$5.95

MIND OVER MATTER®

GUT REACTION

THE FIRST TIME I KNEW

MIGRAINES & BRAIN HEALTH

ONLINE MEMORY TESTS

TOO YOUNG TO FADE

SUBSTANCE USE & ABUSE

Insight into the latest research findings to combat brain aging diseases and what you need to stay **brain healthy longer.**

Women's Brain Health Initiative

WBHI.ORG | VOLUME 7

With Gratitude

THIS EDITION OF MIND OVER MATTER® WAS MADE POSSIBLE THANKS TO THE GENEROUS AND ONGOING SUPPORT AND ENCOURAGEMENT OF OUR PARTNER BRAIN CANADA FOUNDATION AND HEALTH CANADA.

Brain Canada is celebrating our 20th anniversary this year—20 years of supporting and advancing Canada's world-class brain research to the benefit of all Canadians. Since our founding in 1998, we have granted more than $250 million to 281 projects involving more than 1,000 researchers based in 115 hospitals, universities, and research institutes across Canada.

Our research program has been centred on our belief that joining people, labs, and platforms—across the country and around the world—is the best way to accelerate the pace of discovery and to create the conditions to drive innovation. We have proudly been at the forefront of providing funding to enable collaborations across disciplines and institutions, which has led to new thinking and new approaches.

Since 1998, we have partnered with more than 100 private philanthropists and foundations, corporations, research institutes, provincial agencies, and voluntary health organizations. Each one has placed a new lens on our work, and helped us evolve in our role as a funder in providing leadership in areas that need greater attention and investment.

Our collaboration with Women's Brain Health Initiative, which began in 2016, has been particularly transformative. It has helped to raise our awareness of the importance of conducting research that is sensitive to sex and gender considerations, and has inspired us to take concrete measures such as asking researchers applying for grants to describe how they plan to incorporate these considerations into their research.

We have also supported several new projects looking into the effect of hormones on the brain, among other topics. One will be using neuroimaging to study the effect of sex hormone therapy on brain development in adolescents experiencing gender dysphoria – something that has never been studied despite the wide use of sex hormone therapy.

Another will be investigating some of the potential reasons why women experience greater cognitive decline than men, with a specific focus on past pregnancy, motherhood, and genetics. As Dr. Paula Duarte-Guterman, who is conducting this research, says: "Pregnancy's long-term consequences have not received much attention, yet to fully understand women's physiology, reproductive experience needs to be taken into account in research." You can learn more about this project in Brain Canada's 2017 Annual Report, which can be accessed via our website (braincanada.ca).

We are also supporting a study led by Dr. Gillian Einstein, the recipient of the inaugural Wilfred and Joyce Posluns Chair in Women's Brain Health and Aging. Her pioneering work was profiled in the previous issue of Mind Over Matter®. Dr. Einstein's postdoctoral fellow, Nicole Gervais, is studying the effect of natural and surgical menopause on early markers of Alzheimer's disease such as changes in sleep, cognition, and markers of inflammation.

Finally, we are pleased to see that some of the research integrating gender is already having an impact. For example, a study presented at this year's Alzheimer's Association International Conference in Chicago showed that, by adjusting the cut-offs in the "score" for a verbal memory test based on gender, Alzheimer's disease could be detected earlier and more reliably in women. Ignoring sex differences can disguise the existence of Alzheimer's disease pathology, leading to diagnosis at later stages of the illness, when therapies are less likely to work.

While we plan to support more research on women's brain health in the future, we are proud of our track record over the last 20 years, both as a major funder and as a leading voice in changing the way we do research. We invite you to visit our website and social media channels to stay up-to-date on the celebration events that will take place over the next year to mark this special occasion, culminating in a gala in Toronto in June of 2019.

Naomi Azrieli
Chair, Brain Canada Foundation

Inez Jabalpurwala
President and CEO,
Brain Canada Foundation

Brain Canada Foundation

EDITOR'S LETTER

I recently had the opportunity to attend the 2018 Alzheimer's Disease International (ADI) conference in Chicago, along with approximately 1000 other delegates, representing upwards of 100 countries. This experience was both enlightening and heartening. I had the honour of representing Women's Brain Health Initiative (WBHI) on a panel discussion about women and dementia. My co-panelists brought an extraordinary array of expertise from Canada, the U.S., and Europe.

As it happened, all eight of the panelists and the moderator were women – a rarity, I am told. Let that sink in for a moment. We are talking about a disease that overwhelmingly affects women and where women represent the vast majority of caregivers, and yet we rarely see an all-female discussion. It was encouraging that the conference organizers acknowledged the gender realities of dementia. But one audience member asked why our event was not part of a plenary session, where all delegates could attend, as opposed to one of the breakout sessions. We unanimously agreed with the sentiment.

Our panel discussion covered a variety of subjects, including caregiver issues. Individuals living with dementia are overwhelmingly cared for by women, and those women often report experiencing a greater burden than their male counterparts. They tend to pay a higher price both financially and to their career ambitions, and it exacts a greater toll on their psychological health and wellbeing. It is important to continue highlighting those issues.

Maria Teresa Ferretti from Switzerland's Women's Brain Project spoke about some of the most recent research regarding sex differences in dementia, with a title that I appreciated: "The gateway to precision medicine." WBHI proudly champions and supports researchers who believe that we cannot fully understand and treat dementia and other brain-aging diseases without exploring the sex and gender divide.

I was also encouraged to see a paper unveiled recently entitled "Understanding the Impact of Sex and Gender in Alzheimer's Disease: A Call to Action". Prepared by a blue-chip panel of experts from some of the leading health care institutions in the U.S., it is an exhaustive review of the key research findings to date. Its introduction is powerful, timely, and necessary:

"PRECISION MEDICINE METHODOLOGIES AND APPROACHES HAVE ADVANCED OUR UNDERSTANDING OF THE CLINICAL PRESENTATION, DEVELOPMENT, PROGRESSION, AND MANAGEMENT OF ALZHEIMER'S DISEASE (AD) DEMENTIA. HOWEVER, SEX AND GENDER HAVE NOT YET BEEN ADEQUATELY INTEGRATED INTO MANY OF THESE APPROACHES."

I could not agree more. While we have made important strides in incorporating sex and gender into dementia research – with Canada as a world leader – we have much more to do. At WBHI, we are constantly pushing ahead with our mission to educate individuals on how to take positive action to preserve brain health, to support innovative research, and to use our platform to spread the word about the latest advances.

After attending the ADI conference this year, I could not help but reflect on how far we have come in the ten years since I first became involved in raising awareness for the inequity in research for women, and since the launch of WBHI over five years ago. Where once we felt like lone wolves, with the sex and gender divide garnering little attention in the exploding public health crisis of dementia, now more and more people are talking about it and more researchers are integrating sex and gender considerations in their work.

Having just celebrated our own milestone of five years, I would like to pay a special tribute to our friends, colleagues, and supporters at Brain Canada who are marking their 20th anniversary this year. Brain Canada plays a crucial role in funding important research that will make a difference to us all. Congratulations, and thank you for everything you do!

If you are a new reader of Mind Over Matter®, thank you so much for picking up our magazine. WBHI can only do what it does because of our many devoted supporters. I invite you to learn more about our mission through the pages of Mind Over Matter® or to visit our website at womensbrainhealth.org. If you are a member of a book or social club, be sure to check out our initiative in which we provide free copies of Mind Over Matter® so that you can add a discussion of brain health to your next meeting.

Women's brain health needs more attention and thanks to the efforts of many, it is finally starting to get it.

PHOTO: JAYLYN TODD

Lynn Posluns
Founder and President,
Women's Brain Health Initiative

CONTRIBUTORS

AMY CHAPLICK // CONTRIBUTING EDITOR

Amy is a real estate lawyer at DelZotto, Zorzi LLP, one of Canada's top real estate boutique law firms. "Although many people think of dementia as a disease that affects older adults, the disease begins to impact the brain decades before symptoms are even noticed. WBHI is inspiring a new generation of women to take care of our brain health today, since research shows the earlier you protect your brain, the better the cognitive outcome."

VITINA BLUMENTHAL // CREATIVE DIRECTOR

Vitina is creative to her core. An adventurous soul with a passion for travel, a healthy lifestyle (especially all things yoga), and sharing her love of mindfulness with others. She runs a self-discovery business, WanderfulSoul, which focuses on creating unforgettable, transformational experiences that promote mental and emotional well-being. Through WBHI's Young Person's Cabinet, she encourages Millennials to start taking care of their mental and brain health.

STEPHANIE HAHN // WRITER

Stephanie is a writer and yoga instructor living in Waterloo Region, Ontario. It was through the "gift" of back pain that Stephanie learned to slow down, listen to her body and rediscover the joys of moving. "Writing for this magazine allowed me to merge my love of writing with my love of spreading the word that stress relief is critical for health."

DILIA NARDUZZI // WRITER

Dilia is a writer and editor living in Hamilton, Ontario. She's been interested in healthy eating and a balanced lifestyle for almost twenty years. She studied gender dynamics while doing graduate work at McMaster University and was really honoured to write for Mind Over Matter®. "I want the medical profession and all women to know that women's bodies require specialized medical care."

SEAN MALLEN // WRITER

Sean Mallen is a Toronto-based communications consultant, journalist, and writer. His book *Falling For London* is expected to to be published by Dundurn Press in the fall of 2018. Having seen family members deal with dementia, he is a strong supporter of the mission of WBHI.

SUSANNE GAGE // WRITER

Susanne is a marketing/communications agency and events professional, with a solid appreciation for smart thinking. A believer in life balance and healthy body and mind, Susanne is also a passionate advocate for giving back. "As a business woman, wife, mother, daughter and friend, I am inspired by the impact of WBHI and the collaborative opportunities to make a real difference."

AMY SKY AND ZOE SKY JORDAN // ON THE FRONT COVER

Amy and Zoe are both passionate about creativity, healthy living and women's brain health. Both mother and daughter are singer-songwriters, and are each other's biggest fans and supporters. They both believe that awareness, education and prevention are the cornerstones to self-care. They are proud to support the magazine with its message of empowering women to be pro-active in maintaining their vitality, at any stage of life.

CLARE AND CRYSTAL BRAGANZA // ON THE BACK COVER

Advocates of a healthy mind and body, Clare and Crystal are honoured to represent the women's brain health community. A relationship built on support and love, creating lasting memories together has always been a priority for them - cherishing every moment, maintaining a dynamic support system and sharing the gift of brain health.

COVER PHOTOS: JAYLYN TODD

HEADS UP

The Effects of Migraine on Your Brain

For the 10% to 15% of the population who experience migraines, the intense pain can be incapacitating. It is a complex neurological disorder that can affect one or both sides of the brain, and involves varied symptoms including headache, nausea, blurred vision, dizziness, sensitivity to light and sound, and/or aversion to particular smells. Approximately one-third of those with migraines experience "migraine with aura," which is a migraine that occurs with a wide range of neurological symptoms that can include visual disturbances, sensory changes, and speech or language difficulties. Migraines are a major contributor to ill health and disability, affecting an estimated 959 million people worldwide.

Everyone's experience of migraine is unique, with differing times of onset, symptoms, and impact. Shari Orenstein from Toronto began having migraines later in life, commencing around the same time she entered menopause. In the beginning, she would experience one to →

A migraineur is someone who suffers from migraines.

four migraines each month, but now, 12 years later, she might have up to 25 migraines a month. "I can't even remember the last time I had a day when I've been completely OK," Shari said. "Even when I take medication – and I've tried them all – any relief I enjoy is temporary and the rebound effect afterwards comes quickly and can be just as bad as the original migraine, or worse. Like so many migraineurs, when I do have a good day I live in constant fear that the next migraine is right around the corner."

Shari is sharing her story because she wants people to learn that migraines are not just bad headaches. In fact, in some instances, a headache is not even one of the symptoms of a migraine attack. For Shari, the impact on all aspects of her life has been devastating. "Most days I have to sequester myself away in a dark room. I am afraid to make plans as most often I am forced to cancel. I cancelled my own birthday dinner for the last two years, I've missed so many family celebrations, and even had to leave my son's birthday dinner early," she explained. "I feel that I've let everyone down and as a result, I feel depressed, overwhelmed, and terribly isolated."

WOMEN ARE MORE LIKELY TO EXPERIENCE MIGRAINES THAN MEN DUE TO HORMONAL INFLUENCES.

It is estimated that approximately 20% of the female population is affected, with the percentage being the highest during the reproductive years (up to 37%).

MIGRAINE WITH AURA LINKED TO STROKE

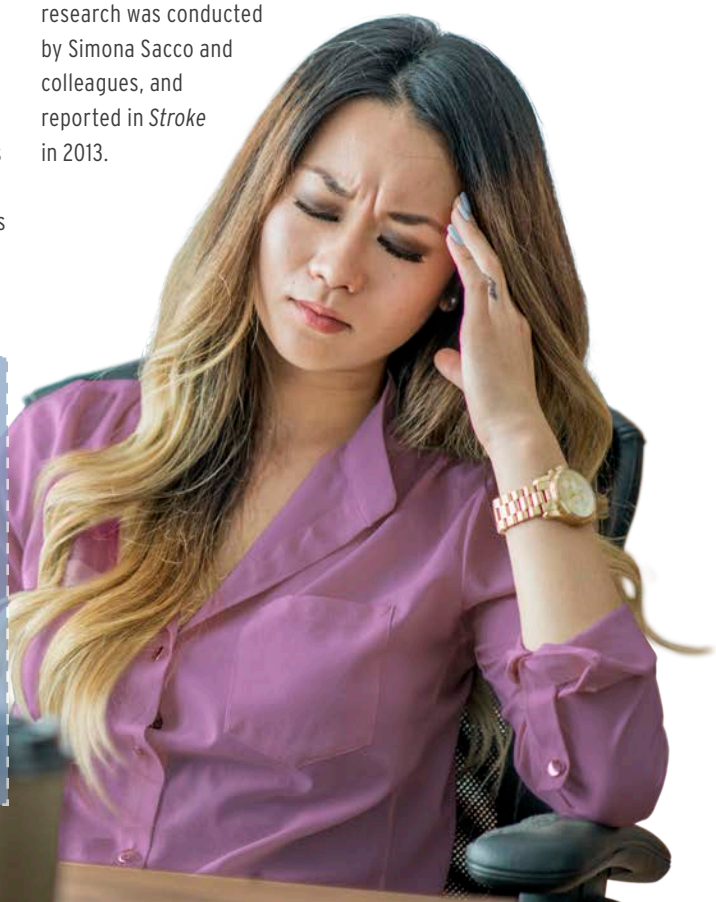
A systematic review conducted by Markus Schürks and colleagues, published in the medical journal *BMJ* in 2009, assessed the findings of nine studies examining the association between migraine and ischemic stroke. The researchers found that migraine with aura was associated with a two-fold increase in the risk of ischemic stroke compared to individuals without migraine, and that the risk was higher among women (compared to men).

A study conducted by Leah MacClellan and colleagues, published in the American Heart Association's journal *Stroke* in 2007, examined the migraine-stroke association specifically in women. The researchers reported that women who suffered from migraines with aura had a 1.5-fold increase in the risk of ischemic stroke compared to women with no migraines. Behavioural risk factors such as smoking dramatically increased the risk of ischemic stroke. Women with migraines with aura who were current cigarette smokers and current users of oral contraceptives had seven-fold greater odds of stroke than women suffering from migraines with aura who did not smoke or use oral contraceptives.

More recently, a meta-analysis of eight studies concluded that

INDIVIDUALS WITH MIGRAINES ALSO HAVE AN INCREASED RISK OF HEMORRHAGIC STROKE COMPARED TO THOSE WITHOUT MIGRAINES

(although the risk was lower than what has been reported for ischemic stroke). The researchers also examined women's risk in particular and found that women who experience migraines have a higher risk of suffering from a hemorrhagic stroke compared with control subjects. The researchers noted, however, that the women-specific findings should be interpreted with caution because only two of the studies contained data relevant to that analysis, and that data did not allow a direct comparison of risk between women and men. This research was conducted by Simona Sacco and colleagues, and reported in *Stroke* in 2013.



There are two types of stroke, ischemic and hemorrhagic. An ischemic stroke occurs when an obstruction (i.e. a blood clot) within a blood vessel blocks the supply of blood to the brain. According to the American Heart Association, ischemic strokes account for the vast majority of stroke cases (approximately 87%). A hemorrhagic stroke occurs when a weakened blood vessel ruptures and causes bleeding into the brain. This type of stroke accounts for approximately 13% of stroke cases.

White matter hyperintensities are lesions in the brain that appear as areas of increased brightness on a magnetic resonance imaging (MRI) or computed tomography (CT) scan.

Silent infarcts are areas of dead brain tissue resulting from blocked or narrowing arteries, which can also be observed on MRI or CT scans. Infarcts are often seen after someone has had a stroke, but in the case of "silent" infarcts, there has not been a corresponding stroke episode.

THE IMPACT OF MIGRAINE ON BRAIN STRUCTURE REMAINS UNCLEAR

A small number of studies have found that migraine with aura, particularly in women, is linked with an increased risk of changes to brain structure – more white matter hyperintensities and silent infarcts, in particular. But a recent study, published in *BRAIN* in 2016, had results that were inconsistent with those earlier findings.

Using the Danish Twin Registry, the researchers identified 172 women between the ages of 30 and 60 years old who experienced migraines with aura, as well as a control group of 139 unrelated women with no history of migraines. Additionally, 34 co-twins who, unlike their participating twin sisters, did not experience migraines with aura, also participated in the study. The women all had magnetic resonance imaging (MRI) brain scans conducted at a single centre, looking for the presence of infarcts and white matter intensities.

"In our study, we found that migraine with aura is not associated with an increased risk of silent brain infarcts or white matter hyperintensities," explained Dr. Messoud Ashina, a Professor of Neurology at the University of Copenhagen and one of the study's authors.

ASSOCIATION BETWEEN MIGRAINE AND COGNITIVE DECLINE ALSO UNCLEAR

Since both stroke and structural brain lesions are linked with an increased risk of cognitive decline, it is not surprising that researchers have hypothesized that perhaps migraine may be associated with increased risk of cognitive impairment or dementia.

> **MANY STUDIES HAVE EXAMINED THE RELATIONSHIP BETWEEN MIGRAINE AND COGNITIVE FUNCTION, AND THE RESULTS HAVE BEEN MIXED.**

Some studies found no differences in cognitive function between individuals with or without migraines, and others found cognitive performance was worse among those suffering from migraines. However, the findings seem to be affected by study design. Some studies looked at cognitive function at a single point in time (cross-sectional) whereas others (prospective) compared cognitive function at different points in time, i.e. measured cognitive decline, which is a more meaningful measure. Prospective studies have not found greater rates of cognitive decline in individuals with migraines compared to those without.

A study conducted by Dr. Pamela Rist and colleagues, published in *BMJ* in 2012, looked specifically at migraines and cognitive decline in women. "Our research revealed that women with migraines did not experience different rates of cognitive decline, compared to women with no history of migraines. This was true for women experiencing migraines with or without aura," said Dr. Rist, Assistant Professor of Medicine at Harvard Medical School and Brigham and Women's Hospital in Boston. "We concluded, based on our own study results and findings of previous studies, that patients with migraines should be reassured that migraines may not have long-term consequences on cognitive function."

WHY WOMEN AND MEN ARE AFFECTED DIFFERENTLY

Sex hormones may play a role in the differences between women and men when it comes to migraines. For most women with migraines, attacks are more likely to occur during the two days before, and first three days of, menstruation. Jelena Pavlovi and colleagues researched the connection between hormones and migraines in women. Their research, reported in *Neurology* in 2016, revealed that women affected by migraines have distinct patterns of estrogen decline leading up to their periods compared to women without migraines. Men do not experience large hormonal fluctuations each month like women do, which may help explain why men are less likely to experience migraines and when they do, why the effects are different than they are for women.

THE NEWEST MIGRAINE DRUGS

There are many drugs to prevent and treat migraines, yet symptoms continue to disable many people. The search continues for new drug therapies, and a new one was approved by the United States Food and Drug Administration (FDA) in May 2018. Aimovig™ is the first and only FDA-approved treatment to prevent migraines in adults by blocking the calcitonin gene-related peptide (CGRP) receptor. It is a monoclonal antibody self-administered once each month via an autoinjector. Research to date has shown that patients who took Aimovig™ experienced 1 to 2.5 fewer migraine days each month. And in the fall of 2018, Eli Lilly is hoping for FDA approval on its own once-monthly self-administered CGRP antibody Emgality™.

TAKE TEN

Ten Minutes of Exercise Daily Can Make a Difference

We know that physical activity is critical to a healthy lifestyle. Exercise helps with muscle strengthening, physical control and coordination, but, most importantly, it helps maintain good blood flow to the brain and may encourage new brain cell growth and survival. Research now suggests that physical exercise can reduce the risk of developing dementia, further confirming the long-believed connection between physical fitness, heart health, and cognitive function.

In fact, a study published in the journal *Neurology* in early 2018 found that

> **WOMEN WITH HIGHER CARDIOVASCULAR FITNESS AT MIDLIFE WERE LESS LIKELY TO DEVELOP DEMENTIA LATER IN LIFE.**

The study involved a group of 191 women who were followed over the course of 44 years, and the results included the following:

5% of women with **HIGH** cardiovascular fitness at midlife developed dementia;

25% of women with **MEDIUM** cardiovascular fitness at midlife developed dementia; and

32% of women who had the **LOWEST** cardiovascular fitness at midlife developed dementia by the end of the study.

The few "highly fit" women who did develop dementia only became symptomatic around the age of 90, which was 11 years later than the "moderately fit" participants in the study. "I'm very surprised that the finding was so strong," said Ingmar Skoog, the senior author of the study and a Psychiatry Professor at The University of Gothenburg in Sweden. "It really shows the importance of exercise. Alzheimer's and other dementias are believed to begin 15-20 years before symptoms even appear, so it makes sense that exercising in mid-life would affect the risk." While exercise alone is not likely to prevent Alzheimer's disease, the study demonstrates that individuals are not helpless in the face of one of the most feared diseases of old age.

Exactly how much exercise is required? And what kind of activity is best to maximize results? According to a report recently published by Western University in London, Ontario, **even a ten-minute aerobic workout can measurably boost one's brain power, improving both problem-solving skills and the ability to focus.** "Some people can't commit to a long-term exercise regime because of time or physical capacity. This study shows that people can cycle or walk briskly for a short duration, even once, and find immediate benefits," noted Kinesiology Professor Matthew Heath, who took part in conducting the study.

Recognizing that an active lifestyle can improve your brain health (even if it is for as little as ten minutes a day), with the real possibility of significantly lowering your risk of dementia over time, →

Exercise tones the legs, builds bigger biceps, and strengthens the heart. But of all the body parts that benefit from a good workout, the brain may be the biggest winner.

The best way to stave off dementia is to move! Exercise builds the size of the hippocampus, the part of the brain where memories are stored, and can knock years off your brain age.

Dr. Jennifer Heisz, Associate Professor, Director of NeuroFitLab.com, Department of Kinesiology at McMaster University in Ontario, shares some practical advice.

Breaking up your work day with short exercise breaks can stimulate the brain to help improve your creativity, focus, and efficiency.

TIP: Activate your mind to improve your focus. Every time you find your mind wandering away from your task, take an exercise break. These breaks could include standing up and stretching, walking to get a drink of water or coffee, or doing a few flights of stairs. This simple act of incorporating exercise into your work day can help you work smarter and more efficiently.

Chronic stress damages brain cells in the hippocampus. Exercise protects your brain against this damage. It does this by growing new brain cells.

TIP: 30 minutes of moderate-intensity aerobic exercise three times per week is best for your mental health.

Exercise is an investment in your future brain health.

Individuals who are inactive have a similar risk of developing dementia as if they were born with a genetic predisposition to Alzheimer's disease. You can't change your genes, but you can change your lifestyle.

TIP: It can be as simple as walking three times per week. And the earlier you start the better!

There is one very important thing about using lifestyle to promote brain health: you actually have to do it.

The physical activity guidelines recommend getting 150 minutes of moderate-to-vigorous aerobic activity per week. In other words, being active once in a while is not enough. Physical activity needs to be built into our schedule, every week.

TIP: Use a calendar to mark the details of your workout ahead of time, including specifics such as when, where, what, and with whom.

should encourage women to engage in some proactive and preventative behaviours.

Women's Brain Health Initiative has had the wonderful opportunity to work with Dr. Jennifer Heisz, an Assistant Professor in Kinesiology at McMaster University. Dr. Heisz's research has long examined the effects of physical activity on brain function to promote mental health and cognition in young adults, older adults, and individuals with Alzheimer's disease. Her current research includes developing physical activity guidelines for the prevention and management of Alzheimer's disease and other dementias.

Some of the most exciting results of her research focus on prevention. "We have found that older adults who exercise early in life, reduce their risk of developing dementia later in life. And physical inactivity is the greatest modifiable risk factor for dementia." Furthermore, her research experience suggests that a woman's physical activity level can influence her dementia risk as much as her genetics.

> "YOU CAN'T CHANGE YOUR GENES, BUT YOU CAN CHANGE YOUR LIFESTYLE,

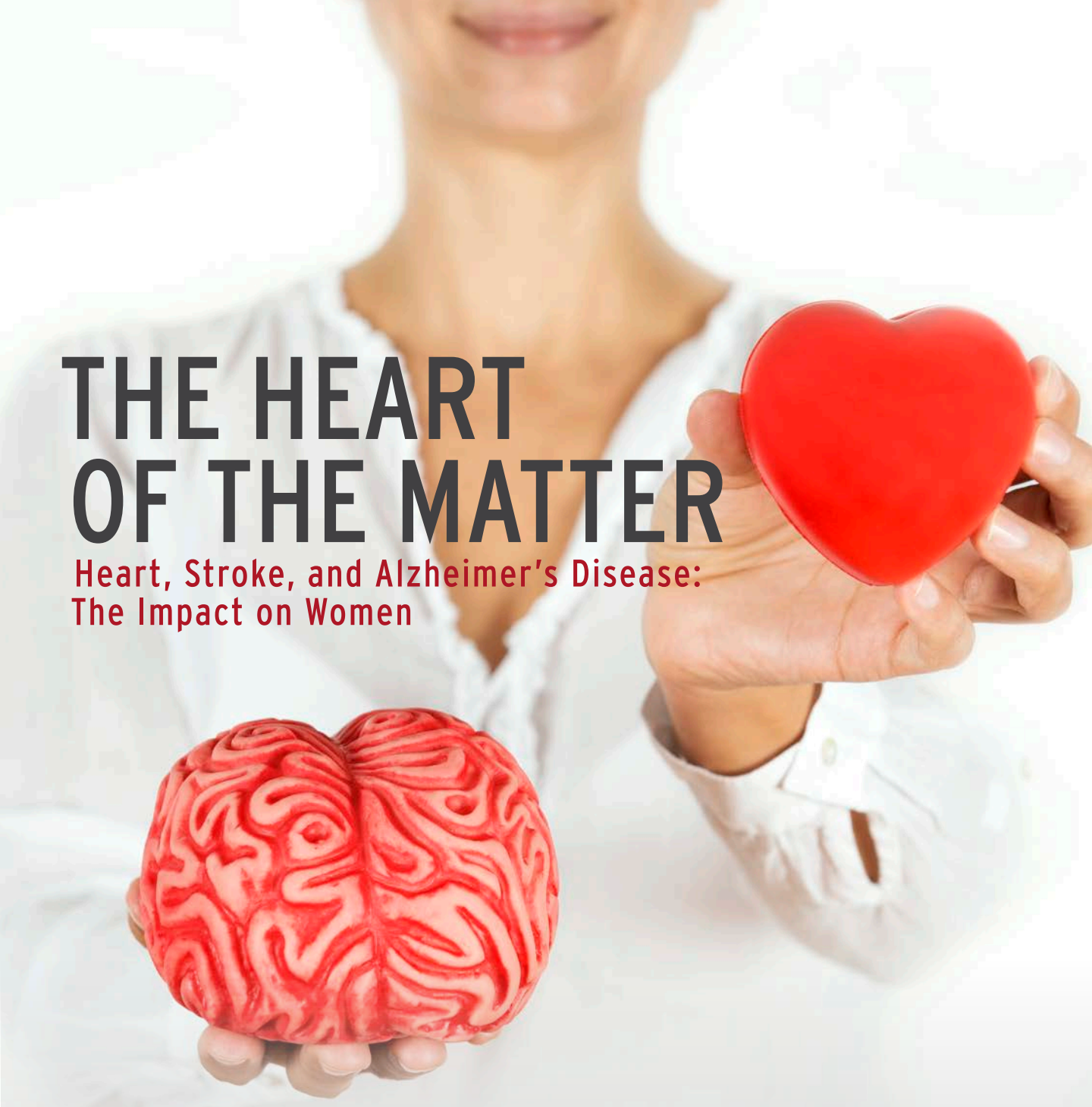
Dr. Heisz added. "Engaging in exercise programs at critical stages will extend autonomy, improve quality of life, and ultimately keep more aging Canadians healthier for longer."

In a 2015 paper published by *Dementia Australia* entitled "Physical Exercise and Dementia," the authors discussed the various benefits of engaging in physical exercise. As the authors observe, individuals who exercise regularly are less likely to experience heart disease and stroke – both of which are associated with an increased risk of developing dementia. Exercise is also essential in reducing the risk of high blood pressure, type 2 diabetes and obesity, all of which are risk factors for dementia. Several prospective studies (where large groups of people are followed up over time) have found that higher levels of physical exercise are associated with less cognitive decline in older adults. Other studies have found that individuals who exercise experience a slower loss of brain tissue as they age.

While more research is being conducted to better understand the relationship between dementia and exercise, regular exercise is recommended as a key strategy for maintaining good physical health, helping to keep the aging brain healthy, and reducing cognitive decline. Of course, you should always consult your doctor before starting any exercise program, particularly where there are other illnesses or disabilities to consider.

THE HEART OF THE MATTER

Heart, Stroke, and Alzheimer's Disease: The Impact on Women



Many women may not realize that heart disease and stroke are the leading causes of premature death for women in Canada. In fact, heart disease and stroke kill 31,000 women in Canada annually, according to the Canadian Heart and Stroke Foundation ("Heart & Stroke"). Two new reports published by the foundation are putting both women and their healthcare providers on alert.

> **WOMEN'S HEART HEALTH – LIKE WOMEN'S BRAIN HEALTH – IS "UNDER-RESEARCHED, UNDER-DIAGNOSED, AND UNDER-TREATED."**

"It's shocking that we are so far behind in our understanding of women's hearts," says Yves Savoie, CEO of Heart & Stroke, "and that

new knowledge is so slow to reach the bedside." For decades, specific therapies were tested in controlled studies on primarily middle-aged, white male subjects. The assumption was that what worked for men, also worked for women, and what was learned "formed the basis of clinical guidelines, diagnostic procedures and therapies that, even today, are widely used for both men and women."

While overall female hearts appear the same as male hearts, "there are important differences that are irrefutable and still poorly understood," says Dr. Karin Humphries, scientific director of the BC Centre for Improved Cardiovascular Health.

> SEX AND GENDER BLINDERS HAVE LED TO TOO MANY WOMEN DYING UNNECESSARILY.

SEX DIFFERENCES IN THE CARDIOVASCULAR SYSTEM

One of the reasons why women's heart health knowledge is vastly behind that of men's is because of the actual physiological differences in men's and women's hearts. "Women's vessels tend to be smaller, their hearts are smaller," notes Dr. Patrice Lindsay, Director of Stroke at Heart & Stroke. This means that when women experience heart attack symptoms, their symptoms might be different than their male counterparts.

As with men, women's most common heart attack symptom is chest pain or discomfort. Women's symptoms, however, tend to be subtler and more ambiguous. Women often experience less severe chest pain than men, which may be described as pressure or tightness rather than the so-called "Hollywood heart attack" (chest-clutching, crushing pain radiating down the arm and up to the jaw).

Women are also more likely than men to exhibit symptoms unrelated to chest pain such as pain or discomfort in one or both arms, the neck, back, jaw, or stomach, as well as shortness of breath (with or without chest discomfort), unusual fatigue and/or nausea, vomiting, or lightheadedness. These symptoms may develop slowly over hours or days, and even come and go.

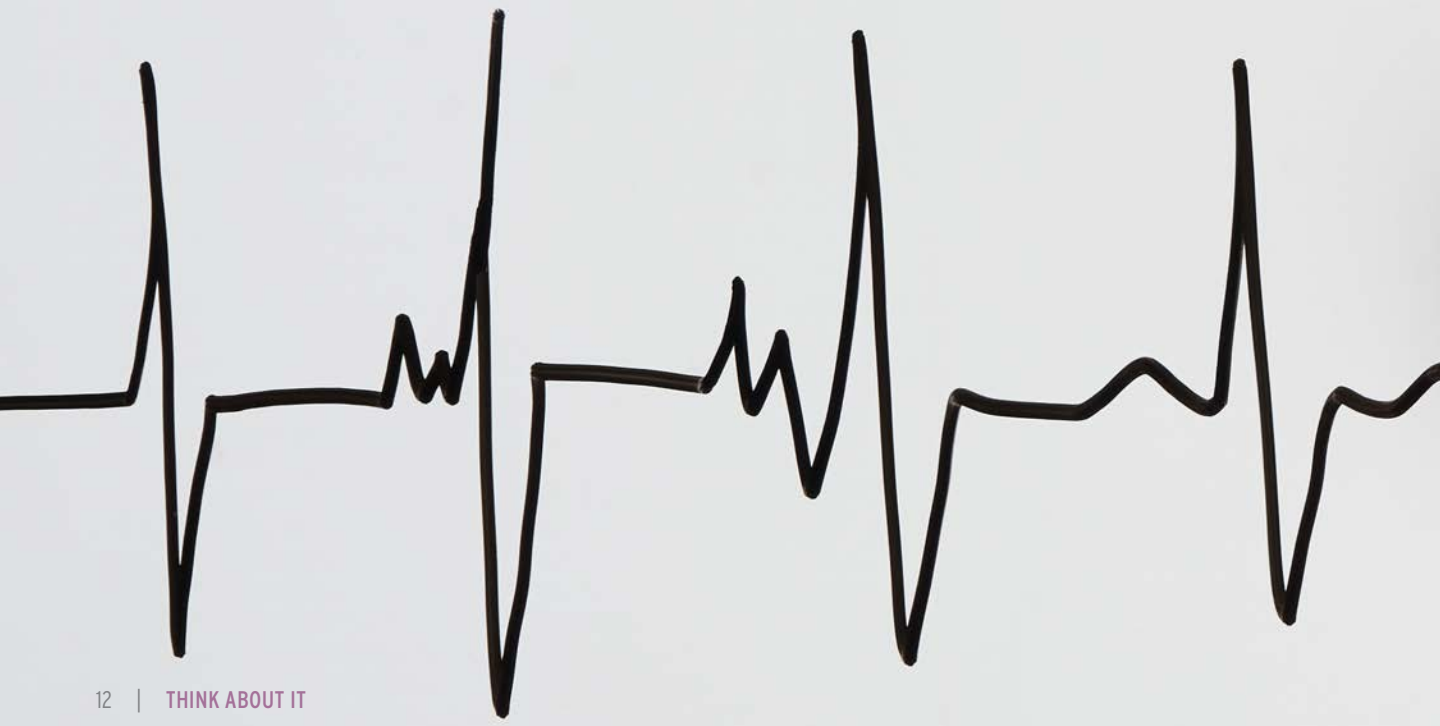
These differences in symptoms can impact the timely identification of heart disease in women, first by the women themselves and later by health professionals. According to a retrospective study published in *Circulation*,

> **EARLY HEART ATTACK SIGNS WERE MISSED IN 78% OF WOMEN**

in the study group, even though these signs occurred repeatedly over a period of weeks or months.

When symptoms are subtle, they are easier to overlook, misdiagnose, or ignore altogether. Women often incorrectly assume that their symptoms are the result of non-life-threatening conditions such as acid reflux, the flu, or normal aging. Consequently, women tend to wait much longer than men before seeking emergency medical services, putting women at greater risk for adverse outcomes.

One study found that the median time women waited before seeking care when experiencing heart attack symptoms was 53.7



hours, compared to just 15.6 hours for men. Other studies have suggested that the median delay times range from two to five hours – exceeding the American Heart Association's recommendation by hours, not minutes.

Once women have arrived at the hospital, it can take them longer to be diagnosed than men, or their condition may be missed entirely and they are sent home.

MANY OF THE SCREENING TOOLS USED TO DIAGNOSE A HEART ATTACK WERE DEVELOPED AND TESTED ON MEN, AND MAY OVERLOOK HEART DISEASE OR A HEART ATTACK IN A WOMAN.

For instance, "women tend to have disease in the small vessels of their heart, while men are more likely to have disease in their major coronary arteries," explains Dr. Tara Sedlak, director of the Leslie Diamond Women's Heart Health Centre in Vancouver.

"The angiogram – the standard diagnostic tool used to detect heart disease – images the major coronary arteries. It does not capture disease in the smaller coronary arteries (microvascular disease)." And when a classic heart health test is not detecting a problem, women might be sent home with an anxiety or menopause-related diagnosis, rather than heart attack or stroke, notes Dr. Lindsay.

What's more, some "medications don't work as well for women versus men," meaning that even when women receive a correct diagnosis, the treatment is not necessarily as effective as it is for men. In fact, certain drugs have been found to cause harmful and even fatal side effects in women, according to Heart & Stroke.

RESEARCH BIAS (AND WHAT'S CHANGING)

There are a multitude of factors that have led to the inequality women still face today regarding their heart health. Historically, research into the testing and treatment of heart disease has had more male participants than female, which began because of safety concerns involving women in drug development (most notably, as a result of the "thalidomide disasters" in the early 1960s, in which a drug used by pregnant women caused major birth defects in a large number of newborns).

Dr. Lindsay says that she does not believe that this disparity was a "deliberate attempt by anyone to bias women," but there has been hesitation on the part of both the research establishment and potential women participants due to this history.

In 1997, Health Canada issued revised guidelines, recommending that women be included in research and clinical trials in order to better understand sex differences. However, over two decades later, researchers are still encountering roadblocks when looking to find female participants for studies and clinical trials.

Structurally, there are exclusions for certain women, says Dr. Lindsay. For example, women of childbearing age, or those who are pregnant or potentially pregnant, are often excluded, usually for good reason because testing new drugs obviously carries a risk. Often, there is also an age cut-off, which "automatically wipes out a lot of older women" who could be trialling drugs, says Dr. Lindsay, and sometimes this exclusion is unwarranted.

Additionally, on an individual level, women tend →

to be more risk averse, says Dr. Lindsay, which means that left to their own choices, men tend to volunteer more for research, than do women. Educating women about participating in research trials is important, then, so that sex-specific results make their way into research findings.

BE YOUR OWN ADVOCATE

"Importantly, major research funding bodies, including Heart & Stroke and the Canadian Institutes of Health Research (CIHR), are now requiring that sex and gender be defined and considered in research findings and reporting," says Dr. Lindsay. CIHR is also offering training resources that educate researchers about the importance of women-specific testing and results. It is a "multi-pronged approach" for change, she says.

While progress has been made recently, it has not been "nearly fast enough to equitably protect women's hearts," says Savoie. "The challenge is to accelerate the pace of change, to gather new knowledge and translate it into better and safer heart health care for women." It is therefore important for women to be their own advocates. Do not be afraid to ask. If your symptoms are not normal for you, you will know that. We are the only ones who truly know what is usual or unusual for our bodies.

IT ALSO HELPFUL TO KNOW THAT THERE ARE A FEW KEY MOMENTS IN A WOMAN'S LIFETIME THAT ARE MAJOR HEART AND STROKE RISK MOMENTS.

The first is pregnancy, says Dr. Lindsay, which is the "first heart stress test for women." Due to hormonal changes, some women experience high blood pressure that can lead to preeclampsia or pregnancy-related diabetes.

Experiencing these conditions during pregnancy means that you may have a much higher risk of suffering from heart disease earlier in life. The second major heart stress test is menopause. After menopause, says Dr. Lindsay, risk of heart disease and stroke increase. Hormone replacement therapy is a double-edged sword, because research shows that while it is protective for heart disease, it actually increases the risk of stroke. Researchers are still trying to determine exactly how women's hormonal changes impact their heart and stroke risk.

PARALLELS WITH ALZHEIMER'S DISEASE RESEARCH

Since we know that brain health is very much connected to heart health (several studies have shown a link between the two, including one in 2016 from the American Heart Association that found that older adults who had healthier cardiovascular systems had less decline over time in brain processing speed, memory, and executive functioning), this lag in understanding women's cardiovascular needs necessarily extends to brain health as well.

As is the case for our hearts, we now know that "there are fundamental differences in the way the brain is organized in terms of connectivity or how the parts of the brain talk to each other, between men and women," says Dr. Pauline Maki, Professor of Psychiatry and Psychology and Associate Director of the Center for Research on Women and Gender at the University of Illinois at Chicago. This means that

MEN'S AND WOMEN'S BRAINS ARE STRUCTURALLY AND FUNCTIONALLY DIFFERENT.

However, the divergence between men's and women's brains – and their experiences of diseases of the brain – is not yet well established.

For instance, researchers have known for nearly two decades that women with the APOE 4 gene are more likely than men with the gene to develop dementia, but still no one understands why this is the case. "[T]he field largely ignored it," says Dr. Maki, "because the field ignored sex differences more generally."

Much more research needs to be conducted in order to understand how sex and gender differences impact an individual's Alzheimer's disease (AD) risk. In fact, Dr. Maki and her colleagues from The Society for Women's Health Research Interdisciplinary Network on AD wrote a paper, published in the June 2018 issue of *Alzheimer's and Dementia*, that outlines twelve priority research areas for clinical research in AD regarding sex and gender, including looking at "potential sex-specific risk factors for AD," like pregnancy or testosterone loss, and paying attention to sex and gender differences "in developing AD therapeutics, from preclinical to clinical studies, and in the design of clinical trials."

One line of research that is relatively new but is showing quite a bit of promise examines the impact of certain hormones, such as estrogen, on a woman's brain. "There's a compelling body of research to suggest that women's brains undergo a pretty considerable change in function and structure during menopause, and people are just beginning to look at whether that critical female-specific life event might in some way set up, at least a proportion of women, for Alzheimer's disease later in life," says Dr. Maki.

Some women show a decrease in memory functioning when they go through menopause, as evidenced by memory tests that are also used to diagnose AD. What's more, 80% of women experience hot flashes during menopause, and Dr. Maki and her colleagues have found that "when you measure them objectively with monitors, they correlate significantly with decreases in memory performance, decreases in brain function, and increases in tiny, little structural changes in the brain that look like very small strokes."

Treating hot flashes, then, is one avenue of treatment that Dr. Maki and her colleagues are currently exploring. Women in menopause also experience sleep-related disturbance, says Dr. Maki, and sleep disruptions "impact the brain's ability to clear out toxins" – so that is another hormonal factor that needs further researching, examination, and treatment in individual women. Of course, as Dr. Maki observes, all women go through menopause and not all of them develop AD, so more work needs to be done to understand why, for some women, this reproductive event could be the "perfect storm."

Similar to heart research, the tide in women's brain research is also shifting. Major U.S. associations like the Alzheimer's Disease Association and the National Institute on Aging are actively soliciting grant applications that focus on sex- and gender-specific manifestations of AD. This year's Alzheimer's Association International Conference held a featured research session on hormonal contributions to dementia risk in women. "I'm happy to say the field is finally coming around," says Dr. Maki.

PREVENTION STRATEGIES FOR WOMEN: DOS AND DON'TS

It is important for women to be proactive and to take better care of their health, including making themselves a priority.

TIPS FROM DR. PATRICE LINDSAY:

- **DO get 150 minutes of exercise per week. Go to the gym or for a walk.**
- **DO focus on healthy nutrition.**
- **DON'T delay regular checkups and don't neglect to monitor risk factors.**
- **DON'T jump into previous roles too quickly after something has happened to your health: allow yourself proper recovery time.**

TIPS FROM DR. PAULINE MAKI:

- **DO get out and socialize and/or join a support group and if you are a primary caregiver, pay special attention. The caregiver role can be toxic due to the chronic experience of stress it carries. Don't neglect caring for yourself while caring for others.**
- **DON'T withdraw if you are busy, irritable, moody, or sad. Our brains respond to social interactions the way they respond to food and sex. Our brains really like it. Some of the best things you can do to prevent brain deterioration are to socialize and engage in new learning.**

COULD IT BE IN YOU TO GIVE?

The Latest on Alzheimer's Blood Tests

With most deadly diseases, an early diagnosis is crucial. Alzheimer's disease (AD) is no different, but it has been challenging to detect. Many people suffer from the disease for years, or even decades, before showing any symptoms. The search for a cure could be helped immeasurably if promising drugs could be tested before the disease progresses to the point where it has caused catastrophic damage to the brain. Even in the absence of a cure, if an individual knows that he or she has AD at an earlier stage, that person can begin making lifestyle changes that might slow the disease's progression.

While doctors can diagnose AD with a high degree of accuracy with a spinal tap or brain scan, these types of tests are costly and, in the case of the spinal tap, invasive – which is why there is an intense international effort underway to find a blood test that could accurately detect AD.

> "HAVING AN EFFECTIVE BLOOD TEST CAN LEAD TO MORE EFFECTIVE TREATMENT BECAUSE WE CAN MORE ACCURATELY STUDY WHO HAS AD AND WHO DOESN'T,

said Dr. Carmela Tartaglia, a cognitive neurologist with Toronto Western Hospital's Memory Clinic and a researcher at the University of Toronto's Tanz Centre for Research in Neurodegenerative Diseases.

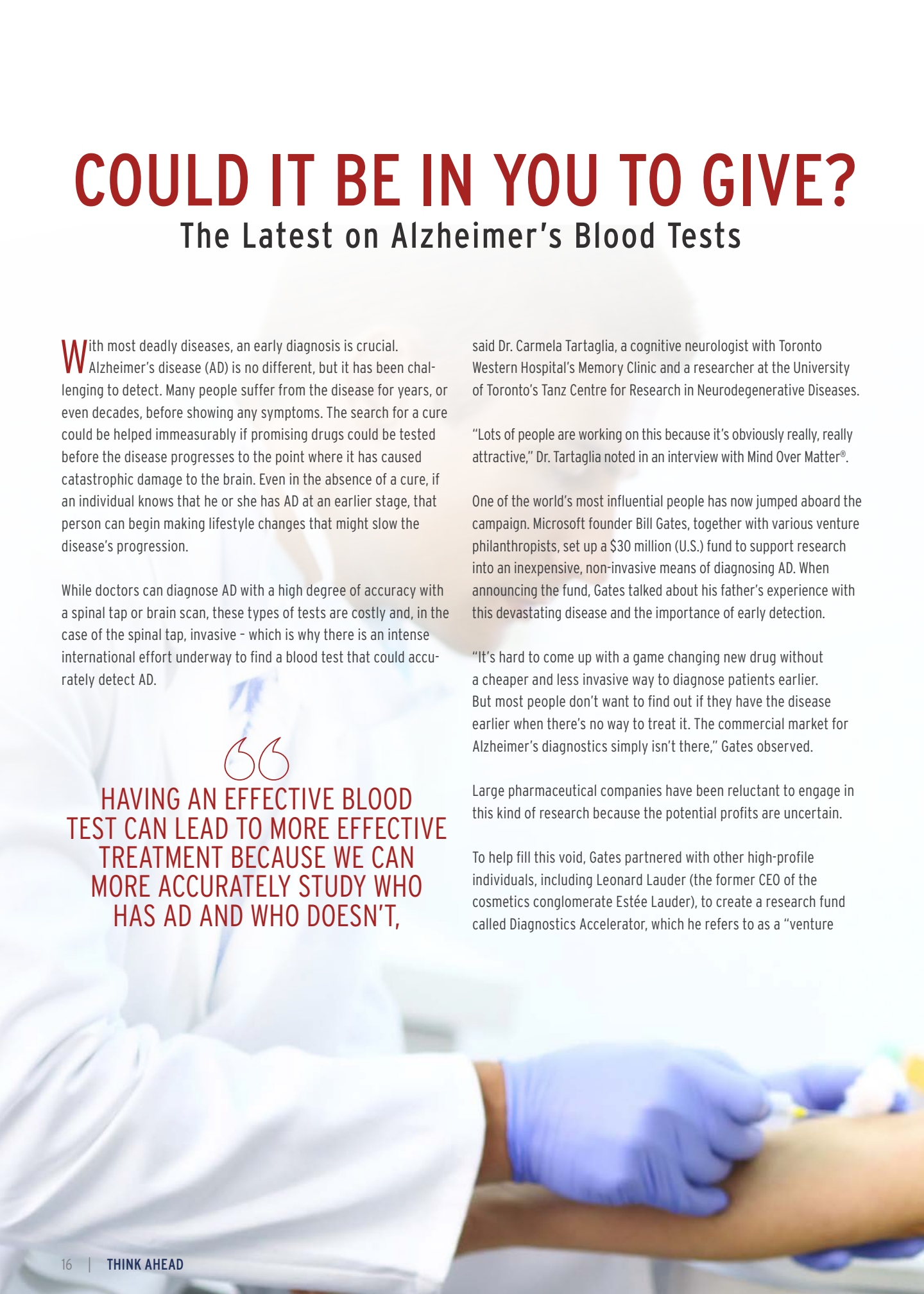
"Lots of people are working on this because it's obviously really, really attractive," Dr. Tartaglia noted in an interview with Mind Over Matter®.

One of the world's most influential people has now jumped aboard the campaign. Microsoft founder Bill Gates, together with various venture philanthropists, set up a $30 million (U.S.) fund to support research into an inexpensive, non-invasive means of diagnosing AD. When announcing the fund, Gates talked about his father's experience with this devastating disease and the importance of early detection.

"It's hard to come up with a game changing new drug without a cheaper and less invasive way to diagnose patients earlier. But most people don't want to find out if they have the disease earlier when there's no way to treat it. The commercial market for Alzheimer's diagnostics simply isn't there," Gates observed.

Large pharmaceutical companies have been reluctant to engage in this kind of research because the potential profits are uncertain.

To help fill this void, Gates partnered with other high-profile individuals, including Leonard Lauder (the former CEO of the cosmetics conglomerate Estée Lauder), to create a research fund called Diagnostics Accelerator, which he refers to as a "venture



philanthropy vehicle" – a means of supporting important work that might not necessarily have a commercial return. Gates describes its goal as developing "a real product for real patients."

Long before this initiative, there were already several research projects underway, some of which have demonstrated promising results.

"Until recently, I would have been extremely sceptical," said Dr. Barry Greenberg, who recently became the director of the new Institute for Prevention and Treatment of Alzheimer's Disease at Johns Hopkins University.

"Now there are research projects that demonstrate a blood test that could be feasible," he said in an interview with Mind Over Matter®.

Early in 2018, a team of researchers from Japan and Australia published a paper in the journal *Nature* in which they reported having developed a blood test that in clinical trials showed a 90% accuracy rate in detecting a marker for AD. The test searches for signs in the bloodstream of a toxic protein called amyloid beta, which accumulates in the brain as the disease progresses. It also has the ability to differentiate between different types of dementia, which can assist doctors with tailoring their methods to fit the diagnosis.

A 2014 study conducted by researchers at Georgetown University and the University of Rochester also claimed a 90% accuracy rate with their blood test in predicting the onset of AD. The researchers observed over 500 seniors (70 years of age and older) throughout a five-year period, examining different forms of fats in their bloodstream as a means of predicting the risk of AD. Although much research still needs to be done, the researchers are optimistic that the test will someday be available in doctors' offices.

BUT EXPERTS SAY THAT ALL OF THE WORK IS STILL AT A RELATIVELY EARLY STAGE, WITH THE TRUE PREDICTIVE VALUE UNPROVEN.

"There's lots of research being done in this area, but I'm not sure we're that close," said Dr. Tartaglia. "For a test to become readily available, it has to show it can pick up amyloid and that it's better than these other tests [brain scan or spinal tap]. It needs to be at least as good, if not better."

Spinal taps and brain scans have an accuracy rate above 90%. If a blood test could reach the same level of reliability, it could act as a screening tool to indicate whether further analysis is required for a more definitive diagnosis.

Dr. Greenberg noted that only a few years ago, the concept of a blood test for brain disorders was difficult to imagine, but technology has been game changing. "What we have now are technical abilities to measure what used to be beneath detection. We can see things we couldn't see before, much as we couldn't see bacteria before a microscope was invented," he explained.

"I would not be surprised to see a validated blood test five years from now." He believes that an effective blood test could eventually become a part of an annual physical, in the same way that doctors test for the potential of heart disease.

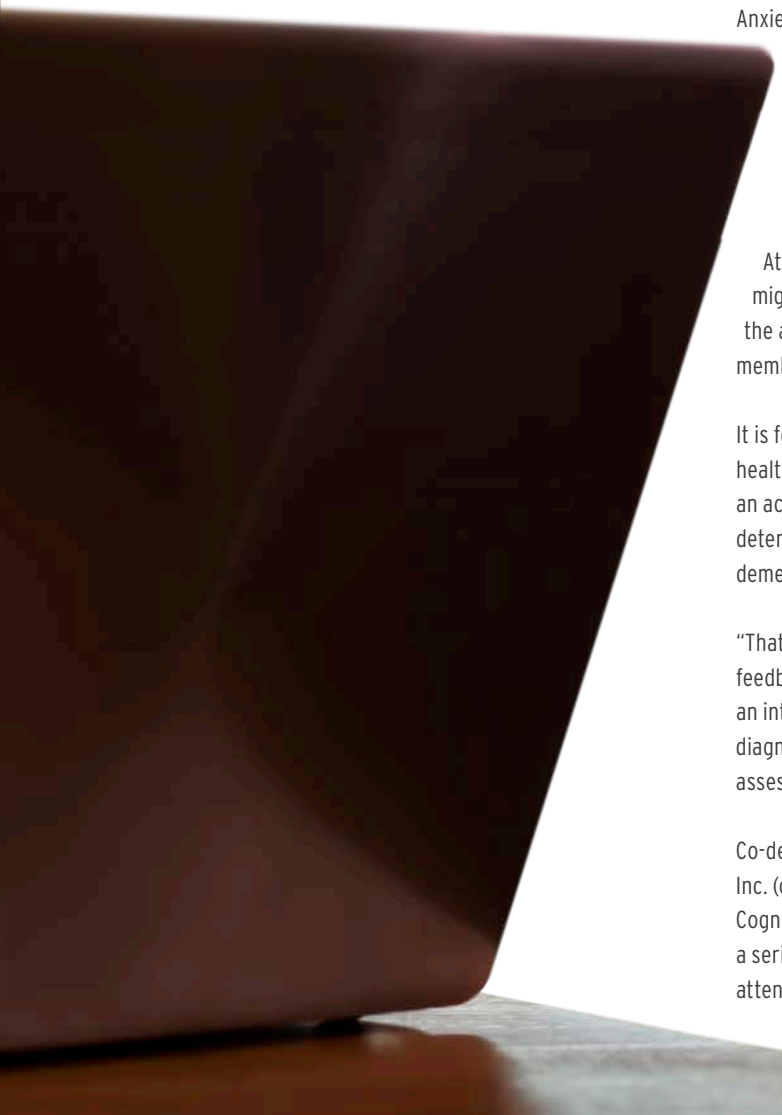
ASSESSING THE 'WORRIED WELL'

Online Memory Testing Tools

As we age, it is normal to experience some decline in our memory function. But with so much public concern about the ever-increasing prevalence of dementia, many of us wonder if our forgetfulness is a sign of something more ominous, even if those fears are usually misplaced. In the past, physicians had often dismissed the memory-related complaints of otherwise healthy individuals as the hypochondria of the so-called 'worried well.' But feeling that one's thought processes are waning could be a sign of something real, and may require further investigation.

"We don't have easy measures for what's normal or not [with memory loss]. It's not like taking your temperature for a fever," explained Dr. Angela Troyer, the Professional Practice Chief of Psychology and the program director of Neuropsychology and Cognitive Health at Toronto's Baycrest Health Sciences. "It's a reasonable worry."

Now the worried will have access to resources that can tell them whether they really have something to be concerned about, without the necessity of seeing a doctor.



THERE ARE A VARIETY OF ONLINE TESTS THAT CAN DETERMINE, WITH A HIGH DEGREE OF RELIABILITY, WHETHER AN INDIVIDUAL IS TRULY SHOWING SYMPTOMS OF DEMENTIA THAT SHOULD CAUSE HIM OR HER TO CONTACT A MEDICAL PROFESSIONAL.

Such online tests can save a considerable amount of time and stress for both patients and the healthcare system.

A definitive diagnosis of dementia can be a complex matter, involving several specialists conducting a battery of tests. It might start with a general practitioner who, if he or she has some expertise in the field, can make a relatively quick assessment. But for less obvious cases of cognitive decline, a geriatrician might be consulted, along with a neurologist and a neuropsychologist who might order blood work and brain imaging, as well as verbal and written tests.

IN SOME CASES, MEMORY LOSS AND CONFUSION CAN BE CAUSED BY PROBLEMS OTHER THAN DEMENTIA.

Anxiety, sleep apnea, chronic stress, depression, diabetes, and side effects from medications and chemotherapy can all impact one's ability to focus, pay attention, and remember. Additionally, a deficiency in vitamin B12 or a urinary tract infection can lead to similar symptoms and, unlike Alzheimer's disease, can be treated.

At the end of a rather exhaustive medical process, the verdict might be that the patient is suffering from nothing more than the average level of memory loss – in which case, he or she is a member of the worried well cohort.

It is for this segment of the population that Baycrest and other health care institutions developed online tests to try to establish an accessible way for those with significant memory concerns to determine whether they may be suffering from actual symptoms of dementia.

"That was the motivation – can we help people to give them some feedback to know what's normal and what's not," said Dr. Troyer in an interview with Mind Over Matter®. Such tests are not a clinical diagnosis, but rather a screening process to help facilitate earlier assessment, diagnosis, and treatment.

Co-developed by the brain health solutions company Cogniciti Inc. (owned by Baycrest and partner MaRS Discovery District), the Cogniciti™ is a free, online brain health assessment comprised of a series of game-like mental challenges that tap into memory and attention performance. Test-takers receive a cognitive health score →

upon completion that indicates where they rank compared to other adults with the same age and level of education. Those who score in the low range are encouraged to print their report and take it to their doctor to start the conversation about their memory concerns. Those who score in the normal range are directed to helpful information about maintaining brain health.

> FOR COGNITION, WHAT'S NORMAL VARIES A LOT," SAID DR. TROYER. "WE KNOW SOME PEOPLE HAVE GOOD MEMORIES, SOME HAVE BAD MEMORIES.

According to the test's creators, the majority of people will score in the normal, healthy range for their age – which will help reassure the worried well.

Prior to its launch in 2014, the developers conducted a study of 400 middle-aged and older adults who had no diagnosis of serious memory problems. The Cogniciti™ team compiled a series of tasks that are sensitive to changes in memory and, working with IT advisors, adapted it to the online environment. The test group performed the various tasks, giving the developers baseline scores to help them determine a cut-off point below which a person could be said to have an issue with memory and attention. The results were published in a peer-reviewed journal before Cogniciti™ was made available to the public – a key point, said Dr. Troyer, for anyone searching for an online dementia test.

"The most important thing people should look for is whether it's been validated scientifically. Any valid one would have a link to a validated study," Dr. Troyer observed.

There are a variety of different products on the market, some of which charge a fee and some of which have not necessarily been well-researched and therefore may not be a good gauge of potential dementia symptoms. However, there is scholarly research to support the notion that a properly-developed test can be helpful for screening purposes.

The Self-Administered Gerocognitive Examination (SAGE) test, developed by the Ohio State University College of Medicine, is another reliable cognitive assessment tool used to identify individuals with mild cognitive impairment or early dementia. A 2017 study published in the journal *Alzheimer's Research & Therapy* compared the digital format of the test (eSAGE) with other neuropsychological tests, as well as clinical assessments of cognitive impairment, and found a "high sensitivity and specificity in detecting cognitive impairment from normal subjects." The study concluded that eSAGE would be valuable in helping to identify early changes in cognition that could be warning signs of dementia.

To date, the Cogniciti™ brain health assessment has been completed nearly 65,000 times and more than 270,000 people have visited the website. Baycrest is currently conducting a follow-up study to confirm the validity of the Cogniciti™ test. Researchers are working with two groups of participants, one of which includes individuals who have memory impairment and one without. While Dr. Troyer is pleased with the results to date, she does not expect online tests to move beyond screening purposes to give an accurate diagnosis of dementia.

"Some clinical judgement is involved. I don't know whether that could be automated."

For more information or to take the Cogniciti™ online brain health assessment, visit www.cogniciti.com

THE STORY IN OUR GENES

Genetic Testing for Dementia

Once on the frontiers of science, genetic testing has in recent years moved into the mainstream. According to industry estimates, the number of people who have had their genes analyzed with direct-to-consumer (DTC) genetic genealogy tests more than doubled during 2017 and currently exceeds 12 million.

THE RESULTS OF A GENETIC TEST, ALSO KNOWN AS A DNA TEST, CAN CONFIRM OR RULE OUT A SUSPECTED GENETIC CONDITION OR CAN HELP DETERMINE AN INDIVIDUAL'S CHANCE OF DEVELOPING OR PASSING ON A GENETIC DISORDER.

Over 1,000 genetic tests are currently in use, and more are being developed. There are also a variety of health-related genetic testing services available through the Internet – some of →

which promise to gauge an individual's susceptibility to cancer, diabetes or obesity, while others claim that an analysis of one's genes can be used to develop specialized training and nutrition programs to build a leaner, stronger body.

Then there is the matter of genetic testing to measure the risk of developing dementia – a controversial subject that has generated discussion amongst both the medical community and individuals living with the disease. A recent survey conducted by Healthline Media of nearly 400 active caregivers in the U.S. found that 34% of caregivers indicated that caring for a loved one with Alzheimer's disease has prompted them to undergo genetic testing for the disease.

THE REPORT ALSO FOUND A DEMOGRAPHIC DIVIDE, WITH MORE MILLENNIALS (49%) SEEKING TESTING THAN OLDER GENERATIONS (GEN XERS 36%, BOOMERS 17%).

At present, the relationship between genetics and dementia is not fully understood. As the Alzheimer's Society observes, while genes play a role in the development of many forms of dementia, the extent of this role varies between dementia types. A person with a parent or sibling living with dementia has on average a higher risk of developing the same condition him or herself, although other factors such as lifestyle can also play a part.

There are two broad categories of genetic testing for dementia: predictive genetic testing and susceptibility testing. **Predictive (or determinative) genetic testing** is used to determine whether an individual has inherited a particular and rare genetic mutation from a relative who has been diagnosed with dementia. If the individual possesses the same mutation, he or she will most likely develop Alzheimer's disease or frontotemporal dementia (FTP) at some point in his or her life (presuming that he or she lives long enough). In contrast, **susceptibility testing** aims to identify the presence of so-called "risk genes" that alter one's risk of developing Alzheimer's disease, as opposed to inevitability causing it.

In the vast majority of people, any genetic risk of developing Alzheimer's disease is linked not to rare mutations but to variations in a large number of susceptibility genes that they have inherited. The most common risk gene is called Apolipoprotein E (APOE), which is the only susceptibility gene for Alzheimer's disease that has been widely confirmed to date (although several others are currently under investigation). Risk genes such as APOE have a more subtle influence on an individual's chances of developing Alzheimer's disease than the genes that are used in tests for the inherited forms of dementia. Advisory committees across the globe have therefore recommended against this type of genetic testing since individuals who have an APOE gene may never develop Alzheimer's disease and individuals with no APOE genes can still develop Alzheimer's disease.

In Canada, there is a substantial amount of screening that patients must go through in order to be eligible for genetic testing, explained Dr. Robin Hsiung, Associate Professor in the Neurology Division of University of British Columbia's Department of Medicine.

PATIENTS NEED TO UNDERSTAND THE DIFFERENCES BETWEEN TESTING FOR A SPECIFIC GENETIC MUTATION OR RISK FACTORS.

"If there's a known family history [of dementia] and we can see a pattern, then they are potentially eligible," Dr. Hsiung said in an interview with Mind Over Matter®. Dr. Hsiung noted that he does not recommend genetic testing for the presence of elevated risk factors. This type of genetic testing does not provide conclusive results and can be challenging emotionally. For those who wish to discover if they have a particular mutation, Dr. Hsiung carefully educates them on the pros and cons of undergoing genetic testing.

The knowledge that an individual will at some point in his or her life develop dementia may affect one's life choices, such as his or her decision about having children. Individuals who exhibit symptoms of dementia often wish to understand as much as possible about the cause of their disease, and to share this knowledge with their relatives to allow them to make decisions about learning their own and any future children's genetic status.

Dr. Hsiung noted that he also considers the potential impact on the individual's mental health.

"We need the patients to be psychologically stable because we don't want them to become depressed. Some people who have

A direct-to-consumer (DTC) genetic test is any DNA test for a medical or non-medical trait that provides interpretation or communication of test results directly to the consumer, rather than through a health care professional. The Internet currently enables unprecedented ease of access for DTC genetic testing, with saliva collection kits posted directly to consumer homes from anywhere in the world. There are several potential harms and consequences of poorly regulated Internet-based DTC testing, which have been well documented. If you are considering any kind of genetic testing, it is important that you speak with your doctor or a genetic counsellor beforehand.

disposition to anxiety or depression may be burdened by the news and will carry this heavy load and make them have a much worse outlook on life."

In a 2017 article published in the *Journal of Neurology*, the authors discuss the critical role of health care professionals in the ever-growing genetic testing market. As the authors observe, "the increasing complexity of the genetic landscape … presents a significant resource and physician training challenge." It is incumbent on practitioners to ensure that individuals are adequately informed, counselled, and supported when making their decision.

Experts in the industry have expressed caution about firms that advertise genetic testing services through the Internet. The U.K. Alzheimer's Society published a position paper warning of the implications for individuals who pay offshore companies to test saliva for the APOE gene, noting that the APOE test has "poor predictive value"– in other words, a positive result does not guarantee that the patient will actually develop Alzheimer's disease. The paper strongly recommends that

> **ANYONE THINKING ABOUT UNDERGOING GENETIC TESTING SHOULD FIRST CONSULT A HEALTH CARE PROFESSIONAL (SUCH AS A DOCTOR OR A CERTIFIED GENETIC COUNSELLOR) – SOMETHING THAT IS NOT OFFERED WITH THE COMMERCIALLY-AVAILABLE GENETIC TESTING.**

There have also been concerns about discrimination based on an individual's genetic characteristics, particularly in the context of the insurance industry. In Canada, parliament passed Bill S-210 in 2017, which prohibits the mandatory disclosure of genetic test results as a condition of providing goods or services (namely, health and life insurance). Canada was the last member of the G7 to pass its own genetic discrimination law. The U.S. had passed similar legislation in 2008.

Dr. Michael Gordon, a leading geriatrician at Baycrest Health Sciences in Toronto, is skeptical of the benefits of genetic testing.

"If someone asks me about it, I say 'what would you do about it [if you had a positive result]?'" he observes. "Can we do anything to change your genetic makeup? No we can't."

Dr. Gordon notes that, in the absence of a cure for dementia, perhaps the best advice is to live a healthy lifestyle. Indeed, as Mind Over Matter® regularly reports, there is much evidence that a healthy diet coupled with exercise, staying mentally and socially engaged, managing stress and getting a good night's sleep can help you maintain a healthy brain, amongst other benefits.

As the Alzheimer's Society observes, there is a lot to think about before undergoing a genetic test for Alzheimer's disease, including:

MOTIVATIONS: Why do you want to take the test? Will it change life decisions such as financial planning or having children?

INFORMED CONSENT: Do you fully understand what the test results will and will not reveal? Are you aware of the possible benefits and risks of taking the test?

CONFIDENTIALITY: Will your test results be kept private? Who will you share the results with?

RISKS: Will the test results affect your family relationships, and/or your mental or emotional wellbeing?

The decision about whether to be tested is a personal and complex one. A geneticist or genetic counsellor can help by providing detailed information about the advantages and disadvantages of a particular test, as well as the social and emotional aspects of genetic testing.

SUBSTANCE USE & ABUSE

Not Just a Problem Among the Young

Substance abuse is commonly considered a problem that affects younger adults, but research has shown that substance use, abuse, and addiction are not limited to a specific age. Historically, older adults have not demonstrated high rates of alcohol or other drug use compared with their younger counterparts or presented in large numbers to substance abuse treatment programs.

These facts have helped to create and perpetuate a misconception that older adults do not use substances and/or do not use substances problematically. However,

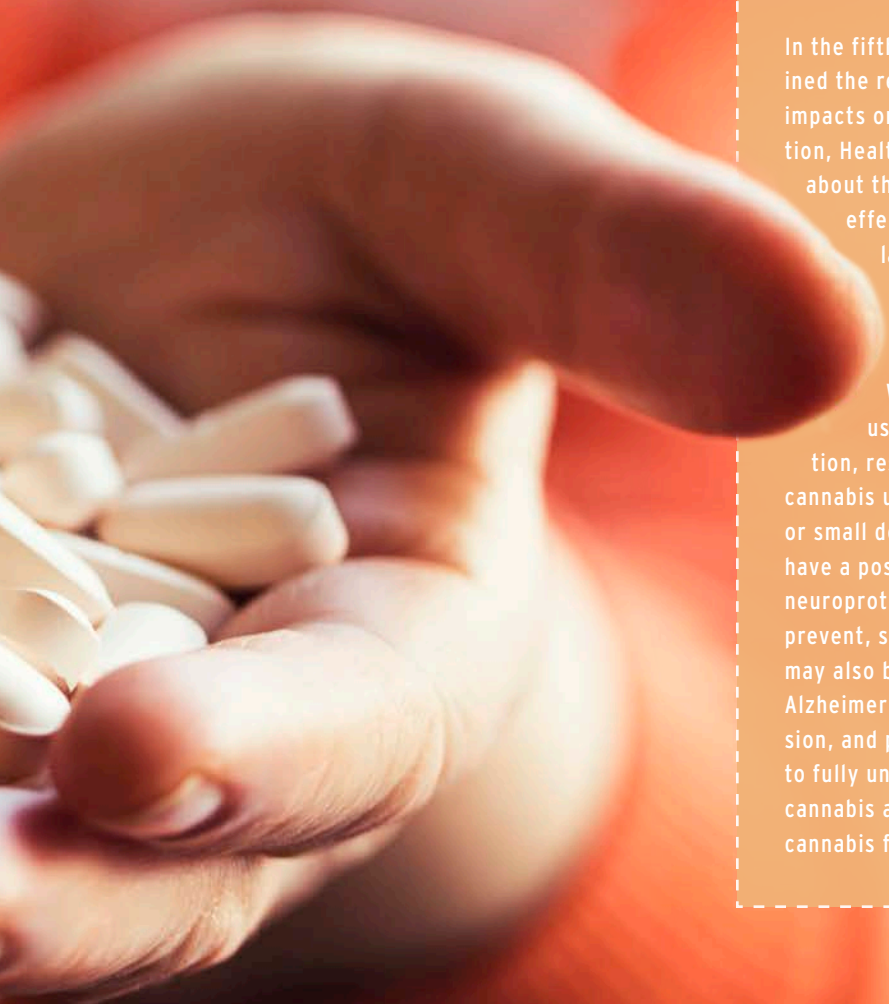
A SUBSTANTIAL AND GROWING PERCENTAGE OF OLDER ADULTS KNOWINGLY OR UNKNOWINGLY MISUSE ALCOHOL, MEDICATIONS, AND ILLEGAL SUBSTANCES.

It is estimated that the number of people aged 50 and over who require treatment for illicit drug problems in the U.S. may increase by as much as 300% by 2020, compared to 2001.

The number of older adults engaged in substance abuse is rising in part because the aging baby boomer population (those born between 1946 and 1964) is simply increasing the number of older people dramatically. But, among the baby boomer cohort, rates of substance abuse tend to be higher than any previous generation, further amplifying the growth in numbers of elderly persons with substance abuse problems.

Alcohol and prescription drugs are the most commonly abused substances among older adults, but illicit drugs are used as well. The types of illicit drugs used by those 50 and older tend to mirror the ones frequently used amongst the general population.

Cannabis is the most commonly used "illicit" drug in the world, with 192.2 million people reported as past-year users in 2016, according to the most recent World Drug Report published by the United Nations Office on Drugs and Crime. ("Illicit" has been used in quotation marks to highlight that cannabis is illegal in many places around the world, but not all.) Opioids are the next most commonly-used type of drug, with 34.3 million past-year users, followed by amphetamines and prescription stimulants (34.2 million), ecstasy (20.6 million), and cocaine (18.2 million). →



CANNABIS IN CANADA

Cannabis became legal in Canada on October 17, 2018. Prior to this date, only prescribed medical marijuana use was legal (as opposed to recreational use).

In the fifth issue of Mind Over Matter®, we examined the research to date on cannabis and its impacts on brain health. Despite its legalization, Health Canada continues to warn the public about the short- and long-term negative effects of cannabis on the brain, particularly for individuals who begin using it at a young age, use it frequently, and over long periods of time.

While it is true that recreational uses of cannabis affect cognitive function, research suggests that some types of cannabis use (for instance, medical marijuana or small doses of isolated components) may have a positive impact on the brain – acting as a neuroprotectant and anti-inflammatory, helping prevent, stop or reverse brain disease. Cannabis may also be helpful in treating symptoms of Alzheimer's disease such as agitation, aggression, and pain. More research is needed, though, to fully understand the association between cannabis and the brain, and how best to use cannabis for therapeutic effect.

OPIOIDS & OPIATES: WHAT'S THE DIFFERENCE?

Some people carefully distinguish between the terms "opiates" and "opioids," while others use the terms interchangeably or have a preference for one or the other. The latest trend, among journalists and politicians in particular, is to use the term "opioids" to encompass all of these types of drugs.

For those who differentiate between the two terms, the difference lies in how the drugs are made. **Opiates** is the term used to refer to drugs that have been extracted or refined from natural plant matter (for instance, poppy sap and fibers). Opium, morphine, codeine, and heroin are all examples of opiates.

Opioids, on the other hand, is the term used to refer to drugs that are synthesized or made in a laboratory, as opposed to derived from natural plant matter. Some of these drugs may be partially synthesized from components of opium (such as hydrocodone, hydromorphone, and oxycodone), while others are completely designed and constructed in laboratories.

The pharmaceutical industry has created hundreds of different opioid molecules. Some of the more widely-used opioids include the following:

- Dextromethorphan (e.g. in over-the-counter products like NyQuil, Robitussin, TheraFlu, and Vicks);
- Loperamide (e.g. in the over-the-counter drug Imodium);
- Hydrocodone (e.g. Vicodin);
- Oxycodone (e.g. Oxycontin and Percocet);
- Methadone (e.g. Dolophine); and
- Fentanyl/fentanil (e.g. Ultiva and Sublimaze).

The World Drug Report further indicates that an estimated one in nine people who use drugs (11%) suffer from "drug use disorders," meaning that their drug use is harmful to the point where they may experience drug dependence and/or require treatment. As of 2016, there were 30.5 million people worldwide who suffer from this disorder. Opioids cause the most harm, accounting for 76% of drug abuse-related deaths.

There are, of course, numerous negative health impacts related to the abuse of prescription and illicit drugs, including the potential to die from an overdose. This article focuses specifically on the impacts to the brain and cognitive function. According to an Alzheimer's Australia fact sheet,

> **ALL SUBSTANCES OF ABUSE DISRUPT NORMAL NEUROTRANSMISSION AND CAN CHANGE THE STRUCTURE OF THE BRAIN, POTENTIALLY INCREASING THE RISK OF DEVELOPING DEMENTIA.**

THE IMPACT OF OPIOIDS

Opioids are drugs used primarily to provide relief from pain (both physical and emotional), but can also be used as a treatment for other conditions such as cough and diarrhea suppression. Some opioids are prescribed drugs, some are over-the-counter medications, and others are considered illicit. When used properly, prescription and over-the-counter opioids can be helpful. However, all types of opioids can induce feelings of euphoria (i.e. feeling high), so they have the strong potential to be misused. It is important to note, though, that only a minority of individuals who use opioids develop an addiction.

Research has shown that opioid misuse can affect the physical structure of the brain. Researchers S.N. Ramage and colleagues conducted post-death examinations of the brains of 34 intravenous drug abusers, who had mainly used heroin and methadone. The brains of 16 additional non-drug users were also examined for comparison (i.e. the control group). The average age across both groups was 26 years old.

The researchers discovered that the drug abusers had a level of brain damage usually seen only in much older adults. In fact,

> **THE BRAIN DAMAGE WAS SIMILAR TO THAT OBSERVED IN THE EARLY STAGES OF ALZHEIMER'S DISEASE.**

Damaged nerve cells were found in key areas of the brain that are involved in learning, memory, and emotional well-being. Those in the drug abuse group were up to three times more likely to have suffered brain damage than those in the control group. These findings were published in *Neuropathology and Applied Neurobiology* in 2005.

Opioid misuse has also been linked to negative changes in cognitive function. A meta-analysis of research findings about the neuropsychological consequences of chronic opioid use published between 1964 and 2010 was undertaken by Dr. Alexander Baldacchino and colleagues, with the results published in *Neuroscience & Biobehavioral Reviews* in 2012.

"Our analysis revealed that chronic opioid exposure is associated with deficits across a range of different neuropsychological domains,"

explained Dr. Baldacchino, Chair in Medicine at the University of St. Andrews in the U.K. "However, the only domains where robust impairment was found were working memory, cognitive impulsivity (risk taking), and cognitive flexibility (verbal fluency)."

Studies of human opioid users can have various confounding variables, though, making it challenging to determine the effects of opioids alone. In other words, there may be other elements at play that affect chronic opioid users' brains and cognitive function. For example, they might use multiple types of drugs or there may be predisposing factors (e.g. some brain abnormalities and functional deficits may have been present before a person started taking drugs, and perhaps made him or her vulnerable to developing an addiction).

Research conducted by Dr. Karen Ersche and colleagues – published in *Science* in 2012 – discovered evidence of such predisposing factors. "Since brain structure is largely inherited and drug dependence runs in families, we wondered if there might be a genetic or epigenetic influence on addiction," said Dr. Ersche, "and we found that might indeed be the case."

The researchers compared brain structure and ability to regulate behaviour in 50 biological sibling pairs. Within each pair, one sibling was dependent on stimulant drugs and the other had no history of chronic drug or alcohol abuse. These sibling pairs were also compared with 50 unrelated, age- and intelligence-matched healthy volunteers. "Our research revealed that impairments and brain abnormalities frequently seen in the siblings with drug addiction were also seen in their non-addicted siblings, suggesting that these impairments had been there before drug use began," Dr. Ersche explained.

THE IMPACT OF COCAINE

Cocaine is a stimulating drug derived from the coca plant that causes an intense euphoric effect. It is used in either powder or rock form ("crack"), and is highly addictive. Cocaine use is known to cause physical structure changes in the brain, as well as to have a negative impact on cognitive function.

A recent academic review by Dr. Kirsten Frazer and colleagues examined the research published about the relationship between cocaine and cognition between the years 1999 and 2016. The majority of studies they reviewed reported statistically significant differences between cocaine users and non-drug-using controls in brain structure, blood-oxygen-level dependent signals, and brain metabolism.

The researchers found differences in cognitive performance between the two groups as well, but limited to just a couple of measures (namely, executive function and working memory). They did not find evidence that chronic cocaine use is associated with broad cognitive deficits. These findings were published in 2018 in *Behavioural Brain Research*.

A confounding variable is a factor that a researcher failed to control or eliminate, thus damaging the validity of the experiment and limiting the conclusions that can be drawn.

An example of a study that found cocaine use to be linked with alterations in brain structure was written by Dr. Karen Ersche and colleagues, and published in 2013 in *Molecular Psychiatry*. In that study, the researchers explored whether cocaine dependence is a "fast-track for brain ageing." They concluded that it might be, after reviewing brain scans of 120 participants aged 18 to 50 years old. Half of the participants were addicted to cocaine and the other half had no history of substance misuse.

"We looked for differences in gray matter volume between the two groups," explained Dr. Ersche, a lecturer in the Department of Psychiatry at University of Cambridge in the U.K. "We discovered that all participants showed a reduction of gray matter volume in cortical and subcortical regions as they aged, but the annual rate of gray matter volume loss in cocaine-dependent individuals was twice the rate of the healthy participants." The accelerated decline in brain volume was most prominent in the prefrontal and temporal cortex – important regions of the brain associated with attention, decision-making, and self-regulation, as well as memory.

MORE INFORMATION ABOUT THE EFFECT OF DRUGS AND ALCOHOL ON THE BRAIN

There have been several other articles about the effect of drugs and alcohol on the brain in Mind Over Matter®:

- See page 31 in this issue to learn about how some prescription and over-the-counter medications can negatively impact the brain and cognitive function;
- See page 10 in Volume 6 for information about the links between alcohol and brain health; and
- For information about the effects of cannabis on brain health, check out the article on page 43 in Volume 5.

ANESTHESIA & DEMENTIA

Memory Loss After Surgery

The administration of general anesthesia (an anesthetic used to induce unconsciousness during surgery), and its potential for long-term cognitive effects, has been under intense scrutiny. Memory loss after surgery affects more than 35% of young adults and 40% of elderly patients at the time of hospital discharge.

> **THREE MONTHS AFTER SURGERY, APPROXIMATELY 6% OF YOUNG ADULTS AND 13% OF ELDERLY PATIENTS CONTINUE TO SUFFER FROM MEMORY DEFICITS AND OTHER FORMS OF COGNITIVE IMPAIRMENT**

– the kind that interfere with the ability to remember names, locate a car in a parking lot, or find a set of keys.

As early as 1955, in one of the first publications to connect anesthesia with cognitive impairment amongst elderly patients, Dr. P.D. Bedford observed that in some cases, "minor dementias and even permanent catastrophic mental impairment may occasionally be the aftermath" of having received a general anesthetic. Since then, researchers have been investigating the relationship between general anesthesia and dementia but have generated inconsistent results.

Research published in the *Journal of Clinical Investigation* in 2014 sought to examine what exactly occurs in the post-operative brain. "One of our fundamental assumptions has always been that once the [anesthetic] drugs were eliminated, the brain goes back to the baseline state," says Dr. Beverley Orser, co-author of the study and Chair of the Department of Anesthesia, as well as a Professor of Anesthesia and Physiology at the University of Toronto. But what Dr. Orser and her colleagues found was that in addition to the "desired, profound anesthetic action, which is due to the drugs interacting directly with the receptors" – which is necessary for the surgery itself – "the memory blocking receptors were hanging around and causing subtle impairment" in animal models after the drugs were eliminated. Specifically, they found issues with memory and problem solving in the mice, she says. Human trials are currently being organized to explore this occurrence further.

According to research published in the journal *Current Opinion in Critical Care* in 2011, postoperative confusion and cognitive problems are more common in elderly patients (over 65 years old) than younger patients, and can be categorized as postoperative delirium, postoperative cognitive dysfunction (POCD), and dementia. The presentation of **postoperative delirium** is variable and patients may exhibit hyperactivity, hypoactivity or mixed hyper-hypoactivity.

Hyperactive patients show increased psychomotor activity, such as rapid speech, irritability, and restlessness, whereas hypoactive patients show a calm appearance combined with inattention, decreased mobility, and have difficulty answering simple questions about orientation. **POCD**, on the other hand, is harder to define since it "is a subtle impairment of memory, concentration, and information processing that is distinct from delirium and dementia."

The symptoms of POCD vary from mild memory loss to an inability to concentrate or process information. "POCD and dementia appear clinically similar," says Dr. Juraj Sprung, an anesthesiologist and professor of anesthesiology at the Mayo Clinic in Rochester, Minnesota, who has published work on this topic in Mayo Clinic Proceedings and has new research findings currently undergoing review at the *British Journal of Anaesthesia*, "the only real difference is that POCD is believed to be transient." Interestingly enough, even though it has been well established that women are at a higher risk for developing Alzheimer's disease, "there is no gender bias at all to any of the perioperative disorders, as far as we know," says Dr. Roderic Eckenhoff, an anesthesiologist at The University of Pennsylvania.

Both postoperative delirium and POCD are "considered to be reversible processes," says Dr. Sprung. The length of recovery from postoperative delirium or POCD varies between weeks or months, depending on the individual. However, suffering from post-operative cognitive deficits for any length of time should not "be undervalued," says Dr. Orser. "If we're looking at months, those are really important decision-making times," she says. For instance, you might be deciding whether your parent should go back home after surgery, or whether he or she should move to a long-term care facility. "So while it's short-term, it's a very critical part of one's life around the time of surgery."

CAN YOU DEVELOP DEMENTIA FROM ANESTHESIA?

Researchers are currently investigating whether lasting cognitive impairment can result from the administration of general anesthesia. "In animal models, there does seem to be a bit of a signal that anesthetics alone can enhance the pathology of some of the neurocognitive diseases," says Dr. Eckenhoff. In humans, "we've known for a long time that there is a cognitive hit from having surgery and anesthesia. But the real controversy at this point is how long it lasts and does it lead to accelerated permanent neurodegeneration. That's the real crux of the question right now, the controversy: Does it lead to long-term decline?"

To date, the results of clinical studies with human subjects have suggested that there is "no association between anesthesia and long-term mild cognitive impairment (MCI) or dementia," says Dr. Eckenhoff. Dr. Sprung agrees: It is clear from most of the recently published literature that you do not develop dementia from anesthesia. Dr. Sprung and his team have found that

> **THERE IS NO SIGNIFICANT ASSOCIATION BETWEEN EXPOSURES TO PROCEDURES REQUIRING GENERAL ANESTHESIA AFTER THE AGE OF 45 AND INCIDENT DEMENTIA.**

For those individuals who do not recover their cognitive abilities after surgery, there are a few explanations for this occurrence, according to Dr. Sprung. Surgery itself is stressful on the body – the body releases steroids and inflammatory cytokines during surgery, which can accelerate the death of brain cells, and dehydration can play a role too, all of which factor into the burden of disease, says Dr. Sprung. In essence, "the sicker you are, there is a greater chance that you will progress towards the state of dementia over time."

It is also a well-established fact that a patient's comorbidities (when an individual has two chronic diseases at the same time) and associated hospitalizations pose a risk for the progression of cognitive impairment in the elderly. In other words, "if you come in with a vulnerability to surgery – let's say you already have MCI, or you have long-term diabetes, or vascular disease, or even sleep apnea – that puts you at increased risk of having cognitive decline caused by both the surgery and the anesthesia," says Dr. Eckenhoff. An individual who is older (and most likely sicker), and who has preexisting conditions, may fare worse after surgery and anesthesia than a relatively healthier younger person, because the older person's burden of disease is likely higher. ⟶

But many researchers believe that the anesthesia is a "pretty minor player," says Dr. Eckenhoff. They believe that it is the neuroinflammation caused by surgery that actually plays a predominant role, but more research needs to be conducted. The brain is "usually protected from inflammatory assaults with a good blood-brain barrier," explains Dr. Eckenhoff, but as we age, that barrier begins to deteriorate and "peripheral inflammatory responses can get into your brain more easily." The ensuing inflammation caused by hip surgery, for instance, can also cause inflammation in the brain.

Other studies have suggested that the type of anesthetic that is used may play a role in how the surgery affects cognition. "Propofol, for example, appears to be a little anti-inflammatory and we do think that this has a bearing on the degree of neuroinflammation and any cognitive decline afterwards. But even having said that, we think the anesthesia plays a small factor," says Dr. Eckenhoff.

Dr. Sprung and his team have hypothesized that individuals who do develop cognitive decline or dementia after surgery were already on the precipice of developing dementia in any event.

> **UNDERGOING SURGERY MAY BE COMPARED TO A 'STRESS TEST' THAT UNMASKS UNDERLYING COGNITIVE DEFICIT,**

says Dr. Sprung. In other words, surgery and anesthesia "can uncover individuals who are on the trajectory to develop cognitive impairment anyway, either mild cognitive impairment (MCI) or pre-dementia, or even dementia." For those who were already on the verge of developing dementia, then, the process can be accelerated by surgery.

It is important to remember, though, that dementia and Alzheimer's disease develop over several years, as opposed to overnight. When an individual is already sick, he says, there is a higher chance that he or she will need surgical procedures and receive a general anesthetic (and then anesthesia incorrectly gets blamed for the cognitive decline). Dr. Sprung and his team examined over 1,700 individuals – approximately half with dementia and half without – and they did not find any direct association between anesthesia and dementia.

Nevertheless, Dr. Sprung still worries when he is administering anesthesia to an older patient. He understands that older patients, particularly those who already suffer from MCI, have "an increased likelihood to fare worse after surgery." If the recovery from cognitive impairment takes longer, or if the individual dies from an unrelated disease in the interim, relatives and medical professionals may misattribute this cognitive deficit to anesthetic exposure, says Dr. Sprung.

Furthermore, researchers have found that individuals who have MCI have a greater propensity of developing postoperative delirium, which has been linked to accelerating the onset of cognitive decline – even in those who test as cognitively normal prior to undergoing surgery. Dr. Sprung believes that postoperative delirium can either accelerate the onset of dementia or, alternatively, those who were testing as cognitively normal may have actually been on the border of normality or on a declining trajectory towards MCI before surgery.

WEIGHING THE SCALE

What do you do, then, when you or a loved one requires surgery but is hesitant to receive general anesthesia?

> **DON'T CANCEL SURGERY THAT YOU NEED BECAUSE OF THIS,**

says Dr. Orser, but "do be mindful of it. Be reassured that we're trying to work hard to identify the extent of this problem and the correctable factors, and meanwhile there's an evolving literature that patients can turn to, to think about what supports they need."

For instance, individuals can visit the Perioperative Brain Health Centre located at Sunnybrook Hospital and/or its website (https://sunnybrook.ca/research/content/?page=dept-anaes-perioperative-brain-health), which is a repository of information. Dr. Eckenhoff says that there are quite a few things that individuals can do to prepare for a surgery. The American Society of Anesthesiologists has a new website through its Perioperative Brain Health Initiative (https://www.asahq.org/brainhealthinitiative), which is meant to help patients over the age of 65 with cognitive recovery after surgery. Individuals can also engage in "prehabilitation," which means "remaining active and exercising right up to the point of surgery," says Dr. Eckenhoff. It is also important to speak with your anesthesiologist before your surgery, as there are things that he or she can do interoperatively in order to reduce the risk of delirium after surgery (such as monitoring blood pressure and using brain vascular monitors to observe how the brain is being oxygenated throughout the procedure).

Dr. Eckenhoff also suggests minimizing the use of certain medications (subject, of course, to your doctor's approval). For instance, elderly individuals "don't tolerate benzodiazepines particularly well," so it is useful to avoid those before, during, and after surgery if possible. After surgery, also ensure that you get your eyeglasses and hearing aids back quickly to orient yourself, if applicable (talk to your doctor or family member beforehand to ensure that this happens) and get sleep, as it is critical for your recovery. Finally, be your own advocate (or be an advocate for a loved one) – it is important to ask questions in order to be as prepared as possible for surgery.

MIND YOUR MEDS

Widely-Used Drugs Can Negatively Impact Cognitive Function

Many people throughout their lives look to drugs – prescribed and/or over-the-counter – to help them cope with a variety of ailments. But some commonly-used drugs have negative consequences for our cognitive function, especially as we age, and may increase one's risk of developing Alzheimer's disease (AD) and other dementias. The following is a summary of some of the latest research findings about widely-used classes of drugs that can negatively impact brain function.

BENZODIAZEPINES

Benzodiazepines are primarily used to treat anxiety and insomnia, as well as to sedate individuals who are critically ill or undergoing surgery. Use of benzodiazepines is consistently high among the elderly in developed countries, ranging from 7% to 43%, despite it being well documented that benzodiazepines can negatively impact memory and cognitive function.

Research has also revealed that benzodiazepine use is associated with an increased risk of developing AD. A study conducted by a team of researchers from France and Canada used the Quebec health insurance program database (RAMQ) to identify nearly 2,000 men and women over the age of 66 who had been diagnosed with AD, as well as over 7,000 age- and sex-matched controls who were randomly selected (i.e., individuals without AD).

The researchers reviewed the drug prescriptions for both groups of participants and found that individuals who took benzodiazepines for three months or less did not have an increased risk of AD. "Their risk was about the same as someone who had never taken one," explained Dr. Yola Moride, a professor at the University of Montreal and one of the researchers for this study. "But individuals who used benzodiazepines for longer than that were found to have higher risk of being diagnosed with Alzheimer's. In fact, the higher someone's cumulative dose of benzodiazepines, the higher their risk." →

INDIVIDUALS WHO USED BENZODIAZEPINES FOR BETWEEN THREE AND SIX MONTHS HAD A 32% GREATER RISK OF DEVELOPING AD AND THOSE WHO TOOK BENZODIAZEPINES FOR MORE THAN SIX MONTHS HAD AN 84% HIGHER RISK.

The type of benzodiazepine consumed also made a difference to one's risk of developing AD. Long-acting benzodiazepines such as diazepam (Valium) or flurazepam (Dalmane) put individuals at greater risk than short-acting benzodiazepines such as triazolam (Halcion), lorazepam (Ativan), alprazolam (Xanax) or temazepam (Restoril).

ANTICHOLINERGIC MEDICATIONS

Drugs with anticholinergic properties are also well recognized for their negative effects on cognitive function, especially for the elderly. More specifically, these types of drugs are known to cause acute impairment of certain aspects of cognition, including working memory, attention, and psychomotor speed. Anticholinergic drugs block the action of acetylcholine – a neurotransmitter that sends brain signals between cells.

Anticholinergic drugs have a long history of use in medicine to treat a wide range of conditions, including seasonal allergies, asthma, overactive bladder and urinary incontinence, depression, and Parkinson's disease. Among older adults, the prevalence of use of anticholinergic drugs is estimated to be between 8% and 37%.

In the past, the general belief amongst the research community was that any cognitive impairment experienced as a result of using anticholinergic drugs was reversible once an individual stopped taking the medication. However, recent studies point to a longer-lasting impact, suggesting that

ANTICHOLINERGIC MEDICATIONS MAY BE LINKED WITH INCREASED RISK OF SUSTAINED COGNITIVE DEFICITS SUCH AS MILD COGNITIVE IMPAIRMENT OR DEMENTIA.

One study, conducted by Dr. Shelly Gray and colleagues, used computerized pharmacy dispensing data to examine cumulative anticholinergic drug use over a ten-year period for nearly 3,500 participants aged 65 and over with no dementia at the commencement of the study. During the study period, 797 participants developed dementia. The researchers analyzed that data to determine whether cumulative anticholinergic medication use was correlated with a higher risk of dementia, and concluded that this was the case.

"The level of additional risk for dementia increased along with amount of exposure to anticholinergic drugs," explained Dr. Gray, a professor in the Department of Pharmacy at the University of Washington. "Participants in the highest exposure category, equivalent to more than three years of usual doses, had a significantly increased risk of dementia compared to those with no use. Even participants with somewhat lower exposure, between 366 days and three years, had a slightly elevated risk."

Another important finding from this research was that among the heaviest users of anticholinergic drugs, there was similar dementia risk whether that heavy use was in the past or more recent. "This finding suggests that the dementia risk associated with anticholinergic use may persist even after someone stops using the drugs," said Dr. Gray. The results of this study were published in *JAMA Internal Medicine* in 2015.

More recent research, conducted by Dr. Kathryn Richardson and colleagues, also examined the association between anticholinergic drugs and dementia risk, and found that dementia risk varied depending on the class of anticholinergic drug consumed. This research suggested that long-term use of only certain types of anticholinergics was linked to higher dementia risk.

In this extensive study, the researchers analyzed over 27 million prescriptions for 40,770 patients in the U.K. aged 65 to 99 with a diagnosis of dementia, and nearly 284,000 controls without dementia. The researchers took into consideration the subclass of anticholinergic drug, as well as its score on the Anticholinergic Cognitive Burden (ACB) scale. They found a link between increased dementia risk and the use of anticholinergic drugs for depression, Parkinson's disease, and loss of bladder control (ones that had an ACB score of 3). However, the researchers found no association between increased dementia risk and many other types of anticholinergic drugs. For example, almost all drugs with an ACB score of 1 were not associated with increased dementia risk, nor were gastrointestinal drugs with ACB scores of 3.

"The associations we found are moderate, but given the high incidence of dementia, they reflect an appreciable level of risk," observed Dr. Richardson, a research fellow at University of East Anglia. "Even though our research suggests there may be no increase in dementia risk as a result of using some anticholinergic medications, we do not dispute the possible short-term harms of all anticholinergics used by vulnerable groups, so we advocate for health

The **Anticholinergic Cognitive Burden (ACB) Scale** was developed by the Aging Brain Program of the Indiana University Center for Aging Research. Drugs were assigned a score of 1, 2 or 3, depending on their anticholinergic effects. Drugs with a score of 1 are "possible anticholinergics," while those with a score of 2 or 3 are "definite anticholinergics." Doctors are advised to avoid prescribing drugs on the list with an ACB score of 3 to elderly patients.

GUIDANCE FOR HEALTH PROFESSIONALS

The **Anticholinergic Cognitive Burden (ACB) Scale** is one tool to help educate health professionals about what drugs to avoid prescribing for older patients. Another widely-used resource is the **Beers List**, which is a list of drugs that may be potentially inappropriate to prescribe to seniors. It was developed by Dr. Mark H. Beers in 1991 and has been subsequently updated by The American Geriatrics Society. Drugs on the Beers List are associated with an elevated risk of adverse effects or a lack of effectiveness in the elderly, or there are safer alternatives available.

professionals to follow current guidance to avoid or limit use of these drugs by older people." This research was published in *BMJ* in 2018.

OTHER DRUGS

There are many other prescription and over-the-counter drugs that are associated with short-term and, in some cases, long-term cognitive impairment. In addition to benzodiazepines and anticholinergics, the list includes widely-used drugs for lowering cholesterol (statins), controlling hypertension (beta-blockers), and helping with insomnia.

Narcotic painkillers (opioid analgesics) are another class of drugs that can impair brain function (examples include morphine, oxycodone, and fentanyl). These prescription painkillers can be highly addictive and consequently are often obtained illegally and used for long periods in doses beyond what a doctor would recommend. For more information about the cognitive effects of opioids, see page 26 in this issue of Mind Over Matter®.

POLYPHARMACY

Polypharmacy is the term used to describe the simultaneous and long-term use of multiple medications in a single individual. Polypharmacy is appropriate when the potential benefits of multiple treatments outweigh the potential harms. However, polypharmacy is commonly associated with a higher risk of adverse drug events, including cognitive impairment (depending on the drugs being consumed).

Polypharmacy is quite widespread among older individuals. According to a 2016 report published by the Canadian Institute for Health Information, 65.7% of Canadian seniors were prescribed five or more different drug classes, with 26.5% being prescribed ten or more, and 8.4% being prescribed 15 or more.

> **EVEN MORE SHOCKING WAS THE PERCENTAGE OF SENIORS TAKING AT LEAST ONE DRUG ON THE BEERS LIST OF DRUGS THAT SHOULD BE AVOIDED BY THE ELDERLY (49.4%).**

As many as 18% of seniors take multiple drugs on the Beers List. The report also contains a list of the top ten chemicals from the Beers List that are prescribed to seniors, and four on that list indicate cognitive impairment or cognitive decline as a potential side effect:

- Lorazepam for anxiety/insomnia is used by 8.8% of seniors (3.6% chronic use);
- Quetiapine for schizophrenia/bipolar is used by 2.8% of seniors (1.7% chronic use);
- Zopiclone for insomnia is used by 2.4% of seniors (1.5% chronic use); and
- Oxazepam for anxiety/insomnia is used by 2.4% of seniors (1.4% chronic use).

(Lorazepam and oxazepam are benzodiazepines, zopiclone is a benzodiazepine-related drug, and quetiapine is an antipsychotic with anticholinergic properties – with an ACB score of 3.)

CONSULT YOUR DOCTOR OR PHARMACIST

If you are taking prescription and/or over-the-counter drugs and are experiencing challenges with memory, thinking or concentration, ask your doctor or pharmacist to review the full list of your medications to explore whether any of them might be causing your symptoms. The good news is that if a particular medication is the source of your cognitive issues, you will likely experience an improvement or reversal of your symptoms after ceasing to use the drug.

It is important that you do not stop, start or change your drug regimen without first consulting your doctor or pharmacist. The health professional will help you make a plan for tapering off unsuitable medications, and possibly switching to appropriate alternatives. This will help prevent any withdrawal symptoms.

> **IT IS ALSO WISE TO KEEP A DRUG LOG TO TRACK SPECIFICS ABOUT WHAT DRUGS YOU ARE TAKING, IN WHAT AMOUNTS, AND WHEN – FOR BOTH PRESCRIPTION AND OVER-THE-COUNTER MEDICATIONS.**

Drug logs are particularly useful for when you conduct medication reviews, which are good to do at regular intervals because your health needs change over time. As you get older, your body's ability to process drugs will change. For example, your kidneys and liver will clear drugs more slowly from the body, keeping drug levels in the blood higher for longer. With age, people tend to gain fat and lose muscle mass, which also affects how drugs are distributed and broken down in the body.

GUT REACTION

Bacteria and Your Brain Health

The human body is host to trillions of microbes. In fact, slightly more than half of the cells found in our bodies are microbes – mostly bacteria, but also fungi, viruses, protozoa, archaea, and other microorganisms. The majority of these microbes reside in the gastrointestinal (GI) tract – commonly referred to as the "gut" – and the rest can be found in different parts of the body, including on the skin, in the urogenital tract, and in the nasal, oral, and otic (ear) cavities. The microbes in the gut are estimated to weigh between one and two kilograms, which is approximately the same weight as the human brain. Collectively, all of these microbes make up what is referred to as the human microbiome.

Microbes handle a variety of essential and beneficial functions in the human body. They play a fundamental role in digestion, nerve cell growth and survival, immunity, and inflammation. →

Interactions between gut microbes and the central nervous system (CNS) – i.e. brain and spinal cord – form the gut-brain axis. This complex communication is bi-directional, meaning that the gut microbes influence CNS function and vice versa.

EVIDENCE IS EMERGING THAT SUGGESTS MICROBES AFFECT COGNITION, BEHAVIOUR, AND MENTAL HEALTH, PARTICULARLY THROUGH INTERACTIONS BETWEEN THE GUT MICROBES AND THE CENTRAL NERVOUS SYSTEM, COMMONLY REFERRED TO AS THE "GUT-BRAIN AXIS."

"In recent years, our appreciation of how important these microbial communities are to many aspects of how the human body functions has grown dramatically," explained Dr. Geraint Rogers, Director of Microbiome Research at South Australian Health and Medical Research Institute and Professor at Flinders University School of Medicine. "For example, we know that animals raised in a germ-free environment show substantially altered immune and metabolic function compared to animals with a normal microbiome. And, evidence has demonstrated that disruption of microbiota in humans is associated with the development of a variety of diseases."

Research has found associations between the composition of the gut microbiome and inflammatory bowel disease, autoimmune arthritis, type 2 diabetes, obesity, atherosclerosis, anxiety, and depression.

THERE IS ALSO EMERGING EVIDENCE THAT LINKS DISTURBANCES TO INTESTINAL MICROBIOTA WITH NEUROLOGICAL CONDITIONS, SUCH AS MULTIPLE SCLEROSIS, AUTISM SPECTRUM DISORDER, PARKINSON'S DISEASE, AND ALZHEIMER'S DISEASE (AD).

In three recent studies set out below, the researchers examined the relationship between the microbiome and the development of Alzheimer's disease.

A review article by Dr. Francesca Pistollato and colleagues – published in *Nutrition Reviews* in 2016 – reported that bacteria in the gut can produce significant amounts of amyloids and lipopolysaccharides, which may play a role in the progression of AD (accumulation of amyloid-beta plaques in the brain is one of the hallmarks of AD). The researchers also explored how certain nutrients affect the composition of gut microbiota, and thus the formation and aggregation of amyloid-beta in the brain.

More recently, a study conducted by Nicholas M. Vogt and colleagues examined the differences between the microbiomes of individuals diagnosed with AD versus those without. The researchers analyzed fecal samples from 25 participants diagnosed with AD and 25 age- and sex-matched controls. The results indicated that the microbiomes of AD participants had decreased microbial diversity and were distinct in composition compared to the controls. "We discovered that the abundance of certain microbes was different in people with dementia due to Alzheimer's, compared to the control group," explained Dr. Barbara Bendlin, Associate Professor at the University of Wisconsin, and one of the authors of the study. "Fourteen of these microbe types were more abundant, while 68 types were less abundant in those with Alzheimer's." These findings were published in *Scientific Reports* in 2017.

One of the topics covered in a review article by Dr. Helen Tremlett and colleagues, published in *American Neurological Association* in 2017, was the association between the oral microbiome and Alzheimer's disease. The researchers noted that poor dental status has been linked to Alzheimer's disease or reduced cognitive function in a number of studies. They also noted that periodontal disease has been associated with increased amyloid in the brain, even in subjects that are cognitively normal.

"TREATMENTS" THAT TARGET THE MICROBIOME

Given what is known so far about the involvement of gut microbiome in human health and disease, it is not surprising that researchers are currently examining the possibility that health could be boosted or disease prevented (or even cured) by targeting the microbiome.

Every individual's microbiome is unique, influenced by whether he or she was born vaginally or by Caesarean section, breastfed or not, genetics, stress, infection, and the environment. Other factors that are known to affect the microbiome, that we usually have some control over, include antibiotic use, diet, alcohol consumption, smoking, and disrupted sleep.

OUT OF THESE POTENTIALLY MODIFIABLE RISK FACTORS, DIET IS ONE OF THE MOST CRUCIAL COMPONENTS, WITH A SIGNIFICANT IMPACT ON THE MICROBIOME.

Experiments have shown that significant changes in diet can cause large shifts in microbial composition within a single day. However, once the new diet has been discontinued, the microbial composition will revert back to its former state within 48 hours. The following are summaries of three recent studies that examined the effects of modifying diet on the microbiome, and the resulting impact on brain health and cognitive function:

In the abovementioned review article by Dr. Francesca Pistollato and colleagues, the researchers found that nutritional interventions involving the use of probiotics and prebiotics, as well as plant-derived nutrients and phytocompounds, might stimulate the gut-brain axis in a positive manner, reduce neuroinflammation, and slow or reverse cognitive impairments associated with AD. The researchers emphasized that more research is needed, particularly involving human subjects, before recommendations about treatments with isolated elements can be made. Nevertheless, they recommend higher intakes of low-fat, plant-derived foods and lower or no intake of meat products as a general strategy that could be safely undertaken to help prevent AD.

In 2017, *Frontiers in Behavioral Neuroscience* published a mini review by Dr. Emily E. Noble and colleagues about the relationship between consumption of a "Western diet," the microbiome, and cognitive impairment. A Western diet is characterized by higher intakes of red and processed meat, refined sugars and grains, alcohol, and high-fat dairy products, with minimal intakes of fruits, vegetables, whole grains, nuts, and fish. "There is substantial evidence linking consumption of a Western diet with cognitive dysfunction," explained Dr. Noble, a post-doctoral researcher at the University of Southern California. "Emerging evidence suggests that the gut microbiome influences cognitive function via the gut-brain axis, and that a Western diet significantly alters gut microbiota."

Dr. Noble continued, "We discovered that there are many potential neurobiological mechanisms involved, linking consumption of a Western Diet with changes in the gut microbiome which then may be contributing to Western Diet-mediated cognitive dysfunction. For example, impairment of the blood-brain barrier may be a factor, or neuroinflammation, or resistance in insulin receptors." Although more research is needed to fully understand the mechanisms underlying the cognitive effects of a Western diet, there is enough evidence to suggest that individuals should try to limit their intake of saturated fats and added sugars.

In another review article, published in *Neuroscience Letters* in 2017, the researchers considered whether a diet that is high in fiber could improve brain health. Dr. Megan W. Bourassa and colleagues focused their research on butyrate (a short-chain fatty acid that is produced by bacterial fermentation of otherwise non-digestible fiber in the colon) and its impact on brain health. High-fiber foods that help butyrate-producing bacteria thrive include resistant starches such as whole grains and legumes, and fructo-oligosaccharides such as bananas, onions, and asparagus.

After reviewing the available evidence to date, the researchers concluded that butyrate has significant potential as a therapeutic for the brain, in dietary and pharmacologic form. The dietary form – in other words, through a high-fiber diet – is particularly appealing since it is a simple, relatively low-risk method to potentially improve outcomes for individuals with brain disorders. While butyrate offers great potential as a "treatment," more research is needed to fully understand its effectiveness as a dietary intervention.

Probiotics are live microorganisms that help to maintain or restore the good bacteria in the gut, which can be consumed in food or supplement form.

Prebiotics are non-digestible food ingredients (e.g., fiber) that selectively stimulate the growth and/or activity of beneficial bacteria in the gut, thereby improving overall health.

Exploration is also underway into the potential for microbiome-targeted treatments to positively impact mental health (with such treatments often referred to as "psychobiotics").

RESEARCH HAS SHOWN THAT INCREASING THE AMOUNT OF GOOD BACTERIA IN THE GUT CAN HELP INDIVIDUALS COPE WITH DEPRESSION AND ANXIETY, LOWER REACTIVITY TO STRESS, AND DECREASE NEUROTICISM AND SOCIAL ANXIETY.

For example, a number of studies have found that some probiotic strains (such as Bifidobacteria, Lactobacillus, and Bacteroides) can have a positive effect on the brain and behaviour. However, substantial work is still needed before any targeted intervention can be rationally recommended.

Although research has revealed interesting relationships between the microbiome and the brain, there is still much to learn. Nevertheless, there is a growing body of evidence to suggest that taking care of your microbiome is critical to your overall health, immune function, mental health, and cognitive function. There are numerous ways to keep your gut bacteria healthy and diverse, such as by consuming substantial amounts of high-fiber foods, limiting your intake of saturated fats and added sugars, only taking antibiotics when absolutely necessary, and limiting your use of antimicrobial products like hand sanitizer (wash well with soap and water instead). It is also important to make other healthy lifestyle choices, such as limiting alcohol consumption, getting enough sleep, and minimizing stress. If you take care of your good bacteria, they will help to take care of you.

YOU CAN LEAD A HORSE TO WATER

Staying Hydrated Boosts Brain Power

Water consumption and brain function are integrally connected. Over 60% of the adult human body is composed of water and every system in the body is dependent on proper hydration, including the activities of the brain and nervous system.

"Brain cells require a delicate balance between water and various elements to operate," says University of Texas neuroscientist Joshua Gowin. "When you lose too much water, that balance is disrupted. Your brain cells lose efficiency." Research has demonstrated that lack of water to the brain can impair short-term memory function and the recall of long-term memory, as well as cause a variety of symptoms such as brain fog, exhaustion, headaches, sleep issues, stress, anger, and depression.

Amongst its many health benefits, water helps with digestion and circulation, as well as helps with the transportation and absorption of nutrients, and helps to limit changes in body temperature in a warm or a cold environment. Drinking water can improve one's brain health by simply increasing blood flow and oxygen to the brain – which, in turn, improves concentration and cognition (supporting memory function) and helps balance moods and emotions, reducing stress and headaches.

Our brains do not have any way to store water, so when our bodies lose more water than the amount being consumed, dehydration sets in and cognitive function is impaired. In fact, studies have demonstrated that

> **PROLONGED DEHYDRATION CAUSES GREY MATTER TO SHRINK IN BOTH SIZE AND MASS, AND CAN CAUSE THE BRAIN TO AGE PREMATURELY.**

In a 2013 study conducted by researchers in the U.K., mild dehydration was found to have a negative effect on the brain's performance, whereas drinking water improved the participants' ability to complete tasks that required a rapid response.

As a natural part of the aging process, our bodies undergo physiological changes that increase our risk of becoming dehydrated. As we get older, our ability to recognize thirst declines, much as our taste buds decrease as we age. Dehydration is one of the most frequent causes of hospitalization of elderly Canadians.

Dehydration is particularly common amongst individuals living with Alzheimer's disease and other dementias. During the early stages of dementia, a person may simply forget to drink because he or she is less sensitive to thirst and/or cannot recall when he or she last consumed a beverage. Individuals with moderate dementia often have difficulty remembering the mechanics of how to drink, such as turning on the faucet or even how to get fluid into a glass. The risk of dehydration is most severe in the advanced stages of dementia due to not recognizing one's thirst, having a complete loss of thirst or being unable to express thirst to others. It is important for family members and caregivers to take time to learn the symptoms of dehydration because early intervention can keep a small problem from becoming a life threatening one.

There are multiple signs that you may not be consuming enough water, including the following:

- You feel fatigued and lethargic;
- You experience hunger pangs;
- Your mouth, skin, and eyes are dry;
- You are overly thirsty;
- Your urine is more concentrated or darker than usual;
- You are disoriented; and
- You have a headache.

SUGGESTIONS TO PREVENT DEHYDRATION IN DEMENTIA PATIENTS AND THE ELDERLY

MAKE IT ACCESSIBLE

Put out bottles or pitchers of water and/or liquids throughout the patient's living space and where he or she spends time, so that he or she is reminded to drink and always have access to liquids.

MAKE IT EASY

Understand the patient's preference for easy consumption (such as water bottles, non-spill cups, and even one-way straws if suction is weak), especially if additional dexterity or coordination is required.

MAKE IT FUN

Set up notices or leave notes as a reminder for your patient to drink regularly. These can be handwritten or electronic reminders.

MAKE IT CREATIVE

If steady plain tap water is getting tiring, try adding slices of lemon, orange or cucumber, or adding a splash of flavouring. Offering fresh juices, smoothies, and teas will not only help the patient stay hydrated, but will also supply him or her with healthy nutrients. Substituting hydrating foods is also a creative idea in an effort to offer alternatives to drinks. High-water content foods (such as broth and cottage cheese, as well as fruits like apples, oranges, berries, and grapes) can help avoid dehydration.

MAKE IT TIMELY

Encourage patients to drink water more often throughout the day rather than right before bed. Sometimes the fear of incontinence can diminish a patient's urge to drink voluntarily.

MAKE IT SAFE

Some medications (both prescription and over-the-counter) can contribute to dehydration. It is therefore important to review medication side effects and work with the pharmacist and doctor to avoid complications.

> **IT IS ALSO IMPORTANT NOT TO UNDERESTIMATE HOW QUICKLY DEHYDRATION CAN OCCUR.**

Merely four to eight hours without water can lead to mild dehydration, and twenty-four hours without water can result in severe dehydration.

THE HARDEST QUESTIONS

Ethics of Capacity, Mandatory Retirement, & Those at Potential Risk

Nearly ten years ago, Dr. Michael Gordon received a panicked phone call from the wife of a physician, a man who was a long-time colleague and friend. She pleaded that it was urgent for Dr. Gordon to see her husband immediately, suggesting vaguely that he was not doing well mentally.

Dr. Gordon is a leading geriatrician and the former chief of medicine at Toronto's Baycrest Health Sciences. One of his residents met with his friend first and emerged wide-eyed from an hour-long session.

"The resident said 'I can't believe he's still in practice. He can't remember anything,'" recalled Dr. Gordon in an interview with Mind Over Matter®.

In his own examination of his friend, Dr. Gordon determined quickly that his friend was "absolutely impaired" and told him that he had to stop practising medicine immediately.

Dr. Gordon then spoke with his friend's fellow physicians at his group practice, where a colleague said "I couldn't report him…it would put him out of business."

Dr. Gordon is now 77 years old and although he stepped down as chief of medicine a decade ago, he is by no means retired. Dr. Gordon is still a professor of medicine at the University of Toronto and the co-director of the ethics program. He is also the oldest person on staff at Baycrest and has no illusions about his own mortality, having ensured that all his personal affairs are in order.

He sits on a committee that examines physician retirement issues and has many friends of a similar age who occasionally speak about how long they should continue working. He points out that the end of mandatory retirement at 65 has changed everything, for physicians and many other professions.

"Most of us like what we're doing and most of us think we're doing a good job. They all said 80 is the new 65!"

Dr. Gordon also undergoes a yearly review at Baycrest, an examination to ensure that he is still able to properly fulfil his duties. "Most of us among older practitioners have no desire to continue to practise when we're no longer able to provide the kinds of service we believe is our duty. I don't have a right to be a doctor. It's a privilege," he said.

As a doctor who studies and treats dementia, Robin Hsiung's days are dominated by thoughts of the disease,

so it is natural that he considers a fateful question about his own future: what happens if he develops dementia? "Yes, I do ask, and I have faced a colleague with the disease and it's a difficult question," said Dr. Hsiung in an interview with Mind Over Matter® from his office at the University of British Columbia, where he is an Associate Professor in the Department of Medicine's Division of Neurology. He is also a staff neurologist at the UBC Hospital Clinic for Alzheimer and Related Disorders.

He pointed out that dementia does not happen overnight. It might begin with mild cognitive impairment and in the early stages most people can function normally, perhaps employing various forms of reminders.

"But doctors need to monitor themselves and stop working if necessary," said Dr. Hsiung. "Their colleagues also have to spot danger signs. A good colleague will bring it up with their friend…and if it's serious might need to bring it up with their superiors." He said in all the cases he has dealt with, the physician was cognizant of the decline and stopped practising.

We trust our health and our lives to our physicians. We expect them to be in top form. By their nature, doctors are high achievers. But for the good of their patients, they must also be honest with themselves about when the time comes to step back from their work.

Professional guidelines published by the Ontario College of Physicians and Surgeons (OCPS) state that "physicians should only care for patients when they are well enough to do so." OCPS advises doctors to "be aware of their own health, which includes being able to recognize when they are not well enough to provide competent care" and recommends that they avoid self-treatment. It also notes that doctors may not recognize when they are incapacitated, which can be a feature of dementia, and so they should seek advice about their own care from another physician.

> **WITH THE ALARMING GROWTH OF DEMENTIA IN THE GENERAL POPULATION, IT IS CRITICAL THAT INDIVIDUALS WHO WORK IN ALL KINDS OF JOBS WITH PROFOUND RESPONSIBILITIES THINK ABOUT THESE ISSUES.**

"It's not just doctors. I've seen lawyers, high-powered lawyers, who have had to stop because they're not serving their clients properly anymore," noted Dr. Hsiung.

In Ontario, the *Law Society Act* and the Law Society of Ontario's *Rules of Professional Conduct* strongly advise lawyers to seek professional assistance if they feel their capacity is compromised – whether as a result of physical illness, addiction problems or any kind of mental health issue. Lawyers are also required to report any concerns about colleagues to the Law Society of Ontario, which has the power to conduct investigations and hearings, as well as restrict or suspend an individual's license to practise law, where warranted.

Commercial airline pilots face perhaps the most rigorous scrutiny of all. In Canada, they are required to undergo a medical examination every six months to a year, depending on their age, which includes an assessment of their "mental status." Airlines also require that co-workers report any abnormal behaviour by pilots.

But these conversations naturally resonate most among health care practitioners who deal with dementia on a regular basis. Dr. Kirk R. Daffner, a professor of neurology at the Harvard Medical School, wrote about his own concerns about cognitive decline in a remarkable column for *The Washington Post*. He recalled how as a young doctor in training he witnessed older colleagues making embarrassingly incoherent presentations, and how he was determined that he would never attempt to continue working when he could no longer perform the job effectively. Now in his 60s, he is attempting to put personal safeguards in place to ensure that he will cease working if his mental faculties decline – despite his wife's insistence that he will never willingly retire.

It is a discussion rife with cruel paradoxes. Nearly 30% of physicians in the U.S. are over the age of 60. The wisdom earned through their years of experience is invaluable and the continued mental stimulation of work is believed to contribute to their personal brain health. However, at the same time, as many as 10% of individuals over the age of 65 suffer from dementia, and 15% to 20% of this age cohort suffer from mild cognitive impairment.

Dr. Daffner has developed a tentative solution, which starts with a detailed document that outlines how he believes he should comport himself if he faces cognitive decline, which he has shared with trusted colleagues. He has identified peers who will assess his work and give him an honest appraisal. In light of the fact that dementia can profoundly change a person's outlook, Dr. Daffner also proposes to record a video outlining his wishes so that he can watch it in the future as a frank talk to himself.

Dr. Gordon believes that his annual reviews at Baycrest will ensure that he does not continue to work if he is unable to do so. He suspects that there are doctors in private practice who are not being reported when their mental health declines, but he also believes that the younger generation of physicians, by nature of their training, have a greater sense of collective responsibility and will be vigilant to ensure that colleagues do not continue to practise if their cognition deteriorates.

Should the day ever arrive for him, Dr. Gordon is prepared to accept the judgement of his peers. "It would be tough because for many physicians it's the source of their identity, but I'd have to do it. There'd be no way that I couldn't do it."

TOO YOUNG TO FADE

Dementia: Not Just a Disease of the Elderly

Dementia is commonly thought of as a disease that affects older adults. While those aged 65 and over certainly do make up the vast majority of individuals with dementia, there is also a growing number of younger adults affected by the disease.

WHEN AN INDIVIDUAL UNDER THE AGE OF 65 IS DIAGNOSED WITH DEMENTIA, IT IS REFERRED TO AS "YOUNG-ONSET DEMENTIA" (YOD).

The number of individuals who have young-onset dementia is not known for certain. A 2014 review of scientific papers reporting on the prevalence of YOD, published in the *European Journal of Neurology*, found that the diversity of research designs has made direct comparison across studies difficult. Accordingly, the researchers (Lambert and colleagues) shared the range of prevalence rates that had been reported in the various studies. Between 38 and 260 people per 100,000 were found to experience the onset of various types of dementia sometime between the age of 30 and 64. Prevalence rates were highest among those at the older end of that age range (as high as 420 people per 100,000 for those between the age of 55 and 64).

How do prevalence rates translate into the number of young adults afflicted with the disease?

- It is estimated that 16,000 Canadians are living with YOD.
- In the U.K., there are approximately 42,325 people with YOD.
- In Australia, the number is estimated to be 13,500 people.
- The Alzheimer's Association has estimated that 200,000 Americans have young-onset Alzheimer's disease (since Alzheimer's disease is just one type of dementia, the number of Americans living with YOD would be higher than this figure).

DIFFERENCES BETWEEN YOUNG-ONSET AND LATE-ONSET DEMENTIA

There are some differences between young-onset dementia and late-onset dementia that relate to the disease itself.

Although Alzheimer's disease (AD) is the most common cause of dementia (regardless of the age-of-onset), the proportion of individuals living with AD is much lower among those with young-onset dementia (15-40%) than it is among those with late-onset dementia (50-70%). If you look at the young end of the YOD spectrum – people under the age of 45 – there are few with AD, and most of these are due to "familial Alzheimer's disease," which is a rare form of the disease passed on through genetics.

Frontotemporal dementia and Huntington disease are more prevalent in YOD, as are secondary dementias (those caused by, or related to, another recognizable disease such as chronic alcohol abuse, HIV, multiple sclerosis or traumatic brain injury. A wide range of rare metabolic, infectious or autoimmune disorders may also cause secondary dementias).

Familial Alzheimer's disease is linked to three rare genes: APP, PSEN 1, and PSEN 2. These are different than the APOE gene that affects Alzheimer's risk in general.

EARLY-ONSET DEMENTIA

Early-onset dementia is another term used to describe young-onset dementia. However, "young-onset" is a clearer descriptor since "early-onset" can be misunderstood to mean early or mild dementia in someone over 65 years of age. An individual experiencing young-onset dementia may be in any stage of dementia: early, mid, or late.

The high proportion of secondary dementias amongst younger individuals means that they are more likely to have treatable conditions causing their dementia (compared to older people). However, in order for interventions to be effective at improving cognition, they usually have to be given early in the course of the disease.

Different causes of dementia result in various symptoms and behaviour changes, and in YOD, memory problems may not be the first symptom to appear.

EARLY SYMPTOMS OF YOD CAN VARY GREATLY AND MAY INCLUDE BEHAVIOURAL CHANGE, DEPRESSION, AND MILD COGNITIVE IMPAIRMENT, AS WELL AS PHYSICAL SYMPTOMS SUCH AS VISUAL IMPAIRMENT, GAIT DISORDER, AND SEIZURES.

Another difference between young-onset and late-onset dementia is the rate of disease progression. Rapid progression is more likely among those with YOD than those with late-onset dementia, although the course of YOD varies quite a bit from person to person and in some cases can remain stable indefinitely.

CHALLENGES UNIQUE TO YOD

A diagnosis of dementia has a devastating impact on an individual and his or her family, irrespective of the age of onset. However, those with young-onset dementia face some unique challenges. To start with, it is common for younger individuals to experience delays in even receiving a proper diagnosis, or to receive a misdiagnosis. Research indicates that on average it takes younger individuals with dementias of all types 4.4 years to receive a diagnosis, compared to 2.2 years for late-onset dementia of comparable severity. The delay in diagnosis for younger individuals is in part due to lack of awareness of YOD among the general public and family doctors (who are usually the first health professionals consulted). Many health care providers simply do not think to →

consider dementia as the potential reason for the presenting symptoms in a young person.

MORE OFTEN, THE SYMPTOMS OF DEMENTIA IN YOUNGER ADULTS ARE MISTAKEN AS SIGNS OF STRESS OR PSYCHIATRIC ILLNESS, PARTICULARLY WHEN COGNITIVE DECLINE IS NOT EVIDENT YET.

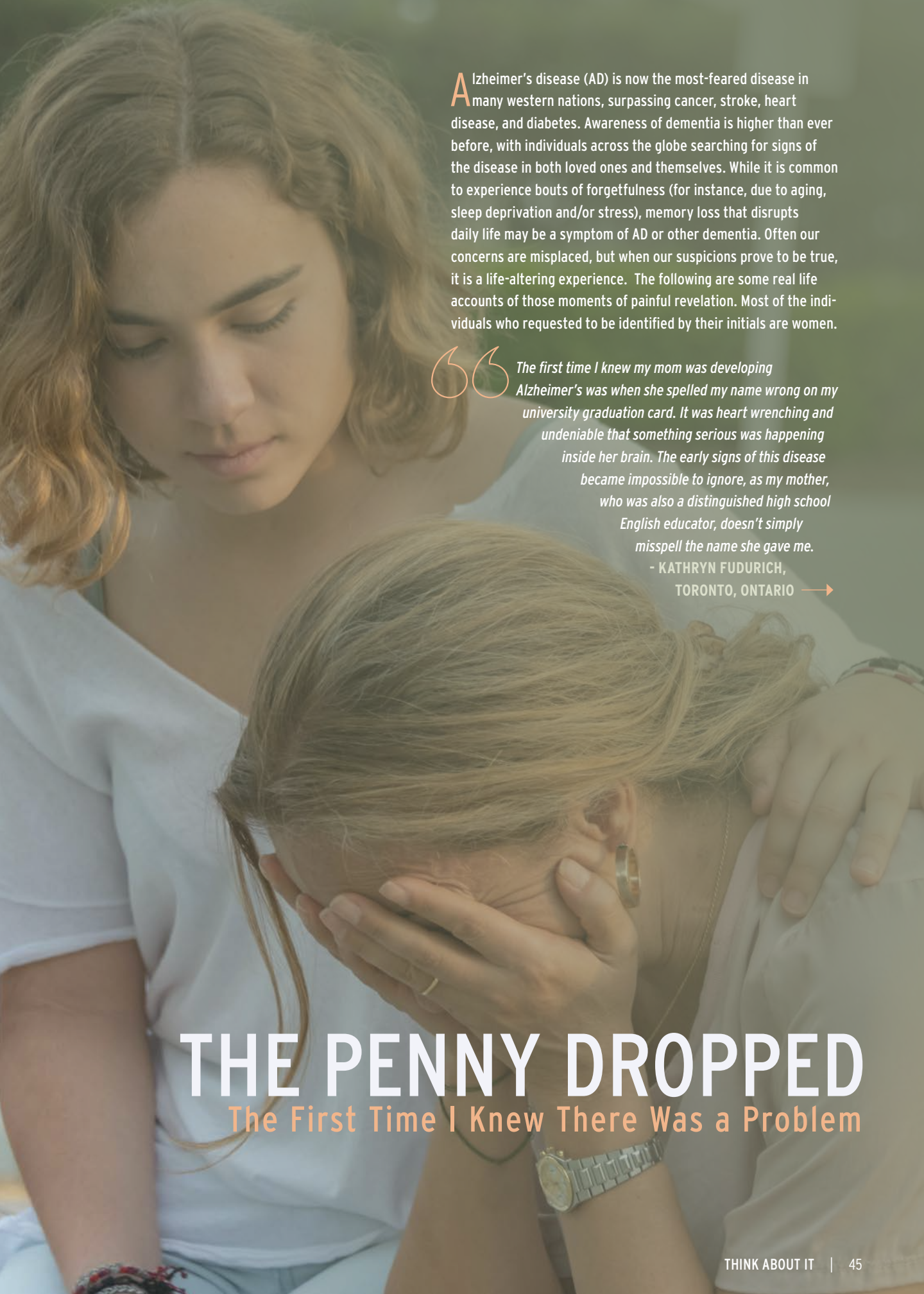
Additionally, individuals with young-onset dementia face the following age-related negative consequences that are not as likely to affect someone with late-onset dementia:

- People around those with YOD are more likely to question or doubt the diagnosis because the disease is associated so strongly with older adults. It can be difficult to believe that someone young has dementia, especially when the early symptoms may not be impacting cognitive function yet.
- People with YOD are more likely to have dependent children, and may be caring for aging parents as well.
- Those with YOD are more likely to still be working when diagnosed and the illness will impact their household income. Initially the person with YOD may have to reduce his or her work hours or change jobs to accommodate the effects of the illness and to be able to attend medical appointments. Eventually, he or she will have to stop working entirely, likely earlier than originally intended. Leaving the workforce early has long-term financial implications since the person may not have worked long enough to qualify for a company pension and/or did not have as much time as planned to save for retirement. The person with YOD's spouse/partner often experiences reduced income as well once he or she shifts into a caregiving role, sometimes full-time.
- There are other work-related consequences that can affect people with undiagnosed YOD. YOD usually begins to affect a person's ability to work long before a diagnosis is received. Without knowing the reason why someone's cognitive performance has declined or behaviour has changed, an employer can easily misinterpret the circumstances (for instance, assume that the employee has a poor attitude or lacks a strong work ethic). Some people with undiagnosed YOD get fired or laid off as a result. Losing a job before being diagnosed can affect eligibility for disability benefits from the employer.
- People with YOD are likely to have financial commitments based on past earning history, e.g., mortgage and car payments.
- People with YOD commonly report that the services and programs available for dementia are difficult to access or do not suit their unique needs as a younger person. For example, a younger person with dementia is usually still physically active and mobile, and is not content to spend time doing sedentary activities with much older people. Caregivers in day programs or long-term care facilities may find the physical strength and energy of those with YOD challenging to handle, and different types of activities and security may be needed.
- When dementia affects younger people, they typically experience emotions unique to their age group. Since they have had less time to achieve their life goals, their sense of grief and loss can be even more profound than for older people. If they have dependent children, they may also feel guilty and inadequate about not being able to fully participate in childrearing.

REMEMBER, YOD IS FAIRLY UNCOMMON

It is important to keep in mind that the vast majority of younger adults who experience challenges with memory do not have dementia. Rather, it is far more likely that they are experiencing cognitive impacts of stress, depression, or anxiety. It is nevertheless important that individuals of all ages – both young and old – focus on making healthy lifestyle choices that support brain health (e.g., physical activity, healthy diet, social connection, brain-stimulating hobbies) and then watch for unusual cognitive or behavioural symptoms. If it appears that the symptoms of dementia are present, it is important to speak with a health professional as soon as possible. Again, since YOD is rare, it is most likely not YOD – but the sooner the diagnosis is received, the better, in order to increase the chances that a treatment could help reverse or halt the disease's progression.

Dementia can be challenging to diagnose at any age. Currently, there is not a single test that confirms whether or not an individual has dementia. Instead, a diagnosis can only be made after a patient undergoes a comprehensive medical evaluation that includes an analysis of his or her medical history, a series of neuropsychological examinations, costly spinal taps and/or brain scans, and a report of behaviour history from an informant (because patients may not be aware of their own behaviour changes or may forget important details).



THE PENNY DROPPED

The First Time I Knew There Was a Problem

Alzheimer's disease (AD) is now the most-feared disease in many western nations, surpassing cancer, stroke, heart disease, and diabetes. Awareness of dementia is higher than ever before, with individuals across the globe searching for signs of the disease in both loved ones and themselves. While it is common to experience bouts of forgetfulness (for instance, due to aging, sleep deprivation and/or stress), memory loss that disrupts daily life may be a symptom of AD or other dementia. Often our concerns are misplaced, but when our suspicions prove to be true, it is a life-altering experience. The following are some real life accounts of those moments of painful revelation. Most of the individuals who requested to be identified by their initials are women.

> *The first time I knew my mom was developing Alzheimer's was when she spelled my name wrong on my university graduation card. It was heart wrenching and undeniable that something serious was happening inside her brain. The early signs of this disease became impossible to ignore, as my mother, who was also a distinguished high school English educator, doesn't simply misspell the name she gave me.*
>
> **- KATHRYN FUDURICH, TORONTO, ONTARIO**

I vividly remember the day we received a troubling phone call from the dentist's office. The receptionist told me that my mother had checked in for her appointment and then promptly left a brief time later. My heart sank. We frantically searched for our mother who had gotten lost on the five-minute drive home from the dentist. I was devastated.

- K.G., SHERBROOKE, QUEBEC

My mother's transformation began while I wasn't paying attention. I was an only child and very close to my mom - but that year I was in the throes of a white-knuckle pregnancy and very focused on myself and my baby. Really, in the first ten years of her slow twenty-year decline, the changes were not cognitive; they were more personality changes. As they progressed, I began to be convinced that her increasing paranoia, and other manifestations, was the war coming home to roost in her after all those years. My fearless mother would call in the middle of the night, terrified, to say she was hiding behind the bed and 'they' were out on the balcony. Eventually, actually fairly soon, she refused to leave her apartment at all.

One day I was relating something to do with my husband at the time sister's husband's brother. My brilliant mother could not grasp the relationship no matter how slowly or how many times I repeated it. That was the moment that the penny dropped and I started to understand what we were dealing with. This illustrates one of the many reasons why the work that WBHI is doing in education and dissemination of information is so important: had I had any notion earlier on that these too could be symptoms of impending dementia, I might have been able to find palpable ways to help her when it might have counted.

- S.SOYKA, THORNHILL, ONTARIO

The first time I realized my mother had dementia, I was very pregnant and she was requesting for me to come over daily to help her with the same tasks. I noticed she had notes and lists written down everywhere of conversations she had with people, shows she had watched, questions she had, etc. I realized then she had cognitive issues, and that we were about to go on a journey together. ***- L. BUNDY, HALIFAX, NOVA SCOTIA***

Both of my parents experienced dementia in their late 70s during an overlapping time period, so mom didn't present as typical. Mom was a caregiver to her husband with Alzheimer's, and simultaneously she was experiencing her own episodic dementia. Stress blurred everyone's reality. Mistrust and suspicion became more prevalent. Medications were hidden like Easter eggs. We reached out to the geriatric psychiatry team for clarification. For dad, a cup of tea was often the antidote to everything, but dozens of cups of tea left in random places, like the inside of the grandfather clock, had us reaching out to a dementia home care agency. *- RYLEY W., KINGSTON, ONTARIO*

Ever since I was a kid, my grandmother was always my favourite person to talk to. She always gave me a sense of peace and comfort anytime we spoke. In her 90s, I began to realize our conversations became shorter, and she would repeat herself more often. As her cognitive decline became worse, sometimes we would just sit together and enjoy each other's company. Those were the best days.

- ANDREW, EDMONTON, ALBERTA

The first time I knew dad might have some form of cognitive challenges was when he started accusing family, friends, and the local coffee shop of stealing his money and not giving him correct change over and over again. At the time, we didn't realize that his paranoia and anger were signs of Alzheimer's, especially coming from a soft-spoken spiritual man all his life. It wasn't until police, paramedics, and the emergency room physician were involved that we were made aware that he may have dementia, specifically Alzheimer's

- RON B., TORONTO, ONTARIO

The first time I knew my dad had dementia was when my mom told me. He had been acting strangely so it was a relief to find out there was an explanation. I didn't suspect dementia because I didn't know anything about it.

- LISA P., CALGARY, ALBERTA

I first found out there might be an issue with my husband, through him. He noticed words and thought processes were not coming fluidly. What followed was a year of appointments, tests, specialists, more tests, waiting, more waiting, and more appointments, then, the diagnosis that he had young onset Alzheimer's disease.

- G. MCLEAN, CALGARY, ALBERTA

We thought dad had a stroke so I took him to the ER where I learned that the symptoms we'd been seeing were dementia. He was so childlike, confused, and scared. That was when I realized that my strong and capable father was gone forever. *- ANGELA MOORE, CHILLIWACK, BRITISH COLUMBIA*

My husband managed a 1.5 million dollar budget when working and I was totally shocked to see he could not count change to buy a cup of coffee. After that, as the pieces fell into place, my denial was replaced with a profound anguish and desperation to understand dementia so we could live the best life possible. ***- C.G., MOOSOMIN, SASKATCHEWAN***

I had been working out of town for a few weeks, a six-hour drive away. My husband came down for a few days to bring me back home. I knew something was seriously wrong when we got home and I found he had left all of the doors to the house wide open. *- SUSAN, WHITEHORSE, YUKON*

CHANGING BODIES, CHANGING BRAINS

The Effects of Hormones on Brain Health

Hormones are regulatory substances produced by various glands (such as the thyroid, pituitary, ovaries, and adrenal) that stimulate specific cells in the body. They are carried by the blood to different parts of the body and are responsible for regulating an extensive variety of psychological and behavioural processes.

> **THE BRAIN RELIES SIGNIFICANTLY ON PROPER HORMONE BALANCE IN ORDER TO FUNCTION APPROPRIATELY.**

In fact, concentrations of estrogen, progesterone, testosterone, DHEA, and other hormones can be higher in the brain than in the bloodstream. Not surprisingly, then, an imbalance of hormones dras- →

tically affects the brain's chemistry and communication between brain cells (i.e. neurotransmission). The detrimental impact to one's health can be physical, mental, and emotional, including issues with growth development, metabolism, sleep, sexual development, diabetes, thyroid, and brain health deterioration.

SPECIFIC HORMONES AND THEIR EFFECTS ON THE BRAIN, COGNITION, AND MEMORY

The following is a brief description of specific hormones that have a substantial effect on brain health, and the common symptoms that an individual may experience if a particular hormone level is too low or too high.

ESTROGEN // Responsible for the sexual and reproductive development in women, estrogen has a profound impact on brain health. A growing body of evidence has documented estrogen's positive effect on learning, memory, and mood, as well as neurodevelopmental and neurodegenerative processes. Among its many benefits in the brain, estrogen also seems to prevent or delay memory and cognitive decline, including diseases such as Alzheimer's and Parkinson's.

- **Too low** – lower libido, difficulty concentrating, mood swings, reproductive issues, breast tenderness, hot flashes, and irregular or absent periods.
- **Too high** – altered sleep patterns, weight gain, hair loss, headaches, memory problems, and changes in appetite (slowed metabolism).

Estrogen, testosterone, and progesterone work directly with the nerve cells in the brain and contribute to blood flow of the brain, protecting against loss of memory and the progression of dementia.

TESTOSTERONE // Produced by the ovaries, testosterone strengthens muscles, arteries, and nerves, including those in the brain, and therefore contributes to mental sharpness and clarity, as well as overall energy levels. Studies from the Baltimore Longitudinal Study of Aging found that low levels of testosterone increased the risk of Alzheimer's disease in men, even when other risk factors for dementia were considered. Along with Alzheimer's, low testosterone has also been associated with other neurodegenerative diseases, such as Parkinson's disease.

- **Too low** – muscle loss, weight gain, fatigue, mood swings, and erectile dysfunction.
- **Too high** – excess body hair, acne, increased muscle mass, changes in body shape, and menstrual irregularity.

PROGESTERONE // Emerging research indicates that progesterone has multiple non-reproductive functions in the central nervous system to regulate cognition, mood, inflammation, neurogenesis, and regeneration. Progesterone has a calming effect on the brain, as well as a protective effect by reducing swelling and improving

THE EVOLUTION OF HORMONES THROUGHOUT A WOMAN'S LIFE

PUBERTY // The luteinizing hormone (LH) stimulates puberty when the hormone is released from the pituitary gland. Once a woman's monthly menstruation cycle begins, the pituitary gland slightly increases production of follicle-stimulating hormones (FSH). Estrogen production increases, causing the lining of the uterus to thicken and progesterone production increases to prepare the lining to receive an egg. The imbalance of these two hormones significantly contributes to premenstrual syndrome (PMS) symptoms.

PREGNANCY // Pregnant women experience immediate and, in some cases, intense increases in estrogen and progesterone as their bodies prepare to support and develop the baby. In fact, a pregnant woman produces more estrogen in one day than a non-pregnant woman generates in three years. This massive fluctuation can also impact several other hormones, resulting in a variety of implications.

Several studies have suggested that pregnancy has a long-lasting effect on a woman's brain. Pregnancy reduces grey matter in specific parts of a woman's brain, to help her bond with her baby and prepare for the demands of motherhood. This change endures for at least two years after pregnancy. The areas of the so-called "mommy brain" that are responsible for focus and concentration are preoccupied with protecting and tracking the newborn child. This can result in what feels like decreased brain power, and increased stress and anxiety when separated from the child, particularly if nursing. The ongoing fluctuation of these predominant hormones, with the simultaneous drop in progesterone, can also cause low moods, leading some women to experience post-partum depression.

PERI-MENOPAUSAL // As women get older, the body's ovaries age and release fewer hormones. The endocrine system tells

mental clarity after a traumatic brain injury.

- **Too low** – mood swings and memory loss, weight gain, low libido, and premenstrual syndrome (PMS) symptoms.
- **Too high** – breast tenderness, bloating, mood swings, dizziness, and susceptibility to yeast infections.

THYROID // The thyroid gland produces hormones that help regulate the body's metabolic rate (energy use), muscle control, brain development, mood, heart and digestive function, and bone maintenance. It can therefore have an impact on thought processes and memory. Thyroid hormone deficiency, even of short duration, may lead to irreversible brain damage, the consequences of which depend on the specific timing of onset and duration of the deficiency.

- **Too high (hyperthyroidism)** – difficulty sleeping, irregular heartbeats, anxiety, thinning hair, and weight loss.
- **Too low (hypothyroidism)** – weight gain, slower metabolism, fatigue, irregular periods, anxiety, difficulty concentrating, short-term memory loss, and depression.

CORTISOL // The primary "stress hormone," cortisol can help reduce inflammation, control blood sugar levels and blood pressure, as well as regulate metabolism. In healthy individuals, cortisol levels naturally increase in response to stressful situations. However, in circumstances in which the body perceives the stress as a severe threat or the stress is prolonged, an excess level of cortisol becomes active in the brain, which can result in adverse effects, such as damage to the hippocampus – an essential part of memory creation.

- **Too high** – severe fatigue, muscle weakness, bone loss, cognitive difficulties, loss of emotional control, high blood pressure, and headaches.
- **Too low** – weakness, weight loss, low blood pressure, salt craving, nausea, and abdominal pain.

VASOPRESSIN // Also referred to as antidiuretic hormone (ADH), vasopressin is a hormone produced by the hypothalamus in the brain and stored in the pituitary gland. Vasopressin regulates the volume of water in the body and also affects blood pressure.

- **Too high** – headaches, nausea or vomiting and, even in severe cases, coma and convulsions.
- **Too low** – causes the kidneys to excrete too much water (frequent urination and dehydration, as well as low blood pressure).

MELATONIN // While previously thought of as a mere sleep aid, recent studies have revealed that melatonin has the ability to reduce brain injury-induced trauma, provide protection against neurogenerative diseases, and boost cognitive functioning, amongst other benefits. →

the body to produce less FSH hormone and there is a decrease in the stimulation of the ovaries resulting in the reduction of estrogen and progesterone levels. Women tend to still experience sporadic menstrual cycles during this time. The fluctuation contributes to hot flashes, fatigue, low libido, and sometimes anxiety.

MENOPAUSE // As the ovaries continue to age, they can no longer properly perform their function to regulate the body's estrogen, progesterone, and testosterone levels. This is the stage when women stop having their periods. At this point, women experience the most significant changes in hormone levels.

POST MENOPAUSE // The female brain becomes more stable after menopause with lower, steadier hormones that translate into a calmer, less emotional brain – one that is not as reactive to stress. However, because of a lower level of estrogen, women at this stage can be at an increased risk for other health conditions such as osteoporosis and heart disease.

On the positive side, though, as the "mommy brain" slows down through this evolution of hormones and the cycle of fluctuations, the individual focus is believed to begin to shift inwards, more often with a greater focus on health and diet, as well as overall well-being.

- **Too low** – tiredness during the day, social withdrawal, irritability, insomnia, anxiety, and depression.
- **Too high** – resets circadian rhythms (internal body clock that tells the body when to rise, eat, and sleep), sleepiness, and drop in the body's core temperature.

Because of the interconnectivity of these hormones, deficiencies and imbalances can result in brain-related symptoms such as poor concentration, forgetfulness, confusion, lack of clarity, and even memory loss. If not properly addressed, these symptoms can have both short-term and long-term effects.

SIMPLE WAYS TO TRY TO IMPROVE HORMONAL IMBALANCE

DIET // Increase your vitamin intake and be smart about how you eat by opting for a more anti-inflammatory diet. For example, healthy fats that are anti-inflammatory include coconut oil, avocados, and salmon. Fish oil and additional Vitamin D and Vitamin B also help balance estrogen. Foods that may increase estrogen include barley, beets, cherries, chickpeas, carrots, cucumbers, dates, fennel, olives and olive oil, papaya, peas, pomegranates, beans, rhubarb, tomatoes, wheat, and yams. For brain-healthy (and great-tasting) recipes, visit **www.memorymorsels.org**.

ALLERGIES // Keeping your immune system in peak form will ensure that your body is in a better position to avoid any inflammation that can result when your system is fighting itself, and increase your body's natural defenses and better regulate hormones.

PHYSICAL AND MENTAL ACTIVITY // Be active. A lack of physical exercise also contributes to high levels of inflammation. Keeping active also includes exercising your mind, such as learning a new language, taking a cooking class, or playing a musical instrument.

TOXINS // Toxins can play a significant role in hormonal imbalance. Limit your exposure to environmental toxins such as pesticides and harmful chemicals as much as possible. This includes being aware of the food that you are consuming in your regular diet that may be injected with growth hormones, as well as your exposure to the chemicals found in plastics. Instead, try to consume high-quality organic meat and dairy products that are hormone-free and drink and eat from glass containers.

WATER // Stay hydrated and drink plenty of water. Water helps with digestion, absorption, and circulation, and it moves waste products and toxins out of the body. It also increases blood flow and oxygen to the brain, which is why dehydration can also impair cognitive function. To learn more about the cognitive benefits of drinking water, see page 38 of this issue of Mind Over Matter®.

STRESS // Learn to manage your stress. Regardless of the cause, addressing all emotional imbalances you are dealing with will naturally help balance your hormones. Stress management strategies include getting regular exercise and plenty of sleep, as well as practicing relaxation techniques such as trying yoga, practicing deep breathing, getting a massage or learning to meditate.

SLEEP // The negative impact of limited sleep and rest cannot be underestimated. Fluctuating hormones contribute to insomnia, which not only impairs memory but also causes additional stress and inflammation in the body because it is not able to fully restore and repair itself at night. Deep sleep is when the brain moves short-term memories into long-term storage. Frequent interruptions in sleep are deadly to memory.

To help support your brain health, enjoy the lifestyle reminders posted on Women's Brain Health Initiative's Instagram account (@womensbrains).

WHAT ABOUT HORMONE REPLACEMENT THERAPY?

Hormone replacement therapy (HRT) is any form of hormone therapy where a patient receives hormones medically to supplement or substitute natural hormone production.

In an interview with Women's Brain Health Initiative, neuroscientist Dr. Gillian Einstein, who holds the Wilfred and Joyce Posluns Chair in Women's Brain Health and Aging, noted that despite all of the research to date, the consensus is still unclear as to whether hormones need to be replaced in menopausal women and whether this would be protective against dementia in an older population.

"Hormone therapy was started to restore what the medical community felt needed to be replaced. It is still a very active area of research," explains Dr. Einstein. "Part of the confusion is the uncertain questions such as, what kinds of hormones need to be replaced, and at what age, what are the critical windows for the most impact, and what dosing schedule should be followed, whether it should be a patch or a pill […] or if they should be given at all. What other body systems might they affect besides the brain (e.g. good and bad effects on the heart and breast)."

"It is not a straight forward answer and the reality is that everyone is different," she added. "The role that your hormones are going to play is completely dependent on a number of variables that are very different for each person, including family

history, other diseases in their backgrounds, the lifestyle they practice, and how they feel."

Dr. Einstein cautions that in addition to all the variables that affect each individual woman, it is also important to understand the impact of hormone loss with younger women, particularly since this subject matter has often been studied in the context of menopausal women.

THE WORK THAT WE ARE DOING, SUPPORTED BY THE POSLUNS CHAIR, IS BEGINNING TO REVEAL THAT HORMONES WHEN YOU'RE YOUNG ARE IMPORTANT TO COGNITION, TO MEMORY, AND THE HEALTH OF DIFFERENT BRAIN REGIONS.

"The kind of hormone deprivation of younger women is different than that which is experienced by older women, whatever the reason (e.g. having ovaries surgically removed vs. natural menopause)," Dr. Einstein observes.

"People with a history of Alzheimer's disease, or who have had their ovaries removed before they would naturally go into menopause, may want to consider hormone replacement, but it is different for everyone. There are many older women who live long and cognitively healthy lives without hormone replacement. The most important question that requires real attention is what is the history of women who have dementia."

Dr. Einstein was recently involved in a research paper entitled *The Many Menopauses*, which identified that there are multiple ways that women can enter menopause that have repercussions on cognitive performance. One of the outcomes is the continuing pressure for research scientists to study distinct populations, since every group is different when it comes to the relationship between hormones and brain health.

CREATIVITY

Therapy for the Mind

Creativity is a broad concept that is often characterized by the ability to perceive the world in novel ways, to make connections between seemingly unrelated phenomena, and to generate innovative and useful solutions. While creativity was once thought to reside in the right hemisphere of the brain, we now know that the entire brain is involved in the creative process, says Dr. Sarah McKay, an Oxford University-educated neuroscientist and the author of *The Women's Brain Book: The Neuroscience of Health, Hormones and Happiness*.

Scientists have started to identify the specific thinking processes and brain regions involved with creativity. Recent research conducted by Dr. Roger Beaty and his colleagues, published in the *Proceedings of the National Academy of Sciences of the United States of America* in early 2018, found that the brains of highly creative individuals were "wired" differently than the brains of less creative thinkers. In particular, individuals with more-creative brains were better able to co-activate brain networks that typically work separately, compared with those with less-creative brains.

In this study, Dr. Beaty and his research team sought to determine what makes some individuals more creative than others. Using functional magnetic resonance imaging (fMRI) scans, the researchers measured changes in blood flow in various areas of the brain while participants were engaged in a divergent-thinking test called the "alternate uses task" (which involves coming up with inven-

tive ways to use everyday objects, such as a gum wrapper or a sock). The researchers then ranked the participants' ideas for originality – common uses received lower scores (for instance, using a sock to warm your feet), while uncommon uses received higher scores (for instance, using a sock as a water filtration system).

The researchers found that those participants who were more innovative had strong connections between three brain systems: the default, executive, and salience networks. The **default network** is a set of brain regions that activate when people are engaged in spontaneous thinking, such as mind-wandering, daydreaming, and imagining. The **executive control network** is a set of regions that activate when people need to focus or control their thought processes. The **salience network** is a set of regions that acts as a switching mechanism between the default and executive networks.

These three networks usually do not get activated simultaneously. For instance, when the executive network is activated, the default network is generally deactivated. Interestingly enough, the more creative participants were capable of activating these three networks in tandem. "It's the synchrony between these systems that seems to be important for creativity," Dr. Beaty says. "People who think more flexibly and come up with more creative ideas are better able to engage these networks that don't typically work together and bring these systems online."

Based on their findings, Dr. Beaty and his colleagues developed a predictive model and tested against brain scan data collected from previously-published studies on creativity. "[W]e wanted to see whether someone with weak connectivity in [these networks] has less-creative ideas than someone with stronger connectivity," Dr. Beaty notes. "And that's what we found across three data sets." According to Dr. Beaty, more research is needed in order to determine whether these brain systems are malleable or relatively fixed. "Creativity is complex, and we're only scratching the surface here, so there's much more work that's needed."

CREATIVITY AND MENTAL HEALTH

A growing body of research suggests that engaging in creative practices can help to alleviate depression and anxiety, while enhancing quality of life and significantly reducing stress. Below are some highlights from recent studies that have explored the link between creativity and mental health:

- A 2012 study, published in *Art Therapy*, examined the psychological effects of art-making in a sample of nearly 60 undergraduate students during examination time. Participants were randomly assigned to either an art-making group (engaging in activities such as painting, colouring pre-designed mandalas, making collages, and modeling with clay) or a control group. The State-Trait Anxiety Inventory (routinely used in the medical sciences to determine the level of situational and long-term characteristics of a person's anxiety) was administered to both groups of participants before and after art-making. The researchers found that a brief period of art-making can significantly reduce a person's state of anxiety.

- According to a study published in 2016 in *ecancermedicalscience*, singing in a choir for one hour boosts levels of immune proteins in individuals affected by cancer, reduces stress, and improves mood, which in turn could have a positive impact on overall health. The researchers examined nearly 200 members of five different choirs before and after their singing practices. They found that positive affect was increased (being happy, relaxed, and feeling connected), negative affect decreased (feeling →

anxious, sad, tense, tired), and cortisol – the stress hormone – decreased. The researchers also found that those with the lowest levels of mental wellbeing and highest levels of depression experienced greatest mood improvement, associated with lower levels of inflammation in the body.

Numerous studies have suggested that writing can calm mental agitation. One recent study from Michigan State University, published in *Psychophysiology* in 2017, found that chronically worried people who engage in "expressive writing" (i.e. writing about their feelings) performed better on an upcoming stressful task than those who did not engage in expressive writing beforehand. "Worrying takes up cognitive resources," says the study's lead author Hans Schroder, a Michigan State University doctoral student in psychology and a clinical intern at Harvard Medical School's McLean Hospital. "Our findings show that if you get these worries out of your head through expressive writing, those cognitive resources are freed up to work toward the task you're completing and you become more efficient."

An article published in *Perspectives in Public Health* in January 2018 examined whether engaging in art-making could improve overall mental wellbeing. Participants were artists who completed questionnaires about art-making, mood, cognition, and state of consciousness. The study found that art-making was significantly associated with positive affect rather than negative affect, both in the present moment and in long-term contexts. Participants were also found to be in the "state of flow" when they created art. Flow is all about "being immersed in a task," according to Dr. McKay, and is "incredibly motivating and has positive impacts on mood."

ART THERAPY AND ALZHEIMER'S DISEASE

Art therapy is a form of expressive therapy that uses the creative process of making art to improve an individual's physical, mental, and emotional wellbeing. Art therapy provides an avenue for non-verbal self-expression, which represents a unique means of intervention for people with limited verbal skills due to a physical, psychological, or neurological incapacity. Art projects can create a sense of accomplishment and purpose.

A wealth of research has suggested that art therapy is particularly positive for individuals living with Alzheimer's disease and other forms of dementia. "[B]eing involved in creative endeavours for their own sake is satisfying, and experiencing positive emotions is so important for overall health," says Dr. McKay. Watercolours, oil painting, making collages or pottery, and enjoying music are just a few of the creative therapies that are available to people living with cognitive disorders.

"It is not just about finding a cure, it's about improving the lives of those living with dementia today," says Nalini Sen, Director of Research for the Alzheimer's Society of Canada.

> **ART THERAPY SHOWS GREAT PROMISE FOR BOOSTING THE QUALITY OF LIFE OF THOSE LIVING WITH COGNITIVE DISORDERS.**

Art therapy consists of a "non-directive approach centred on the person, which encourages free and spontaneous expression," says Sen.

When participating in art therapy, patients with Alzheimer's disease are stimulated cognitively, emotionally, and through their senses, and "they experience improvement in feelings of wellbeing and mood." Anxiety levels can decrease, and art-making or participatory practices can help to validate personal experiences and histories, says Sen. The social interaction involved in art therapies is another significant piece of the puzzle as well. "[E]specially for individuals with dementia, it can reduce the risk of increased decline within the disease," says Sen, as various studies have now demonstrated. While it will not eliminate the disease, the creativity and happiness that art therapy brings can make all the difference in the life of a loved one who has been progressively in decline.

AMPLIFY YOUR CREATIVE SIDE

According to Dr. Sarah McKay, we all have the ability to maximize our creativity. The following is a list of some of her top tips on how to amplify your creative side:

1. TAKE A SHOWER. "Having a shower is one of the few places in our crazy modern world where you can switch off – you do not have sensory input, you're relaxed, warm, and safe." The nurturing environment can often enhance creativity.

2. HAVE A NAP. "Lots of people use afternoon naps to hit a creative insight or to intentionally try to solve problems. It's called dream incubation. It's a way of forcing your mind to wander and shut off."

3. GIVE YOURSELF A LIMIT. As Dr. McKay observes, Dr. Seuss wrote *Green Eggs and Ham* when challenged to write a book of only fifty words, which is quite restrictive. "Try a self-imposed limit. It can be a restrictive limit or an expansive one." On the expansive side, you could try brainstorming 100 unique solutions to a particular problem before choosing one to work with.

4. EMBRACE EXTREME MOODS. We know that positive moods can help boost our creativity, but so can so-called negative ones. "Anger and frustration can often, in the right environment, force a creative solution."

SUGAR & SPICE

And What's Not Nice for Your Brain

Eating a balanced diet is vital for good health and overall wellbeing. Food provides our bodies with the energy, protein, essential fats, vitamins, and minerals to live, grow, and function properly. Sugar and salt are present in many, if not all, of the foods that we consume as part of our everyday diets. Although both play several essential roles in our health (the brain needs sugar for energy, and muscles need salt to contract, for instance), they can also lead to a variety of adverse health conditions when consumed in excess.

TOO MUCH SUGAR

One in every five calories that Canadians consume comes from sugar. This dietary sugar →

may occur naturally (for instance, in fruit, vegetables, and milk) or it may have been added to foods and beverages to improve palatability. According to Statistics Canada, Canadians consume an average of 110.0 grams of sugar a day – the equivalent of approximately 26 teaspoons. This figure amounts to 21.4% of Canadians' total daily calorie intake.

THE WORLD HEALTH ORGANIZATION RECOMMENDS A DAILY MAXIMUM OF 10% OF CALORIES FROM "FREE SUGARS"

(i.e. sugars added to foods by the manufacturer, cook, or consumer, as well as sugars naturally present in glucose, fructose, honey, and fruit juices), which translates to approximately 12 teaspoons. The American Heart Association (AHA) recommends no more than 6 teaspoons (25 grams) of added sugar per day for women and 9 teaspoons (38 grams) for men. Many popular drinks have more than half of the recommended daily sugar intake. For instance, one can of pop typically contains about 10 teaspoons of added sugar.

High-sugar diets have been associated with an increased risk of numerous diseases, including heart disease, stroke, obesity, diabetes, high blood cholesterol, and cancer. "We know that excess sugar is not good for the body or the heart and we also know that having risk factors for heart disease is also bad for the brain," says Dr. Matthew Pase, Senior Research Fellow at Melbourne Dementia Research Centre in Melbourne, Australia. Dr. Pase and his colleagues sought to investigate just how detrimental sugar is for the brain and, specifically, the ways in which sugary beverage intake impacts the brains of those with preclinical markers of Alzheimer's disease.

The study, published in the September 2017 issue of *Alzheimer's & Dementia*, involved nearly 4,000 participants with an average age of 54 who completed a food frequency questionnaire and underwent magnetic resonance imaging (MRI) scans. The researchers found that the

PARTICIPANTS WHO MORE FREQUENTLY CONSUMED SUGARY BEVERAGES TENDED TO HAVE SMALLER TOTAL BRAIN VOLUMES, POORER MEMORY, AS WELL AS SMALLER HIPPOCAMPAL VOLUMES

– which is particularly noteworthy because the hippocampus is one of the first areas that is affected in Alzheimer's disease.

A different team of researchers from Australia sought to examine the impact of sugary beverages on the early-life brain, using a rodent model. Their study, published in the January 2016 online issue of *Frontiers in Molecular Neuroscience*, found that early-life exposure to high amounts of sugar produced the same ill effects on the brain as early-life traumatic experiences (namely, lesser brain volume, inflammatory effects to the hippocampus, and the misprocessing of the stress hormone cortisol). Additionally, both learning capacity and memory function were compromised by the consumption of a high-sugar diet.

More research needs to be conducted to better understand the relationship between sugar, mental health, and physical brain health. Some studies have suggested that high sugar intake is linked to greater instances of depression – a finding that is particularly concerning in light of the fact that many young adults are eating too much sugar at the same time that mental health concerns among this segment of the population are on the rise.

Many individuals who consume too much sugar are also consuming too much saturated fat. According to a study published in *Frontiers in Behavioral Neuroscience* in 2017, consumption of a "Western Diet" (a diet that consists of both high levels of saturated fat and added sugars) negatively impacts cognitive function.

THE HIPPOCAMPUS – A BRAIN REGION ASSOCIATED WITH THE CONTROL OF CERTAIN LEARNING AND MEMORY PROCESSES – APPEARS TO BE PARTICULARLY VULNERABLE TO THE DELETERIOUS EFFECTS OF A WESTERN DIET.

The researchers suggest that the Western Diet's negative effects on the brain might be the result of a disturbance of the gut microbiome (the collective genome of microbes residing in the gastrointestinal tract). In rodent studies, the gut microbiome was "profoundly altered by early life sugar [consumption]," notes Dr. Scott Kanoski, one of the study's authors and Assistant Professor of Biological Sciences at the University of Southern California. The microbiome is a "very new field of research," says Dr. Kanoski, so more research needs to be conducted in order to determine how it relates to brain outcomes. (For more on the microbiome, see page 34 of this issue of Mind Over Matter®)

According to a longitudinal study involving over 5,000 individuals (mean age 66), published in the April 2018 issue of *Diabetologia*, increasing blood sugar levels are associated with cognitive decline. While previous studies have linked cognitive decline with diabetes, this study is one of the largest to establish the direct relationship between HbA1c (levels of glycated haemoglobin, a measure of overall blood sugar control) and subsequent risk of cognitive decline. Interestingly enough, the researchers found that high-circulating HbA1c levels were correlated with cognitive decline, whether or not the participant was diabetic.

To date, researchers have not conclusively proven a cause-and-effect link between sugar and cognitive impairment. While we know that dietary factors are associated with memory and cognitive impairments in humans, "what's harder to do is

to isolate specific dietary factors," says Dr. Kanoski. Nevertheless, Dr. Kanoski (amongst others) believes that limiting intakes of simple sugars is a good idea "not just for brain outcomes, but also for metabolic outcomes, which are of course linked."

TOO MUCH SALT

According to Statistics Canada, the majority of Canadians are consuming nearly twice the recommended intake of salt every day – approximately 3,400 mg, far exceeding the recommended limit of 2,300 mg. Both of these numbers are consistent with those in the U.S. While our bodies require a small amount of sodium to be healthy, too much can lead to adverse health consequences, including an increased risk of developing cardiovascular diseases, osteoporosis, and stomach cancer.

> THE DANGER OF SALT IS NOT SO MUCH THE SALT THAT COMES FROM THE SHAKER, BUT THAT SALT THAT IS EMBEDDED IN THE FOOD WE EAT. PROCESSED FOODS USE AN EXTRAORDINARY AMOUNT OF SALT,

says Dr. Costantino Iadecola, director of the Feil Family Brain and Mind Research Institute and a Professor of Neurology and Neuroscience at Weill Cornell Medicine. "In population studies, [communities that] consume higher levels of salt tend to have more strokes, more vascular problems, and more dementia."

In order to better understand why this is the case, Dr. Iadecola and his colleagues performed several experiments with mice, where some were fed a high-salt diet (comparable to the excessive proportion of salt found in some human diets). Within a few weeks, the salty diet led to dysfunction of endothelial cells (the cells that line blood vessels and modulate vascular tone), a reduction in cerebral blood flow, and cognitive impairments in several behavioural tests, without any changes in blood pressure. However, when the mice were returned to a normal diet, both brain blood flow and cognition improved, suggesting that the effects of excessive salt consumption could be reversed.

Notably, the salty diet also increased the numbers of T Helper 17 (TH17) white blood cells in the gut and increased the levels of a pro-inflammatory molecule these cells release, called the interleukin 17 protein (IL-17). Once in the bloodstream, IL-17 interacts with the brain's endothelial, vascular cells, inhibiting "the ability to produce a critical chemical called nitric oxide that the brain needs to work correctly," explains Dr. Iadecola.

The researchers found that it was this increase in IL-17 in the bloodstream (and corresponding lack of nitric oxide) that caused the high-salt diet's negative effects on cerebrovascular function and behaviour. In a final experiment, the researchers treated the mice with a drug known to increase the level of nitric oxide in endothelial cells, called ROCK inhibitor Y27632. The drug reduced circulating levels of IL-17 and the mice showed improved behavioural and cognitive functions. "[D]espite being on the high-salt diet, [the mice] did not develop dementia," says Dr. Iadecola, which means that there could be some interesting pharmaceutical developments in the future as a result of these findings. This study was published in the January 2018 issue of *Nature Neuroscience*.

While much more research is needed before any definitive link can be made between cognitive impairment and high-salt and high-sugar diets, these findings highlight the importance of cutting out excess salt and sugar from our diets.

THE ROOT TO BETTER

The Nutritional Value of Beets

Beetroots, commonly known as beets, are a popular root vegetable used in many cuisines across the globe. While you may not find them on your typical grocery list, beets are packed with essential vitamins, nutrients, and plant compounds, making them one of the healthiest vegetables that you can consume. Adding more beets to your diet can help boost longevity, from aiding weight loss to preventing chronic diseases (such as cancer), and can even help improve mental and cognitive function.

According to Leslie Beck, one of Canada's preeminent registered dieticians and author of several books about food and health, including *The Plant-Based Power Diet*, "beets, due to their bright red colour, are an excellent source of antioxidants," which are compounds that fight inflammation in the body. Specifically, beets contain the antioxidant polyphenols and betalains, the former of which is a phytochemical (a compound naturally produced by plants, which is thought to provide several health benefits) and the latter of which is a naturally occurring pigment responsible for the red colour of the beet vegetable.

Research published in 2001 in the *Journal of Agriculture and Food Chemistry* identified betalains as a new class of antioxidants and suggested that "red beet products used regularly in the diet may provide protection against certain oxidative stress-related disorders in humans." In light of the fact that recent research has shown a connection between inflammation and the occurrence of dementia, anything that fights inflammation in the body and the brain is a step in the right direction.

> "NUTRIENT WISE, BEETS ARE A GREAT SOURCE OF THE B VITAMIN, FOLATE, "WHICH HELPS TO MAKE AND REPAIR DNA IN THE BODY, AND IS A GOOD SOURCE OF POTASSIUM, WHICH HELPS TO KEEP BLOOD PRESSURE IN CHECK,

says Beck. They are also high in dietary fibre and in betaine, which, according to research published in *The American Journal of Clinical Nutrition*, has been found to maintain liver, heart, and kidney health, as

BRAIN HEALTH

well as is an important nutrient for the prevention of chronic disease.

BEETS AND BRAIN HEALTH: WHAT DOES THE RESEARCH SAY?

Recent research presented at the American Chemical Society's national meeting in March 2018 found that betanin, a subset of the antioxidant betalain category, "shows some promise as an inhibitor of certain chemical reactions in the brain that are involved in the progression of Alzheimer's disease." While the precise cause of Alzheimer's disease remains unknown, one of the prime suspects is a protein called beta-amyloid that accumulates in the brain and disrupts communication between brain cells (i.e. neurons). Researchers are now hypothesizing that much of this damage occurs when beta-amyloid attaches itself to metals such as iron and copper, which can cause beta-amyloid peptides to bind together in clumps. This, in turn, can promote inflammation and oxidation, ultimately killing surrounding neurons.

"There is often a high amount of copper, or iron, present in the plaques of patients with Alzheimer's," says Cole Cerrato, a PhD candidate in the Department of Chemistry at the University of South Florida. "[U]nregulated metals in the body don't tend to do what you want them to do." For instance, they can accelerate the accumulation of beta-amyloid proteins, as well as create oxidation in the brain, which is damaging to the brain as a whole.

Cerrato and his doctoral supervisor, Dr. Ming, added betanin (a compound found in beets) to copper-bound beta-amyloid mixtures in the laboratory, and found that doing so reduced oxidation by as much as 90% – in essence, seemingly neutralizing the beta-amyloid's negative effects. "[It is] always the well-regulated chemistry that our bodies need and we found that it is the unregulated chemistry that betanin seems able to prevent," notes Cerrato. While more research needs to be conducted, this compound could potentially be used as part of a drug for Alzheimer's sufferers in the future.

Other scientific research published in the *Journals of Gerontology: Medical Sciences* in 2017 examined the impact of beetroot juice on the aging brain. Researchers out of Wake Forest University in North Carolina wanted to determine how beetroot juice, combined with exercise, affected the brains of hypertensive older adults. It is well known that exercise has positive effects on overall health, →

including brain health. Individuals with high blood pressure, for instance, are encouraged to exercise in order to lower their blood pressure and to maintain cardiovascular health, which we know is linked to brain health.

As Beck observes, anything that keeps the heart healthy, keeps the brain healthy. Accordingly, the researchers provided participants (aged fifty-five and older) with a beetroot juice supplement before they engaged in a moderately vigorous 55-minute treadmill walk in order to determine whether beetroot juice had a better effect on brain neuroplasticity (the ability of the brain to form and reorganize synaptic connections) than exercise alone. Participants engaged in the treadmill exercise three times a week over the course of a six-week period. Using functional magnetic resonance imaging (fMRI) scans, the researchers found that the beetroot juice supplement, which contained dietary nitrate, combined with exercise improved brain function in subjects. In particular, connectivity between brain regions was improved.

> “SUPPLEMENTING WITH BEETROOT JUICE “MAKES THE BRAINS APPEAR MORE SIMILAR TO THOSE OF A YOUNGER ADULT,

says Dr. Daniel B. Kim-Shapiro, Director of the Translational Science Center: Fostering Independence in Aging at Wake Forest. “The active ingredient in the beet juice is nitrate, which gets converted to nitrite, and eventually to nitric oxide” by the body, says Dr. Kim-Shapiro. “In the end, it’s the nitric oxide that’s thought to be active.” Nitric oxide is a vasodilator, which means that it increases blood and oxygen flow, including flow to the brain.

While the body makes nitric oxide naturally, consuming foods that are high in nitrate is one way to boost nitric oxide production. Many vegetables are high in nitrate (such as spinach and other leafy greens), and there are also beetroot juices on the market now that have been created specifically for their high-nitrate content.

Earlier research conducted by Dr. Kim-Shapiro and his colleagues, published in the journal *Nitric Oxide* in 2011, found that a high-nitrate diet – which included both drinking beetroot juice and eating beets – improved the regional brain perfusion (blood flow) in older adults in critical brain areas known to be involved in executive functioning.

OTHER HEALTH RESEARCH ON BEETS

In the past decade, there has been an ever-increasing amount of research focusing on the compounds contained in beetroot juice and beets. Supplementing with or consuming beets and beetroot juice (high in dietary nitrate) has been found to enhance the physiological response to exercise, such as muscle efficiency and oxygenation, according to a paper published in *Sports Medicine* in 2014.

Similarly, 2012 research published in the *Journal of the Academy of Nutrition and Dietetics* examined whether beetroot consumption could improve running and overall athletic performance. Although the study was relatively small, the researchers found that consumption of whole beetroot acutely improves running performance in healthy adults. Additionally, research published in *Nutrients* in 2017 found that beetroot juice supplementation improved the cardiovascular performances of athletes.

HOW TO ENJOY BEETS AND BEETROOT JUICE

“Beets are just one part of a healthy diet, and we just don’t have the data yet to say that beets should be included in the diet X times per week for optimal health,” says Beck. Nevertheless, including beets in one’s diet a few times a week or even every day has been recommended.

While cooking beets can sometimes be labour intensive and even messy, grating them raw is a tasty way to enjoy this “superfood,” or you can purchase pickled beets and snack on them (although this option would have a higher sodium content). For those more adventurous, you could try making your own beet chips by thinly slicing beets and adding a bit of olive oil and salt.

You could also consider drinking beetroot juice, but be careful if you have hypotension (since this beverage can lower blood pressure) or if you are susceptible to kidney stones. Nitric oxide is an antiplatelet agent as well, so if you are taking daily aspirin or other drugs such as warfarin for cardiovascular reasons, drinking beetroot juice may not be for you. It is important that you speak with your doctor before you start drinking beetroot juice as a supplement.

Whether juiced raw, cooked, pickled or fermented, beets offer a wide array of health benefits, and may be the root to better brain health.

WOMEN'S BRAIN HEALTH INITIATIVE HONOURARY BOARD

Jeanne Beker
Journalist, Author & Fashion Entrepreneur

Catherine Delaney
President, C.A. Delaney Capital Management Ltd.

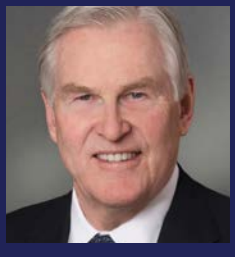
Arlene Dickinson
CEO, Venture Communications

Rosie MacLennan
Olympic Gold Medalist

Heather Reisman
Founder, Chair & CEO, Indigo

Fran Sonshine
National Chair, Canadian Society for Yad Vashem

Kirstine Stewart
President & CRO, TribalScale



Hon. Michael Wilson
Chairman, Barclays Capital Canada Inc.

WOMEN'S BRAIN HEALTH INITIATIVE OFFICERS & BOARD OF DIRECTORS

Lynn Posluns
President & CEO, Women's Brain Health Initiative

Ken Aber
Founding Partner, Blueprint Business Architecture

Lisa Borsook
Executive Partner, WeirFoulds LLP

Dr. Vivien Brown
MDCM, CCFP, FCFP, NCMP, Vice President Medisys Health Group

Mark Girard
CFO, Cedarpoint Investments

Susan Hodkinson
COO, Crowe Soberman LLP

JoAnne Korten
Executive Director, Women's Brain Health Initiative

Mark Lash
Founder & President, Mark Lash

Ellen Rachlin (U.S.)
Managing Director, J.P. Morgan

Mark Raynes Roberts
Crystal Artist & Designer

Sarah Widmeyer
Director, Wealth Strategies Richardson GMP Limited

Confit Campari® and Salmon

SERVES 4 TIME: 45 MIN

INGREDIENTS

8 fresh garlic cloves
1/2 bunch fresh thyme
1/2 bunch fresh tarragon
2 lb salmon filet
16 SUNSET® Campari® tomatoes
1 Tbsp whole black peppercorns
Sea salt for seasoning

INSTRUCTIONS

1. Preheat oven to 225 F.

2. Place garlic and herbs in a loaf pan large enough to fit all ingredients, then add salmon to the centre of the pan. Place tomatoes around the salmon and sprinkle peppercorns around and on top of salmon. Put the pan on a baking tray and bake for 35 minutes.

3. Remove tray from oven and very gently move tomatoes directly to service platter using a slotted spoon. Using two spatulas, gently move salmon and herbs to platter. Drizzle a couple of tablespoons of the oil from the pan over the salmon, as it is infused with the flavor of all the herbs. Sprinkle with sea salt and serve hot.

salmon

A diet rich in fatty oils, such as Omega 3s found in salmon, can help prevent the progression of dementia.

MEMORY**MORSELS**®

A WOMEN'S BRAIN HEALTH INITIATIVE

This volume's recipes are brought to you by award-winning chef, cookbook author, and restaurateur as well as a celebrated Food Network and Cooking Channel personality, Roger Mooking Courtesy of SUNSET®.

For more recipes, morsels, and the latest from our Featured Foodie, Roger Mooking, visit memorymorsels.org.

Blistered Shazam!™ Shishito Peppers and Chili Lime Soy Sauce

SERVES 4 | TIME: 12 MIN

BLISTERED SHAZAM!™ SHISHITO PEPPERS

1 package SUNSET® Shazam!™ Shishito peppers
1/8 cup vegetable oil
1 tsp kosher salt

CHILI LIME SOY SAUCE

1 lime, zested
3 1/2 tbsp freshly squeezed lime juice
1 tsp finely chopped red finger or Thai chilies
4 tbsp low sodium soy sauce or tamari

INSTRUCTIONS

1. **Blistered Shazam!™ Shishito Peppers:** Preheat oven to broil.

Rinse, drain, and pat dry the peppers with clean towel or paper towel.

Place whole peppers evenly on a baking sheet. Pour vegetable oil over the peppers. Sprinkle with salt and mix until peppers are well coated.

Place baking sheet in the oven on the top rack under the broiler. Once you hear the peppers start popping, about 4 minutes, shake the tray and leave in the oven for another minute or so. Peppers will be blistered and lightly charred in spots. Remove the tray from the oven.

2. **Chili Lime Soy Sauce:** In a small bowl, mix all ingredients, then pour into a small service vessel.

Transfer to a serving plate and serve warm, making sure your guests know to discard the stems.

peppers

Packed with vitamins and minerals, these popular Japanese peppers help reduce inflammation and boost immunity.

Your diet is crucial to the maintenance of a healthy brain and functional independence as you get older. Memory Morsels® is a website dedicated to delicious, brain health recipes, brain health tips (our morsels), and great information to help keep your brain functioning the way you want.

EVOO

A significant source of Vitamins E and K to help keep your memory sharp.

Eggplant Pizzas

SERVES 4 | TIME: 50 MIN

INGREDIENTS

1 package SUNSET® baby eggplants, cut into 1/3 slices
1 tsp kosher salt
1 tbsp olive oil
1/2 tsp freshly ground black peppercorns
1/2 cup Angel Sweet® tomatoes, sliced
1/2 cup grated Mozzarella
1 cup basil dressing (visit sunset-grown.com for recipe)

INSTRUCTIONS

1. Preheat oven to 400 F.

2. Toss eggplant with salt and let stand for 10 minutes. Pat dry with paper towels.

3. Place eggplant on lined baking sheet and lightly brush both sides with olive oil and sprinkle with pepper.

4. Roast for 10 minutes, until eggplant is just cooked through. Remove from oven and turn on broiler.

5. Top with tomatoes and cheese.

6. Broil for about 2 minutes or until cheese is golden and bubbly.

7. Remove from heat and let stand for 5 minutes.

8. Dollop a small amount of basil dressing over each slice.

9. Garnish with additional basil leaves and sea salt.

JULY 2018 | PRESENTED BY RBC WEALTH MANAGEMENT | CITÉ | CHICAGO

THERE'S NO HEALTH WITHOUT BRAIN HEALTH

(L-R) Elizabeth Soto, Justin Ferdula, Dr. Pauline Maki, Dr. Yves Joanette, Angie O'Leary, Lynn Posluns, Stacie Herron, Tara Marszewski, Walter Chapman, Teresa Soppet

BRAIN BUZZ

Support for WBHI and women's brain health continues

AUGUST 2018 | HAUTE GOAT FARM

YOUNG PERSON'S CABINET

Back Row (L-R) Lyndsay McDonald, Tiffany Wanklin, JoAnne Korten, Vitina Blumenthal, Sandy MacKenzie, Lynn Posluns, Ken Aber, Shannon Gaudet
Front Row (L-R) Kathy Kelaidis, Leah Henderson, Nicole Roberts, Laura Best, Nazeefah Laher, Julia Hamer, Martin Reader
Behind the Lens: Mark Girard

APRIL 2018 | CO-HOSTED WITH AGE-WELL AT AUTODESK

MIND MATTERS

// WOMEN, TECHNOLOGY & HEART HEALTH

(L-R) Dr. Azadeh Yadollahi, Dr. Elizabeth Chertkow, Dr. Heather Ross

JUNE 2018 | CO-HOSTED WITH AGE-WELL AT AUTODESK

MIND MATTERS // WOMEN, TECHNOGY & PAIN

(L-R) Sarah Sheffe, Dr. Babak Taati, Mimi Lowi-Young, Lynn Posluns, Dr. Vivien Brown

MARCH 2018 | PRESENTED BY RBC | LOYALTYONE

ENGAGING MILLENNIAL MINDS // STRESS AT WORK

(L-R) Julia Hamer, Vitina Blumenthal, Dr. Ellen Choi, Matteo Tino

MAY 2018 | HOSTED BY SHAARE ZEDEK HOSPITAL

THE KURT & EDITH ROTHCHILD HUMANITARIAN AWARD PRESENTATION

Lynn Posluns, the Hon. Linda Frum

JUNE 2018 | PRESENTED BY RBC | VERITY CLUB

ENGAGING MILLENNIAL MINDS // SUGAR & BRAIN HEALTH

(L-R) Jessica Morris, Dr. Angela Assal, Samantha Goren, Dr. Elizabeth Chertkow

MAY 2018 | PRESENTED BY RBC | AT RBC

ENGAGING MILLENNIAL MINDS // YOUNG CAREGIVER

(L-R) Lynn Posluns, Matteo Tino, Kathryn Fudurich, Kelly Rivard, Julia Hamer, JoAnne Korten

WHY WE MATTER

Women's Brain Health Initiative (WBHI) is the only charitable organization solely dedicated to protecting the brain health of women.

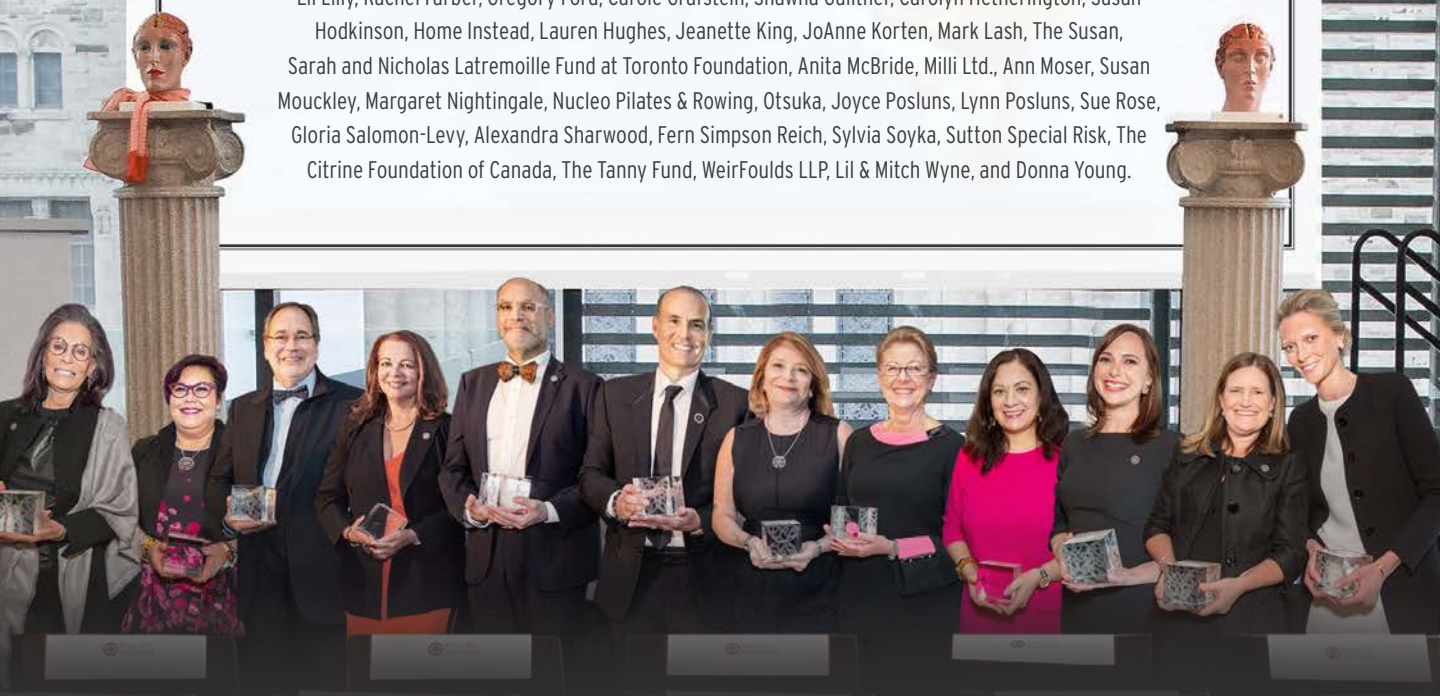
A Canadian and U.S. registered charity established in 2012, WBHI empowers women to help themselves and each other: by educating them on how to best protect their brain health as they age; by funding vital gender-based research; by providing access to the latest information to help maintain our cognitive vitality; and by highlighting the need for policies and care geared to women's unique requirements.

WE ARE TRULY GRATEFUL TO:

Brain Canada Foundation

And all those who generously supported this publication:

AGE-WELL, The Honourable W. David Angus, Sephi Band, Beverly Bushfield Harden Fund, Dave Blake, Lisa Borsook, Dr. Vivien Brown, C.M. Odette Philanthropic Foundation, Joy Cherry, Crowe Soberman, Eli Lilly, Rachel Farber, Gregory Ford, Carole Grafstein, Shawna Guiltner, Carolyn Hetherington, Susan Hodkinson, Home Instead, Lauren Hughes, Jeanette King, JoAnne Korten, Mark Lash, The Susan, Sarah and Nicholas Latremoille Fund at Toronto Foundation, Anita McBride, Milli Ltd., Ann Moser, Susan Mouckley, Margaret Nightingale, Nucleo Pilates & Rowing, Otsuka, Joyce Posluns, Lynn Posluns, Sue Rose, Gloria Salomon-Levy, Alexandra Sharwood, Fern Simpson Reich, Sylvia Soyka, Sutton Special Risk, The Citrine Foundation of Canada, The Tanny Fund, WeirFoulds LLP, Lil & Mitch Wyne, and Donna Young.



WBHI recently honoured those individuals who have made an outstanding effort to advance women's brain health and support the work that we've done since our launch in 2012. Each of these "catalysts" received a beautiful sculpture, designed by crystal artist and Board Member Mark Raynes Roberts – magnificently etched with our iconic Hope-Knot symbol.

L-R: Meryl Comer, Mary Michael, Dr. Yves Joanette, Lisa Borsook, Ken Aber, Mark Lash, Dr. Vivien Brown, Margaret Nightingale, Inez Jabalpurwala, Lyndsay McDonald, Lorraine Chan, Elizabeth Fisher (Absent: Heather Reisman, Sylvia Soyka)

Remembering Jacquie

As David Angus speaks about his daughter Jacquie, his otherwise sad memories are infused with glee, admiration, and occasional laughter. The obvious joy in his voice seems counterintuitive, given that she passed away five years ago after a tumultuous journey, but he is a father who both mourns the loss of his first-born child and celebrates her life.

"She was this very bubbly, blonde, blue-eyed vivacious little girl. We were so proud of Jacquie," he said in an interview with Mind Over Matter®.

Jacquie had struggled bravely with mental illness since her early childhood and when she died at the young age of 47, Mr. Angus harnessed his grief as a spur to action. He joined the board of Brain Canada, which is one of the key supporters of Women's Brain Health Initiative and Mind Over Matter®. As well, he decided to make an ongoing and substantial commitment to support mental health causes generally, as well as the mental health mission at the McGill University Health Centre (MUHC) in particular. He wanted to share Jacquie's story in the pages of this magazine, both to honour her memory and to spread awareness that mental illness must not be stigmatized and that individuals suffering from it need much more support.

"We decided that rather than being secretive, the best thing we could do was to speak out, because our society at all levels is so bad at understanding mental illness and supporting people and families who are afflicted."

Mr. Angus, a retired Senator and prominent Montreal lawyer, draws from his painful, first-hand experiences. He recalls Jacquie as a happy baby whose personality drastically changed after an illness at the age of one. She acted out through grade school and at age 16 was diagnosed with paranoid schizophrenia. Despite having key connections in the community, his family's search for guidance was endlessly frustrating in the 1960s and 70s. Mr. Angus and his family looked in vain across the country for appropriate facilities to help them manage Jacquie's illness and to provide her with an opportunity to live a relatively normal life.

"We had trouble dealing with the stigma surrounding young people and others with mental health issues and we found there was no well-structured or organized system in place to help or direct families trying to cope with such problems," Mr. Angus said. "We learned poignantly first hand that mental illness can and usually does wreak havoc in families and frequently tears them apart. It's not just the individuals afflicted who need therapy and support, but their loved ones as well."

Although in recent years society has become much more open about discussing mental health issues, Mr. Angus believes that we still fall far short.

"What I'm trying to get across is that even now, in 2018, our society and health care system have only minimal resources for people with these diseases. The mentally ill are a very important and significant segment of our society. Because mental illness generally has a kind of domino effect, creating big problems for many others besides the individuals directly afflicted, the cost and damage to society can be and usually is far more widespread than with other serious health issues like heart disease and cancer."

Mr. Angus recalls Jacquie constantly striving to overcome her diagnosed illness, describing her determination as both extraordinary and heart-warming.

"She was brilliant, when not dealing with psychosis. She was a Type A personality and it frustrated her greatly when these terrible mental swings took her over. She'd be hospitalized sometimes for more than six months at a time in very tough and scary facilities."

But she refused to give up. In her 40s, she managed to obtain a doctor's certificate allowing her to apply for a driver's license. Mr. Angus has a vivid memory of the look of joy on Jacquie's face when she was able to finally sit behind the wheel of a car – an act that is so mundane for most of us felt like winning the lottery for her.

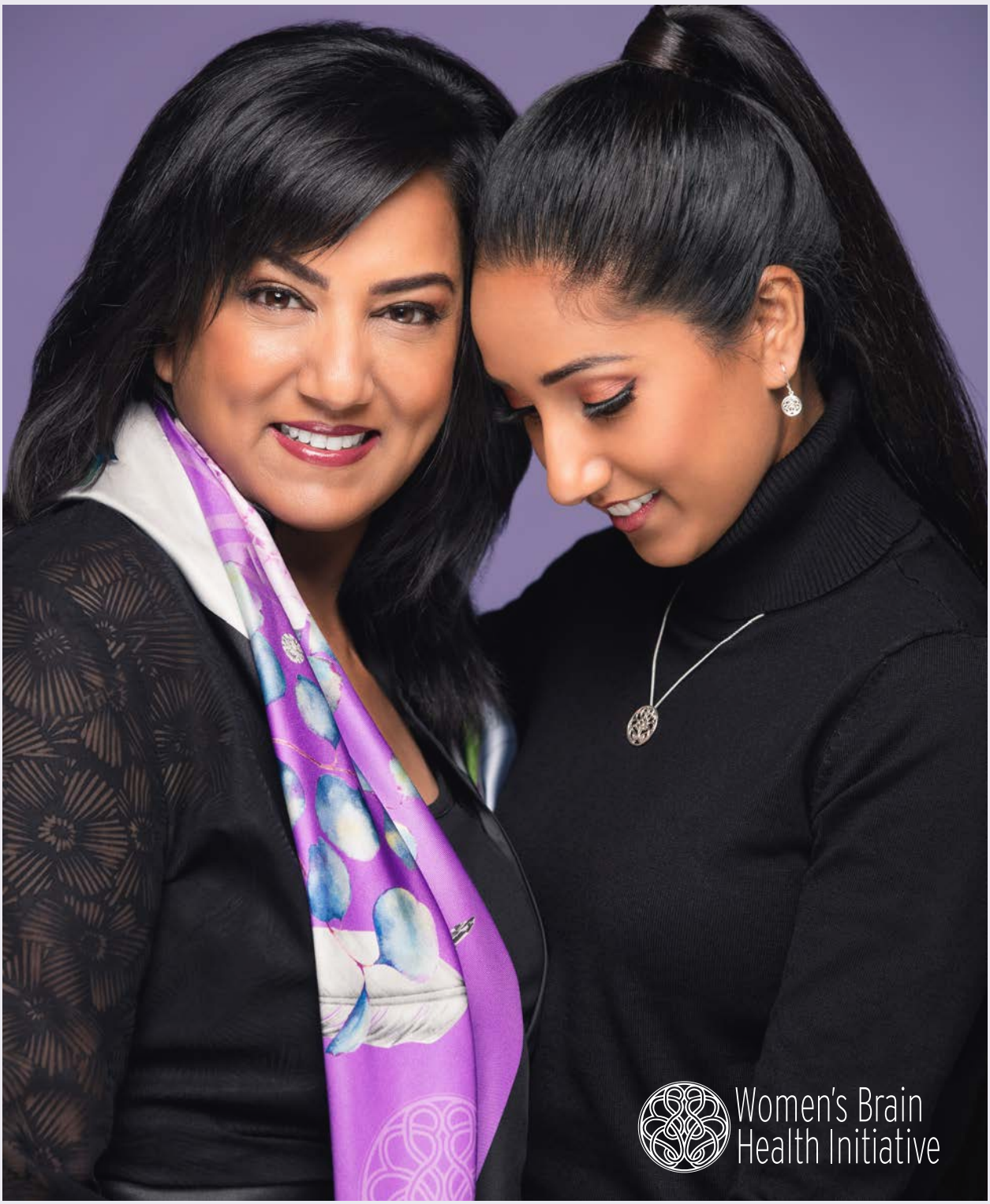
Jacquie took endless courses, trying hard to improve her résumé and qualify herself for useful employment. She craved independence, but her illness seemed to frustrate her aspirations at every turn. Mr. Angus recalls one of her valiant efforts working as a volunteer in the MGH Auxiliary cafeteria. "She proudly rose to the trusted position of cashier. She wore her three-year service pin as if it were the Order of Canada!" Mr. Angus said with a chuckle.

Having witnessed the abysmal state of care facilities and wishing to create a tangible tribute to his daughter, Mr. Angus made substantial donations to the Montreal General Hospital to modernize the psychiatric Intensive Care Unit and to assist in the creation of the Jacqueline G. Angus Mental Health Emergency Unit – a place where individuals in crisis can find specialized help in their time of need. A plaque with Jacquie's picture and story hangs on the wall of the unit.

He sees the mission of Women's Brain Health Initiative and the important messages of Mind Over Matter® as a natural fit for his promotion of mental health causes, particularly as they affect women.

"Women's issues are not always the same as the men's. They are severe and need appropriate support and hands-on treatment," he said, citing the example of postpartum depression. Mr. Angus says that fundraising for mental health causes remains challenging and therefore he feels compelled to contribute – both financially and through sharing his time and own experiences.

"I've been fortunate in my life and I believe in the principle of giving back and this is an area that came naturally to me because our family was so profoundly affected."



Give All the Women in Your Life the Gift of Brain Health.

SUPPORT THE INITIATIVE. WEAR A HOPE-KNOT.

hopeknot.org // 1.888.927.2011

Charitable No: 80099 3206 RR0001 | 501(c)(3) Tax-Exempt Organization