



PERIOPERATIVE BRAIN HEALTH CENTRE

**Sunnybrook Health Sciences Centre
2018-2019 ANNUAL REPORT**

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THE FIRST PERIOPERATIVE BRAIN HEALTH CENTRE IN THE WORLD...

OUR VISION

We envision a future with surgery and anesthesia approaches that preserve and restore brain health.

Message from Co-founding Leaders

Welcome to the first Annual Report of the Perioperative Brain Health Centre (PBHC). The centre was established at Sunnybrook Health Sciences Centre (SHSC) in 2018 with the goal of developing strategies to optimize brain health for the hundreds of millions of patients who undergo anesthesia and surgery worldwide each year. Fortunately, most patients recover from surgery without complications. However, many experience brain-related problems in the postoperative period, including confusion, delirium, reduced mental abilities, chronic pain and depression. Patients at greatest risk with adverse brain outcomes are those who are older, have undergone major surgery or cardiovascular procedures and are

exposed to certain medications. The PBHC has created a platform for studying new treatments. It has also become a resource for patients and a tool to promote the use of available prevention strategies to optimize brain health.

We have embarked on exciting projects in both the preclinical and clinical arms. Ultimately, we aim to create a fully integrated, translational research program, a true bench-to-bedside enterprise.

What have we done?

This Annual Report provides a sampling of the projects that have been completed or are underway by the researchers, healthcare providers, advocates and volunteers in the PBHC.

Thank you for your financial support of this growing program. Those who would like to know how they can help to optimize brain health after anesthesia and surgery may contact brainhealth@sunnybrook.ca or visit <https://donate.sunnybrook.ca/one-time>.

Highlights of our year:

- Established the first Professorship in Perioperative Sciences through the generosity of the Department of Anesthesia at Sunnybrook Health Sciences Centre. Dr. Stephen Choi, Co-director of the PBHC, is the Professorship awardee.
- Helped develop the first internationally accepted nomenclature to describe perioperative neurocognitive disorders.
- Collaborated in development of the first published best practice guidelines for perioperative brain health.
- Launched a drug treatment study that aims to reduce the incidence of long-term cognitive changes after cardiac surgery and anesthesia.
- First reported the mechanisms of action of the only drug available that reduces the incidence and duration of delirium in the postoperative period.
- National and international recognition of our research team.



Dr. Stephen Choi
MD, MSc, FRCPC

Co-founding Leader, PBHC
Co-director of (Clinical) Research,
Dept. of Anesthesia, SHSC
Associate Professor, Dept. of Anesthesia, U of T



Dr. Sinziana Avramescu
MD, PhD, FRCPC

Co-founding Leader, PBHC
Assistant Professor, Dept. of Anesthesia, U of T



Dr. Beverley A. Orser
MD, PhD, FRCPC, FCAHS

Co-founding Leader, PBHC
Co-Director of (Preclinical) Research,
Dept. of Anesthesia, SHSC
Professor and Chair, Dept. of Anesthesia, U of T





Perioperative Brain Health Centre Website

The Perioperative Brain Health Centre website is committed to improving patient education about brain health and to discovering “best anesthetics” and therapeutic strategies for prevention and treatment of postanesthetic cognitive deficits.

Regular updates are provided in areas such as ongoing research, advocacy and news. An exciting educational infographic on delirium that was developed this year by the Perioperative Brain Health Centre can be found on the website. Patients and healthcare providers can access the website for up-to-date information.

To learn more, please visit:

<http://www.perioperativebrainhealth.com>

New Clinical Terms for Cognitive Changes Affecting Surgical Patients

An international panel developed a unified nomenclature that was simultaneously published in six leading anesthesiology journals. The panel recommended a new set of terms to describe cognitive changes after anesthesia and surgery. This consistent nomenclature will help with the diagnosis and management of perioperative cognitive impairment (*Br J Anaesth. 2018 121(5):1005-1012*).

Best Practice Recommendations for Perioperative Brain Health

A consensus from international leaders provides best practice recommendations for clinical assessment and management of postoperative brain health (*Anesth Analg. 2018 127(6):1406-1413*).

Two Steps to Evolve Patient Care

We established a program that is designed to develop new medicines/treatments and better diagnostics in brain and mental health – an area that represents a tremendous social and economic burden for Ontario.

Step 1.

Preclinical Research

Step 2.

Clinical Research

We will grow the program by focusing on:

- *Basic Brain Science:* To discover and decipher novel cellular pathways related to human brain physiology
- *Clinical Research:* To preserve and restore brain health for our patients
- Collaborations and knowledge transfer
- Patient involvement and precision medicine
- Patient and economic benefits



Preclinical Advancements

The preclinical laboratory team is exploring how anesthesia and surgery changes the brain with the aim of identifying potential new treatments. We recently published the first evidence explaining the ability of a drug, called dexmedetomidine, to prevent cognitive deficits after surgery in critically ill patients. These insights will lead to better use of dexmedetomidine in the perioperative period. In another study, we identified how gabapentin, a widely used analgesia drug, causes sedation and confusion (*EBioMedicine*, *in press*). Finally, we continue to work close with the US Food and Drug Administration and *SmartTots* (SmartTots.org) to examine the potential neurotoxic effects of anesthetics in the developing brain. We published a commentary in the leading journal, *The Lancet*, that addresses cognitive changes in children after anesthesia and surgery.

Clinical Advancements

The research program of the PBHC is well underway, with two major clinical studies: **COGNIGRAM** and **CODEX**.

COGNIGRAM is a prospective, observational study aiming to examine postoperative cognitive outcomes or trajectories and to identify risk factors leading to worsening cognitive function after total hip and knee arthroplasty. These surgeries are among the most commonly performed in Canada (~130,000 yearly). While the improvements in physical quality of life are well documented, cognitive outcomes have yet to be studied rigorously. Over the past 18 months, 550 patients have generously volunteered to participate in the study.

CODEX is a multicentre, randomized controlled trial aiming to determine whether dexmedetomidine sedation administered immediately after cardiac surgery reduces postoperative cognitive impairment (i.e., 3 months after surgery). Our study just launched at Sunnybrook, with funding from the AFP Innovation Fund. We have recently been awarded a major international grant from the Dana Foundation's Clinical Neuroscience Research Grant Program, which will be used to spearhead expansion of the trial across cardiac centres within the University of Toronto and throughout the province.



New Professorship in Perioperative Sciences

Department of Anesthesia University of Toronto

Scientific and clinical research plays a fundamental role in the evolution of medicine by providing knowledge and insight that further improves patient care. This year, the Sunnybrook Anesthesia Academic Partnership undertook a novel approach to allocate and expand resources available for such research by launching the Professorship in Perioperative Sciences within the Department of Anesthesia at the University of Toronto.

This professorship creates a structure whereby our clinical department allocates protected funds to enable research while partnering with the University of Toronto to seek matching donors from the community. By working with both the university and the community, we are striving to maximize the resources available for impactful research.

We would like to thank the Sunnybrook Anesthesia Academic Partnership for their generous donation which has established the Professorship in Perioperative Sciences at Sunnybrook through the Department of Anesthesia at the University of Toronto. We are very grateful to Dr. Oskar Singer for his invaluable contribution in facilitating the interactions between the Sunnybrook Anesthesia Academic Partnership and the University of Toronto.

Collaborations at Sunnybrook

Dr. Fahad Alam



Dr. Alam's research program focuses on developing immersive reality, e-learning and cognitive learning theories for use in clinical research and medical/patient education. PERFECT-VR, a study led by Dr. Alam, investigates anxiety in psychiatric patients before electroconvulsive therapy (ECT) and aims to enhance patients' knowledge about ECT and thereby decrease treatment misconceptions. This innovative study has been featured on multiple media platforms over the past month. Dr. Alam is the Director of Research at the Sunnybrook Canadian Simulation Centre and Co-director of the Collaborative Human Immersive Interaction Laboratory (CHISIL), a laboratory advancing the use of immersive reality and technology-enhanced learning in medical education. The CHISIL is also a collaborator with PBHC, aiming to provide resources for clinical, medical and patient education.

Dr. Benjamin Goldstein

Dr. Goldstein's collaboration with PBHC investigators focuses primarily on a Health Canada-approved randomized controlled trial of two anesthetics, midazolam and nitrous oxide, for the treatment of refractory depression among adults with bipolar disorder. This study is an example of image-guided therapeutics, with the secondary outcome being regional cerebral blood flow, measured via arterial spin labelling MRI. An NMDA-antagonist, nitrous oxide is also known to modulate cerebral blood flow, which is modified toward an increased anterior-to-posterior perfusion gradient. The anesthetics are delivered while the participant is in the MRI scanner, with real-time, repeated measures of cerebral blood flow and resting-state functional connectivity. The study treatment team includes two anesthesia assistants and an anesthetist, in addition to imaging staff and psychiatry team members. Dr. Beverley Orser and Dr. Susan Belo are co-investigators on this project, which was supported earlier this year by a pilot grant from the Sunnybrook Department of Psychiatry.



The Centre for Seniors Health



The Centre for Seniors Health is an initiative funded by Peter Cipriano through a \$10 million donation to create a centre to introduce the "first-ever patient-centred model of care to keep seniors healthy in their community". The PBHC is partnering with this initiative to help address perioperative brain disorders using a multidisciplinary approach.



Focus on Trainees

The year 2018 has been a very successful year for the trainees of the preclinical laboratory. Trainees contributed to several research articles that were published in peer-reviewed journals. The graduate students from the lab were also awarded prestigious scholarships, as listed below:

- **Shahin Kodaei** – Canadian Institute of Health Research Frederick Banting and Charles Best Canada Graduate Scholarship
- **Winston Li** – Canadian Institute of Health Research Graduate Scholarship
- **Marc Manzo** – Dr. Kirk Weber Award in Anaesthesia and Graduate Stimulus Package
- **Arsene Pinguelo** – Dr. Kirk Weber Award in Anaesthesia



Dr. Orser's laboratory team, 2018. Top, left to right: Winston Li, Arsene Pinguelo, Marc Manzo. Bottom, left to right: Shahin Khodaei, Dr. Dianshi Wang, Dr. Beverley Orser, Dr. Lilia Kaustov, Dr. Ali Ghavanini.

Past and Present Team Members

Several new members have joined our research team.

Dr. Angela Jerath, from the University Health Network, joined us as a Clinician Scientist. Dr. Jerath's expertise covers clinical epidemiology, health services and advanced biostatistics.



Dr. Angela Jerath

Dr. Lilia Kaustov joined us as a Research Manager. She is a scientist with experience in both biomedical and academic sectors. Dr. Kaustov works closely with the investigators, coordinating clinical and research programs to fulfill the department's strategic research goals.



Dr. Lilia Kaustov

Dr. Ali Ghavanini joined us as a postdoctoral fellow after working at the Karolinska Institute and the Centre for Toxicology in Sweden. Dr. Ghavanini has a background in toxicology to the human brain and in understanding long-term changes in genes that regulate behavior. He has a wide range of skills, including immunohistochemistry, flow cytometry, confocal laser microscopy and protein biochemistry. He is excited to join the team and expand his expertise in translational science as it relates to perioperative care.



Dr. Ali Ghavanini

Dr. Josiane Mapplebeck is a neuroscientist who trained under the mentorship of Dr. Michael Salter at the Hospital for Sick Children. She joined us as a Research Coordinator and will bring a wealth of expertise in pain biology and sex/gender differences in neuroscience.



Dr. Josiane Mapplebeck

We bid a fond farewell and express our gratitude to **Drs. Sinziana Avramescu, Shelly Au** and **Gang Lei**. Dr. Avramescu, one of the co-founding members of the PBHC, is working at Humber River Hospital and continues to provide valuable collaboration on our projects. Dr. Au moved to Vancouver and is working at the Djavad Mowafaghian Centre for Brain Health at the University of British Columbia. Dr. Lei is working at the Lunenfeld-Tanenbaum Research Institute under the mentorship of Dr. Graham Collingridge.



Public Media

Under the knife and unaware?

What happens when we're under anesthesia

CBC's Mike Finnerty interviewed Dr. Beverley Orser in June 2018 about the current understanding of anesthesia and recent developments in anesthesia research. [Click Here](#) to listen to Dr. Orser on CBC's *The Current*.

Our Goals and Aims:

Position Sunnybrook Health Sciences Centre and U of T as international leaders in perioperative brain health

Aim 1. Patient Education

- Carefully monitor cognitive function in all surgical patients at Sunnybrook Health Sciences Centre.
- Educate Sunnybrookers and our patients on ways of promoting brain health before and after surgery.
- Help to establish and collaborate in delivering the Seniors Health Program at Sunnybrook.

Aim 2. Perioperative Sciences – Educational Program in Perioperative Brain Health

- Establish a perioperative sciences program at U of T.
- Train 3 - 5 graduate students, 1 - 2 post doctoral fellows and 3 - 5 co-op and summer students annually.
- Continue to develop curriculums for international meetings.
- Develop a cross-disciplinary training program.

Aim 3. Advancement, Communication and Outreach

- Advocate and fundraise for a chair in perioperative brain health.
- Increase media/web presence and social media.
- Continuously submit publications and be successful on grant applications.

Awards, Publications and Funding Updates

Awards

Dr. Stephen Choi received the U of T Department of Anesthesia Merit Award. This award supports talented investigators to foster sustained growth of research in the department. Dr. Benjamin Goldstein received the Dr. Samarhji Lal 2018 Award, which recognizes an outstanding Canadian researcher in the area of psychiatry. Dr. Fahad Alam received the Annual Sunnybrook Education Conference Best PODIUM 2017 and 2018 Awards. Dr. Beverley Orser was recently recognized by several awards and honours, including a Fellowship in the Royal Society of Canada, elected membership in the US National Academy of Medicine and the 2018 American Society of Anesthesiologists Excellence in Research Award.

Publications

The PBHC has already established a prolific publication record. Since its founding, PBHC-supported research has been published in more than 30 articles in a wide variety of journals, including *The Lancet*, *Anesthesia & Analgesia*, *Anesthesiology*, *Scientific Reports* and the *British Journal of Anaesthesia*. See below for links to the publication records of our leading members:

Dr. Sinziana Avramescu:

<https://www.ncbi.nlm.nih.gov/pubmed/?term=sinziana+avramescu>

Dr. Stephen Choi:

<https://www.ncbi.nlm.nih.gov/pubmed/?term=Choi+S%5BAuthor%5D+and+sunnybrook>

Dr. Beverley Orser:

<https://www.ncbi.nlm.nih.gov/pubmed/?term=Orser+B%5BAuthor%5D>

Funding updates

Dr. Choi's clinical trial on dexmedetomidine, the **CODEX** study, was supported by a prestigious Dana Foundation Award. This is an international peer-reviewed grant valued at \$300,000 USD that funds his clinical research in connection with perioperative neurocognitive disorders after cardiac surgery. This grant will spearhead expansion of the trial across cardiac centres at the University of Toronto and throughout the province. The Dana Foundation is a philanthropic organization committed to developing a better understanding of the brain and its functions. Founded in 1950, this foundation works to achieve its goals through grants to institutions engaged in innovative neuroscience research and through public outreach efforts. Dr. Orser's laboratory continues to be supported by a Foundation Grant from the Canadian Institutes of Health Research and other funding sources.

Acknowledgements



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(SEAC)

AHSC AFP Innovation Fund



For more information, please visit:
www.perioperativebrainhealth.com

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