 5 ppb higher NO_2 concentration was associated with 0.14-points lower MoCA (95% CI -0.19, -0.09; p<0.0001) and 0.52 lower DSST (95% CI -0.85, -0.19; p<0.0001) scores. $PM_{2.5}$ was not associated with silent brain infarction. Each 5 ppb higher NO_2 concentration was associated with higher odds of silent brain infarction (Odds Ratio (OR)=1.12; 95% CI 1.00, 1.26; p=0.048).

Conclusion: In a cohort of healthy Canadian adults, $PM_{2.5}$ and NO_2, considered indicators of traffic-related air pollution, were associated with lower cognitive assessment scores, while only NO_2 was associated with higher odds of silent brain infarction. Further analyses are ongoing to examine effect modification by sex and by neighbourhood characteristics such as walkability, greenspace, and proximity to roads.

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Clinical predictors of post-mortem cerebral small vessel disease in middle-aged to older adults

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Background: Amongst vascular aetiologies implicated in cognitive impairment, sporadic cerebral small vessel disease (CSVD) is a particularly prevalent group of processes known to affect the ageing brain[1, 2]. Rather than imaging-related lesions[3], we aimed to identify clinical predictors associated with pathologically-confirmed CSVD in middle-aged to older adults.

Methods: We relied on a retrospective sample of 160 autopsied cases from the Edinburgh Brain Bank that included middle-aged and older adults (defined as individuals aged 40 years and older) covering the spectrum of healthy aging through to common forms of dementia (i.e., highly-prevalent aetiologies such as Alzheimer's disease (AD) and vascular cognitive impairment (VCI)). We developed and tested risk models using binomial logistic regression to predict a pathological diagnosis of non-amyloid CSVD (i.e., arteriolosclerosis) and amyloid CSVD (i.e., cerebral amyloid angiopathy (CAA)[4]). Selected potential predictors included demographics, lifestyle habits, traditional vascular risk factors, chronic medical conditions, presence of the APOE4 allele, and clinically determined cognitive status. Sample splitting and cross-validation methods were performed to ensure internal validity. External validity was assessed post-hoc in a sample of cases with atypical dementias (n=24).

Results: A clinical diagnosis of dementia was present in 40% of our sample (AD=33, VCI=26 and mixed=5), while others were cognitively healthy (n=96). The mean age at death was 73.8 (SD 14.1) years and 40% were females. The presence of none-to-mild versus moderate-to-severe non-amyloid CSVD was predicted by our model with high accuracy (AUC=0.84, SEN=72%, SPE=95%), the most significant clinical predictors being age, history of cerebrovascular events, and cognitive impairment. The presence of CAA pathology was also predicted with good accuracy (AUC=0.86, SEN=93%, SPE=79%). Significant predictors included alcohol intake, history of cerebrovascular events, and cognitive impairment. In our subset of atypical dementias, our models provided poor predictive performance for both non-amyloid CSVD (AUC=0.50) and CAA (AUC=0.43).

Conclusions: CSVD pathology can be predicted with high accuracy from clinical factors in patients within the spectrum of AD, VCI and normal aging. Whether this prediction can be enhanced by the addition of fluid-based and neuroimaging biomarkers warrants further study. We believe that improving our understanding of clinical determinants of vascular brain health is a step toward the development of personalized preventive and therapeutic strategies addressing vascular contributions to cognitive decline and related dementias.

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Level variations in brain and blood of the antioxidant glutathione in healthy aging, Alzheimer's disease and vascular dementia: A systematic review

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Background: Oxidative stress (OS) plays an important role in healthy aging, and diseases like Alzheimer's disease (AD) and vascular dementia (VaD) [1]. Glutathione (GSH) is the most prevalent antioxidant protecting against OS [2] but its alterations with aging, AD and VaD have not been systematically assessed. We aim to address this knowledge gap by conducting a systematic review.

Methods: PubMed searches were conducted upto February 2023. 39 keyword-combinations were used to identify studies investigating GSH levels in (a) brain (in vivo using magnetic resonance spectroscopy (MRS) and in autopsy tissue using biochemical assays) and/or (b) blood using biochemical assays (Fig1A). We categorized age groups as young (18 39), middle-aged (40-59), and old (≥60) [3].

Results: 45 studies met inclusion criteria (Fig1A, B).
BRAIN: 12 MRS studies reported good-to-excellent reproducibility. For studies investigating age-specific changes in cognitively unimpaired adults (CU; N=6), GSH levels were reduced in half of the brain regions investigated (temporal, occipital, limbic) in old- versus young- or middle-aged adults (Fig2A). In AD, 5/7 studies found lower brain GSH levels compared to CU, while MCI studies lacked consensus. No brain VaD studies met our inclusion criteria.
BLOOD: Blood GSH levels were lower (a) with increasing age in CU (5/7), and (b) in AD (7/9) and VaD (3/3) compared to age-matched CU (Fig2B).
GSH and COGNITION: Two studies investigated the relation between GSH levels and cognition in CU but found no significant association. The majority (4/7) of AD continuum studies found poorer cognitive function with lower GSH levels in both brain and blood. No studies explored GSH variations with cognition in VaD.

Conclusions: Our systematic review demonstrates that in vivo MRS measurements of GSH are reliable. GSH levels in both brain and blood generally decrease in (a) CU with increasing age, and (b) AD relative to age-matched CU, with lower GSH being associated with cognitive impairment. While blood GSH levels were reported decreased in VaD relative to CU, our review identified a lack of GSH studies in the brain. Results suggest that oxidative stress may play a role in both healthy and pathological aging.

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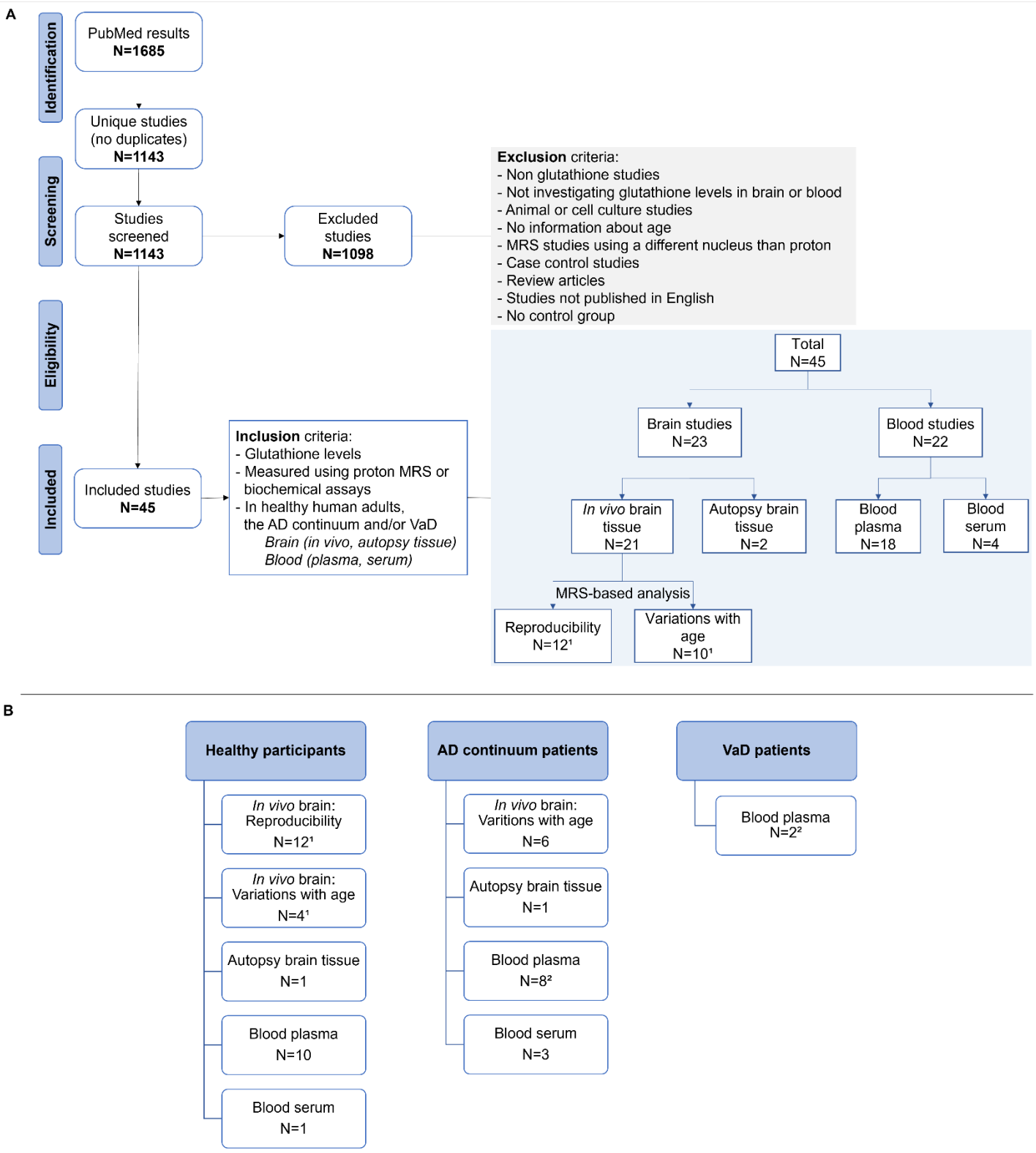

Figure 1: Flowcharts and demographics of studies that met inclusion criteria
A) Flowchart for study selection; and B) Study repartition of healthy aging, AD continuum, and VaD participants, ¹one study is common to both the GSH reproducibility section and the GSH variations with age category, resulting in 21 papers in the *in vivo* MRS studies; ²two studies are in common in the AD continuum and the VaD sections, resulting in 18 plasma studies in total. Note that no VaD studies in brain met our inclusion criteria. Abbreviation: AD, Alzheimer's disease; GSH, glutathione; MRS, magnetic resonance spectroscopy; VaD, vascular dementia.

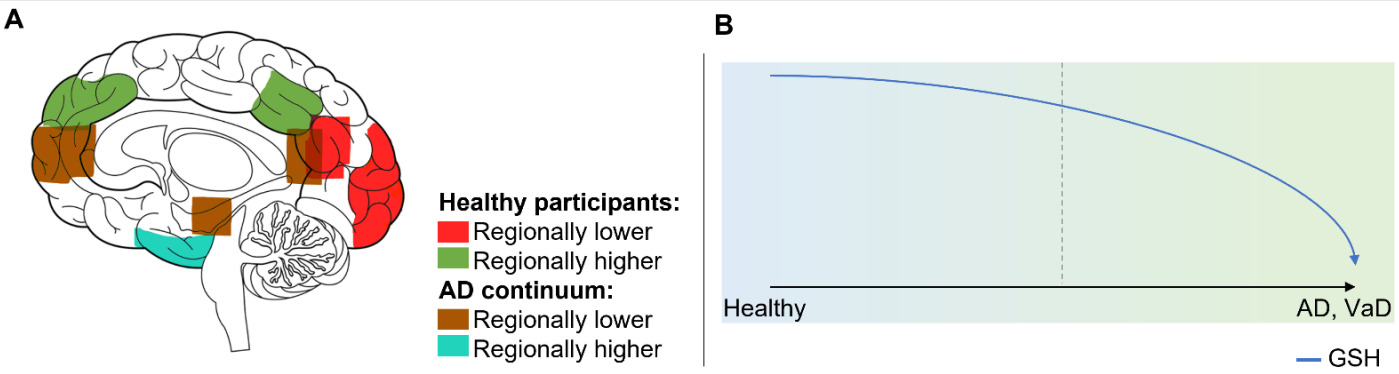

Figure 2: GSH variations in brain and blood
A) In brain, a region-specificity pattern can be observed, especially for healthy participants where GSH levels are lower in posterior regions. In patients, the decreases are more spread out throughout the brain; and B) in blood, GSH levels are lower with age, and are further decreased in both AD and VaD patients. Lower GSH levels are indicative of higher OS with increasing age and disease severity. Abbreviation: AD, Alzheimer's disease; GSH, glutathione; VaD, vascular dementia.

Astrocytic nitric oxide in response to cholinergic stimulation in mouse somatosensory cortex.

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Background: Neurovascular coupling (NVC), the close relationship between neuronal activity and the local increase in blood perfusion, is essential for brain function. NVC is impaired in neurodegenerative diseases such as Alzheimer's disease[1]. Among vasoactive messengers involved, nitric oxide (NO) is a major vasodilator[2] known to be produced by neurons and the endothelium through the so-called neuronal NO synthase (nNOS) and endothelium NO synthase (eNOS), respectively. However, astrocytes also actively participate in NVC[3] and express eNOS[4] but this pathway has never been explored. Acetylcholine (Ach) has the potential to induce increased calcium and reactive oxygen species production via eNOS in cardiomyocytes[5]. The aim of this study was to investigate astrocytic NO production by eNOS in response to acetylcholine stimulation.

Methods: To test this hypothesis, we used electronic microscopy and immunohistochemistry to subcellularly localize eNOS in astrocytes. Furthermore, to monitor astrocytic NO production in response to Ach, we used fluorescent NO indicator DAF-FM *in vitro* and *ex vivo* of wild-type (WT) mice and knock-out mice for eNOS ($eNOS^{-/-}$) and nNOS ($nNOS^{-/-}$).

Results: Our team showed by electron microscopy and immunohistochemistry that astrocytes express eNOS preferentially in perineuronal processes (71 ± 5%, mean ± sem) than perivascular processes (29 ± 5%) and are spatially connected to cholinergic terminals. Moreover, we show *in vitro* that Ach induces 21.8% increase in NO production that mostly relies on eNOS signalling as there was no production in $eNOS^{-/-}$ mice and at a smaller extend in nNOS signalling (11.8% increase in $nNOS^{-/-}$ mice). In brain slices, Ach induces localized NO synthesis in astrocytes and NO intensity was reduced in $eNOS^{-/-}$ (11.5%) and $nNOS^{-/-}$ (11.1%), compared to WT group (22%). Subsequently, we will observe *in vivo* this astrocytic NO production by combining biphotonic microscopy, fluorophore labelling and electrical stimulations of the nucleus basalis of Meynert, a cortical cholinergic source.

Conclusions: These results show a new source of eNOS-derived NO by astrocytes in response to Ach. This project will allow us to better understand the role of astrocytes and NO in the neurovascular coupling during cholinergic activations and could be a source of the vascular alterations observed in neurodegenerative diseases.

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The plasma sphingolipid and glycerophosphocholine lipidome identifies metabolic correlates of depression in a clinical population with Coronary Artery Disease

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Background: Coronary artery disease (CAD) is characterized by inflammation with extravasation of immune cells into the subendothelial space of coronary arteries contributing to atherosclerotic plaques.[1] CAD is the leading cause of mortality in the developed world. Prognosis is exacerbated by comorbid depressive symptoms, which affect up to 45% of CAD patients and exacerbate the risk of mortality.[2] Consequently, there is a need to better understand the biological processes associated with depression in CAD patients. Studies have suggested that altered lipid metabolism may link vascular disease to depression.[2,3] We and others have demonstrated that the abundances of platelet-activating factor (PAF) phospholipids, sphingolipids, and tryglycerides are altered in CAD with comorbid depression.[1-5]

Methods: A cohort of 36 patients with CAD without depression and 34 with depression from Coronary Artery Disease Randomized Omega-3 (CAROTID) trial were included in this study. Depression severity was assessed using the Hamilton Depression Rating Scale (HAM-D). Plasma samples were collected prior to trial treatment and again after 12 weeks of daily dietary supplementation with omega-3 or omega-6/9 fatty acids (Ocean Nutrition). Sphingolipids and glycerophosphocholines were isolated using a modified Bligh and Dyer protocol. Targeted lipidomics analyses were performed and our in-house computational lipidomics platform was used to assign molecular identities, quantify lipid abundances, and identify metabolic pathways disrupted and enriched in each cohort further validated by univariate, multivariate statistics and machine learning feature selection.

Results: Using novel lipidomic pathway analysis methodologies, we identified both sphingolipid and glycerophosphocholine pathways that discriminated non-depressed CAD patients from depressed CAD patients compared to cognitively normal healthy controls. We further assessed whether these lipidomic profiles and associated pathways could be ameliorated by supplementation with omega-3 or omega-6/9 fatty acids and whether these changes associated with modulation of depressive indices. We describe here the alterations in circulating metabolic biomarkers of sphingolipid and glycerophospholipid associated with CAD and depression and describe the changes elicited by dietary supplementation in this context.

Conclusions: This research can broaden our knowledge of lipidomic biomarkers that link depression with CAD, which can lead to the identification of potential novel treatment targets for affected patients.

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Heritability enrichment identifies systemic tissue-specific signatures for white matter hyperintensities and other brain-MRI-derived complex phenotypic traits

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Introduction: White matter hyperintensities (WMHs), an established MRI-detected marker of cerebrovascular abnormality, demonstrates high heritability, and has been associated with Alzheimer's disease (AD) and related dementias (ADRDs). While there is growing awareness of the bidirectional communication between the brain-body axis and brain health, the interrogation of systemic tissue-specific genetic signatures for brain phenotypes, such as WMHs, is lacking. We address this gap by characterizing common genetic bases and idiosyncrasies across multiple cell-type-groups in the body for (i) WMHs, (ii) other brain-MRI-derived complex traits and (iii) ADRDs.

Methods: We conducted heritability-analysis using the linkage-disequilibrium score regression (LDSC) pipeline [1] on available GWAS summary statistics for (i) WMH studies (N=2), (ii) ADRDs, namely AD (N=3), Parkinson's (PD; N=2), Lewy-body dementia (LBD, N=2), and (iii) 1960 UKBiobank imaging-derived phenotypes (IDPs) [3](Table.1). We used stratified-LDSC (SLDSC) for partitioning heritability of the phenotypes across cell-type-group-specific annotations [2]. Per phenotype, enrichment of SNPs associated with each cell-type group was calculated. Enrichment p-values were corrected by the standard error and log-transformed (- log(p/SE). We sub-grouped IDPs according to the functional category naming convention of UKBiobank and used an averaged -log(p/SE) per sub-category.

Results: We systematically assessed the 3 most-enriched cell-type-groups per phenotype. WMHassociated-SNPs were most enriched in liver, kidney, connective bone, and skeletal muscle cells. In common with WMH findings, total-WMH-volume-associated-SNPs showed enrichment in liver-cells, while the remaining IDPs'-associated-SNPs were most enriched in connective bone- (10/10) and skeletal muscle-cells (4/10) (Table.2). ADRD-associated-SNPs demonstrated overlap with WMHs for the following cell-type-groups: (i) liver and connective bone (AD), (ii) kidney, connective-bone, and skeletal-muscle (PD), and (iii) skeletal-muscle (LBD). Several common (e.g., CNS-, cardiovascular-cells [IDPs, PD, LBD]) and unique (e.g., immune-cells [AD]) signatures were found within and between IDPs and ADRDs (Table.2).

Conclusion: Phenotypes exhibited unique enrichment signatures across cell-types, with specific commonalities between phenotypes. WMH-associated-SNPs were highly enriched in liverand kidney-cells, agreeing with emerging literature associating WMHs with non-alcoholic fatty liver and chronic kidney diseases [4,5]. Overall, our work provides novel information on genetic commonalities that should be considered when addressing etiology, diagnosis, and treatment questions concerning phenotypes.

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The impact of cortical microvasculature hypoxia on measures of brain function in people with Multiple Sclerosis

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Background: People with Multiple Sclerosis (pwMS) may experience vascular dysfunction due to chronic inflammation in the central nervous system (CNS)[1]. Using frequency-domain near-infrared spectroscopy (fdNIRS), we showed that ~40% of pwMS experience cortical microvasculature hypoxia[2]. We also showed that cortical hypoxia is associated with reduced brain functional connectivity (FC) in pwMS[3]. This study was designed to confirm this relationship, and determine if the reduced FC is associated with cognitive impairment (CI) in pwMS.

Methods: We recruited 14 healthy controls (HCs) and 39 pwMS. Those with tissue oxygen saturation (S_tO_2) values, measured with fdNIRS, lower than 2SD below the HCs mean (S_tO_2<55.7%), were defined as hypoxic. Functional NIRS (fNIRS) was applied during rest, finger-tap, and paced auditory serial addition test (PASAT), a test to measure auditory processing speed, and working memory. FC was quantified using wavelet coherence in a low-frequency window (LFW: 0.01-0.069 Hz) which relates to vasomotor reactivity, and a high-frequency window (HFW: 0.07-0.3 Hz) which relates to cerebral autoregulation.

Results: We found that 43% of pwMS are hypoxic. There was a significant difference between HC, normoxic pwMS, and hypoxic pwMS in resting-state prefrontal cortex (PFC) inter-hemispheric coherence (p=0.013 for HFW, p=0.012 for LFW). Coherence was lower in hypoxic pwMS when compared to the normoxic pwMS (p=0.009 for HFW, and p=0.008 for LFW), and the HCs (p=0.012 for HFW, and p=0.006 for LFW). Group differences in the PFC inter-hemispheric coherence were present during PASAT (p=0.039 for HFW). Coherence was lower in hypoxic pwMS when compared to the HCs (p=0.015 for HFW). Moreover, we showed that during PASAT, cognitive Z-scores and PFC interhemispheric coherence were positively correlated (r=0.54, p=0.002 for HFW).

Conclusions: Microvasculature hypoxia in pwMS may relate to impaired brain function based on reduced FC. Also, reduced FC is associated with CI measured with validated neurocognitive tests. Our findings suggest that NIRS measures of hemodynamic coherence in MS could provide novel information on brain function, and be a biomarker of disease progression.

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AcT-Cog: Cognitive outcomes in the Alteplase compared to Tenecteplase (AcT) Trial

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Background: Stroke is a leading cause of morbidity and mortality resulting in both physical and neurological deficits. The AcT trial (Alteplase (tPA) compared to Tenecteplase (TNK)) compared two acute stroke treatments and showed non-inferiority of TNK on functional outcomes, measured by the modified Rankin scale (mRS)[1]. However, the mRS is a coarse functional scale, biased towards mobility and mortality that does not capture cognitive or participation metrics well[2]. Earlier phase II data suggested that TNK may achieve faster reperfusion[3], which could reduce cognitive impact. Therefore, we investigated cognitive changes as a secondary endpoint in the AcT trial.

Methods: Prospective cognitive outcomes were collected at 90-180 days from participants in the AcT Trial. All patients enrolled in the parent trial (treated with either tPA or TNK) who were able to complete the parent trial's primary outcome independently were eligible for AcT-Cog. Able patients were invited to complete the telephone Montreal Cognitive Assessment (T-MoCA range 0-22; scores <19 consistent with cognitive impairment)[4] and an online cognitive assessment using the Cambridge Brain Sciences (CBS with memory, reasoning and verbal domains)[5]. Differences in T-MoCA and CBS assessments between tPA and TNK was assessed using an ANCOVA and linear regression models adjusted for age, sex, education and 90-day mRS.

Results: 409 people (39% female) completed T-MoCA, ages 66y±13, mRS 1±1, with no difference between groups. 242 of these completed CBS. tPA and TNK groups did not differ on T-MoCA (tPA:16.1 ± 3.6 and TNK:16.4 ± 3.5, $F(1,392) = 0.33$, $p=0.57$) or any cognitive domains of CBS: Short-Term Memory ($\beta = 0.018$, $p=0.89$), Reasoning ($\beta = -0.054$, $p=0.65$), Verbal ($\beta = 0.035$, $p=0.81$).

Conclusions: No differences in cognitive outcomes were noted between patients treated with tPA or TNK. In both groups, the majority of patients exhibited cognitive impairment on T-MoCA, despite high prevalence of good outcomes.

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A Novel Phenotype of Older Adults with Dual Decline in Gait and Cognition at Higher Risk of Dementia. A Metabolomics Analysis

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Background: Older adults presenting with dual-decline in cognition and gait speed are at a 6-fold higher risk for dementia compared with those showing no decline in both cognition and gait speed [1,2]. Biochemical characterization of metabolic perturbations in this novel clinical group might assist in early identification of those at elevated dementia risk. We hypothesized that dual decliners would have a unique metabolomic profile. Our objective was to identify and characterize the metabolomic profile of older adults with dual decline at a high risk of dementia.

Methods: From the Gait and Brain Cohort, 76 participants, matched by time of follow up (3 years) with equal distribution (N=19) across the 4 groups were examined: pure-cognitive-decline, pure-motordecline, dual-decline, and no-decline. Cognitive and gait decline were operationalized as decrease of ≥2 points in Montreal Cognitive Assessment score, and reduction ≥10 cm/second in gait speed between baseline and the final assessment, respectively. Untargeted plasma metabolomics analyses were performed in the plasma samples collected at baseline prior to knowing which group the participants were going to belong to after 3 years across the 4 groups using Liquid Chromatography Mass Spectrometry. Pair-wise comparison of detected compounds was done with Compound Discoverer, version: 3.2.0.421.

Results: Principal components analysis and hierarchical clustering analysis did not detect any cluster separation in metabolomes across groups. However, 4 compounds (17-Hydroxy-12-(hydroxymethyl)-10-oxo-8 oxapentacyclomethyl hexopyranoside, Fleroxacin, Oleic acid, and 5xi-11,12-Dihydroxyabieta-8(14),9(11),12-trien-20-oic acid) were in significantly higher concentration ($p< 0.05$) among the dual-decliners compared with non-decliners in both cognition and gait speed.

Conclusions: Dual decliners showed similar metabolomic profiles at baseline; however, 4 compounds were identified at higher concentration when compared with non-decliners. We plan to follow-up metabolomics analyses of the groups. Results may point to modifiable pathways.

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The PREVENT VCI Study: Application of Rich-Club Behavior in the Human Brain Connectome as a Potential Novel Early Biomarker of Cognitive Decline

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Background: Transient ischemic attack (TIA) patients have a substantially increased risk of early dementia, representing an ideal population to investigate preclinical dementia. Since microstructural changes in the brain start years before cognitive impairment occurs, they are promising potential biomarkers for cognitive decline before its onset. One such indicator of microstructural changes is alterations in the rich club organization. The rich club phenomenon describes a densely connected set of hub nodes, and is thought to play an important role in brain communication, including facilitating global integration and local segregation[1]. Disruptions to the rich club have been observed in established dementia such as Alzheimer's disease[2] and small vessel disease[3], suggesting its sensitivity to WM connectivity changes in various clinical manifestations of dementia. In this study we thus aim to examine early disruptions in the rich club effect by determining whether its prominence and characteristics differ between TIAs and controls at baseline and 5-year post-event.

Methods: TIA patients (n=28) and controls (n=26) underwent T1 anatomical scans and diffusion tensor imaging at baseline and 5-year post TIA or recruitment. Whole-brain tractography utilizing anatomically constrained tractography (ACT) and constrained spherical deconvolution (CSD) was performed to construct whole-brain connectomes. In-house code was used to analyze the connectomes and to generate rich club coefficients, which indicate how interconnected a group of nodes are. The maximum rich club coefficient (Φ max) was then used as an indicator of the prominence of the rich club effect.

Results: Mean age was 64 and 62 for TIA and controls, respectively, while 43% and 65% were female. Φ max was not significantly different between TIA patients (mean [SD]: 1.11 [0.04]) and non-TIA controls (1.11 [0.05]) at baseline (p=0.700). However, TIA patients (1.09 [0.04]) showed a significantly less prominent rich club effect at 5-year compared to controls (1.12 [0.05]; p=0.029).

Conclusions: This preliminary data applying brain network analysis to the PREVENT VCI study subjects shows a significant decrease in rich club prominence (indicated by Φ max) seen in TIA patients and thus supports that it may be a novel biomarker that has the potential for predicting for future cognitive decline in TIA patients.

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IL-17A Contributes to the Angiotensin II-induced Neurovascular Coupling impairment through Oxidative Stress

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Background: Hypertension is the most prevalent modifiable risk factor for neurovascular and neurodegenerative diseases, including stroke and Alzheimer's disease [1]. It has been demonstrated that angiotensin (Ang) II, a peptide known to be involved in the development of hypertension, is a powerful modulator of the immune system. Neurodegenerative diseases have been associated with higher concentrations of circulating interleukin (IL)-17A [2, 3]. However, the possible role that IL-17A plays in linking hypertension with neurodegenerative diseases remains to be established. Cerebral blood flow regulation may be the crossroads of these conditions because regulating mechanisms may be altered in hypertension, including neurovascular coupling (NVC) [4, 5]. Therefore, our hypothesis is that NVC impairment induced by chronic Ang II administration is mediated by IL-17A and the subsequent increase in NADPH oxidase 2-dependent superoxide production. The main objective of this study is to investigate whether IL-17A contributes to the NVC impairment induced by chronic administration of Ang II by maintaining a high level of NADPH oxidase 2-derived ROS production.

Methods: Therefore, Ang-II induced hypertensive C57BL/6J mice (600 ng/kg/min, for 14 days) were injected with a neutralizing anti-IL-17A antibody, an IL-17RA receptor antagonist or with an IgG isotype control (0.5 µg/µL). NADPH oxidase 2 depleted mice and mice treated with Tempol, a superoxide dismutase mimetic agent, received a chronic administration of a recombinant IL-17A (50 pg/kg/h) to further investigate the mechanism behind its effect on NVC. NVC was assessed by monitoring cerebral blood flow responses to whiskers stimulation by laser-Doppler flowmetry in anesthetized mice. Oxidative stress was assessed ex-vivo with dihydroethidium immunostaining.

Results: Our results show that IL-17A neutralization or specific inhibition of its receptor IL-17RA prevent the Ang II-induced NVC impairment ($p<0.05$). These treatments also reduce the Ang II-induced cerebral oxidative stress ($p<0.05$). Moreover, Tempol and NADPH oxidase 2 depletion prevent NVC impairment ($p<0.05$), and the increased superoxide anion production ($p<0.05$) induced by chronic recombinant IL-17A administration.

Conclusions: These findings suggest that IL-17A, through superoxide anion production, is an important mediator of cerebrovascular dysregulation induced by Ang II. Therefore, targeting this cytokine in hypertension is a promising approach to prevent cerebrovascular dysfunctions and neurodegenerative diseases.

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Thanks for joining us.

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