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MIND OVER MATTER®

HEALTH UPSHOTS OF VAPING

COGNITIVE BENEFITS OF CANNABIS

BRAIN HEALTH RESEARCH THAT BETTER MEETS WOMEN'S NEEDS

LIFELONG IMPACTS OF PREGNANCY ON YOUR BRAIN

DO GAMES GIVE YOUR BRAIN A BOOST?

CELEBRATE WOMEN'S BRAIN HEALTH DAY

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 10

BRAIN CANADA:
FUNDING BRILLIANCE DAILY

Brain Canada is a national, charitable organization that enables and supports brain research. Our vision is to understand the brain, in health and in illness, to improve lives and achieve societal impact. For two decades, Brain Canada has made the case for the brain as a single system with commonalities across neurological disorders, mental illnesses, and brain and spinal cord injuries. Looking at the brain as one system underscores the need for collaboration, and a smarter way to invest in brain research.

WE FUND BRILLIANCE DAILY

You will learn about a few of the brilliant minds we fund in this issue, the eighth we have sponsored through our partnership with Women's Brain Health Initiative.

In *Bear it in Mind* (p. 13), you will learn about **Dr. Paula Duarte-Guterman**'s research, which explores whether multiple pregnancies could increase the risk of Alzheimer's disease.

With *Sink Your Teeth Into It* (p. 25), **Dr. Brett Finlay** explains how diseases that involve the whole body can produce oral signs and symptoms. These, in turn, could play a role in cognitive function and dementia.

Finally, in *The First Step* (p. 29), **Dr. Ian Graham** highlights the role exercise can play in stroke recovery.

We fund brilliance daily because we believe that new ideas, tested through research, and leading to innovation and discovery, hold the promise of reducing the burden on Canada's health care system, improving productivity, and enhancing the health of individuals and our communities.

To find out more about our work and the research we are supporting, please visit **BRAINCANADA.CA**

Fondation
Brain Canada
Foundation

OUR IMPACT OVER 20 YEARS

$250M Invested in brain research

300 Grants awarded

1000+ Researchers funded

Funding in **115** Institutions across Canada

100+ Partners leading to a more collaborative and coordinated research ecosystem

367 Scientists from Canada and other countries have served as reviewers

Multidisciplinary team grants connecting **75+** disciplines

1,173 Publications in scientific journals

Over **90%** of funds go directly to research

EDITOR'S LETTER

I am so proud to welcome you to the tenth edition of Mind Over Matter®. As we go to press, we are all dealing with the extraordinary disruptions to our lives caused by the COVID-19 pandemic. I hope you are all keeping well, despite the health and economic challenges. It is a difficult and scary time, but as many have said, we are in this together and together we will get through it.

Because of the long deadlines in magazine production, the articles you will be reading in this edition were all prepared before the pandemic took hold. But it is all important information about an ever-growing health challenge that will in its own way have a profound impact on our lives.

Reaching this landmark has been quite a journey for Women's Brain Health Initiative (WBHI). In my editor's letter for our inaugural issue, I wrote about the important progress that WBHI had made since its official launch in 2013, citing "tremendous strides in raising awareness about the inequity in brain-aging research funding for women." Nine issues later, our relentless drive to educate and raise awareness is delivering tangible results on several fronts.

Let's start with the Canadian Consortium on Neurodegeneration in Aging (CCNA) – the largest initiative in dementia research ever undertaken in Canada. The CCNA brings together more than 350 researchers and clinicians across the country that have been assembled into 19 research teams under the broad categories of prevention, treatment, and quality of life. WBHI, along with our partner Brain Canada, now funds a "cross-cutting program" that requires each team to incorporate relevant sex and gender considerations into their research.

This is a crucial innovation – the importance of which cannot be overstated. The more we learn about how sex and gender influence health, the more we can improve the health and well-being of everyone. For far too long, the majority of research on brain-aging diseases focused primarily (if not entirely) on men, even though more than two-thirds of new Alzheimer's patients are women. Until very recently, most studies included male subjects exclusively (in both human and animal studies), which we now know has serious implications for women's health.

In this edition of Mind Over Matter®, we introduce you to some of the scientists who are working on the CCNA project – brilliant, committed people who are searching for answers to one of the most pressing health challenges. We give you a glimpse into their fascinating discoveries about the differences between the brains of women and men. With our involvement, Canada has quickly become a global leader in this previously-neglected aspect of research.

While we have made incredible progress, there is much more to be done. This past year, WBHI transformed December 2nd into a special day on the national health calendar – Women's Brain Health Day – so that every year more and more individuals and organizations can help raise funds and awareness for this important cause.

The first-ever Women's Brain Health Day was marked by thousands of people across the globe turning themselves upside down (literally) in a campaign that was both a fundraiser and an awareness-raising initiative.

The Stand Ahead™ Challenge called upon participants to perform a headstand in order to stand up against research bias and stand ahead for women's brain health. We were heartened to see so many people taking part in the challenge, sharing their gesture on social media, and encouraging others to do the same.

Our great partner and supporter Brain Canada helped bolster the campaign with an offer to match all of the donations that we raised for women's brain health research up to $250,000. I am elated to report that we exceeded our goal! Thanks to the generosity of so many supporters, we raised enough money to qualify for the full matching amount. That means a minimum of half a million dollars more for research into women's brains.

For all who took part, many of whom are faithful readers of Mind Over Matter® and WBHI supporters, I extend my deepest gratitude and appreciation. To learn more about the Stand Ahead™ Challenge, I invite you to visit standahead.org.

With the success of the first Women's Brain Health Day, I hope that next December 2nd many more individuals and organizations will be encouraged to support the cause. At WBHI, we are already exploring new ideas to celebrate the second Women's Brain Health Day. Look for more information in the next issue of Mind Over Matter®.

As always, the mandate of Mind Over Matter® is to bring our readers the latest news about scientific advances in brain research highlighting the unique risks for women, as well as to offer practical advice on how to protect our cognitive vitality. We're committed to doing this in a way that is both accessible and thought-provoking. It is a conversation that touches us all in one way or another.

Thank you for joining us on a journey that we hope will continue to make a difference. Please stay healthy and take care of yourselves.

PHOTO: JAYLYN TODD

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

THINK ABOUT IT

THINK TWICE

HELPFUL THINKING

BETTER THINKING

LOOKING FOR MORE COPIES?

mom@womensbrainhealth.org

CONTRIBUTORS

AMY CRYSTAL // 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 now shows that the earlier you protect your brain health, the better the cognitive outcome."

VITINA BLUMENTHAL // CREATIVE DIRECTOR

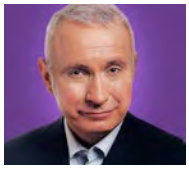
Vitina, founder of Align Creative Minds, is creative to her core with a passion for a healthy lifestyle (especially all things yoga), and sharing her love of mindfulness with others. Through WBHI's Young Person's Cabinet, she encourages millennials to start taking care of their mental and brain health.

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 magiazine 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 Narduzzi is a writer and editor living in Hamilton, Ontario. She has been interested in the benefits of a healthy lifestyle for twenty years. She studied gender dynamics while doing graduate work at McMaster University and is truly honoured to be using those skills 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, media trainer, and writer. Having seen close family members deal with dementia, he is a passionate supporter of WBHI's mission and is inspired by telling the stories of researchers who are expanding our knowledge of women's health. Sean's first book, *Falling for London: A Cautionary Tale* from Dundurn Press, is widely available across Canada, the U.S., and the U.K.

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."

ANNE-MARIE & MURIEL MEDIWAKE // ON THE FRONT COVER

Being in the public eye comes naturally to Anne-Marie Mediwake, the co-host of CTV's Your Morning program, but not as easily for her mother Muriel. So it was a rare treat for them to appear together on the cover of Mind Over Matter®. "I love the opportunity to be photographed with her. I'm proud of her. She's a role model," says Anne-Marie. Muriel described it as a privilege. "It's an honour. I'm very proud of Anne-Marie, and I'm very impressed with the magazine because it is raising awareness and helping women stay brain healthy longer."

COVER PHOTO: JAYLYN TODD

FULL THROTTLE

SEEKING THE IDEAL EXERCISE "PRESCRIPTION" FOR BRAIN HEALTH

Your risk of developing dementia is influenced by a combination of genetic, environmental, and lifestyle factors. While there is nothing you can do about the genetics that you are born with, and there are only certain environmental factors that you can change, you do have complete control over the lifestyle choices that you make. It can be quite empowering to realize just how much of an impact lifestyle factors (particularly physical activity) have on your cognitive function and dementia risk. ⟶

THERE IS A RAPIDLY GROWING BODY OF RESEARCH SUGGESTING THAT REGULAR PHYSICAL ACTIVITY AND/OR HIGH CARDIORESPIRATORY FITNESS LEVEL HELPS PREVENT COGNITIVE IMPAIRMENT AND LOWERS THE RISK OF DEMENTIA.

CARDIORESPIRATORY FITNESS refers to how well a person's heart, lungs, and muscles perform during sustained physical activity (i.e. how effectively the circulatory and respiratory systems deliver oxygen to the muscles). Exercise helps improve cardiorespiratory fitness.

In several studies, individuals with high cardiorespiratory fitness for their age have been found to have 36% to 88% lower risk of developing dementia compared to those who were unfit.

The findings from a study published in 2017 in *Journal of Alzheimer's Disease* emphasize just how great a role physical activity plays in reducing dementia risk. That study, involving over 1,600 Canadians followed over a five-year period, found that sedentary older adults who have no genetic risk factor for dementia (i.e. are not carriers of the APOE e4 gene variant) may be just as likely to develop dementia as individuals who are genetically predisposed to the disease (i.e. are carriers of APOE e4).

"Our research revealed that inactivity dramatically increases the risk of dementia among non-carriers of APOE e4, so much so that it appears to completely negate any protective effects of having healthy, low-risk genes," said Dr. Jennifer Heisz, an Assistant Professor at McMaster University and co-author of the study.

WHAT'S THE IDEAL EXERCISE "PRESCRIPTION" FOR YOUR BRAIN?

There is extensive research suggesting that exercise is good for your brain. But there are lots of different ways that a person can exercise. Is there an ideal exercise "prescription" for maintaining cognitive function and preventing dementia? At this point, it is not clear what exercise regimen is best for your brain.

Determining an ideal exercise prescription for brain health is challenging because the study of physical activity and its benefits is very complex. There are many potential variables to consider, including:

- **TYPE OF EXERCISE** – Is it better to engage in cardiovascular/aerobic exercise or strength training, or both? Is there a difference between various types of cardiovascular activities (e.g. walking/jogging, swimming, or cycling) or between different types of strength training?
- **LENGTH OF EACH EXERCISE SESSION** – How many minutes of exercise should one do each time?
- **FREQUENCY OF SESSIONS AND OVERALL DURATION** – How many times each week should one exercise? How many weeks or years does it take to have an impact? (Sometimes researchers will look at the effects of "acute" exercise, meaning they assess the impact of a single session of exercise, rather than a long-term program.)
- **INTENSITY** – How vigorously should you exercise?

Things are further complicated by elements of research design, which impact the strength of the results and how they can be interpreted. Do the researchers measure actual fitness level, or physical activity (and assume it is a reasonable indication of fitness)? Do they obtain their data about physical activity from self-reports by participants or from a device that directly measures movement? What measurement is used to determine fitness level or exercise intensity (e.g. heart rate or maximal oxygen uptake)?

EVEN THOUGH RESEARCHERS CANNOT YET POINT TO AN IDEAL EXERCISE PRESCRIPTION FOR BRAIN HEALTH, THERE IS A LOT THAT THEY HAVE DISCOVERED ALREADY.

Here are some highlights of what is known so far.

ALL TYPES OF MOVEMENT SEEM TO PROVIDE SOME LEVEL OF BRAIN BENEFIT

Many studies over the years have pointed to the brain benefits

APOLIPOPROTEIN E (APOE) is the gene most commonly associated with late-onset Alzheimer's disease (AD). One of its three types (or "alleles"), APOE e4, is linked with increased risk of AD.

of engaging in different types of exercise. For instance, various types of cardiovascular training and strength training appear to be beneficial. In past issues of Mind Over Matter®, we have covered the benefits of weight training (issue no. 4), dancing (issue no. 5), walking (issue no. 5), and even using balloons as a resistance training tool (issue no. 9).

All past issues of Mind Over Matter® can be read online at **https://womensbrainhealth.org/mind-over-matter-magazine.**

EVEN A SHORT EXERCISE SESSION OFFERS BENEFITS

Research has explored the benefits of exercise sessions of varying lengths.

> **ONE OF THE MOST IMPORTANT TAKEAWAY MESSAGES IS THAT EVEN SHORT EXERCISE SESSIONS CAN GIVE YOUR BRAIN A BOOST.**

Issue no. 7 of Mind Over Matter® contains an article about how just ten minutes of exercise a day can make a difference.

LOW-INTENSITY EXERCISE BENEFITS THE BRAIN

In issue no. 9 of Mind Over Matter®, we shared some exciting research findings that showed that low-intensity exercise can have a positive impact on the brain and cognitive function. This was particularly good news for older individuals or those with health or mobility challenges that make it difficult to follow the *Canadian Physical Activity Guidelines*, which currently recommend engaging in moderate- to vigorous-intensity exercise.

SOME RESEARCH SUGGESTS HIGH-INTENSITY IS BEST

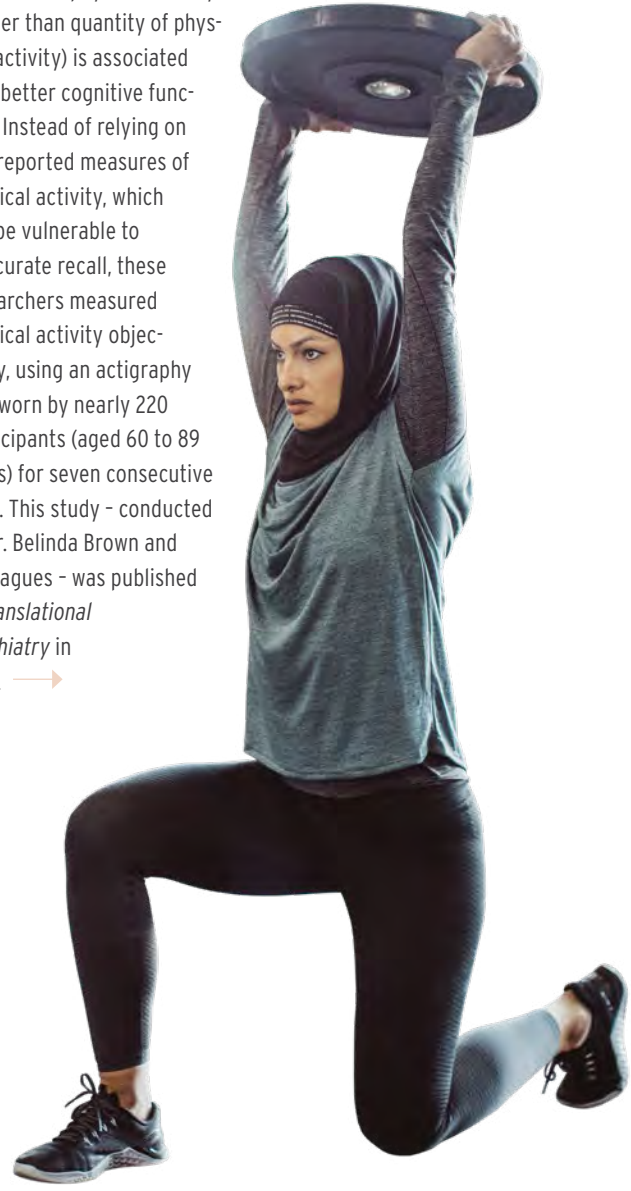
While it is valuable to know that small amounts of light-intensity exercise can be beneficial for your brain health, it is also important to realize that higher levels of intensity have been found to be beneficial too, and perhaps even more beneficial.

Some studies suggest that engaging in high-intensity exercise yields the greatest benefit for cognitive health, compared with low-intensity exercise. For example:

A study conducted by Dr. Maaike Angevaren and colleagues, published in December 2007 in *European Journal of Cardiovascular Prevention and Rehabilitation*, found that intensity of physical activity is related to cognitive function, while duration is not. Over 1,900 healthy women and men from the Netherlands (aged 45 to 70) took part in the study. Physical activity was assessed using an extensive questionnaire, and cognitive function was measured by a battery of neuropsychological tests.

IN PARTICULAR, HIGHER INTENSITY OF WEEKLY PHYSICAL ACTIVITY WAS FOUND TO BE ASSOCIATED WITH BETTER PROCESSING SPEED, MEMORY, AND MENTAL FLEXIBILITY, AS WELL AS OVERALL COGNITIVE FUNCTION.

A later study conducted by researchers in Australia also found that intense physical activity (rather than quantity of physical activity) is associated with better cognitive function. Instead of relying on self-reported measures of physical activity, which can be vulnerable to inaccurate recall, these researchers measured physical activity objectively, using an actigraphy unit worn by nearly 220 participants (aged 60 to 89 years) for seven consecutive days. This study – conducted by Dr. Belinda Brown and colleagues – was published in *Translational Psychiatry* in 2012.



More recently, researchers at McMaster University in Canada found that high-intensity aerobic exercise improves memory in older adults. For this study, which was published in October 2019 in *Applied Physiology, Nutrition, and Metabolism*, nearly 65 sedentary (but healthy) adults aged 60 to 88 were divided into one of the following three groups, each completing three sessions of their assigned type of movement every week for over 12 weeks:

1. the high-intensity interval training group, which participated in intense treadmill workouts that got heart rates up to 90% to 95% of maximum for short bursts of time, followed by short intervals of lower-intensity walking;

2. the moderate continuous training group, which participated in moderate-intensity walking on a treadmill, getting heart rates up to 70% to 75% of maximum; or

3. the control group, which engaged in gentle stretching exercises only.

"The high-intensity interval training led to the greatest improvement in memory, boosting performance by up to 30% on average, while participants in the other two groups saw no improvement," explained Dr. Heisz, co-author of the study. "Exercise intensity seemed to matter less for executive functioning, though, as we observed positive trends for executive functioning in both the high-intensity and moderate-intensity groups."

Recent research conducted in Germany has revealed that physical activity performed at a level intense enough to have a beneficial effect on the heart and improve cardiovascular fitness results in positive changes to the brain itself. Dr. Katharina Wittfeld and colleagues evaluated the cardiovascular fitness of over 2,100 participants aged 21 to 84 between 2008 and 2012, and examined their brains using magnetic resonance imaging (MRI) scans.

The researchers found that higher cardiovascular fitness was associated with larger brain volume in several brain regions.

THIS RESEARCH SUGGESTS THAT BY EXERCISING TO IMPROVE CARDIOVASCULAR FITNESS, YOU CAN POSSIBLY SLOW DOWN THE LOSS OF GREY MATTER VOLUME THAT HAPPENS WITH AGE OR DISEASE, THEREBY IMPROVING YOUR BRAIN HEALTH.

One of the particularly exciting findings in this research was that the effect of improving cardiorespiratory fitness appeared to be stronger in individuals aged 45 years and older, suggesting it may never be too late to improve your brain health through exercise. These findings were published in the January 2020 issue of *Mayo Clinic Proceedings*.

DON'T OVERDO THE INTENSITY, THOUGH

Keep in mind that it is possible to overdo it when it comes to intensity. A review conducted by Dr. Jennifer Norman and colleagues published in 2018 in *Current Pharmaceutical Design* explains that while exercise has been shown to have beneficial effects on brain health, there can be adverse effects if that exercise is extreme or too vigorous (e.g. exercising to exhaustion or at a level far too high for your current level of fitness).

PERHAPS MODERATION IS KEY

Some researchers have found that it is *moderate* physical activity that improves cognitive function. It is possible that the relationship between physical activity and cognitive performance can be represented by an inverted U-shape, meaning that there is a sweet spot in the mid-range for physical activity where cognitive performance reaches a peak, but that as exercise moves away from that mid-point in either direction – in other words, moving toward very high intensity or very low intensity – cognitive performance diminishes.

HOW INTENSELY SHOULD YOU EXERCISE?

Given the current uncertainty about what level of exercise intensity is best for your brain health, what should you do?

IT SEEMS CLEAR THAT MOVING YOUR BODY IN SOME WAY AT ANY LEVEL OF INTENSITY (OTHER THAN EXTREMELY HIGH) BENEFITS YOUR BRAIN AND COGNITIVE FUNCTION.

You therefore should aim to do what you can, knowing that engaging in even small amounts of light-intensity exercise is better than being sedentary. However, if your health and mobility allow it, you might want to choose more vigorous activities that get your heart pumping to potentially boost the brain benefits.

"Keep in mind that what counts as high-intensity will vary for each individual and will change over time as a person becomes more or less fit," explained Dr. Heisz. "Each person needs to choose exercise tailored to their current fitness level. And anyone starting a new fitness program or dramatically changing their exercise pattern should see their doctor first."

PURPLE HAZE

VAPING IS NOT A HARMLESS FAD

Use of vaping devices has grown rapidly in the past decade. While initially promoted as a smoking cessation aid for adults addicted to conventional cigarettes, vaping devices have become incredibly popular among young people, many of whom are attracted to their enticing flavours, alluring advertisements, and the belief that they are safer than cigarettes.

In a recent study, for example, researchers found that the number of Canadian participants aged 16 to 19 who reported vaping in the previous month increased by 74% in just one year (rising from 8.4% in 2017 to 14.6% in 2018). That same study – conducted by Dr. David Hammond and colleagues and published in 2019 in *BMJ* – found that 37% of Canadians aged 16 to 19 reported having tried vaping in 2018, compared to 29.3% in 2017. →

THIS TREND IS OF GREAT PUBLIC HEALTH CONCERN BECAUSE IT IS BECOMING INCREASINGLY CLEAR THAT VAPING IS NOT HARMLESS.

WHAT IS VAPING?

Vaping is the act of inhaling and exhaling an aerosol that is created when a liquid is heated up inside an e-cigarette or similar device. These devices come in varying shapes and designs, and include vape pens, vapes, mods, tanks, and other electronic nicotine delivery systems (ENDS). Recently, the e-cigarette brand JUUL has become so widespread among youth that "JUULing" is also used as a common verb for all e-cigarette use. Disposable devices (such as Puff Bars and Bidi Sticks) have also become very popular.

Typically, each device has a power source, a heating element, and a reservoir for the liquid. Yet, there are vastly differing appearances across devices. For example, some devices look similar to a conventional cigarette or a pen, while others look like a USB flash drive or a unique contraption, unlike any other everyday object.

The latest generations of e-cigarettes, including JUUL, use a specific type of nicotine called "nicotine salts" in their e-liquids. This newer form of nicotine allows for much higher concentrations of nicotine to be inhaled with less irritation to the throat. In essence, these newer products have figured out a way to increase nicotine levels in a palatable way.

The contents of vape liquids also vary substantially, but most contain a base of some kind – propylene glycol or glycerin – along with nicotine in different doses and flavourings. The liquids can also contain colourings, sweeteners, and other chemicals, some of which are considered toxic. Some e-liquids contain THC (tetrahydrocannabinol), the component of the cannabis plant responsible for its psychoactive effects (i.e. the "high"). This article focuses on the vaping of nicotine-containing products.

While e-liquids themselves have been found to contain over 60 chemical compounds, the aerosol created once the liquid is heated contains even more.

"Heating liquids in these vaping devices causes thermal decomposition and changes the e-liquid chemicals that some have said 'pose limited danger' into known toxicants," explained Dr. Ilona Jaspers, an inhalation toxicologist and Professor at University of North Carolina at Chapel Hill.

STUDIES HAVE FOUND THAT VAPE AEROSOL CAN CONTAIN VARIOUS CARCINOGENS, KNOWN RESPIRATORY IRRITANTS, AND VOLATILE ORGANIC COMPOUNDS (SUCH AS BENZENE, WHICH IS FOUND IN CAR EXHAUST FUMES), AS WELL AS HEAVY METALS SUCH AS CADMIUM, LEAD, NICKEL, TIN, AND COPPER.

"Because what chemicals and how much of them can be added to e-liquids is not regulated, it is impossible to clearly establish what people are actually inhaling. Furthermore, it's important to realize that just because something isn't in the base liquid doesn't mean that your lungs will not eventually be exposed to it," emphasized Dr. Jaspers.

WHAT DO WE KNOW ABOUT THE HEALTH IMPACTS OF VAPING?

Since vaping is a relatively new phenomenon, there is currently limited research on the direct and long-term health effects of inhaling propylene glycol or other ingredients in e-cigarettes, as well as the potential health consequences from second-hand exposure. However, a recent outbreak of "e-cigarette or vaping product use-associated lung injury" or "EVALI" demonstrates the negative impact of this habit on respiratory health. Researchers have found that these lung injuries resemble those seen after exposure to toxic chemical fumes, poisonous gases, and toxic agents.

As of November 2019, more than 2,000 cases of vaping-associated lung illness had been reported to the U.S. Centers for Disease Control and Prevention, including 39 confirmed deaths. Dr. Jaspers noted that

> **THE NUMBER OF CASES OF OTHERWISE HEALTHY YOUNG PEOPLE WHO HAVE BEEN HOSPITALIZED AND, IN SOME CASES, DIED FROM VAPING-ASSOCIATED LUNG INJURY IS ALARMING.**

Vaping has also been found in some studies to be associated with cardiovascular disease, oral disease, and increased carcinogenic potential. In addition, more than 100 seizures and other neurological problems linked to vaping have been reported to the U.S. Food and Drug Administration in the past decade.

HOW DOES NICOTINE AFFECT THE BRAIN?

Almost all vaping liquids contain nicotine, and the impact of nicotine on the brain has been studied quite extensively. Nicotine increases the release of acetylcholine neurotransmitters that suppress appetite, enhance pleasure, and help with relaxation. Low doses of nicotine have been found to temporarily boost cognitive function, including some aspects of attention and memory. These are some of the effects of nicotine consumption that may contribute to its initial appeal.

However, high doses of nicotine are associated with impaired memory consolidation, and nicotine abstinence after habitual use seems to impair cognitive function temporarily (i.e. when regular users stop using nicotine, they will experience short-term negative impacts on cognition during withdrawal).

It is important to note that chronic smoking of combustible cigarettes has been linked with decreased cognitive performance in middle age, as well as increased risk of cognitive decline and dementia in older age. These effects may be the result of exposure to nicotine and/or other components of regular cigarette smoke. At this point in time, though, it is unknown what the long-term effects of vaping are on cognitive function and dementia risk.

AMOUNT OF NICOTINE IN VAPING PRODUCTS

How much nicotine one is exposed to from vaping can vary widely depending on many factors, including how much nicotine is in the liquid, the type of nicotine, the type of device used and whether that device has been modified, and the intensity of inhaling. The amount of nicotine in e-cigarettes can reach or exceed that found in regular cigarettes.

It is also important to know that mislabeling of the nicotine content in e-liquid is common. Although some brands of vape products offer a zero-nicotine liquid option, many brands do not – including some of the most widely-used brands like JUUL.

YOUNG PEOPLE ARE PARTICULARLY VULNERABLE TO THE NEGATIVE EFFECTS OF NICOTINE ON THEIR BRAINS.

After reviewing the available research, the U.S. Surgeon General issued an advisory on e-cigarette use among youth in 2018, warning that "nicotine exposure during adolescence can harm the developing brain," negatively impacting learning, memory, and attention. Other risks from exposing developing brains to nicotine include addiction, mood disorders, and lower impulse control. →

While nicotine is a highly addictive substance for everyone, young individuals are particularly susceptible to developing an addiction to nicotine because of its effect on key receptors in their developing brains. (The brain continues to grow and develop until approximately the age of 25.) It also appears that nicotine can prime the adolescent brain for future addiction to other drugs.

IS VAPING SAFER THAN CIGARETTE SMOKING?

Because e-cigarettes do not expose users to the combustible "smoke" of regular cigarettes, it has been suggested that vaping might be safer than cigarette smoking. However,

E-CIGARETTE AEROSOL EXPOSES USERS TO DIFFERENT SUBSTANCES – SOME OF WHICH MAY BE AS BAD (OR EVEN WORSE) THAN WHAT IS CONTAINED IN REGULAR CIGARETTE "SMOKE."

Even though regular cigarettes and e-cigarettes do have some similarities – e.g. both are products one inhales and they commonly contain nicotine – they are very different in many ways and should not be compared, according to Dr. Jaspers. "E-cigarettes expose users to different chemicals, in a fundamentally different way," she explained. "With cigarettes, one inhales a mixture created by combusting tobacco plants and other chemicals within. Whereas, with e-cigarettes, one inhales an aerosol created from a liquid. By definition, these are very different exposures. Just as we would not compare smoking cigarettes to smoking crack, even though both involve inhaling, we should not compare vaping with smoking cigarettes."

RESEARCH TO DATE SUGGESTS THAT VAPING POSES UNIQUE HEALTH HARMS, SO COMPARISONS WITH REGULAR CIGARETTE SMOKING MAY BE IRRELEVANT.

"The recent outbreak of vaping-associated lung injuries proves the point that vaping is having a uniquely negative impact on health," said Dr. Jaspers.

"The symptoms doctors saw in these patients are not something that would ever be seen in someone who had been smoking cigarettes or marijuana for just a few months. Since doctors are seeing these severe diseases in vapers after relatively short exposures, does that make vaping more harmful than cigarettes? Are these effects truly linked to a single compound like Vitamin E acetate contained in bootlegged products, as some have suggested? More research is needed to answer these questions."

WHAT'S THE IMPACT OF SECOND-HAND EXPOSURE?

Although some e-cigarette manufacturers and retailers have claimed that what a person exhales after using an e-cigarette is "water-only vapor" that is harmless to others, there is actually more than just water being released into the air.

Some of the components that are contained in the aerosol as it is inhaled by the user can linger once it is exhaled, potentially exposing bystanders to nicotine, as well as the respiratory irritants, heavy metals, volatile organic compounds, and various cancer-causing chemicals. Exposure to second-hand vaping aerosol should be avoided, especially by vulnerable populations such as pregnant women and children.

VAPING MAY BE MORE HARMFUL THAN WE KNOW

There is still so much that is unknown about the health impacts of vaping, including its long-term effects. "It's likely that vaping has dangers that could take years for scientists to even know about," warned Dr. Jaspers.

> **IT TOOK DECADES FOR EPIDEMIOLOGISTS TO DISCOVER THAT CIGARETTE SMOKING CAUSED LUNG CANCER, FOR EXAMPLE, SO WE SHOULD BE CAREFUL NOT TO ASSUME THAT E-CIGARETTES DON'T HAVE HIDDEN DANGERS THAT MIGHT TAKE YEARS TO MANIFEST TOO.**

Research on vaping is challenging, in part because the devices and liquids keep evolving quite quickly.

As scientists continue to study the health effects of vaping, it is important to remember that the absence of *evidence* of harm is not the same as absence of harm. There is a lot that we do know already about the negative health impacts of vaping, so it would be wise to err on the side of caution and think twice about vaping, particularly if you are under the age of 25.

BEAR IT IN MIND

LIFELONG IMPACTS OF PREGNANCY ON A WOMAN'S BRAIN

Women are disproportionately affected by many brain disorders. For example, it is estimated that almost 70% of individuals diagnosed with Alzheimer's disease are women. Women's Brain Health Initiative and the Brain Canada Foundation have been advocating for the inclusion of women in research studies to help determine what is behind the sex differences in brain health and how that impacts potential treatment. Historically, research studies often included only male subjects, which kept research design and analysis less complicated. ⟶

THANKFULLY, THERE HAS BEEN AN INCREASING AWARENESS IN THE RESEARCH COMMUNITY OF THE IMPORTANCE OF STUDYING SEX DIFFERENCES, AND A CORRESPONDING INCREASE IN THE INCLUSION OF FEMALE SUBJECTS IN STUDIES.

However, in order to make substantial progress in the study of women's health, researchers need to go even further and consider variables among women. In other words, while we do need to study what makes women and men different, we also need to study differences *between* women. For example, research suggests that there are brain health differences between women based on variables related to pregnancy (e.g. whether a woman has had a pregnancy, how many children she has had, and her age when she gave birth).

Dramatic changes occur in a woman's body during pregnancy and into the postpartum, affecting her physiology (e.g. cardiac, immune, and metabolic function), as well as endocrinology (e.g. hormones). A woman's estradiol and progesterone levels, for example, rise by up to 300-fold during the 40 weeks of pregnancy. It is therefore not surprising that such changes have an impact on a woman's health – including her brain health – in the short-term.

BUT IT MAY BE SURPRISING TO SOME TO LEARN THAT PREGNANCY ALSO APPEARS TO HAVE LONG-TERM IMPACTS, AFFECTING THE BRAIN AND COGNITIVE FUNCTION INTO MIDDLE AGE AND BEYOND.

COGNITIVE PERFORMANCE DURING PREGNANCY AND POSTPARTUM

Many women notice cognitive changes during pregnancy, such as increased forgetfulness and distractibility, and difficulty thinking of words. But, are these subjective self-reports of change consistent with objectively-measured assessments of cognitive performance?

A recent review on the short- and long-term effects of pregnancy and motherhood on the brain was conducted by Dr. Duarte-Guterman and colleagues and published in 2019 in *Frontiers in Neuroendocrinology*. Dr. Paula Duarte-Guterman received a 2017 Alzheimer's Association Research Fellowship, co-funded by the Brain Canada Foundation and Alzheimer's Association, to explore the impact of pregnancy and motherhood on the brain to better understand the short- and long-term effects on cognition and brain health, including Alzheimer's disease.

"Research findings have varied somewhat from study to study, but the latest meta-analyses on human cognition during pregnancy suggest that pregnant women do experience small, but significant, deficits in some aspects of cognitive function, namely, free recall, delayed free recall, working memory, and executive function," said Dr. Duarte-Guterman, a postdoctoral research fellow in the laboratory of Dr. Liisa Galea at the University of British Columbia. "Interestingly, one aspect of memory – recognition memory – was found to improve slightly during pregnancy."

What happens to a woman's cognitive function in the postpartum period, after the baby is born? "Although research is more limited on this subject, the available evidence suggests cognitive deficits may be experienced in the early postpartum that are similar to what is experienced during pregnancy," said Brain Canada-funded Dr. Duarte-Guterman. "In recent studies, the evidence suggests that in the period two to six months postpartum, executive function is enhanced in mothers compared to non-mothers."

THERE ARE SOME SURPRISING VARIABLES THAT SEEM TO AFFECT COGNITIVE PERFORMANCE DURING PREGNANCY AND POSTPARTUM, WHICH MAY ACCOUNT FOR DIFFERENCES IN COGNITIVE FUNCTION AMONG PREGNANT WOMEN.

For example:

- A study conducted by Dr. Claire Vanston and Dr. Neil Watson published in *NeuroReport* in 2005 found that the **sex of the fetus** was unrelated to maternal performance on several cognitive tests, but on difficult tests of working memory and spatial ability, "women pregnant with boys consistently outperformed women pregnant with girls." In this study, participants' cognitive performance was tracked from early pregnancy through to resumption of menstruation post-birth.

- In a study involving 254 women, Dr. Laura Glynn investigated if **parity** affects verbal recall memory performance during pregnancy and at three months postpartum. She found that the adverse effects of pregnancy on memory reported in previous studies were compounded with successive pregnancies. In other words, increasing parity was linked to cumulative negative effects on

PARITY refers to the number of pregnancies a woman has experienced to 20 weeks or more of gestation, whether the baby was born alive or stillborn.

memory. These findings were published in October 2012 in *Journal of Women's Health*.

Psychiatric symptoms, such as depression and anxiety, experienced during pregnancy may impact cognitive function. Research conducted by Dr. Eeva Leena Kataja and colleagues, and published in August 2017 in *Journal of Affective Disorders*, found that pregnant women experiencing a high or moderate level of psychiatric symptoms made significantly more visuospatial working memory errors compared to mothers with low levels of symptoms.

Together, the evidence collected to date in human studies suggests that "the effects of pregnancy on cognitive function may be subtle, but can be more pronounced in certain groups of women, including those experiencing depression and anxiety, those who have given birth before, and those who are carrying a female fetus," summarized Dr. Duarte-Guterman.

CHANGES IN BRAIN VOLUME DURING PREGNANCY AND POSTPARTUM

Not only does a woman's cognitive function change during pregnancy and the postpartum period, but the brain itself also physically changes.

Research conducted by Dr. Angela Oatridge and colleagues, published in 2002 in *American Journal of Neuroradiology*, found that a woman's total brain volume decreases during pregnancy, reaching its smallest size at the time of childbirth and rebounding in size by six months after delivery. Later studies conducted by various researchers found that the changes in brain volume during postpartum differed depending on which brain structure was imaged.

For example, Dr. Pilyoung Kim and colleagues found that grey matter volume increased in areas involved in maternal behaviours and motivation – such as the amygdala, hypothalamus, and prefrontal cortex – during the first three to four months postpartum versus the first two to four weeks postpartum. These findings were published in 2010 in *Behavioral Neuroscience*.

Yet, when Dr. Elseline Hoekzema and colleagues compared brain images of women pre-conception versus postpartum, they found reductions in grey matter volumes in multiple areas postpartum, including the hippocampus. Additionally, most of the grey matter reductions noted at two months postpartum were still present two years after birth. These findings were published in 2016 in *Nature Neuroscience*.

> **SOME PARTS OF THE BRAIN SHRINK AND OTHERS ENLARGE, AT VARIOUS POINTS DURING PREGNANCY, EARLY POSTPARTUM AND BEYOND.**

"The effects of pregnancy on brain matter volume remain understudied, but it is evident that the impacts are time- and brain region-dependent," observed Dr. Duarte-Guterman.

PREGNANCY'S LONG-TERM EFFECTS ON COGNITIVE PERFORMANCE

Research findings about the effect of pregnancy on cognitive performance later in life are inconsistent. Nulliparity (i.e. no pregnancies experienced beyond 20 weeks of gestation) and lower parity are associated with better cognitive function in later adulthood in some studies, but not in others.

The number of pregnancies experienced is not the only variable involved, though. There are other factors related to reproductive history and endogenous estrogens that appear to impact cognition over the long-term, including length of reproductive period (i.e. number of reproductive years), age at first and last pregnancy, and duration of breastfeeding.

A study of nearly 1,000 French women aged 65 and older conducted by Dr. Joanne Ryan and colleagues revealed that having a first child at a young age was associated with worse global cognitive performance and verbal fluency in later life. That same study also found that a higher number of reproductive years (i.e. more time between first menstruation and menopause) was associated with better verbal fluency. These findings were published in February 2009 in *Psychoneuroendocrinology*.

Another study of older women involving 830 naturally menopausal women was conducted by Dr. Roksana Karim and colleagues. The researchers found, amongst other things, that having a baby later in life had a positive effect on cognitive function. Having a last pregnancy after the age of 35 was positively linked with verbal memory later in life. These findings were shared in the November 2016 issue of *Journal of the American Geriatrics Society*.

"Multiple studies of older women have found that measures of higher endogenous estrogens – such as lower parity, longer reproductive period, and shorter breastfeeding period – are associated with better cognitive performance," said Dr. Duarte-Guterman. "In other words, women who experience higher lifetime exposure to endogenous estrogens, regardless of what variable provided that →

ENDOGENOUS hormones are those produced by the body.

EXOGENOUS hormones come from external sources (e.g. from oral contraceptives or hormone replacement therapy).

higher exposure, seem to enjoy better cognitive function later in life. Estrogens appear to be neuroprotective."

REPRODUCTIVE HISTORY AND LONG-TERM RISK OF BRAIN DISORDERS

Numerous studies have examined the impact of parity on the risk of brain disorders. "In our review, we found studies that showed amount of parity is positively associated with an increased risk of Alzheimer's disease," said Dr. Duarte-Guterman. "Grand multiparity – sometimes defined as having three or more children, sometimes five or more – has been linked to an increased risk of developing Alzheimer's disease."

Research has also found higher parity is associated with increased levels of hallmark changes in the brain associated with Alzheimer's disease, as well as earlier onset of the disease.

"It's important to note, though, that not all studies have found links between parity and increased risk of Alzheimer's disease," emphasized Dr. Duarte-Guterman. "It's possible that genetics play a role, interacting with parity to influence risk of Alzheimer's and timing of onset. This is something that I am currently investigating as part of a study funded by Brain Canada." For more information about Dr. Duarte-Guterman's research, visit: **https://braincanada.ca/research-stories/the-effect-of-pregnancy-on-brain-aging-in-women/**.

LOOKING AHEAD

The more we know about the differences between women – whether due to differences in reproductive history, genetics, or other variables – the better. Findings from research like that conducted by Dr. Duarte-Guterman and others have important implications for the development of treatments. It is possible that unique treatments will be needed for various subsets of women as they may have varied responses depending on their unique health history and genetics.

"Further research is needed to unravel the specifics of what makes women unique from men, what makes women who've experienced pregnancy different from women who have not, and how to apply that knowledge to the development of treatments," said Dr. Duarte-Guterman. "I'm very pleased to be a part of this important area of ongoing research."

LEVELLING THE FIELD

Among Equals

Sex & Gender Neurodegenerative Disease Research

Proof of the changing times in Canadian scientific research can now be found at the highest levels of government, set out in black and white on the Prime Minister's letterhead.

In Justin Trudeau's mandate letter to the Minister of Health, Patty Hajdu, dated December 13, 2019, Ms. Hajdu was mandated to work with her colleagues and, through established legislative, regulatory, and cabinet processes, deliver on top priorities, including working with the Canadian Institutes of Health Research (CIHR) to "integrate sex- and gender-based analyses, as well as diversity analyses, to ensure research takes diversity factors into account to improve women's health care."

This particular mandate may not have drawn much attention in the mass media's post-election analysis, but it was most certainly noticed and championed by Dr. Cara Tannenbaum, the Scientific Director of the CIHR Institute of Gender and Health. CIHR is the largest funder of health research in Canada, and is a key partner with the Canadian Consortium on Neurodegeneration in Aging (CCNA) – a multifaceted national research effort involving more than 350 researchers and clinicians who are studying age-related neurodegenerative diseases, including Alzheimer's disease and other types of dementia.

"The government recognizes that CCNA's integration of sex and gender needs to become the norm and gold standard for everyone else conducting health research in Canada. I'd call that a win," said Dr. Tannenbaum in an interview with Mind Over Matter®.

There are 19 different research teams within the CCNA that are exploring diverse aspects of dementia under the themes of prevention, treatment, and quality of life. But there is also a cross-cutting program of Women, Sex, Gender and Dementia (WSGD) that works with all research teams, advising and collaborating to ensure the proper integration of relevant sex and gender considerations into their studies.

Importantly, CIHR now requires all grant applicants to describe how sex and/or gender considerations are incorporated into their research, and, within the CCNA, Women's Brain Health Initiative (WBHI) initiated and is funding the WSGD program to help CCNA researchers do just that. Brain Canada is also a major funder.

"It's sort of like a business pitch. If you want to get funded, you have to think of a way to do this. CCNA was the first research consortium to apply such an approach in Canada. It was actually quite novel. The sex and gender strategy was embedded at the very core of the CCNA from its planning stage back in 2014," explained Dr. Tannenbaum.

> **"THERE WAS UPFRONT ACCOUNTABILITY FOR MAKING SURE THAT WOMEN AND FEMALE BIOLOGY WOULD NOT BE IGNORED IN THE RESEARCH."** ⟶

Dr. Howard Chertkow, Scientific Director for the CCNA, told Mind Over Matter® that when the project was first launched, the researchers who were incorporating sex and/or gender considerations in their studies were in the minority, but now most researchers are on board.

"It was impossible to just pay lip service; you really had to be thinking about it. Consequently, everyone is looking at sex differences much more than previously," said Dr. Chertkow, who is also the Chair in Cognitive Neurology and Innovation at the Rotman Research Institute, as well as the Director of both the Clinical Trials Unit and the Kimel Family Centre for Brain Health and Wellness at Baycrest in Toronto.

"It's proving to be very important. When you start looking you find all sorts of stuff. But the first step is getting them to look." He credits the influence of both CIHR and WBHI.

"Lynn Posluns [the Founder and President of WBHI] is an important, additional voice in sex and gender playing a significant role. We have these two voices to encourage us to do the right thing, which we would have hopefully done anyway," said Dr. Chertkow.

Dr. Gillian Einstein of the University of Toronto contributed to the WSGD program in its first phase, and has been the Lead of the WSGD in its second phase for the past year.

DR. EINSTEIN SAYS THAT SHE HAS WITNESSED A GROWING INTEREST IN SEX AND GENDER CONSIDERATIONS AMONG RESEARCHERS.

"There are still some people who need to be convinced or helped on how they could do it. But the spirit is willing, whereas earlier on it took more convincing," she said to Mind Over Matter®. It is a field of study Dr. Einstein knows intimately, as she currently holds the Wilfred and Joyce Posluns Chair in Women's Brain Health and Aging – the first Chair of its kind in the world, which seeks to enhance women's brain health through the study of cognitive aging and associated disorders.

She says that the CCNA collaboration is already benefitting her research, particularly as her team can access data from the largest study of its kind ever launched in Canada: the Comprehensive Assessment of Neurodegeneration and Dementia (COMPASS-ND). CCNA researchers are currently in the process of recruiting more than 3,200 older adults, including individuals who show no signs of illness, as well as those with a wide array of neurodegenerative diseases (such as Alzheimer's disease, Parkinson's disease, and vascular dementia).

Among the data being collected are important elements in sex and gender studies, including hormone levels in the blood and the history of each participant – for example, the number of children that a female participant has had, whether her ovaries have been removed, and whether she was ever subject to sexual and/or verbal abuse.

"So we've really tried to gear the collection toward a lot of the kind of details that one would need to have to really understand the background upon which women might have mild cognitive impairment or Alzheimer's," said Dr. Einstein.

She says that her role in overseeing the WSGD cross-cutting theme is to support all of the teams with suggestions, and in some cases funding, to assist their research.

EACH OF THE 19 TEAMS HAS A "SEX AND GENDER CHAMPION" – A RESEARCHER WHO IS RESPONSIBLE FOR PROMOTING AND INTEGRATING SEX AND GENDER CONSIDERATIONS THROUGHOUT THE LIFETIME OF THE RESEARCH PROJECT.

Each Champion possesses (or acquires) expertise in the study of sex as a biological variable and/or gender as a social determinant of health, and takes on the role of an educator, mentor, consultant, facilitator, advocate, co-investigator, or principal applicant.

Dr. Einstein and the Champions participate in a conference call bi-monthly to discuss the progress of research, review relevant papers on sex and gender, review their own teams' manuscripts for sex and gender considerations, and collectively form what she calls a "community of practice" to develop the best approaches.

Dr. Tannenbaum says, because this is a relatively new field of research, there is still work to do in improving best practices. Scientists need consistency and clarity in how they gather, interpret, and report data on sex and gender differences.

"[Following] best practices means that if the research shows a difference between men and women, then the next step is to ask why. It's that 'why' which is really the key to discovery," explained Dr. Tannenbaum.

Other countries are now looking to the Canadian model and are beginning to emulate it. "I'm extremely encouraged by the progress," said Dr. Tannenbaum. "The CCNA is setting an example for all other research that we're doing in Canada. We've developed a successful model that's bearing fruit. You know you're a successful leader when others want to follow you."

Dr. Howard Chertkow points to this as one of the greatest achievements of the consortium. "We're very proud of it, proud that we're sort of ahead of the wave, so to speak. There haven't been many national efforts in any area of medicine which have put sex and gender front and centre of the whole enterprise."

LEVELLING THE FIELD

An Ounce of Prevention

Sex & Gender Differences in Alzheimer's Prevention Research

When she was a graduate student some decades ago, Dr. Margaret Fahnestock was told that scientific research involving female subjects was challenging. The rationale was that a woman's hormonal cycle would ruin or interfere with the data in biochemical studies. That was then. Thankfully, attitudes have changed – albeit slowly – over time. Exploring sex and gender differences in the brain is now at the heart of her work on dementia, as part of a team supported by the Canadian Consortium on Neurodegeneration in Aging (CCNA).

Dr. Fahnestock, a Professor of Molecular Neuroscience at McMaster University, observed firsthand just how much things have changed when she attended a conference last year of the Organization for the Study of Sex Differences (OSSD) in Washington, DC. The OSSD was founded by scientists from the Society for Women's Health Research, whose mission is to eliminate imbalances in health care for women.

She listened to dozens of speakers discuss how researchers have focused for far too long on only male subjects, and how that, in turn, resulted in the scientific community not knowing as much as it should about women. "And this turns out to be really bad for medicine because there have been instances where women were given inappropriate treatments because they were prescribed drugs that we knew worked in males, but didn't know if they worked at all that way in females."

For Dr. Fahnestock, the OSSD conference was truly an eye-opener, as she heard many colleagues speak about their latest discoveries in a long-neglected field.

"I WAS ABSOLUTELY AMAZED TO HEAR THAT THERE ARE DIFFERENCES EVERYWHERE THROUGHOUT THE BODY IN HOW MALES AND FEMALES FUNCTION, NOT JUST IN THE BRAIN, BUT THERE HAVE BEEN NO EFFORTS UNTIL RECENTLY TO STUDY FEMALES AT ALL. WE'RE MISSING HALF THE POPULATION."

Dr. Fahnestock's graduate school teachings about the alleged challenges of studying female participants were thoroughly debunked. "Studying females is not nearly so difficult," she said. In fact, she spends her days examining the brain molecules of both women and men, finding important differences.

Her subgroup of researchers in the CCNA effort is working on the theme of prevention, with the goal of developing a greater understanding of the molecular and cellular basis of memory loss in diseases such as Alzheimer's. Exploring the differences between women and men is central not only to her work, but also is a "cross-cutting" theme across CCNA projects, which means that while each team may be investigating different aspects of dementia, all are encouraged to include relevant considerations of sex and/or gender. Both Women's Brain Health Initiative (WBHI) and Brain Canada are providing funding for this aspect of the work, which carries the official title of the Women, Sex, Gender and Dementia (WSGD) Program.

Dr. Fahnestock and her colleagues are studying particular neurons in the brain that are necessary for learning and memory, which are the same neurons that degenerate and lose contact with each other in the early stages of Alzheimer's disease. "My work is of a fundamental nature. A necessary precondition to finding a good way to →

prevent a disease is to understand it," she said. Some of the most novel findings have come through examining a particular type of mice called "triple transgenic" or "3xTg", whose brains mirror what is often found in humans with Alzheimer's disease. In particular, these mice possess amyloid beta plaques (deposits that appear as spots on images of the brain), as well as tangles within brain cells.

Her colleague at McMaster University, neuroimmunologist Dr. Boris Sakic, noted that the 3xTg mice also have a severe autoimmune dysfunction. In autoimmune diseases, the immune system mistakenly attacks the body instead of protecting against harmful agents. Dr. Sakic observed that there was a notable difference between the male and female mice. In particular,

> **THE FEMALE MICE HAD A LOWER SEVERITY OF THE AUTOIMMUNE DISEASE, BUT A GREATER PREVALENCE OF PLAQUES AND TANGLES IN THE BRAIN.**

While the autoimmune dysfunction affected the males more significantly, with greatly enlarged spleens, they had fewer plaques and tangles.

Dr. Sakic developed a hypothesis that autoimmunity could be protective – in other words, if the mice have more autoimmunity, they have fewer of the plaques and tangles associated with Alzheimer's disease. But it was more complicated. Although the male mice had fewer plaques and tangles, they actually performed worse than the females on learning and memory tests.

"So we have a big puzzle with these mice to try to figure out what's going on," said Dr. Fahnestock. Her team is now running tests to try to determine whether it is autoimmunity that is causing the differences between female and male mouse brains or whether it is sex hormones.

The findings speak to the evolving nature of Alzheimer's research. For decades, scientists focused on plaques and tangles, developing drugs that could eliminate them in the hope that it could be a successful treatment option. However, clinical drug trials over the past few years have failed and the search for a cure remains elusive.

"That's the short form of the history of why we've been so unsuccessful at curing Alzheimer's disease," Dr. Fahnestock explained. "It's not really clear how plaques and tangles fit into the memory loss. They contribute for sure. But I've studied postmortem brains of people that have lots and lots of plaques, but when they died they were sharp as a tack. There was no memory loss at all."

Researchers are now branching out and exploring other potential factors. Immune dysfunction is one of them, and Dr. Fahnestock's team is using the male-female difference to try to develop a better understanding of how the immune system interacts with the brain. "So far, we're coming up with more puzzles than answers. That's not unusual. Research always leads to more questions. That's why it's such a fun field to be in. I'm never going to be out of business!"

Another CCNA research team within the prevention group, led by Guylaine Ferland, a Professor in the Department of Nutrition at the Université de Montréal, is exploring topics that are frequently discussed both within and outside of the scientific community: nutrition, exercise, and lifestyle.

> **"THERE IS ALREADY MUCH RESEARCH INDICATING THAT DIET CAN PLAY A ROLE IN PRESERVING BRAIN HEALTH."**

There is now a Brain Health Food Guide, co-authored by Dr. Carol Greenwood and Dr. Matthew Parrott, that was unveiled in 2017 at Baycrest Health Sciences in Toronto. Inspired by the Mediterranean diet, the guide encourages the consumption of berries, leafy green vegetables, and nuts, while avoiding highly-processed meat and baked goods.

Dr. Ferland and her team have conducted an exhaustive survey of the existing literature and focused on a group of nearly 1,800 study volunteers from Quebec known as the NuAge (for nutrition and age) cohort. The NuAge group was comprised of healthy individuals between the ages of 67 and 84. Starting in 2003, the researchers tracked the participants for a number of years in order to gain a better understanding of the effects of nutrition and aging. Although the focus of the initial study was not cognition, Dr. Ferland's team is mining the data in search of new insights, including a greater understanding of sex and gender differences.

Her colleague, Dr. Alexandra Fiocco of Ryerson University, is in the final stages of preparing a research paper that analyzes sex, gender, nutrition, and cognition. While Dr. Ferland noted that it is too early to speak publicly about the conclusions, Dr. Fiocco's paper promises to be an important addition to our knowledge, because this is an understudied field. "There's virtually nothing with respect to brain health and that's what we plan to address as part of our team," said Dr. Ferland.

They are currently in the process of recruiting a new group of study volunteers in Toronto for the next stage of their research. Titled LEAD (lifestyle, exercise, and diet), the project will focus on individuals between the ages of 60 and 85 who are experiencing at least two of three health challenges (namely, high blood pressure, high cholesterol, and diabetes), and who are noticing their memories are deteriorating.

The participants will be divided into two groups: one will be given general dietary advice and the other who will receive more specific information about the Brain Health diet. Every participant will be put on an exercise program. The researchers will examine the participants over a period of six months and will look not only for differences between the two test groups, but also between male and female subjects. "It's something we will incorporate in our future analyses as much as possible because it's really important from a public health view," said Dr. Ferland.

LEVELLING THE FIELD

Equitable Remedy

Sex & Gender Differences in Alzheimer's Treatment Research

It seems to be one of the inescapable realities of getting older – more things start to go wrong with your body. There are many diseases of aging and several are interconnected. For instance, if you live long enough, there is a strong chance that you will develop high blood pressure, which also happens to be a contributing risk factor for dementia. Researchers are exploring those relationships, hoping that they can further our understanding of each disease, as well as the best course of treatment.

A 2019 Statistics Canada study estimated that approximately 90% of Canadians will suffer from hypertension at some point, often developing it in midlife. As with many diseases, high blood pressure affects the sexes differently, with the study finding that men suffer from high blood pressure at a higher rate than women.

The elevated risks of developing dementia are similar for both sexes, but there are outstanding questions regarding the differing impacts of drug therapies. This is a key element of a research study led by Dr. JoAnne McLaurin, a senior scientist at Toronto's Sunnybrook Health Sciences Centre.

> **"WHAT WE'RE TRYING TO DO IS UNDERSTAND WHAT MIDLIFE HYPERTENSION DOES TO THE BRAIN AND WHY THAT MIGHT HEIGHTEN THE RISK OF DEMENTIA, INCLUDING AN EXPLORATION OF THE EFFECT OF DRUGS."**

Dr. McLaurin explained that even though hypertension can be successfully treated with drugs, the risk of developing dementia remains elevated even if the individual's blood pressure returns to normal. It remains unclear as to why this is the case, and there is minimal understanding about what the various medications do to our brains. "There's a plethora of drugs out there to treat hypertension, but no one thought to check what the effects might be on the brain," she said.

Her team has already made some interesting observations, such as discovering that female lab rats are more sensitive to hypertension drugs than their male counterparts – a revelation that forced the researchers to reduce the dosages for the females by 30%. Dr. McLaurin and her team cannot yet explain the reason for the difference between the sexes, partly due to the fact that most →

of the research conducted to date involved male rats exclusively, and nothing in the literature suggested that the sexes would react differently. "There are lots of possibilities. It was a big surprise."

Dr. McLaurin will not speculate on whether there might be a similar effect on human beings. There is a huge variability among individuals, not only between women and men, but also among the variety of hypertension drugs consumed. Some of the medications work well for some and not for others.

DR. MCLAURIN AND HER COLLEAGUES ARE NOW EXPLORING WHETHER DIFFERENT HYPERTENSION MEDICATIONS HAVE DIFFERENT IMPACTS ON FEMALES AND MALES.

The research could inform treatment of high blood pressure, as well as enhance our understanding of its link with dementia. The results of their work could ultimately affect drug policies. "Which drug candidates would be the ones to choose to help your brain, while also treating hypertension? Maybe none of them do, or do a bit or not enough," said Dr. McLaurin. That is just one thread of a research effort that is revealing a variety of differences between the sexes.

Her colleague, Dr. Shawn Whitehead of Western University, has demonstrated that hypertension has varying effects on the brains of female and male rats. In particular, it appears that the females have more damage to white matter, which is the insulation that covers your nerves to assist your neurons in communicating with each other more efficiently – an essential brain function. "This is significant," said Dr. McLaurin.

Dr. McLaurin's team is also exploring another risk factor for dementia: covert strokes. This type of stroke occurs when a small blood vessel in the brain is permanently blocked. Although cells around the affected area die, a covert stroke causes no obvious immediate physical damage and does not affect muscle or motor skills. However, covert strokes do real damage to the brain, weakening the connections necessary for executive functions such as memory, navigation, planning, decision-making, and reasoning. Having a stroke more than doubles the risk of developing dementia. Covert strokes are responsible for at least one-third of all dementia, according to the Heart and Stroke Foundation.

AFTER MENOPAUSE, WOMEN ARE MORE PRONE TO COVERT STROKES THAN MEN AND TEND TO NOT RECOVER AS WELL.

"We need to know what's causing covert strokes, because then we can figure out mechanisms for stopping them and decreasing your risks," said Dr. McLaurin. "That's what we're trying to understand. We don't understand it yet. This is a fairly new area."

She is a participant in the major dementia study supported by the Canadian Consortium on Neurodegeneration in Aging (CCNA) and is part of the group exploring the theme of treatment. The cross-cutting theme across all of the projects is sex and gender, ensuring that researchers integrate sex and gender considerations into their research designs, methods and analyses, and interpretation and/or dissemination of findings when appropriate. The Women, Sex, Gender and Dementia (WSGD) Program is supported by funding from Women's Brain Health Initiative (WBHI) and Brain Canada.

Each group includes a "Sex and Gender Champion," a researcher who encourages and supports other team members on the subject of sex and gender differences. In Dr. McLaurin's group, this role is filled by Dr. Steffany Bennett of the University of Ottawa. According to Dr. Bennett, the role of the Sex and Gender Champion is "not only to keep peoples' ideas focused on the idea that not everything is the same for men and women, but to also assist in the statistical analyses."

"I'm both a resource and a champion to assist with really interesting interpretations." Dr. Bennett's own research focuses on lipids, the natural fats in our blood systems. Our lipid metabolisms change when we develop diseases such as Lewy body dementia or Parkinson's. They develop imbalances, with a buildup of potentially toxic by-products.

Dr. Bennett is searching for biomarkers among our lipids – clues that might provide early indications as to whether individuals are susceptible to those kinds of diseases. She is studying whether there are metabolic changes that are happening before an individual displays any symptoms, which could help with earlier diagnosis and potentially also identify whether certain individuals are more resistant and why.

She already has surprising and important results, observing that women and men metabolize certain lipids differently. "It's quite exciting. You still get [the diseases], but through slightly different routes, which is important for treatment," she explained. Dr. Bennett believes that it is possible that the metabolic differences might be part of the explanation as to why there is a disparity between the sexes in the prevalence of these diseases.

ALZHEIMER'S DISEASE IS MORE COMMON IN WOMEN, BUT MEN GET LEWY BODY DEMENTIA AT A HIGHER RATE.

Dr. Bennett says that the previous practice of focusing exclusively on male subjects hindered our search for a better understanding of the human brain and contributed to the failure to find a cure for dementia. She believes that the new emphasis on exploring sex and gender differences makes it an exciting time to be a researcher. "We're finding out a lot more things. And it all needs to be considered or we're missing an entire population of people – half of humanity."

LEVELLING THE FIELD

To The Fullest

Sex & Gender Differences in Quality of Life Research

The journey of dementia is marked with wrenching life changes. As memory diminishes, so does independence. For many, one of the most heartbreaking transitions is the loss of the ability to drive.

Some individuals with Alzheimer's disease come to their own realization when it is time to stop driving. But far too often, family caregivers and health care professionals must deal with the delicate and devastating matter of taking away the keys from an individual who angrily, tearfully, and profoundly resists. It is an ethical, moral dilemma for loved ones. Your mother or father has become potentially a risk to herself or himself and others, but in removing that risk you must deal an awful blow to her or his independence and identity.

> **"THE WHOLE PROCESS OF PERSONS WITH DEMENTIA HAVING TO ACCEPT THEY NEED TO STOP DRIVING IS ONE THAT IS OFTEN FRAUGHT WITH EMOTION, AND AS A CONSEQUENCE IT CAN BE A SOURCE OF CONFLICT WITH FAMILY MEMBERS AND WITH HEALTH CARE PROVIDERS,"**

says Dr. Gary Naglie, a geriatrician and Vice-President of Medical Services and Chief of Staff at Baycrest, and Professor of Medicine and holder of the Hunt Family Chair in Geriatric Medicine at the University of Toronto.

He is co-leading a major study of driving and dementia for the Canadian Consortium on Neurodegeneration in Aging (CCNA), along with Dr. Mark Rapoport, a geriatric psychiatrist at Sunnybrook Health Sciences Centre and Professor of Psychiatry at the University of Toronto. →

Together with research associate Elaine Stasiulis, they have conducted an exhaustive review of the existing literature and have spoken with many individuals dealing with dementia. In the process, they found serious gaps in the availability of information and support.

"It's often a subject that people end up avoiding because of the emotional aspects and the challenges it poses. They avoid it because they don't have the knowledge and tools to approach it," Dr. Naglie told Mind Over Matter®.

Another member of the research team, Dr. Stephanie Yamin of St. Paul University, noted that research to date has tended to focus on how to identify when a person with dementia should stop driving, but we need to know more.

"We've gotten better at determining when to stop driving. Not perfect, but we're better at it. But one of the areas that really has been neglected is 'okay, but then what?' Once you've identified that someone is unsafe and we're at a point when they have to stop driving, what then? How do we support this person?" she said.

THE CCNA DEMENTIA AND DRIVING PROJECT PROPOSES TO FILL THE GAP BY CURATING ALL OF THE INFORMATION THAT IT HAS COLLECTED AND DEVELOPING AN ONLINE RESOURCE AVAILABLE TO THE PUBLIC.

"We're building a webpage that's going to have portals for people with dementia, family caregivers, and a third portal for health care providers where they will be able to identify information, tools, and resources related to issues pertaining to decision-making around driving cessation, but also to providing support for people after they have to stop driving," said Dr. Naglie.

Dr. Rapoport encourages family members to start the conversation about driving cessation as early as possible in the course of the disease, so that it is less of a shock when the time comes to stop driving.

IT IS IMPORTANT TO DEVELOP A PLAN FOR TRANSPORTATION ALTERNATIVES AFTER DRIVING CESSATION TO MINIMIZE SOCIAL ISOLATION, LOSS OF FUNCTION, AND DEPRESSION.

The online resource will also include advice for medical professionals on how to sensitively communicate the necessity of such a life-changing event.

The researchers hope to launch the webpage in 2020, but are first testing its effectiveness, collaborating with an Advisory Committee comprised of individuals living with dementia and family carers. The Murray Alzheimer Research and Education Program at the University of Waterloo helped put the committee together. The researchers have also called upon Alzheimer's Societies to evaluate its implementation and gather feedback from individuals with dementia, family members, and community providers.

As with all of the CCNA dementia projects, the project includes an exploration of sex and gender considerations – a cross-cutting theme supported with funding from Women's Brain Health Initiative (WBHI) and Brain Canada.

"We need to recognize that men and women may react differently to the issue of driving cessation, and we must personalize our approaches to recognize these differences," said Dr. Naglie.

THE RESEARCHERS HAVE FOUND THAT WOMEN WITH DEMENTIA WERE TWICE AS LIKELY TO GIVE UP DRIVING AS MEN.

"While that was the case with this cohort of older drivers with dementia, it could be different in the future," noted research associate, Elaine Stasiulis. "The important element about this is recognizing that there are sex and gender differences related to driving, and that it's important to have an awareness and sensitivity about this in helping to address the challenge of driving cessation," added Dr. Naglie.

Dr. Stephanie Yamin acts as the "Sex and Gender Champion" for the research team, where she is responsible for ensuring that her colleagues take into consideration relevant sex and gender differences. She also collaborates with other CCNA teams to ensure best practices are being followed.

In the context of the driving and dementia study, this means examining how women and men might react differently to the challenges of driving cessation. Dr. Yamin, a clinical psychologist, has already observed in her practice that the loss of driving for men can have an impact on their sense of identity. She is hoping to learn more as data is collected from the major COMPASS-ND research project that has been launched by CCNA in which more than 3,200 older adults are being studied. "By examining sex and gender differences in driving and dementia research, we might be able to tailor driving cessation programs and interventions to the particular needs of each group."

"The CCNA provides a perfect opportunity, given the large number of investigators involved, to create a body of knowledge in dementia and neurodegeneration, to document areas where there are sex and/or gender differences, and take these things into account to create better solutions," said Dr. Naglie.

For Dr. Yamin, the sex and gender aspect of the project brings personal satisfaction as well. "Research tends to overlook the impact of sex and gender, which can be significant. As a woman, I find it meaningful that in this work we do not assume that we are all the same and have the same experiences, and there is value at looking at those differences."

SINK YOUR TEETH INTO IT

GOOD ORAL HEALTH MAY BOOST YOUR BRAIN HEALTH

Considerable research has been conducted in recent years to examine the relationship between oral health and cognitive function. Much of that research has found that poorer oral health is linked with greater cognitive decline. ⟶

STUDIES HAVE SHOWN THAT OLDER ADULTS WITH CERTAIN ORAL CONDITIONS (E.G. PERIODONTAL DISEASE, DIFFICULTY CHEWING FOOD, OR HIGHER NUMBERS OF MISSING TEETH OR CAVITIES) ARE MORE LIKELY TO HAVE LOWER COGNITIVE PERFORMANCE AND/OR HIGHER RISK OF DEVELOPING DEMENTIA, COMPARED WITH INDIVIDUALS WITHOUT THOSE CONDITIONS.

ABOUT GUM DISEASE

GINGIVITIS is the first phase of gum disease, when the gums are inflamed by bacterial plaque that has accumulated on the surface of the teeth. Gingivitis that goes untreated can progress to PERIODONTITIS, where the infection in the gums has spread to the bone that supports the teeth.

Periodontal disease is quite common. According to a 2019 press release from the American Academy of Periodontology, in the U.S., more than half of the population aged 30 and older has some form of periodontal disease, and for those aged 65 and older, the prevalence rate increases to 68%.

For example, an academic review conducted by Dr. Ingar Olsen and Dr. Sim Singhrao – published in 2015 in *Journal of Oral Microbiology* – sought to examine whether oral infection may be a risk factor for Alzheimer's disease. The researchers concluded that there was "increasing evidence for an association between chronic periodontitis and late-onset Alzheimer's disease."

More recently, a study conducted by researchers in South Korea found that chronic periodontitis could be linked to a higher risk of dementia. Dr. Seulggie Choi and colleagues explored the relationship between chronic periodontitis and dementia using health information from over 262,000 individuals (aged 50 and older) throughout a ten-year period. The findings – shared in *Journal of the American Geriatrics Society* in 2019 – revealed that the individuals with chronic periodontitis had a 6% higher risk for dementia than those who did not have periodontitis.

Another interesting study revealed that oral health behaviours may also be linked with risk of dementia – which makes sense given that taking good care of your teeth and gums can help prevent the oral conditions that have been associated with cognitive impairment. In their research involving nearly 5,500 older adults in California followed over an 18-year period, Dr. Annlia Paganini-Hill and colleagues discovered that among the participants with their own teeth (i.e. not wearing dentures), those who did not brush their teeth daily had a 22% to 65% greater risk of developing dementia than those who reported brushing three times a day. These findings were reported in *Journal of the American Geriatrics Society* in August 2012.

ALTHOUGH VARIOUS STUDIES HAVE FOUND A RELATIONSHIP BETWEEN ORAL HEALTH HABITS AND COGNITIVE FUNCTION, THIS RESEARCH DOES NOT CONCLUSIVELY PROVE THAT POOR ORAL HEALTH CAUSES DECREASES IN COGNITIVE FUNCTION.

It may even be possible that the reverse is true – in other words, perhaps impaired cognitive function leads to poor oral health. It seems plausible that individuals experiencing cognitive decline might not take care of their teeth as well as they used to – because they forget to brush and floss regularly (or do not do a thorough job due to struggles with motor skills) or do not go to the dentist – thereby negatively impacting their oral health.

An academic review of 36 research studies – conducted by Dr. Suzanne Delwel and colleagues, and published in 2018 in *Clinical Oral Investigations* – concluded that older individuals with dementia are, in fact, more likely to have oral health problems related to oral soft tissues (such as gingival bleeding, periodontal pockets, and reduced salivary flow) compared to cognitively-intact older adults, as a result of a decline in self-care and motor skills. Additionally, the severity of cognitive decline appeared to play a role in the oral health of individuals with dementia, with more plaque and oral disease in individuals with greater cognitive decline.

It is also possible that there is a third variable (such as poor nutrition) that is the underlying cause of poor oral health and diminished cognitive function.

While there has indeed been much research that reported a clear association between oral health and cognitive function, there is not a firm consensus about this subject. An academic review conducted

by Dr. Bei Wu and colleagues – published in April 2016 in *Journal of the American Geriatrics Society* – found the collective body of research on this subject inconclusive.

The researchers examined findings from 56 studies published between January 1993 and March 2013 on the association between oral health and cognitive status. Some of the studies found a significant, but relatively weak, association between periodontal disease and cognitive decline, while other studies found no such association.

The link between cavities and cognition was also inconsistent across studies. As for the relationship between tooth loss and cognitive decline, the findings were even more complex, with some studies finding a positive association, others finding no association, and others finding a negative association.

The researchers ultimately concluded that it was unclear how or whether oral health conditions and cognitive status are related. The inconsistent findings may be due to methodological limitations (i.e. characteristics of study design that impact how findings can be interpreted).

A group of Australia-based researchers wondered if the relationship between oral health and cognitive function might be more clear if specific aspects of cognitive function were examined, rather than using broad, overall assessments based on a brief screening and/or dementia status. Dr. Matthew Nangle and colleagues conducted a review of 23 studies that focused on how oral health relates to specific cognitive abilities in older adults, and shared their findings in 2019 in *Gerontology*.

"Our review revealed that oral health is linked with certain aspects of cognitive function in older adults, namely, learning and memory, complex attention, and executive function," explained Dr. Nangle, a senior lecturer at the School of Dentistry, University of Queensland. Results were less clear for other cognitive domains, such as language and perceptual motor function. "So, our research suggests that certain types of cognitive function are indeed linked with oral health, while others may not be."

The potential association between oral health and cognitive function has been an extremely popular topic among researchers in recent years. A search of relevant scientific databases in September 2019 revealed that more than half of all research articles on the topic had been published in just the previous five years. Recognizing this rapid, recent growth in scientific study on the subject, Dr. Nangle and Dr. Nithin Manchery prepared a review of the existing research in order to summarize the most up-to-date understanding of this complex relationship. Their review was published in the March/April 2020 issue of *Current Opinion in Psychiatry*.

"Our review, incorporating all of the latest findings, revealed a growing body of evidence suggesting there may be bidirectional causal associations between oral disease and dementia," said Dr. Nangle. "So, it looks like poor oral health might directly contribute to cognitive decline and cognitive decline might play a causal role in poor oral health, creating a cycle of impairment. But, more research is needed, particularly randomized controlled trials, to further our understanding of the subject."

Assuming there is some relationship between oral health and cognitive function, what might explain the connection between the two? What do your mouth, teeth, and gums have to do with your brain?

ONE POTENTIAL EXPLANATION IS THAT UNHEALTHY ORAL MICROBES (AND/OR THE TOXINS THAT THEY PRODUCE) MIGHT BE FINDING THEIR WAY TO OTHER PARTS OF THE BODY, INCLUDING THE BRAIN, AND TRIGGERING INFLAMMATION AND BRAIN DAMAGE.

Indeed, some studies have found higher levels of gum disease-related bacteria in the brains of individuals with Alzheimer's disease compared to the brains of those without the disease.

Oral health, it turns out, has implications well beyond your mouth. "The mouth is known to reflect overall health at any stage of life," explained Dr. Brett Finlay, a researcher and Professor at University of British Columbia and co-author of *The Whole-Body Microbiome: How to Harness Microbes – Inside and Out – for Lifelong Health* (which includes a chapter on oral health). Dr. Finlay is the Co-Director of the CIFAR Humans & the Microbiome program, co-funded by Brain Canada. "Most systemic diseases – ones that involve the whole body or many organs – produce oral signs and symptoms, so it's not surprising that →

MICROBES are tiny micro-organisms that live all around us – in water, soil, and the air – and also on and inside our bodies. The most common types of microbes are bacteria, viruses, and fungi. While some microbes can make us sick, others play an important role in keeping us healthy. Collectively, the microbes on/in the human body are known as the microbiome.

The oral cavity contains millions of microbes, some of which are swallowed as part of saliva, and others that manage to cling to the tongue, teeth, gums, and inside of the cheeks.

Chronic inflammation associated with aging is sometimes referred to as "INFLAMMAGING."

oral health might play a role in cognitive function and dementia."

The human mouth is home to complex communities of microbes. When all is going well, the "good" microbes outnumber the "bad" ones and our oral health is strong. However, in some instances, the "bad" microbes begin to colonize in large numbers and thrive, creating the conditions for cavities, gum disease, and/or tooth loss. Plaque-induced oral conditions, like periodontitis, are known to be associated with changes in the oral microbiome.

"Plaque on your teeth is old biofilm material from bacteria that has calcified," explained Dr. Finlay. "As soon as it's removed at the dentist, it begins accumulating again, particularly in spots that are hard to clean at home." As plaque builds up in those hard-to-reach places, our gums are irritated by it and become inflamed. Prolonged and repeated bouts of such inflammation can damage the underlying tissue and lead to periodontitis in some individuals.

"As periodontitis progresses, the oral microbiome shifts toward a higher number of pathogenic microbes. In other words, there's more of the negative, disease-causing bacteria present," said Dr. Finlay. "We know that people with periodontitis have distinctly different oral microbes than people without the condition. Porphyromonas gingivalis and Treponama denticola are often among the microbial culprits."

The human body is equipped with systems – the gums, the gut barrier, and the blood-brain barrier – to keep pathogens out of the blood and brain. "Sometimes as one gets older, these systems become more permeable, so they don't do as good a job as they once did at keeping the 'bad' microbes out of our blood and brain," explained Dr. Finlay. "When pathogenic microbes seep across these barriers, we experience low-grade chronic inflammation. This inflammation can lead to tissue damage, including brain damage."

IT IS IMPORTANT, THEN, TO DO ALL THAT YOU CAN TO MAINTAIN GOOD ORAL HEALTH. IT WILL BENEFIT YOUR MOUTH AND TEETH, AND MAY WELL BOOST YOUR BRAIN HEALTH TOO.

Aside from regular brushing and flossing, and visits to the dentist, you might also want to consider giving these tips a try to further boost your oral health:

- **ADDRESS DRY MOUTH.** Saliva flow is important for oral health; saliva is antibacterial and helps to wash away undesirable microbes. However, decreased saliva production tends to happen naturally with age and can be exacerbated by certain medications. To address dry mouth, try sipping water throughout the day, chewing sugarless gum, and avoiding drinks that are sugary or heavily caffeinated.

- **CHEW PROBIOTIC GUM**. You can give your oral cavity a boost of "good" microbes to help keep pathogens and periodontal disease at bay by chewing probiotic gum. For example, Cultured Care gum with BLIS K12® contains a bacterial strain that can help you chew your way to better oral health.

- **TRY COCONUT OIL SWISHING**. Coconut oil has anti-microbial and anti-inflammatory effects that may boost oral health (and whiten teeth) when swished around the mouth and through the teeth for approximately five to twenty minutes, then spit out as part of daily oral care. Oil swishing (or oil "pulling"), which can be done with many different kinds of edible oils, is an ancient Ayurvedic technique that has many supporters. More scientific research is needed to determine the effectiveness of oil swishing.

You might wonder about the effectiveness of mouthwash for maintaining a healthy oral microbiome. Well, it turns out that common over-the-counter mouthwashes are good for rinsing away food particles, but do not effectively eliminate cavity-causing microbes, especially those that are below the gumline. Further, antibiotic mouthwashes do not help your oral microbiome because they kill off both the bad and the good microbes. Dr. Finlay predicts in his book that in the future there will be probiotic mouthwashes that help boost oral health, so watch for that type of product to be launched.

POOR ORAL HEALTH IS NOT INEVITABLE FOR INDIVIDUALS WITH DEMENTIA

Even though research has shown that individuals with dementia are more likely to experience oral health problems, this can be avoided. A 2016 academic review conducted by Dr. Bei Wu and colleagues (published in *Journal of the American Geriatrics Society*) found that when individuals with dementia had good dental care, their oral health remained comparable to that of patients without dementia. These findings suggest that good oral health can be maintained by those with dementia if they maintain oral hygiene (on their own or with assistance) and visit the dentist regularly.

THE FIRST STEP

GETTING STROKE SURVIVORS MOVING

Worldwide, one out of every six people will have a stroke in their lifetime. Thankfully, a large number of those individuals will survive the stroke, but many of those survivors will experience long-term disability. In Canada alone, it was estimated that at least 405,000 people were living with long-term stroke disability in 2013, and that number is projected to grow dramatically over the next 20 years to 726,000.

Stroke survivors experience a wide range of complex post-stroke consequences, including impairments in movement, balance, speech, vision, memory, and cognition. Each person is affected differently depending on what part of the brain is affected, how extensive that area is, and how long the brain tissue is deprived of oxygen.

Physical inactivity increases the risk of stroke. Individuals who have had a stroke often become even less physically active, as exercising is more challenging post-stroke for a variety of reasons, including fatigue.

> **WHEN STROKE SURVIVORS ARE SEDENTARY, THEY BECOME MORE AND MORE PHYSICALLY "DECONDITIONED," WHICH NEGATIVELY IMPACTS THEIR ABILITY TO PERFORM DAILY LIVING ACTIVITIES, AND CORRESPONDINGLY INCREASES THEIR RISK OF FALLS AND RECURRENT STROKE, AS WELL AS OTHER HEALTH CONDITIONS LIKE DIABETES.**

Engaging in exercise post-stroke can help reverse that negative cycle, providing numerous physical and psychosocial benefits. It also provides cognitive benefits that are especially important given that up to two-thirds of people who experience a stroke suffer from cognitive impairments as a result. →

Stroke survivors need exercise programs specifically designed for their unique needs.

Stroke survivors may find it difficult, impossible, or unsafe to participate in exercise programs offered to the general public for a variety of reasons, including the degree of their disability, lack of prior experience with exercise, fear of injury, lack of transportation, and program cost. Some prefer to participate in exercise classes with others who have also experienced one or more strokes, as they are not comfortable being included in generic classes with individuals who do not have disabilities or limitations.

POST-STROKE EXERCISE BOOSTS BRAIN FUNCTION

A recent meta-analysis conducted by Dr. Lauren Oberlin and colleagues – published in 2017 in *Stroke*, a journal of the American Heart Association – examined the findings from 14 studies published between 2001 and 2016 on the effects of physical activity on post-stroke cognitive function. After combining and analyzing the collective results, the researchers found a positive overall effect of physical activity training on cognitive performance. The cognitive benefits were achieved in as little as 12 weeks, with programs that combined both aerobic and strength training providing the largest cognitive gains (compared with either aerobic or weight training alone).

This research also revealed a very important, new finding: it is never too late to reap the cognitive benefits of exercise after a stroke. "Doctors used to believe that most cognitive improvements post-stroke would be experienced in the acute and subacute phase, within three months after the stroke," said Dr. Oberlin, a postdoctoral fellow at Weill Cornell Medicine. "However, our research shows that exercising has a positive impact on cognition well beyond that. We found that participants who started exercising on average 2.6 years after a stroke still experienced cognitive gains."

BRAIN SCANS SHOW THE IMPACT OF POST-STROKE EXERCISE

Researchers from the Florey Institute of Neuroscience and Mental Health conducted a study using magnetic resonance imaging (MRI) scans and memory tests to track how exercise affects neuron regeneration after a stroke. The 35 participants were divided into groups that performed aerobic, strength, and resistance exercises. Preliminary findings showed that exercise led to new neuron growth on the side of brain with the stroke-associated lesions and slowed or stopped atrophy on the opposite side of the brain. The researchers noted that these findings – shared in July 2019 in *Alzheimer's & Dementia* – were early and encouraging, but emphasized that more testing in larger studies is needed.

HOW TO GET STROKE SURVIVORS MOVING

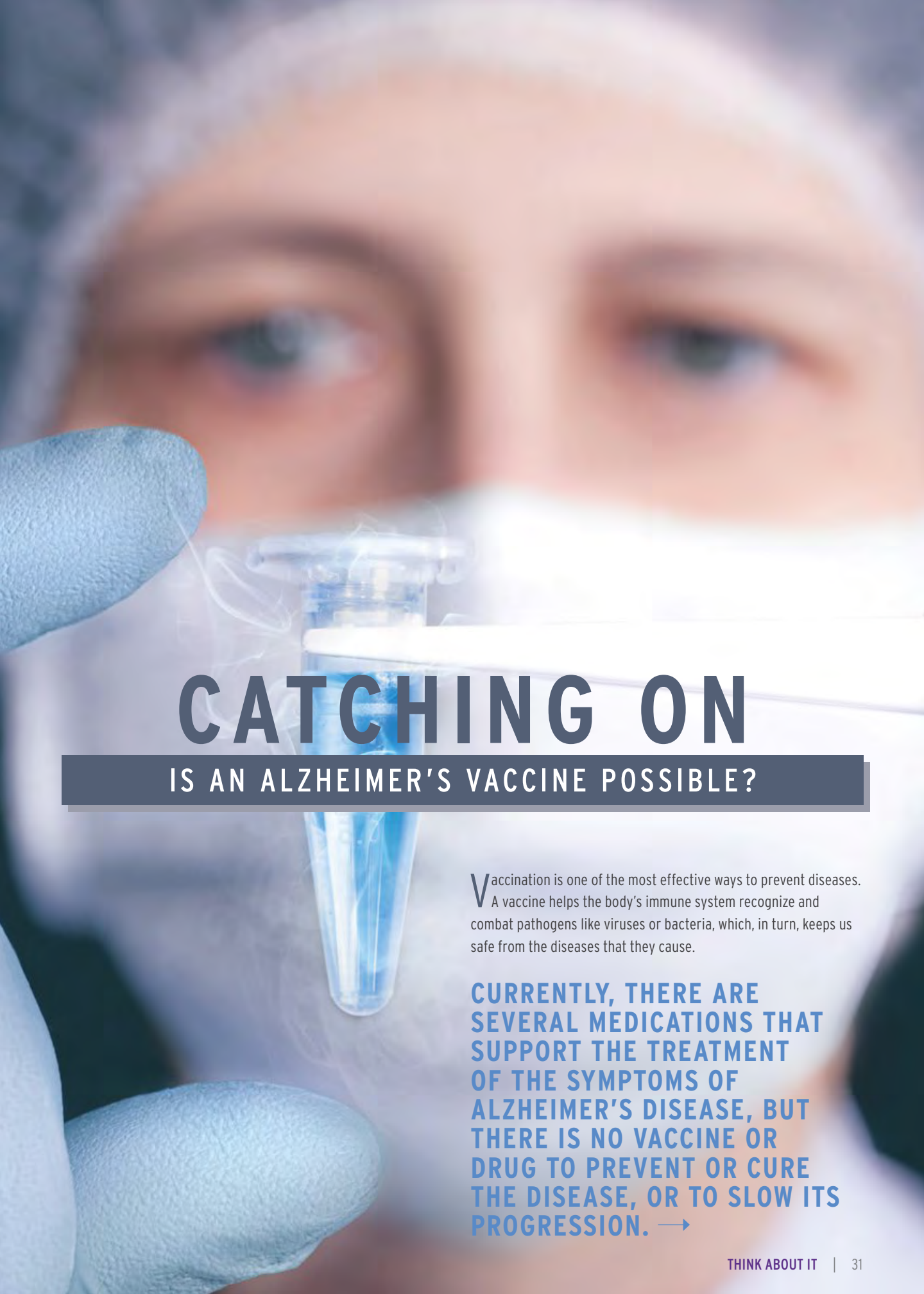
It is clear that exercise has the potential to help stroke survivors in numerous ways, yet many are not getting the physical activity that they need. Most stroke survivors do not have access to quality exercise programs customized for their unique needs. To address this situation, Dr. Ian Graham is co-leading a project, funded by Brain Canada and the Heart and Stroke Foundation Canadian Partnership for Stroke Recovery, to scale-up the implementation of sustainable, evidence-based community exercise programs for stroke survivors.

> **"THERE IS STRONG EVIDENCE THAT EXERCISE IMPROVES MOTOR RECOVERY, QUALITY OF LIFE, AND COGNITIVE FUNCTION FOR STROKE SURVIVORS, YET THERE ARE MANY BARRIERS TO EXERCISE FOR THIS POPULATION,**

said Dr. Graham, Senior Scientist at Ottawa Hospital Research Institute and a Professor at the University of Ottawa. "So, our project team is working to develop and field test a guidebook that will help community groups plan and deliver top-quality exercise programs to these individuals."

The guide does not provide recommendations about specific exercise regimens; rather, it outlines core program elements and safety guidelines, and presents three examples of existing Canadian programs that are operating with success. "The planning approach we outline in the guide is designed to be generic, so that the guidance can be applied to any exercise program a given community might choose," explained Dr. Graham, a Brain Canada-funded researcher. "Each community is different, so our guide focuses on high-level guidance to help with considering and pulling together all of the factors essential to a program's success."

A draft version of the guide has been prepared by the project team and is currently being tested in communities of various sizes across the country. The researchers will be tracking whether the pilot programs are successful at finding participants, if those participants experience improvements and are satisfied with the program, and obtaining feedback from the communities to further refine the contents of the guide. The final guide, which is slated to be ready in September 2021, will be open-access – i.e. available for any interested community to use to help get (and keep) stroke survivors moving.



CATCHING ON

IS AN ALZHEIMER'S VACCINE POSSIBLE?

Vaccination is one of the most effective ways to prevent diseases. A vaccine helps the body's immune system recognize and combat pathogens like viruses or bacteria, which, in turn, keeps us safe from the diseases that they cause.

CURRENTLY, THERE ARE SEVERAL MEDICATIONS THAT SUPPORT THE TREATMENT OF THE SYMPTOMS OF ALZHEIMER'S DISEASE, BUT THERE IS NO VACCINE OR DRUG TO PREVENT OR CURE THE DISEASE, OR TO SLOW ITS PROGRESSION. →

Although a number of studies and clinical trials are working on the development of a vaccine, there have been various challenges along the way.

One of the difficulties in the pursuit for an Alzheimer's vaccine is that many studies on Alzheimer's disease and other types of dementia target individuals over the age of 60, when research now suggests that the onset of symptoms can occur much earlier. Additionally, findings in mouse models of Alzheimer's disease have been notoriously difficult to replicate in humans, which contributes to a longer research cycle and delays the development and production of a solution.

ONE OF THE MOST SIGNIFICANT CHALLENGES RESEARCHERS FACE IS THAT THE UNDERLYING PATHOLOGY OF ALZHEIMER'S DISEASE IS CURRENTLY UNKNOWN.

Some scientists believe that a buildup of beta-amyloid (in deposits known as plaques) and/or a buildup of tau proteins (which form neurofibrillary tangles) in the brain are to blame, while others believe that another mechanism, such as inflammation is at play.

Recently, researchers have recognized that many previously-failed Alzheimer's treatments have focused either on beta-amyloid or tau protein reductions exclusively, but never both. Research now suggests that it is a synergic relationship between the two toxic proteins that may be responsible for degeneration of the brain. This latest revelation is pivotal in bringing the medical community one step closer to developing an Alzheimer's vaccine.

GLOBAL EFFORTS

Earlier studies targeting the plaques with antibodies have been able to successfully clear plaques and reverse cognitive deficits in mouse models. However, clinical trials using these antibodies resulted in serious brain-swelling side effects.

In a recent study published in *Alzheimer's Research and Therapy* in November 2018, a DNA vaccine tested in mice reduced the accumulation of beta-amyloid and tau proteins in the brain without triggering severe brain swelling or inflammation.

IF BETA-AMYLOID AND TAU ARE INDEED THE CAUSE OF ALZHEIMER'S DISEASE, THEN THIS COULD BE A POTENTIAL THERAPY THAT COULD DRAMATICALLY DECREASE THE NUMBER OF PEOPLE AFFLICTED WITH THE DISEASE.

"If the onset of the disease could be delayed by even five years, that would be enormous for the patients and their families," said Dr. Doris Lambracht-Washington, the study's senior author. "The number of dementia cases could drop by half."

Other companies in the early stages of research for a vaccine include a biotech company in Dublin, Ireland called United Neuroscience. The lead researcher, Dr. Chang Yi Wang, and her daughter, Mei Mei Hu, have developed a vaccine that reduces the build-up of the beta-amyloid plaque, and they have already started to see some positive results in their small group of human clinical trials, with no significant side effects.

Another study at the University of New Mexico is also in the process of testing a potential Alzheimer's vaccine and reported that mice given the vaccine developed antibodies that cleared tau protein tangles in their brains. Those mice also performed better on memory tests than those that did not receive the treatment.

BREAKTHROUGH DIFFERENTIATOR: PREVENTATIVE AND CURE

Nikolai Petrovsky, a Professor at Flinders University in South Australia, has been working with his colleagues on developing an Alzheimer's vaccine for the past two decades, and recently achieved a major breakthrough that differentiates his research from the others.

In his study involving mice – which were genetically engineered to exhibit some of the symptoms of Alzheimer's disease – the vaccine successfully generated antibodies that both prevented and removed the aggregation of beta-amyloid and tau proteins in the brain.

According to Professor Petrovsky, the vaccine was designed to be a preventative measure and a cure. In other words, the vaccine could help an individual from developing dementia, and could also help to reverse the process of an individual's early onset of symptoms. The impact of this research is extraordinary.

"In the animal models, we can both use it to prevent the development of memory loss by giving it before the animal starts to get these build-ups of proteins," Professor Petrovsky said. "But we can also show that even when we give it after the animals have proteins, we can actually get rid of the abnormal proteins. It's actually designed to be both a prophylactic and a therapeutic."

Professor Petrovsky's research is being led and funded by the Institute for Molecular Medicine and University of California. For that reason, human clinical trials will most likely begin in the U.S., but efforts are being made for the trials to also include Australia. Today, there are nearly 436,000 Australians living with dementia and by 2050, that number is expected to climb to 1.1 million. In the U.S., the figures are just as staggering, with close to 5.8 million Americans suffering from Alzheimer's disease, with the number expected to rise to 14 million by 2050.

As for timing, there is encouraging progress that the human clinical trials may begin by late 2021 or early 2022. Mind Over Matter® spoke with Professor Petrovsky directly about his research and his outlook for the future. In particular, we asked if he observed any differences between the female and male mice in his research.

> **WE HAVE SEEN SEX DIFFERENCES IN THE PREDISPOSITION TO DEMENTIA DEVELOPMENT IN TRANSGENIC MOUSE MODELS, AND THIS REFLECTS CURRENT DATA SHOWING HUMAN WOMEN ARE ALSO MORE SUSCEPTIBLE TO DEMENTIA, FOR REASONS THAT ARE STILL NOT FULLY UNDERSTOOD.**

Professor Petrovsky also discussed some of the biggest challenges that he has experienced over the years working on an Alzheimer's vaccine, including the "great skepticism" of other scientists and the industry more generally, driven by the failures of previous research attempts. "Nothing great is achieved without initial setbacks and our aim is to learn from these previous failed attempts. Everest wasn't conquered on the first attempt," said Professor Petrovsky. "Notably, the current vaccines we are helping to develop are almost one thousand times better than previous candidates, giving us hope that this time we may in fact be able to succeed."

In terms of overall brain health, Professor Petrovsky also emphasized that prevention is always easier than a cure. "Having a healthy diet, exercising regularly, keeping control of your weight and blood pressure, avoiding excessive stress, and regularly exercising your brain by reading books and doing mental puzzles are some of the best ways to keep your brain healthy and avoid age-related declines in mental function."

A STAND AGAINST RESEARCH BIAS

UPDATE ON THE STAND AHEAD™ CHALLENGE

It was a campaign launch like no other in the short history of Women's Brain Health Initiative (WBHI).

December 2, 2019 was a cold, snowy day in downtown Toronto. WBHI's supporters gathered in a room at Artscape Daniels Launchpad, an airy space with large windows and an expansive view of the waterfront. It had the feel of a yoga class, as several people removed their outer garments, revealing workout clothing, and rolled out mats. But this was not a fitness class. They had gathered to make a statement for an important cause that touches us all.

At the appointed hour, with broad smiles, a few giggles, and news cameras rolling, they collectively stood on their heads.

The Stand Ahead™ Challenge was officially underway.

THAT DECEMBER 2ND WAS MARKEDLY SPECIAL. AT WBHI'S INSTIGATION, HEALTH CANADA HAD DECLARED IT THE VERY FIRST NATIONAL WOMEN'S BRAIN HEALTH DAY.

Since its inception in 2012, WBHI has enjoyed spectacular growth in reach, influence, and impact – supporting educational programs on brain health and funding important research, including the Wilfred and Joyce Posluns Chair in Women's Brain Health and Aging at the University of Toronto. Held by Dr. Gillian Einstein, it is the first (and only) research chair for women's brain health and aging in the world.

While WBHI has principally relied on funding from major donors and corporate sponsors, the Stand Ahead™ Challenge was something different.

"We wanted to try a grassroots campaign, with small donations from a larger group of donors – a campaign that people could rally behind and have some fun with. That was the impetus that drove the Stand Ahead™ Challenge," said WBHI Founder and President, Lynn Posluns.

"And in the process, we wanted a campaign in which more people could learn how to protect their brain health, and about the importance of equity in research."

The idea was to base the initiative on social media, with the added benefit of reaching younger individuals, a key target for WBHI.

The concept was relatively simple: encourage people who were safely able to perform a headstand to take a picture or video of the feat, and to make a statement about the importance of research equity and protecting one's brain health. Participants were encouraged to say that they were "standing up" for something and/or someone, to make a donation to WBHI, challenge two other people to do the same, and to share their message on social media with the #standahead hashtag.

Mindful that not everyone can (or should) attempt a headstand, supporters were advised that they could designate someone else to perform a headstand on their behalf.

Vitina Blumenthal, a member of WBHI's Young Person's Cabinet, became one of the most visible faces of the campaign. Vitina is also a yoga instructor and not only shared advice on how to safely perform a headstand, but also was the model on the standahead.org website.

SEVERAL PROMINENT CANADIANS PARTICIPATED IN A POWERFUL VIDEO TO SUPPORT THE CAMPAIGN, ELOQUENTLY SPEAKING TO THE CENTRAL MISSION OF WBHI.

Journalist, entrepreneur, and member of WBHI's honourary board, Jeanne Beker, said she was standing ahead for her mother. Juno Award winner Sean Jones said that he was standing ahead for his two-year-old daughter. Global TV's Jennifer Valentyne: her daughter and sister. CP24 anchor Pooja Handa: her mother and mother-in-law. Broadcaster Karman Wong: her three daughters. CTV's Anne-Marie Mediwake: her mom and her brain health. Entertainment Tonight host Cheryl Hickey: her father, adding "because good research needs to include everyone." Postmedia Network Executive Chair Paul Godfrey: his wife, his daughters-in-law, and his granddaughters. Co-host of Breakfast Television on CITY TV Dina Pugliese: her mom, sister, cousin, and "every woman watching this."

Brain Canada, a key partner in the production of Mind Over Matter®, gave the campaign a massive boost with a commitment to match all donations for women's brain health research up to $250,000.

"Brain Canada has invested more than $3.25 million in six research projects across Canada that examine differences between women and men in brain research, and we are excited to have committed matching funds for the 2019 Stand Ahead™ Challenge. This enables us to expand our support of women's brain health research, through a longstanding partnership with Women's Brain Health Initiative," said Naomi Azrieli, Board Chair of the Brain Canada Foundation.

Stand Ahead™ was a leap into the unknown, but it paid off in both donations and awareness.

There were thousands of social media postings from around the world, mainly in Canada and the United States, but as far abroad as the U.K., Australia, and Israel. Members of the WBHI Young Person's Cabinet braved winter's cold to stand on their heads in front of Toronto City Hall.

The campaign launch brought substantial media coverage. Lynn Posluns and Vitina Blumenthal appeared on Global News Morning in Toronto, and CTV Toronto interviewed Lynn at the launch event.

> **THE DONATIONS POURED IN – MORE THAN ENOUGH TO ACHIEVE THE MAXIMUM MATCHING AMOUNT FROM BRAIN CANADA.**

"It was just great," said Lynn. "Not only because of the amount of money raised, but also because much of it came from people who had never donated before. People who learned about WBHI for the first time. People who believed in standing up against research bias and standing ahead for women's brain health."

Plans are currently underway for the next Stand Ahead™ campaign and for the second Women's Brain Health Day. Lynn says that she is open to all ideas and encourages you to send your suggestions to **standahead@womensbrainhealth.org**.


(L-R) Lynn Posluns, Dr. Gillian Einstein

(L-R) Vitina Blumenthal, Laurie Piltz, Laura Best, Matteo Tino, Katie Black

(L-R) Mario Tino, Monica Berger, Brain Canada Director of Philanthropy, Gabriella Tino, Vincenza Pietropaolo, Toronto Public Health

UP YOUR GAME

DO BRAIN GAMES KEEP YOUR MIND SHARP AS YOU AGE?

Challenging your brain with games and puzzles (e.g. crosswords, Sudoku, chess, and computer brain-training games) is commonly believed to help maintain or improve brain health. In a 2015 survey of Americans aged 40 and older, conducted by the American Association of Retired Persons (AARP), respondents considered several activities "very important to brain health," including sleep, diet, exercise, and managing stress. When respondents were asked what activity they considered the "most important," though, challenging the mind with games and puzzles was the most commonly reported answer. That same survey found that 40% of respondents do games and puzzles specifically because they think that it is good for their brains.

However, is the belief that "brain games" give a boost to cognitive function supported by scientific evidence? There is currently no consensus on this subject, partly due to the inconsistency in research design, including how the study defines brain games, how cognitive function is measured, and what population of people is being studied (e.g. their age and current cognitive status).

COGNITIVELY-STIMULATING ACTIVITIES BOOST BRAIN HEALTH

If you consider the broader question of whether or not cognitively-stimulating activities (i.e. not just games) provide benefits for brain health, then the answer is yes.

In March 2017, experts with the Global Council on Brain Health (GCBH) reviewed the research on cognitive stimulation, focusing on the strongest evidence available to date – i.e. from well-designed randomized control trials and epidemiological observational studies that had large numbers of participants, and were published in peer-reviewed journals. One of the conclusions that they reached was that cognitively-stimulating activities over the life course, such as engaging in formal or self-initiated informal educational activities, continuing to engage in work experiences, learning a new skill, or engaging in leisure activities that are mentally challenging, provide benefits for adults' brain health.

> **THE REPORT RECOMMENDS CHOOSING ACTIVITIES THAT PROVIDE NOVELTY, VARIETY, AND A HIGH-LEVEL OF ENGAGEMENT AND MENTAL CHALLENGE, WHILE ALSO BEING ENJOYABLE.**

You could learn a new language, volunteer in the community, take up painting, or learn to play a musical instrument, for example. There really are endless ways that you can challenge your brain. And, certainly games that challenge your brain in this way could qualify as a cognitively-stimulating activity.

WHAT ABOUT COMPUTERIZED BRAIN GAMES, IN PARTICULAR?

A subset of cognitively-stimulating activities is playing computerized brain games, an increasingly popular pastime. Although the broader category of cognitively-stimulating activities has been found to provide brain benefits, there is disagreement in the research community about the effects of computerized brain games.

In 2014, a group of more than 70 scientists published a consensus statement arguing that computerized brain-training interventions are not a scientifically-proven method for improving cognitive function or preventing cognitive decline. In response, a group of over 120 researchers issued their own statement counter-arguing that there was indeed evidence in support of the cognitive benefits of brain training. Despite the discrepancy between the main conclusions of these two statements, the two groups of scientists did agree on some things, including that:

- some claims being made by brain game companies were unsubstantiated by research;
- there is currently no evidence that brain games help reverse dementia; and
- more research is needed on computerized cognitive training (CCT).

Later reviews further contributed to the uncertainty around the benefits of CCT. For example:

- A review conducted by Dr. Daniel Simons and colleagues, published in October 2016 in *Psychological Science in the Public Interest*, found "extensive evidence that brain-training interventions improve performance on the trained tasks, less evidence that such interventions improve performance on closely-related tasks, and little evidence that training enhances performance on distantly-related tasks or that training improves everyday cognitive performance." In other words, they found that playing brain games improved performance at playing brain games and perhaps very similar tasks, but there is not much evidence that the skills learned in these games are transferrable to everyday real-world situations.

The previously-mentioned GCBH review also looked specifically at computerized brain games and concluded that the evidence (as of March 2017) about the benefits of playing such games was "weak to non-existent." They also warned that the claims made by brain game companies are often exaggerated.

More recently, another review was conducted by Dr. Philip Harvey and colleagues, and published in November 2018 in *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging*. One area of focus for their review was the effect of CCT on healthy older adults. They reviewed the four largest randomized controlled trials and several recent meta-analyses on the subject, noting that the CCT interventions studied varied widely, ranging from casual games to structured scientifically-derived exercises. According to Dr. Harvey, Leonard M. Miller Professor of Psychiatry and Behavioral Sciences and Chief of the Division of Psychology at the University of Miami Miller School of Medicine, after reviewing the research to date,

> **"THERE IS CONSISTENT EVIDENCE THAT COMPUTERIZED COGNITIVE TRAINING IMPROVES COGNITIVE PERFORMANCE AND SOME ELEMENTS OF REAL-WORLD FUNCTION IN HEALTHY OLDER ADULTS."**

He continued, "the real-world functions that were improved were skills that had been previously acquired, such as driving. These studies did not prove that cognitive training leads to skills learning without targeted skills training intervention. We believe that the controversy around whether CCT provides brain benefits was caused by elements of research design, including overly narrow definitions of CCT and overly narrow definitions of learning transfer."

There are several variables that make it challenging to study the effects of CCT, including the following considerations:

- What is the training like, and what cognitive domains does it target?
- What is the length of each training session, how many sessions are done each week, and how many sessions are completed in total?
- Is the training done independently, or with supervision or facilitation of some kind?
- Is the training done at home, or in a clinical or educational setting?
- Do sex, education level, current health status, or other personal factors impact the effectiveness of a given intervention?

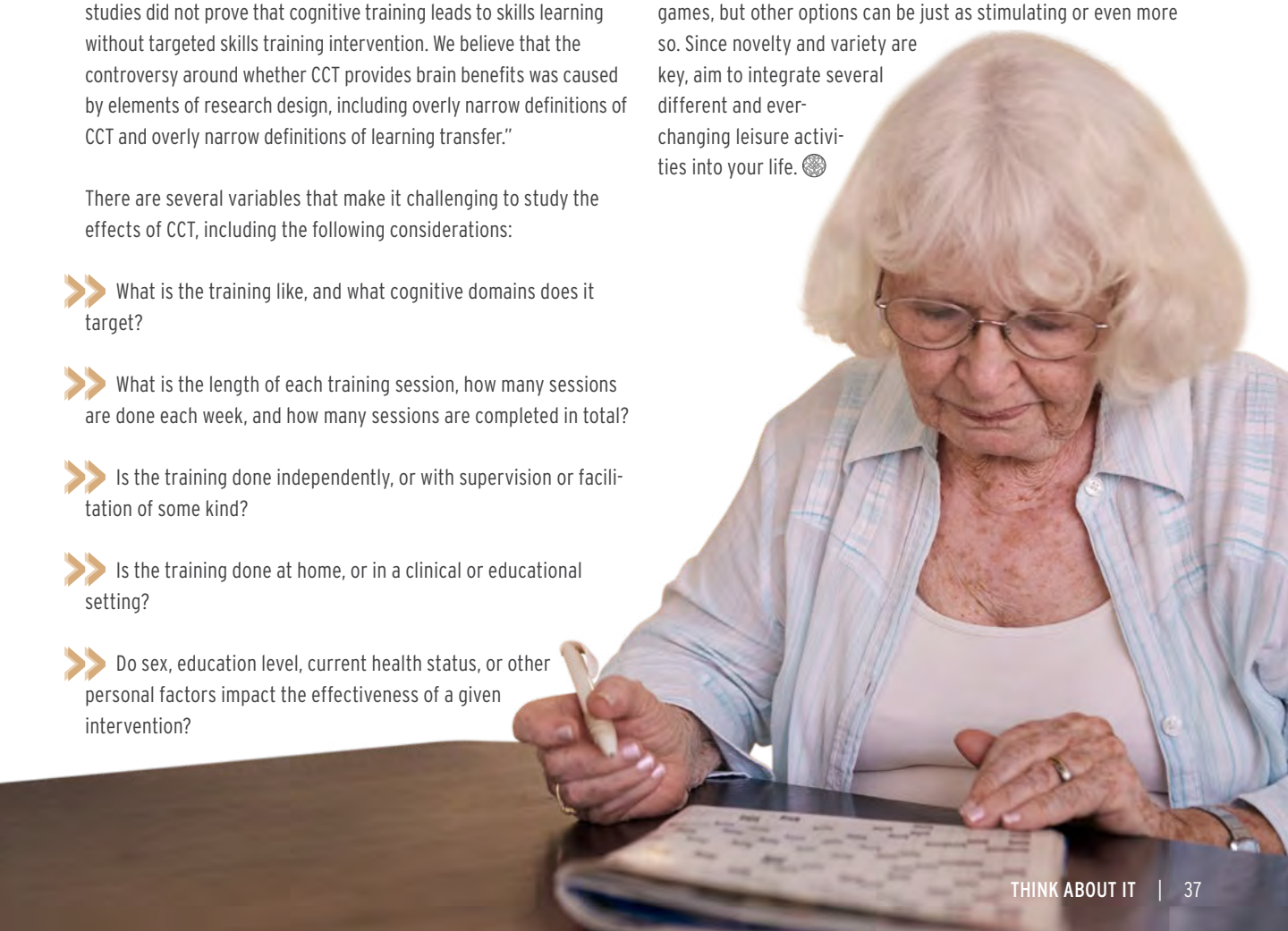
It is possible that there are multiple elements of research design that influence the inconsistent conclusions being reached by researchers. If one type of CCT delivered in a particular way to a certain group of people does not improve cognitive function in some way, that does not necessarily mean that all CCT is ineffective. What is clear, though, is that more research is needed on this subject.

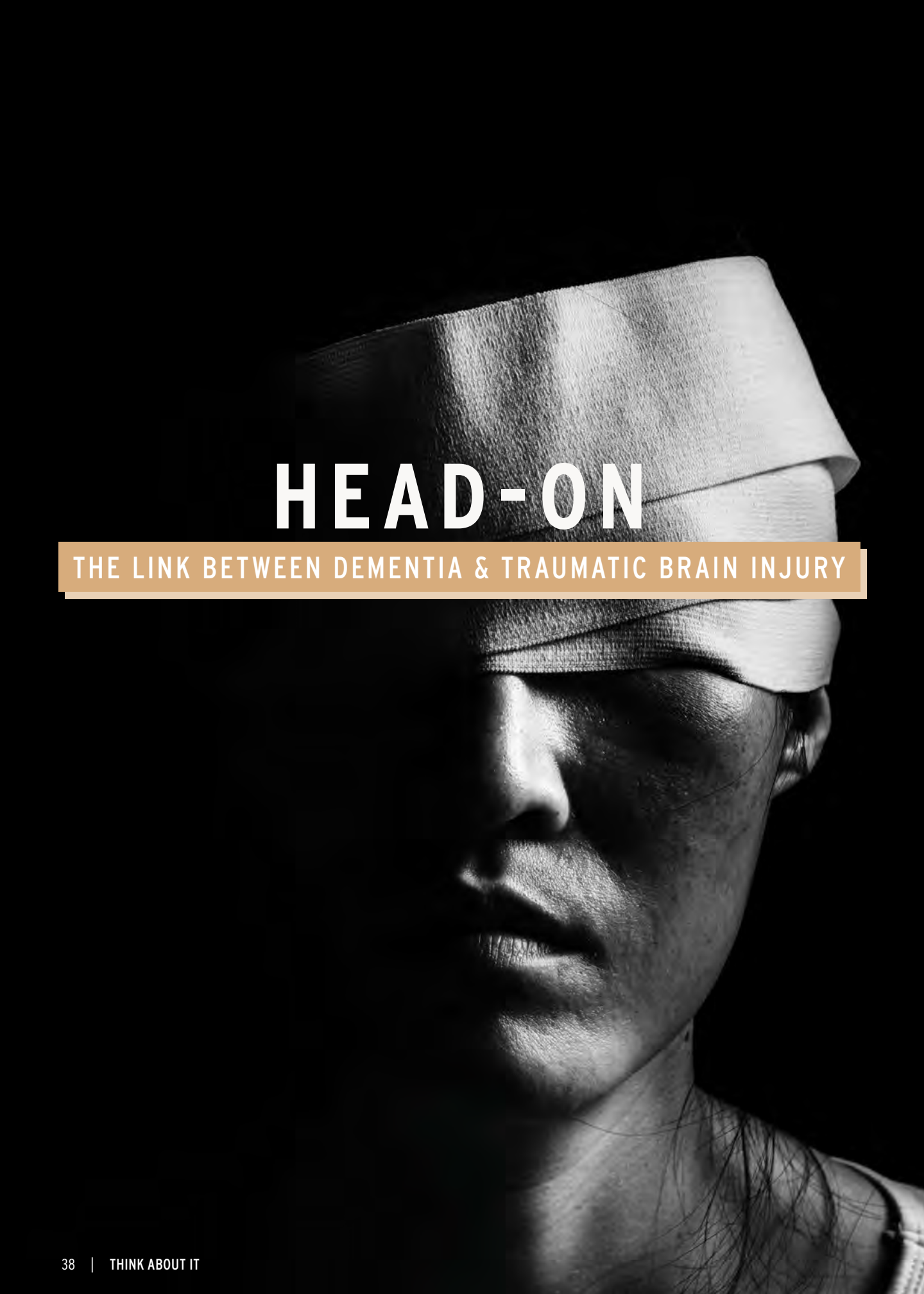
USE IT OR LOSE IT

The brain is constantly changing throughout one's lifespan, growing new neurons, and developing new neural connections. It is empowering to know that you can have an impact on how your brain changes as you age, in part by engaging in cognitively-stimulating activities of some kind. For maximum brain-boosting benefits, choose activities that are challenging – ones that force your brain to work and learn new things.

Computerized brain games are one option that you might want to include in your cognitively-stimulating line-up of activities. When choosing a computer-based brain game, the GCBH suggests that you look carefully at what is being offered and review the evidence that the company is using to substantiate any claims they make about the potential benefits.

Remember, you can learn new things and challenge your brain at any age. Perhaps you will choose to play computer-based brain games, but other options can be just as stimulating or even more so. Since novelty and variety are key, aim to integrate several different and ever-changing leisure activities into your life.





HEAD-ON

THE LINK BETWEEN DEMENTIA & TRAUMATIC BRAIN INJURY

In recent years, there has been an increasing awareness of the importance of preventing, identifying, and treating concussions, particularly in physical sports such as hockey, baseball, skiing, and even cycling, where helmets are mandatory. This heightened awareness, and education, has undoubtedly evolved as more and more of us become concerned about protecting our brain health.

While there are many reported incidents of concussions and brain injuries, experienced through sport as a child or adult, through a fall, or even an accident, the question that many people are asking (and are concerned about) is whether suffering a traumatic brain injury (TBI) increases your chances of developing longer-term brain health issues, including Alzheimer's disease or other types of dementia.

In a large-scale study published in *The Lancet Psychiatry* in April 2018, the researchers analyzed data from nearly three million people in Denmark over a ten-year period, identifying those who had and those who had not suffered a brain injury, and reported a correlation between brain injuries and a 24% increased risk of dementia.

Additionally, the researchers found that

THE RISK OF DEVELOPING DEMENTIA APPEARS TO BE HIGHER THE YOUNGER YOU ARE WHEN YOU SUFFER A BRAIN INJURY.

More specifically, the risk was greatest in those who had suffered the injuries in their 20s (who were 63% more likely to get the condition at some point in their life). Individuals who suffered a TBI in their 30s were 37% more likely to develop dementia later in life, while those who had suffered a TBI in their 50s were only 2% more likely to develop the disease.

Despite the correlation, it is worth noting that the risk of developing dementia following a TBI is still relatively small: 4.5% of individuals with no history of a TBI developed dementia, compared with 5.1% who had a TBI.

THE RESEARCHERS NEVERTHELESS CONCLUDED THAT GREATER EFFORTS TO PREVENT TBI, AND TO IDENTIFY STRATEGIES TO AMELIORATE THE RISK AND IMPACT OF SUBSEQUENT DEMENTIA, ARE NEEDED.

In another study out of Sweden, and published in *PLOS Medicine* in January 2018, the researchers tracked all diagnoses of dementia and TBI in Swedish nationwide databases from 1964 through 2012. The researchers found that in the first year after TBI, the risk of dementia is increased by four- to six-fold and thereafter the risk decreased rapidly, but was still significant more than 30 years after the trauma. Overall, the risk of dementia diagnosis was increased by approximately 80% during a mean follow-up period of 15 years. The researchers also found that the risk of developing dementia was higher for individuals who had suffered a severe TBI or multiple TBIs, and was similar in both women and men.

However, since the development of dementia can be a risk factor for accidents resulting in a TBI, it is possible that in some cases the onset of dementia preceded the TBI. The researchers therefore caution against making causal inferences.

Moreover, since the above-noted studies took a significant period of time to track, monitor, and report, it may be misleading to assume that suffering the TBI was the trigger for the disease, as opposed to another potential cause or trigger. For example, an individual's overall health, lifestyle, and geographic location may also be contributing factors that may have skewed the study results.

HOW TO CONFIRM THE SEVERITY OF YOUR TBI

In light of the short-term and long-term effects of brain injuries, there is a growing need to prevent and better understand treatments to minimize the impact that a TBI can have and to reduce one's chances of suffering long-term damage or developing dementia.

In addition to the typical medical tests, like computed tomography (CT) scans, there are two new studies that show that blood tests can actually identify protein biomarkers such as glial fibrillary acidic protein (GFAP) that can help detect TBI and, in particular, subconcussive injuries (i.e. those head traumas that do not necessarily exhibit the traditional symptoms of concussions). Problematically, CT scans frequently miss the subtle signs of subconcussive brain injury, which results in those who have suffered head trauma without concussion symptoms being classified as having "no injury."

Dr. Linda Papa, lead author of one of the studies and an emergency medicine physician at Orlando Health, notes that subconcussive trauma has been of particular concern in military personnel and athletes, as "repetitive subconcussive impacts have the potential for long-term deleterious effects."

Dr. Papa and her colleagues analyzed the biomarkers associated with brain injury in more than 700 children and adults who visited the emergency room within four hours of potential trauma. The →

TRAUMATIC BRAIN INJURY (TBI)

Traumatic Brain Injury (TBI) is caused by a concussion (a blow or jolt to the head) or loss of blood and oxygen supply to the brain. TBI survivors are often told that they may have a headache and be a bit emotional for a few days. In fact, the consequences of suffering even "mild" TBI can be disabling, and include:

- **Problems with memory and vision, fatigue, headaches, and migraines;**
- **Sexual dysfunction, including lost libido and infertility;**
- **Sensitivity to light, sound, and motion;**
- **Emotional swings, from depression to euphoria, from attention-deficit/hyperactivity disorder (ADHD) to explosive anger;**
- **Sleep disturbances, including insomnia or an inability to stay awake for more than a few hours;**
- **Slowed thoughts, word recall, and reaction times; and**
- **Loss of skills, including the ability to read, learn, recognize faces, and organize everyday tasks like shopping and cooking.**

participants were divided into three groups of patients based on their level of trauma: (1) those with overt symptoms of a concussion; (2) those with a head trauma, but without any apparent signs of concussion; and (3) those with a body trauma that did not involve head trauma or a concussion.

The researchers found that GFAP levels in the blood increased after head trauma, but were not elevated after body trauma, making it very specific to brain injury. Additionally, ubiquitin carboxyl-terminal hydrolase L1 (UCH-L1) levels were higher than GFAP levels in patients with non-concussive trauma, and this was especially true in the pediatric patients. The results of this study – which were published in the August 2019 issue of *BMJ Paediatrics Open* – may inform the development of a standard blood test for this type of injury.

In another study published in *The Lancet Neurology* in October 2019, the researchers were able to successfully identify TBI in patients with normal CT scans.

> **BLOOD-BASED BIOMARKERS REPRESENT THE NEXT STEP IN DIAGNOSING AND TREATING TBI,**

said Dr. Geoffrey Manley, senior author of the study, a Professor of Neurosurgery at the University of California-San Francisco, and a member of the Weill Institutes for Neurosciences. "We are finding that not only are they more sensitive than [CT scans] in identifying TBI, but they may also be more accurate than the current standard of [magnetic resonance imaging]."

DOMESTIC VIOLENCE

Aside from athletes and the military, another group at risk for traumatic brain injuries, who are often overlooked due to the sensitive circumstances of their injuries, are the victims of domestic violence – most often women. And, women experience concussions differently than men, and have an increased risk of suffering a TBI.

Disturbingly, statistics indicate that in 2000, approximately 4.8 million women were known to experience physical violence by an intimate partner each year. The actual numbers are likely much higher.

> **NEWER ESTIMATES SUGGEST THAT TBI FROM DOMESTIC VIOLENCE MAY AFFECT UP TO 20 MILLION WOMEN (REPRESENTING 6% OF THE POPULATION).**

While this may dwarf the numbers from the military and athletes combined, TBI from domestic violence receives little attention.

Whether a TBI is suffered through a fall, a sports-related injury, a car accident, or an assault, there is a definite link to post-injury symptoms and an increased chance of developing dementia.

To protect your brain and do your best to avoid brain injury, you should wear a helmet and/or protective gear when playing sports, and be cautious around potential tripping hazards both indoors and outside (e.g. carpets, slippery stairs and floors, ice on sidewalks, and uneven pavement). In addition, if ever faced with a brain injury, remember that early treatment for a concussion can improve one's recovery time.

5 REASONS WHY WOMEN SUFFER CONCUSSIONS DIFFERENTLY THAN MEN

Current research indicates that women suffer from concussions differently than men. Women have an increased risk of getting a concussion, have more severe symptoms, and take longer to recover.

Dr. Tracey Covassin, an Associate Professor and Director of the undergraduate athletic training program at Michigan State University in East Lansing, studies concussions in female athletes. Her research in sports-related concussions focuses on sex differences in concussion outcomes, epidemiology, and risk factors. According to Dr. Covassin, there are five key ways that women suffer concussions differently than men.

1. WOMEN EXPERIENCE LONGER AND MORE SEVERE SYMPTOMS THAN MEN

Not only do women take longer to recover from a concussion, but they also have more severe symptoms. "Women actually had symptoms three to four weeks later, where typically the males recover 10 to 14 days after [a head injury]," Dr. Covassin noted. "Women had neurocognitive impairments a lot longer than males and had difficulty remembering and concentrating." As Dr. Covassin observed, women may take longer to recover than men because of neuroanatomical differences in their brains. Women have slower nerve signals while men have faster nerve impulses in their brains, which could lead them to have a quicker healing process.

2. WOMEN SUSTAIN MORE CONCUSSIONS DURING PRACTICES AND GAMES THAN MEN IN SIMILAR SPORTS

In previous research, Dr. Covassin found that women in college soccer sustained more concussions during practices and games than men in the same sport. Soccer was also found to be the women's sport with the highest rate of concussions (over basketball, lacrosse, softball, and gymnastics). She attributes this to the nature of soccer, in which players often collide with each other accidentally. She also says that women could be more at risk of concussions than men because they have a greater "ball-to-head size ratio," or smaller heads compared with the ball. "There's a greater transmission of forces that are occurring," she explained. Heading the ball continuously and playing in a sport with no helmets or protective gear could also lead to more head injuries.

3. WEAKER NECK MUSCLES IN WOMEN MAY RESULT IN MORE BRAIN INJURIES

Simply put, a woman's weaker neck muscles cannot withstand the impact of a hit the way that a man with firmer shoulders and neck muscles can. As a result, there is a greater risk for the head to move dangerously following an impact. The risk is the same for young children who do not yet have fully-grown strong neck muscles.

4. A WOMAN'S HORMONES MAY AFFECT HER HEALTH OUTCOMES FOLLOWING A CONCUSSION

A woman's menstrual cycle and her hormones can influence her concussion symptoms. For example, "the levels of sex hormones, such as progesterone, which is known to have a calming effect and can improve cognition, memory, and mood, can change after a concussion, too. When women receive a blow to the head during the luteal phase, progesterone production slows to create a sense of withdrawal, making concussion symptoms, such as headache, dizziness, and nausea, worse." Furthermore, researchers have found that women who were injured during the last two weeks of their menstrual cycle, when progesterone was at its highest (i.e. the luteal phase), had worse post-concussion symptoms compared with women injured during the first two weeks, when progesterone was low (i.e. the follicular phase), and with those who were taking contraceptive pills. This research was published in the January 2017 issue of *Journal of Head Trauma Rehabilitation*.

5. WOMEN ARE MORE LIKELY TO REPORT THEIR SYMPTOMS THAN MEN

Dr. Covassin says that men typically hide their symptoms in order to not let their coaches or other team members down. She also says that men have more opportunities to play in a professional setting, so they do not want to put their careers on the line for the sake of a head injury. "Males will not be completely honest and report those injuries because they do have a chance to go pro sport. Females, on the other hand, even if we go pro sport, we really don't make any money," she said. "For us, it's generally not about going pro and making millions of dollars."

LET THE TRUTH BE TOLD

MISDIAGNOSIS & DOCTOR BIAS

Could your diagnosis be wrong? Doctors are human and sometimes make mistakes. Perhaps a cluster of symptoms suggests a few different diagnoses, and a lack of time or an incomplete set of diagnostic criteria may result in a patient receiving a diagnosis that either does not seem appropriate, turns out to be incorrect, or may cause greater injury or even death.

Research published in *Canadian Medical Association Journal* in May 2004 found that between 9,000 and 24,000 deaths occur in Canada each year due to "adverse events" in the hospital setting (with an adverse event being defined as an unintended injury or complication that is caused by health care management, rather than by the patient's underlying disease, and that leads to death, disability at the time of discharge, or prolonged hospital stays). According to the researchers, approximately 37% to 51% of these adverse events have been judged, in retrospect, to be potentially preventable.

Medical errors may include administering the wrong medication or dosage and misreading a laboratory result. Misdiagnosis – receiving the wrong diagnosis for your ailment – is the top offender. According to research published in *JAMA* in September 2012, cases of delayed, missed, and incorrect diagnosis are common, with an incidence in the range of 10% to 20% Additionally, research published in *BMJ Quality and Safety* in October 2013 found that in the United States, among malpractice claims, diagnostic errors appear to be the most common, most costly, and most dangerous of medical mistakes.

While there are several factors that can lead to a medical misdiagnosis, including miscommunication between medical professionals and technology glitches, doctor bias has been found to play a considerable role.

IMPLICIT BIAS AND THE MEDICAL COMMUNITY

Some biases are explicit, such as overt racism or sexism, and are therefore easier to detect and condemn. However, often times an individual's bias is implicit, which makes it more difficult to track and unpack. "Implicit bias is the automatic associations that your mind makes about a person or situation that you're really not aware of," explained Dr. Elizabeth Chapman, the lead author of an article on physicians and implicit bias published in the November 2013 issue of *Journal of General Internal Medicine*. She is also a clinical Assistant Professor at the University of Wisconsin's Department of Medicine, Division of Geriatrics and Gerontology. →

IMPLICIT BIAS IS PARTICULARLY CHALLENGING BECAUSE EVEN THOUGH YOU DO NOT REALIZE IT IS OCCURRING, IT IS NEVERTHELESS INFLUENCING YOUR BEHAVIOUR, AND IT IS HIGHLY DEPENDENT ON THE RACIAL, ETHNIC, GENDER, AND OTHER STEREOTYPES THAT ARE PREVALENT IN SOCIETY.

Doctors can possess the same kinds of implicit bias as anyone else, and, problematically, their unconscious beliefs about others can influence the kinds of treatments that they offer. "It's one thing to have a negative social interaction, but it's a completely different thing when that social interaction is in a clinic when you're supposed to be making a diagnosis," said Dr. Chapman. Doctors are frequently under time constraints and do not have complete information (including appropriate medical tests and/or equipment), which further amplifies the effects of implicit bias, said Dr. Chapman.

IMPLICIT BIASES THAT CAN AFFECT A MEDICAL DIAGNOSIS INCLUDE GENDERED, RACIAL, WEIGHT, AND AGE-BASED BIAS.

For example, multiple studies have shown that it takes a woman longer than a man to receive a diagnosis for a physical ailment. One study published in *BMJ Open* in June 2010 found that being a woman was independently associated with higher odds of three or more pre-referral consultations for bladder cancer and renal cancer. In other words, it took women much longer to receive the appropriate diagnosis. The researchers therefore concluded that there are notable gender inequalities in the timeliness of diagnosis of urological cancers.

AS A RESULT OF GENDER BIAS, WOMEN'S CONCERNS ARE OFTEN ATTRIBUTED TO STRESS AND ANXIETY.

One study published in *Chest* found that in a hypothetical situation, men were more often correctly diagnosed with chronic obstructive pulmonary disease (COPD) than were women, until the appropriate testing was ordered. "By and large, the men were thought to have COPD, which is lung disease due to smoking. The women patients who were absolutely identical, except female, were more likely to be thought of as having some sort of psychiatric disease," explained Dr. Chapman. "So maybe they're anxious or there's something going on that isn't necessarily explained by a physiologic diagnosis."

With autoimmune diseases, such as multiple sclerosis, celiac disease, and rheumatoid arthritis, which disproportionately affect women, an American Autoimmune Related Diseases Association study found that the average time for diagnosis of a serious autoimmune disease is 4.6 years. During that period, the patient typically has visited 4.8 doctors, and 46% of the patients were told initially that they were too concerned about their health or that they were chronic complainers. The connections between women and hysteria have historical roots and this bias is still well-established today – even if referred to as other names, such as anxiety or stress.

Implicit biases can also factor into whether or not an individual with a mid- or dark-skinned complexion is appropriately diagnosed with a health condition. For example, Dr. Chapman noted that if a physician has implicit bias where race is concerned – if they "tended to think that African Americans were more likely to be uncooperative" or less "likely to follow through on treatment" – those beliefs could impact how the doctor treats that patient. One study found that "if someone had higher implicit bias, they were less likely to recommend guideline indicated treatment for chest pain in people of colour and women." In this example, "African-American women fared the worst, which is unfortunately pretty common," said Dr. Chapman.

OLDER ADULTS MAY FACE ADDITIONAL PROBLEMS IF THEIR DOCTORS HAVE CERTAIN IMPLICIT BIASES TOWARDS AGING.

Dr. Chapman noted that some physicians may not necessarily understand what constitutes "normal" aging, which can lead to missed diagnoses. Certain early signs of Alzheimer's disease or other types of dementia, for example, can mimic the symptoms of depression or anxiety, especially for women, which means that symptoms might again be linked to psychological issues.

MUCH OF THE PROBLEM WITH IMPLICIT BIAS IS SYSTEMIC, AND THE MEDICAL SYSTEM REFLECTS THESE BIASES.

Women have only routinely been included in medical trials since

the early 1990s, when feminist mobilization led the National Institutes of Health in the United States to mandate women's inclusion in government-funded health research. The same can be said for African-American participants, who have also been historically excluded from large-scale medical data.

In a recent study, published in the October 2019 issue of *Science*, researchers found that a medical technology commonly used in hospitals in the United States was skewed towards helping Caucasian patients over African-American patients. The algorithm used patients' past medical costs to predict how much they were likely to cost the health-care system. However, for socioeconomic and other reasons, African-American patients have historically incurred lower health-care costs than Caucasian patients with the same conditions. As a result of this faulty metric, the wrong individuals were being prioritized for certain health care programs. Importantly, the research team is partnering with the developer of a widely-used algorithm to help eliminate this bias.

WHAT CAN BE DONE TO OVERCOME BIAS

A more diverse physician population will help to lessen the effects of implicit bias, said Dr. Chapman. In the meantime, doctors should be aware that implicit bias exists and should be proactive in overcoming these biases. A first step for a doctor, Dr. Chapman suggested, might be to take the Implicit Association Test (developed by psychologists at Harvard University, the University of Virginia, and the University of Washington) to discover what unconscious biases she or he possesses (available online at **https://implicit.harvard.edu/implicit/canada/takeatest.html**).

AS PATIENTS, WE MAY HAVE TO ADVOCATE FOR OURSELVES.

Samaria Nancy Cardinal knows this truth all too well. She has personally suffered from the ill effects of not receiving the correct diagnosis for her health issues. Now, Cardinal is a volunteer patient advocate with the Canadian Patient Safety Institute, an organization whose mandate is to inspire and advance a culture committed to sustained improvement for safer healthcare. Cardinal shares her story with others so that they might avoid some of the hardships that she has endured.

Many years ago, Cardinal, who is of Métis descent, was struggling with mental health issues. Her father had to experience the devastating effects of the residential school system, and as a result "didn't know how to parent," said Cardinal, and he was abusive. Cardinal was traumatized from a young age and ran away from home. At one point, she was hospitalized due to severe post-partum depression and was eventually diagnosed with bi-polar disorder. However, Cardinal was not offered counselling; instead, she was prescribed various medications and at one point was taking fifteen different medications and received bi-weekly shock treatment for several years. "I entrusted doctors to help me, but instead I lost fifteen years of my life," said Cardinal.

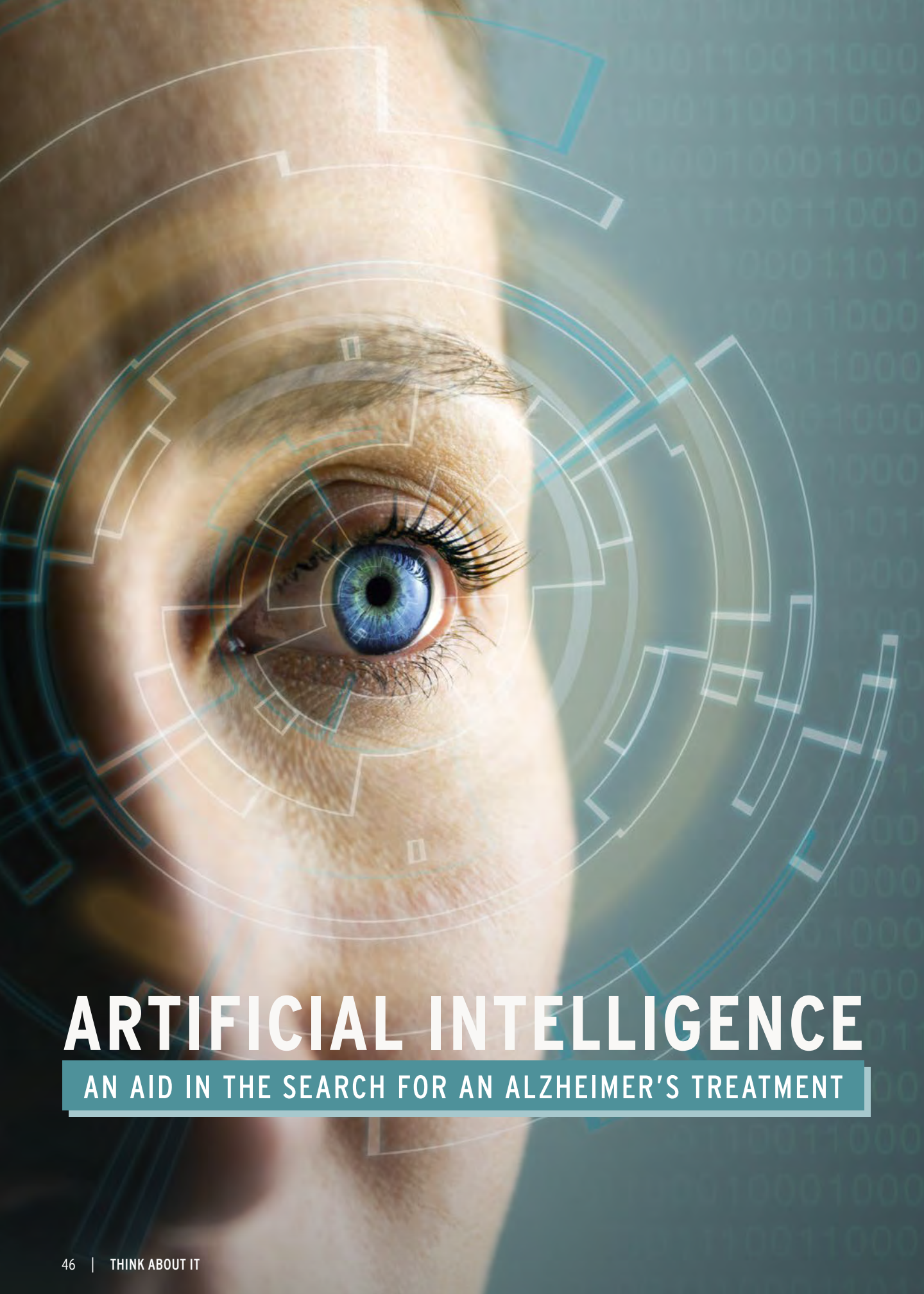
Fortunately, Cardinal was able to turn her life around when someone she met encouraged her to take an active role in her health care. She gained the strength she needed and found two new doctors – a family physician and a psychiatrist – who were able to work with her. The psychiatrist helped her get off of the medications that she was on, a process that took approximately two years. "The doctors say now that I have PTSD; I never had bipolar. I was treated totally wrong. If I'd had sufficient counselling, I would have been okay."

Today, Cardinal is back in university, and owns her own house and business. "I found my way back, but there's many people who never do." Cardinal believes that implicit bias played a role in her misdiagnosis, or at least lack of knowledge. "I believe that if the Canadian health care system and doctors would have understood what Indigenous people have gone through, the intergenerational trauma, they wouldn't have diagnosed me as bipolar. It would have been PTSD."

WHAT YOU SHOULD DO IF YOU ARE WORRIED THAT YOU HAVE RECEIVED AN INCORRECT DIAGNOSIS

It is important to remember that doctors are not perfect and may make mistakes. "When I was younger, I thought doctors were Gods," said Cardinal. "I thought they knew everything. I no longer think that way." If you do not feel comfortable with your diagnosis or particular course of treatment, then do not hesitate to vocalize your concerns, ask questions, and/or seek a second (or third or fourth) opinion. "You have to get pushy. It's your life. Doctors aren't living your life. They're consultants in your life." By being actively involved in your own health advocacy, you not only gain a greater sense of control, but also a better understanding of your condition and greater satisfaction with your care.

SAMARIA NANCY CARDINAL



ARTIFICIAL INTELLIGENCE

AN AID IN THE SEARCH FOR AN ALZHEIMER'S TREATMENT

Alzheimer's disease is the most common cause of dementia, responsible for approximately 60% to 80% of dementia cases. It presents a massive, expensive healthcare challenge and, currently, there is no treatment to slow down the development of the disease or to stop its progression.

According to Alzheimer's Disease International, 50 million people were living with dementia worldwide in 2018, and that number is forecasted to rise to 152 million by 2050. The total estimated global cost of dementia was US$1 trillion in 2018, and alarmingly, is expected to double by 2030.

Alzheimer's disease develops over a long period of time, with changes in the brain starting decades before symptoms appear.

THERE IS A LONG "PRE-CLINICAL" STAGE OF THE DISEASE THAT USUALLY GOES COMPLETELY UNNOTICED BECAUSE OF THE LACK OF SYMPTOMS, BUT DAMAGE IS OCCURRING IN THE BRAIN.

Typically, by the time that an individual is diagnosed with Alzheimer's disease, the brain damage that has already materialized is extensive and irreversible.

Increasingly, researchers are wondering if treatments tested to date may have failed because the disease was already too far advanced, and perhaps emerging treatments will be effective if the disease is targeted in the earliest stages (i.e. during the preclinical and mild cognitive impairment (MCI) stages).

A BIOMARKER is a measurable substance that indicates the severity or presence of a disease. For example, blood sugar levels are evaluated to determine if someone has diabetes.

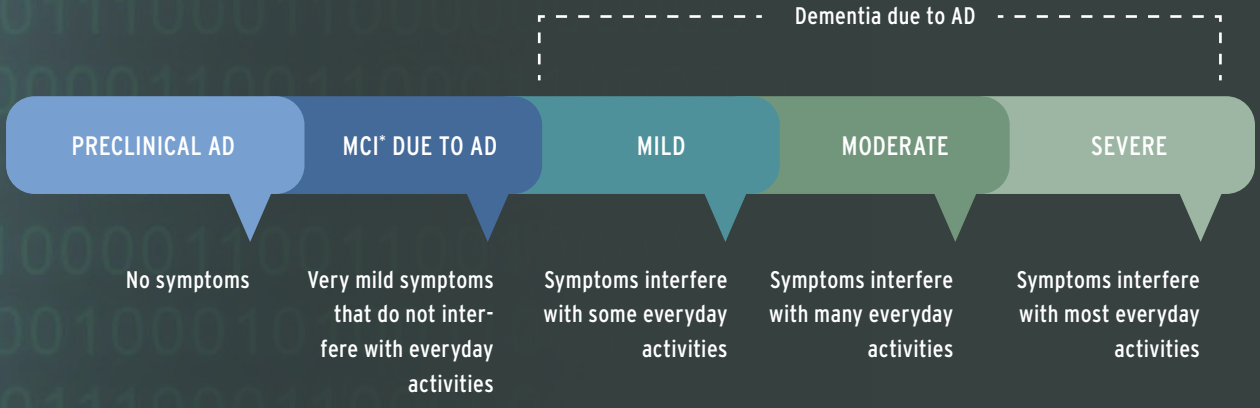
In order to develop treatments targeting these stages, though, scientists need to be able to diagnose Alzheimer's disease early or determine how to accurately predict who is likely to develop the disease.

Diagnosing the disease at any stage is complex; dementia is a syndrome with multiple potential causes, and there is not a single test for dementia due to Alzheimer's disease. Diagnosing the disease in the early stages or predicting the likelihood that MCI will progress to Alzheimer's disease (i.e. determining a prognosis) is especially challenging.

THANKFULLY, ARTIFICIAL INTELLIGENCE (AI) IS SHOWING PROMISE AS A TOOL TO HELP WITH EARLY DIAGNOSIS AND MORE ACCURATE PROGNOSIS.

AI is capable of spotting small changes or patterns that humans →

THE STAGES OF ALZHEIMER'S DISEASE (AD)



Mild cognitive impairment

The ALZHEIMER'S DISEASE NEUROIMAGING INITIATIVE is a global project that connects researchers with large quantities of study data (including MRI and PET images, genetics, cognitive tests, and cerebrospinal fluid and blood tests) in order to help scientists learn about the progression of Alzheimer's disease.

may not be able to detect and can analyze vast amounts of data quickly and consistently, in some cases taking into consideration a number of variables at once.

Within the last decade, there has been exponential growth in research to develop AI methods for the diagnosis and prognosis of Alzheimer's disease. Researchers are using varied AI methods to analyze different variables that have been associated with Alzheimer's disease, collected in different ways.

Some of these variables are potential biomarkers of the disease (e.g., amyloid-beta and tau levels, glucose metabolism in the brain, or brain atrophy), collected using brain scans, or extraction of cerebrospinal fluid or blood. Examples of other variables studied include clinical and neuropsychological assessments, as well as sociodemographic data.

To give you a glimpse into how AI is being applied to the diagnosis and prognosis of Alzheimer's disease, below are highlights from just a few examples of the studies that have been completed to date.

AI PREDICTS ALZHEIMER'S BASED ON GLUCOSE UPTAKE IN THE BRAIN

Alzheimer's disease has been linked with changes in glucose uptake in certain brain regions, but these changes are very subtle and can be challenging to detect. Researchers from the University of California trained a "deep learning algorithm" to look for these subtle patterns in FDG-PET (18-F-fluorodeoxyglucose positron emission tomography) scans. In this type of scan, FDG (a radioactive glucose compound) is injected into the blood and then the PET scan measures the uptake of FDG in brain cells, an indicator of metabolic activity.

Using a large number of FDG-PET brain scan images obtained from the Alzheimer's Disease Neuroimaging Initiative (ADNI), the algorithm was trained to detect metabolic patterns that are associated with Alzheimer's disease. Then, that learning was tested in a small sample to see how well the trained algorithm could predict a final clinical diagnosis.

THE AI PERFORMED WELL, ACHIEVING 100% SENSITIVITY AT DETECTING ALZHEIMER'S DISEASE ON AVERAGE MORE THAN SIX YEARS BEFORE THE FINAL DIAGNOSIS.

"We were very pleased with how well the algorithm performed," said Dr. Jae Ho Sohn, one of the researchers involved in the study, from the Radiology and Biomedical Imaging Department at the University of California in San Francisco. "It was able to predict every single case that advanced to Alzheimer's disease."

Dr. Sohn cautioned, though, that the testing sample was small and more work needs to be done to further validate their findings. "Overall, our study demonstrates that AI can be used to predict AD diagnosis from FDG-PET scans with high accuracy," he continued. "With further validation using larger and more diverse datasets, our algorithm may prove to be a useful tool to assist radiologists as they interpret scans and improve the accuracy of prognosis." These findings were published in 2019 in *Radiology*.

AI PREDICTS ALZHEIMER'S BY ANALYZING MULTIPLE VARIABLES

A team of Canadian researchers have developed an AI algorithm that analyzes data on multiple variables spanning up to six years – magnetic resonance imaging, genetic and demographic details, and cognitive assessments – looking for patterns that suggest an individual's cognitive function is likely to decline and lead to Alzheimer's disease. The researchers shared their findings in September 2018 in *PLOS Computational Biology*.

Like the scientists in the previously-described study, these researchers also used data from the ADNI to train their algorithm – in this case, data on 800 seniors, some with normal cognitive function, some experiencing MCI, and others diagnosed with Alzheimer's disease. The results were then replicated in a separate sample of individuals who were part of the Australian Imaging, Biomarkers, and Lifestyle Study of Ageing.

"The algorithm that we developed can help predict whether an individual's cognitive function is likely to deteriorate towards Alzheimer's disease within the next five years," said Dr. Mallar Chakravarty, one of the study's authors and an Assistant Professor in McGill University's Department of Psychiatry and the Douglas Hospital Research Institute.

BY HELPING WITH EARLY DETECTION OF INDIVIDUALS AT RISK FOR COGNITIVE DECLINE, OUR ALGORITHM COULD AID IN ACCURATE, EARLY PROGNOSIS OF ALZHEIMER'S DISEASE.

"However, more research is needed," continued Dr. Chakravarty. "We are currently working on further testing with new data, to help refine predictions and see if we can predict even farther into the future than five years."

AI PREDICTS CONVERSION FROM MCI TO ALZHEIMER'S USING ONLY EASILY-COLLECTED DATA

There are many variables that have been linked to the risk of developing Alzheimer's disease, and the ease and cost of collecting data for each variable ranges widely. Brain imaging and the collection of cerebrospinal fluid, for example, tend to be expensive and/or invasive, whereas the collection of sociodemographic information and neuropsychological testing are not.

One group of researchers set out to develop an algorithm to predict conversion from MCI to Alzheimer's disease based only on information that can be collected non-invasively, quickly, easily, and inexpensively in a clinic setting. These researchers also used data from the ADNI – from 550 individuals who had MCI. In particular, they investigated the predictive role of sociodemographic characteristics, subtypes of MCI, clinical dementia scale ratings, and neuropsychological test results.

The algorithm that they developed to predict three-year conversion to Alzheimer's disease among MCI subjects demonstrated high predictive accuracy using just information that can be easily collected in a doctor's office. However, the researchers noted that further testing is required in order to explore potential interactions between the multiple predictors that they examined.

In their paper – published in July 2019 in *Frontiers in Neurology* – the researchers explained how their algorithm has promising potential as a screening tool that could be used as a first step to identify individuals who should undergo additional testing because they appear to be at high risk of developing Alzheimer's disease.

BY REDUCING THE NUMBER OF PEOPLE WHO REQUIRE ADDITIONAL EXAMINATION USING MORE COSTLY AND INVASIVE TOOLS, THEIR ALGORITHM COULD HELP REDUCE THE BURDEN OF ALZHEIMER'S DISEASE.

PREDICTING ALZHEIMER'S EARLY IS IMPRECISE, BUT CRITICAL

Any prognosis, including ones aided by artificial intelligence, is just a prediction, not a certainty. However, knowing that an individual has a high likelihood of developing Alzheimer's disease is helpful, even if it involves a degree of imprecision. Not only is early diagnosis or prognosis helpful for research to find potential treatments, it is also beneficial for individuals and their families.

Learning early on that you are at high risk of developing Alzheimer's disease allows time to plan for the future while cognition is still intact and, most importantly, it can provide motivation to make lifestyle changes in support of brain health, including exercising, making healthy food choices, minimizing stress, and engaging in cognitively-stimulating leisure activities.

THROUGH THE WEEDS

POTENTIAL BENEFITS & RISKS OF LATE-LIFE CANNABIS USE

Use of cannabis by young people up to 25 years of age is discouraged because it can have detrimental effects on their developing brains. But, what is the impact of using cannabis for adults, particularly older adults? This is an important question because more and more older adults are using medical or recreational cannabis.

Older adults can be drawn to using cannabis in an attempt to alleviate various age-related symptoms and diseases that are not adequately controlled with other available treatment options, and now, because of changes in the legality of cannabis in some places such as Canada, it is easier to access cannabis than ever before.

RESEARCH SUGGESTS THAT OLDER ADULTS MAY BENEFIT FROM CANNABIS TREATMENT FOR A VARIETY OF COMMON AGE-RELATED SYMPTOMS, INCLUDING CHRONIC PAIN, TROUBLE SLEEPING, AND POOR APPETITE.

Cannabis may also help with some aspects of dementia. However, the research available on cannabis for older populations is very limited at this point in time, and the conclusions are not always consistent.

LATE-LIFE CANNABIS USE MAY (OR MAY NOT) IMPROVE COGNITION

One recent systematic review conducted by Dr. Emmi Scott and colleagues examined the findings from 26 studies about the neurocognitive effects of medical or recreational cannabis use by older adults, some healthy and some with neurocognitive disorders,

CANNABIS is a flowering plant that has been used for thousands of years for its medicinal effects. Its phytochemical contents can vary widely, but the two most commonly-studied components are THC (tetrahydrocannabinol) and CBD (cannabidiol).

THC is responsible for the psychoactive effects, or the "high," while CBD produces a physical effect without the "high"; in fact, CBD is thought to dampen down or offset the psychoactive effects of THC. Many medical uses of cannabis are CBD-oriented. Labels on legal cannabis describe the amounts of each of these two components.

Use of medical cannabis by older adults is on the rise, with prevalence rates estimated to range from 7% to more than one-third, depending on the country.

including dementia and Parkinson's disease. They found that with higher doses and heavier lifetime use, generally modest reductions in cognitive performance were detected.

The researchers noted, though, that variation in the cannabis product used, the outcomes measured, and the quality of the research studies limited the conclusions that they could make. And, they emphasized the need for more high-quality research on this subject. These findings were published in October 2019 in *Current Addiction Reports*.

However, another recent review conducted by Dr. Galit Weinstein and Dr. Sharon Sznitman, and published in May 2020 in *Ageing Research Reviews*, reached a somewhat different conclusion. These researchers also noted that evidence on late-life cannabis use and cognitive health is limited, and that more research is needed.

But, after reviewing available animal and human studies on the subject, they concluded that cannabis use in old age may not be linked with poorer cognitive function and may, in fact, be associated with improved brain health.

"There is definitely a big gap in the current knowledge about late-life cannabis use and cognitive health, but the limited evidence available on this important topic suggests that the known detrimental effects of early-life cannabis use may not translate to use in older ages," said Dr. Weinstein, Associate Professor of Neuroepidemiology at the University of Haifa School of Public Health in Israel.

> "CANNABIS USE IN OLDER AGE LOOKS LIKE IT MIGHT BE NEUROPROTECTIVE, ALTHOUGH FIRM CONCLUSIONS CANNOT BE REACHED AT THIS POINT.

CANNABIS MAY HELP WITH SOME DEMENTIA SYMPTOMS

While there is currently no research that proves cannabis or cannabis-based products can prevent, stop, slow, or reverse →

Individuals with dementia do not just experience loss of memory and thinking skills. It is estimated that 90% of people with dementia also experience **behavioural and psychological symptoms of dementia (BPSD)** – also referred to as **neuropsychiatric symptoms of dementia (NPS)** – which can include agitation, physical and verbal aggression, depression, anxiety, delusions, hallucinations, decreased inhibition, wandering, and sleep and eating disorders.

See "When Push Comes to Shove" starting on page 50 of issue #8 of Mind Over Matter® to learn more about BPSD and non-drug approaches for managing them.

dementia, there is some evidence that suggests cannabis can help with managing some of the symptoms of dementia, including the particularly challenging behavioural and psychological symptoms of dementia (BPSD). This is good news because the current pharmaceutical options for addressing BPSD have limited effectiveness and can have significant side effects that often outweigh their benefits.

Again, there is some inconsistency in the findings to date, though. For example:

- A meta-analysis conducted by Dr. Myuri Ruthirakuhan and colleagues – published in *The Journal of Clinical Psychiatry* in 2019 – compiled the data from six studies involving a combined total of 251 participants, examining the efficacy of cannabinoids on agitation and aggression in individuals with Alzheimer's disease (AD). Cannabinoids are the bioactive components of the cannabis plant. There are at least 140 different cannabinoids with varying effects. Cannabinoids can be naturally derived or synthetically produced.

  These researchers found that overall the evidence about the efficacy of cannabinoids on agitation and aggression in patients with AD was inconclusive, and warned that any usage should be closely monitored to ensure safety because cannabinoid treatment was associated with increased sedation.

- However, another recent systematic review and meta-analysis – conducted by Dr. Anees Bahji and colleagues – examined the use of cannabinoids for neuropsychiatric symptoms of dementia, synthesizing data across nine trials involving 205 participants. They found that cannabinoids were well-tolerated and led to significant improvements across neuropsychiatric symptom instruments.

  "Although the overall quality of the studies we analyzed was low, we concluded that there is preliminary evidence for the efficacy and tolerability of cannabinoids as treatments for the neuropsychiatric symptoms of dementia," explained Dr. Bahji, a resident in the Department of Psychiatry at Queen's University School of Medicine in Canada. "More research is needed to determine the real-world effectiveness, but cannabinoids show promise as a potential treatment for NPS." These findings were published in December 2019 in *The Canadian Journal of Psychiatry*.

WHY ARE THE FINDINGS INCONSISTENT?

Research conducted to date is quite limited, and differences in research design and quality may be contributing to the inconsistent findings.

For starters, "cannabis" is not a single substance; rather, it consists of hundreds of phytochemicals, some of which are cannabinoids and others that are not. The amounts of each phytochemical can vary across strains of the plant, and across batches of strains. Many factors influence the concentration of phytochemicals in a cannabis plant, including nutrition, humidity, temperature, the age of the plant, when it was harvested, and how it was stored.

Additionally, the effects will vary depending on whether the whole cannabis plant is used, or just an individual component or combination of components, and whether those components are naturally derived or synthetically produced.

There are even more variables that affect how an individual responds to cannabis or cannabinoid use, including the dose, how it is consumed, and differences in individual physiology.

MORE RESEARCH IS NEEDED

While much of the research to date is promising, it is also inconclusive. More research is required in order to flesh out what cannabis "product" – at what dose and frequency – is best for which people, with what symptoms or conditions (if any).

SYNERGY MIGHT BE KEY

Some researchers have found an "entourage effect" with cannabis, where it seems to work better in certain instances when it is administered as a whole-plant extract, rather than as an isolated phytochemical part(s).

AS ADDITIONAL STUDIES ARE BEING CONDUCTED, RESEARCHERS SHOULD BE SURE TO CONSIDER THE POTENTIALLY UNIQUE EFFECTS ON DIFFERENT POPULATIONS.

For example, older adults may need to take special caution in using cannabis because of other drugs that they already take, differences in how drugs are absorbed, metabolized, and eliminated in old age, or increased cardiovascular risk.

Sex and gender differences should be considered, too. "As with all substances, there is a wide range of sex- and gender-related factors that influence how substances are consumed, and their physical, mental, and social impacts," said Dr. Lorraine Greaves, clinical professor at the University of British Columbia and senior investigator with the Centre of Excellence for Women's Health in Canada.

> **IN PARTICULAR, FEMALES ARE MORE AFFECTED BY CANNABIS, IN LOWER AMOUNTS, THAN MALES. WOMEN OFTEN 'TELESCOPE' TO DEPENDENCE MUCH FASTER THAN MEN.**

"Sex-related factors include the biological, physiological, anatomical, and genetic differences that impact how cannabis affects female versus male bodies, while gender-related factors include the effects of gender norms, relations, and identity," continued Dr. Greaves.

"Men, for example, use cannabis more often and in larger amounts, and are more likely to smoke it. All research on cannabis should take sex and gender into account, analyze data accordingly, and report on it so that more precise recommendations can be made for men and women, but this is an area that needs considerably more attention and growth."

IN THE MEANTIME, SHOULD YOU OR A LOVED ONE TRY CANNABIS?

Because of the promising findings to date, people might be tempted to investigate cannabis for dementia or other common symptoms of older age, without waiting for further research.

If you find yourself wanting to explore the potential therapeutic benefits of cannabis for yourself or a loved one, and you live in a place where medical cannabis is legal, it is best that you seek out the advice of a cannabis prescriber and/or a health professional in your area. Do not just purchase and use recreational cannabis, even if it is legal.

A HEALTH PROFESSIONAL SHOULD PROVIDE YOU WITH A PERSONALIZED PRESCRIPTION AND MONITOR YOUR RESPONSE TO THE TREATMENT.

A research paper published in November 2019 in *Journal of Clinical Medicine* provides doctors with a suggested treatment protocol for medical cannabis specifically for older adults. The researchers' recommendations provide an idea of what you might expect if you get a prescription for medical cannabis. They advise that medical cannabis should be considered carefully and individually for each patient after a risk-benefit analysis, and followed by frequent monitoring for efficacy and adverse events.

> **IT'S IMPORTANT TO NOTE THAT CANNABIS TREATMENT IS NOT SUITABLE FOR ALL PATIENTS AND SHOULD ONLY BE USED AFTER OTHER EVIDENCE-BASED TREATMENTS HAVE FAILED,**

explained Dr. Ran Abuhasira, lead author of the study, and a doctor at Soroka University Medical Center and Ben-Gurion University of the Negev in Israel. "While there are no absolute contraindications for cannabis treatment in the geriatric population, doctors must consider the potential risks of treatment. In particular, we suggest avoiding cannabis treatment if someone has severe cardiovascular disease, an existing psychotic disorder, or a history of addiction. Caution is also needed for patients with gait instability, nervous system impairment, polypharmacy, or reduced drug elimination mechanisms."

"The preferred method of administration of medical cannabis for older adults is sublingual – oil placed under the tongue. Smoking cannabis should be avoided because of the negative impact on lung and respiratory function," Dr. Abuhasira continued. "Most importantly, we recommend starting with a low dosage, raising it slowly if necessary, and keeping it as low as possible."

POLYPHARMACY refers to the simultaneous use of multiple drugs by an individual.

GREAT EXPECTATIONS

WHAT TO EXPECT AFTER YOUR LOVED ONE RECEIVES A DEMENTIA DIAGNOSIS

Insight courtesy of Lakelyn Hogan, MA, MBA,
Gerontologist and Caregiver Advocate, Home Instead Senior Care®

Receiving a diagnosis of Alzheimer's disease or another type of dementia can bring mixed and complex emotions. For some, it may be a relief that there is finally an explanation for symptoms. For others, it may trigger fear and/or anxiety about the unknowns that lie ahead. For those providing care and support to individuals with a new diagnosis, it is difficult to know what to expect. The following article provides some helpful tips and insights for caring for a loved one with dementia.

THERE IS A LOT TO LEARN. If you are a first-time caregiver, there will be a learning curve. It is important to realize that dementia is a progressive disease that causes the brain to fail over time. You will want to learn more about the disease progression, symptoms, and dementia-related behaviours that can result.

> **MOST IMPORTANTLY, YOU WILL WANT TO DISCOVER THE BEST APPROACH FOR SUPPORTING YOUR LOVED ONE TO HELP MAINTAIN HER OR HIS DIGNITY AND RESPECT.**

When searching for information, be sure to seek out reputable sources for information such as the Alzheimer Society of Canada, **HelpForAlzheimersFamilies.ca**, or **Womensbrainhealth.org**.

THE JOURNEY IS DIFFERENT FOR EVERYONE. While there are common dementia-related behaviours and symptoms, individuals experience dementia differently. People move through the early, middle, and late stages of the disease at varying rates. On average, a person lives four to eight years after a diagnosis, but others can live as long as 20 years with the disease. It is important for caregivers to understand where their loved one is in the disease process.

PLAN AHEAD. It is critical to do as much planning as possible in the early stages of dementia. This provides your loved one with an opportunity to make her or his wishes known. Planning ahead also helps family caregivers understand the options for care and will allow for informed decision making along the way.

CREATE A SUPPORT SYSTEM. The demands of caregiving may be overwhelming at times. It is important to identify your support system early. Support can come from family, friends, neighbours, your faith community, and/or professional services, such as in-home care. Those in your support system may directly help with the care of the individual living with dementia and also support you as the caregiver.

> **WHEN PEOPLE ASK HOW THEY CAN HELP, KEEP A FEW IDEAS ON HAND.**

For example, let a friend pick up your children from school or ask a neighbour to reach out the next time she or he goes grocery shopping. Another way to find support is by joining a support group (in-person or online) to connect with people who are going through similar experiences.

FIND A HEALTHY OUTLET FOR EMOTIONS. Emotional highs and lows are a normal part of the caregiving journey. There may be days when you are feeling frustrated, resentful, and guilty. Other days you may experience joy, happiness, and contentment. Do your best to accept your emotions for what they are and try not to judge your feelings. Find a healthy way to release your emotions. Consider journaling your feelings, or talking to a family member, friend, and/or mental health professional. Yoga, meditation, and exercise are also great ways to release emotions and boost your overall mood.

BE AN ADVOCATE. As a caregiver, you will likely accompany your loved one to medical appointments, assist with paperwork, and help arrange support services. During these activities, you may find the need to advocate on behalf of your loved one to ensure that her or his unique needs are being met and that hers or his voice is being heard.

> **REMEMBER, YOU KNOW YOUR LOVED ONE BEST AND YOU CAN BE A CHAMPION FOR HER OR HIS WELL-BEING.**

PRIORITIZE SELF-CARE. If you do not take care of yourself, you will not be able to be the best caregiver that you can be. Find opportunities to step away from the caregiving situation. Ask a family member, friend, or neighbour to provide temporary care while you tend to your own physical and emotional needs. You can consider hiring a professional care provider to give you a break and time to recharge, and there are respite grant programs available. More information can be found at **HelpForAlzheimersFamilies.ca**.

> **WHILE A NEW DIAGNOSIS OFTEN LEAVES FAMILIES WITH MORE QUESTIONS THAN ANSWERS, IT IS IMPORTANT TO KNOW THAT YOU ARE NOT ALONE.**

Millions of family caregivers are going through a similar experience. The good news is that there are numerous resources and support to help you along the way. For more tips on navigating the challenges of caregiving, visit **CaregiverStress.com**.

LAKELYN HOGAN

DOS AND DON'TS FOR FAMILY CAREGIVERS

- Don't delay important conversations.
- Don't assume your loved one can no longer do things on her or his own.
- Don't be afraid to ask for help.
- Don't let yourself become isolated.
- Do put a plan in place for the future.
- Do find ways to enhance your loved one's independence and offer support without taking over.
- Do seek out supportive services to help ease burden and stress.
- Do reach out for support when needed and consider joining a support group.

TO PUT IT MILDLY

HELPING CHILDREN UNDERSTAND DEMENTIA

Children are highly attuned to their environment and readily notice changes in those around them. If a family member has Alzheimer's disease or other type of dementia, children, depending on their age and how often they see that person, will inevitably notice that something is different with their loved one. They may have questions about the changes in their family member, or they may be hesitant to voice their concerns, or perhaps not even know how to express themselves about the situation. While it is natural to want to protect children from difficult or upsetting situations, it is important to explain to children what to expect and how to react to their loved one's cognitive decline.

TIPS FOR A PARENT OR CAREGIVER ON HOW TO DISCUSS DEMENTIA WITH A CHILD

1. BE HONEST.

"One of the crucial things is you've got to be open. People often think that they should shield kids from bad news and not tell them. That's always a mistake," says Dr. Robert B. Santulli, an Honorary Associate Professor of Psychiatry at the Geisel School of Medicine, and a Visiting Associate Professor in the Department of Psychological and Brain Sciences, at Dartmouth College in Hanover, New Hampshire. He is also co-author of the book *The Emotional Journey of the Alzheimer's Family.*

"Honesty is extremely important," agrees Toby Haberkorn, author of *When My Grammy Forgets, I Remember: A Child's Perspective on Dementia*, a book for children that stimulates discussion about compassion and dementia. "If you try to hide the fact that grandpa or grandma has dementia, children are going to know that something is wrong and for some reason it is too bad or too frightening to talk about," says Dr. Santulli.

2. CONTROL THE NARRATIVE AND LABEL APPROPRIATELY.

It is essential that parents take an active role and "control the narrative," according to Haberkorn. With the Internet at their fingertips, children can search their own information, and some of what they find may not be accurate or will not be age appropriate. →

HOW YOU EXPLAIN THE SITUATION TO YOUR CHILDREN WILL DEPEND ON THEIR AGE, AS WELL AS THEIR RELATIONSHIP TO THE LOVED ONE WITH DEMENTIA.

Although the language that you use or how much detail you go into will vary, it is important to explain that the child's loved one is ill, says Dr. Santulli. This will help your child understand why the person may be behaving differently than usual or forgetting more often. Although the news may be distressing, children may find it a relief to know that their loved one's behaviour is part of an illness and is not directed at them. This is particularly important with children, as they may attribute the behavioural changes to their own actions.

With teenagers, Dr. Santulli believes that parents should speak more openly and identify the disease as dementia. Having accurate, age-appropriate information can empower teenagers, says Haberkorn, and will position them as having a role in a "significant family situation."

3. ASK QUESTIONS AND REASSURE.

Parents can direct the conversation based on the particular questions that the child asks or how much information she or he seems interested in hearing about. Some questions that you could ask your child include "how do you feel about this?" or "grandma called you by somebody else's name, why do you think that happened?"

PARENTS MAY BE SURPRISED BY HOW CHILDREN INTERPRET THE SITUATION, AND ASKING YOUR CHILDREN POINTED QUESTIONS WILL START AN IMPORTANT DIALOGUE ON THE SUBJECT.

Often, children may be fearful that because Alzheimer's disease or other types of dementia are illnesses, they may develop the illness too or that their parents will. You can explain to the child that dementia is not contagious, like a cold or chicken pox, says Dr. Santulli. "Children need to be reassured that the family is okay, and that mommy and daddy are safe," says Haberkorn. In other words, children need to understand that they will not develop the disease simply by being around their loved one. You can also explain to a concerned child that those who develop these brain diseases are typically older adults.

4. ENGAGE EMOTIONS AND HIGHLIGHT UNCONDITIONAL LOVE.

When they realize that a loved one is ill and that her or his behaviour has changed, children will likely experience a wide range of emotions, including uncertainty and fear. "Children are afraid because they just don't understand it," says Dr. Santulli, and explaining the disease will therefore be of great assistance. Children may also experience jealousy if their family member lives in the same house and is receiving additional attention from their parents, says Dr. Santulli. They may be sad that their relationship with their loved one is different now, particularly if they have been close over the years, and they may have to learn how to be more patient as well.

Once the child knows what is going on, Haberkorn suggests using a practice called "compassionate modeling," where parents offer compassionate care to the loved one with dementia. "If we are compassionate toward the person with dementia, [children] will be compassionate," which is a skill that a child can use beyond the family dynamic. It is critical to show and inform a confused child that the love we have for the person with dementia and the love that she or he has for us in return still exists, even if her or his behaviour has changed.

> **CHILDREN NEED TO BE REASSURED THAT LOVE IS UNCONDITIONAL, THAT THE PERSON WITH DEMENTIA IS PART OF THE FAMILY, AND WE AS A FAMILY CONTINUE TO LOVE AND CARE FOR EACH OTHER,**

says Haberkorn. Embodying this love is the central theme of Haberkorn's book.

5. INVOLVE YOUR CHILDREN.

Try to find ways to involve your children in providing care and stimulation for their loved one with dementia. This will help make the situation seem more normal for them and will prevent them from feeling excluded. It is important to show children that they can still interact with their loved one, and can engage in fun activities together, such as listening to music, working on a puzzle, colouring, singing songs, and reading stories – all of which can be positive, says Dr. Santulli.

Spending time together can be beneficial for both children and the loved one with dementia. However, do not give your children

(particularly younger children) too much responsibility, or let caregiving tasks consume too much of their time. Make sure that your children have time for their own interests and needs, such as playing with friends, participating in extracurricular activities, or doing homework.

CONSIDERATIONS FOR ADULT CHILDREN COPING WITH A PARENT'S YOUNG-ONSET DEMENTIA

Approximately 16,000 Canadians under the age of 65 are living with young-onset dementia. According to the Alzheimer Society of Canada, young-onset dementia accounts for an estimated 2% to 8% of all dementia cases. A dementia diagnosis is difficult at any age, and comes with unique challenges – for both the person diagnosed and her or his loved ones – when an individual is diagnosed in her or his 40s or 50s.

A paper published in a special issue of *International Psychogeriatrics* in December 2014 reported that adult children (between the ages of 20 and 37) of a parent with young-onset dementia experienced great burdens and feelings of neglect during the development of their parents' dementia, both by their family and by health and social services. Stress was increased within the family, and depending on sibling dynamics and positionality (i.e. gender, age, and relationship to parents), reactions to the circumstances varied. However, in all of the interviews conducted, adult children expressed a great need for information and support.

As Dr. Santulli observes, young-onset dementia can be particularly complex and challenging because "the parent who is the care provider now is the person who needs care," and he has witnessed individuals in their teenage years have to cope with this situation. An adult child's feelings in these circumstances can be an intense combination of sadness, anger, confusion, and fear. Professional counselling is often extremely valuable as a way to understand and cope.

Another paper published in the same issue found that adolescent children (between the ages of 15 and 27) living with a parent with young-onset dementia had difficulties managing all of the responsibilities and showed concerns about their future.

ALTHOUGH MOST ADULT CHILDREN WERE INITIALLY RELUCTANT TO SEEK PROFESSIONAL CARE, SEVERAL OF THEM EXPRESSED THE NEED FOR PRACTICAL GUIDANCE TO ADDRESS THE CHANGING BEHAVIOUR OF THEIR PARENT.

The children felt more comfortable speaking with someone who was familiar with their situation, and who had specific knowledge of young-onset dementia and the services available. These findings reinforce the need for a personal, family-centered approach to young-onset dementia, as well as the demand for more accessible and specific information about the diagnosis and development of the disease.

Additionally, a 2015 study published in *Journal of Multidisciplinary Healthcare* found that growing up with a parent with young-onset dementia has a great impact on the child's situation and experiences of personal development. The researchers concluded that children of a parent with young-onset dementia are a group with unmet needs for support. It is critical for children of all ages to receive support, as well as access to information on the course, treatment, and management of the disease, when a loved one is diagnosed with dementia. Fortunately, there are now more resources and support systems available, including The Change Foundation and Carers Canada.

ON THE COVER

WITH ANNE-MARIE AND MURIEL MEDIWAKE

Becoming a parent has a way of changing any of us. When it happened to journalist Anne-Marie Mediwake, the impact was threefold, given that she gave birth to triplets. In her case, parenthood caused her to start paying more attention to her overall health. But it was only more recently that she started tuning into the importance of looking after your brain health.

"I study a lot of research, but it was research that I hadn't read," said Anne-Marie, the co-host of the CTV program Your Morning. "When I started to learn the statistics on women's brain health, and the lack of research on women's health concerns more generally, it really made me pay attention."

After discovering the disconnect between research funding and the disproportionate number of women facing dementia, Anne-Marie was inspired to take part in a powerful video in the fall of 2019, along with several other prominent Canadians, highlighting the need for research that explores the differences between men and women. It was all part of the Stand Ahead™ Challenge, Women's Brain Health Initiative's fundraising and educational campaign that was launched on Canada's first official Women's Brain Health Day, December 2nd.

Now, Anne-Marie is taking it a step further, by appearing on the cover of Mind Over Matter® alongside her mother Muriel. In a joint interview with the magazine, they spoke about their growing understanding of brain health and the ways in which you can help protect your cognitive vitality.

For Muriel Mediwake, this awareness came later in life. "I think as a parent I was just so busy, I didn't have enough time to think about it," she said.

A native of Scotland, she met and married Sri Lankan native Mervyn Mediwake in London, and later moved to his home country, where Anne-Marie was born. However, growing civil unrest caused them to move back to the UK, where Muriel gave birth to Anne-Marie's sister. Then it was off to Canada, where they finally settled in southern Alberta.

"Each country was different, each time we moved my lifestyle was different. In Alberta, I ended up getting into real estate and was extremely busy. So, then you have the challenges of having a family plus a business," said Muriel.

Life experience brought greater understanding of the importance of a healthy lifestyle. About ten years ago, her husband's heart problems caused them both to change their diets. Muriel was also

moved by the challenges faced by her sister back in Scotland, whose husband developed dementia.

"I watched how she struggled to take care of him, especially in the later years, before he passed away. It's very difficult," said Muriel. "Only in the last five years have I really become aware of how our body is interconnected, and how our physical bodies affect our emotions and our brains, and just the effect on our overall health."

Anne-Marie similarly watched a friend have to deal with caring for parents with dementia. "It was very sobering to watch that journey, to see their health start to decline as well, and to see them become both emotionally and physically exhausted."

When she was offered the opportunity to host a national morning show, the career advancement also brought the personal challenge of learning to adjust to a workday that begins in the middle of the night. It is a shift where everyone obsesses about sleep and everyone struggles to get enough. "The first year was brutal. I was tired all the time. Sicknesses lasted longer. It took two years before I finally got into a rhythm," she said.

Never one to go to the gym, Anne-Marie ultimately decided that she needed to improve her fitness and hired a personal trainer. While her first workout was rocky – she had brought the wrong shoes and forgot her water bottle – the regimen soon paid off and, in the process, she was taking a step that has proven to be important for brain health. "Adding in exercise was 100% different. I wanted more energy and to be stronger. I didn't want to be tired all of the time."

One benefit of the morning show hours is that she has afternoons available to spend more time with her two daughters and her son, who turn 13 in June. Her husband, Darryl Konynenbelt, a former journalist, works in communications. The arrival of the triplets happily meant closer contact with her parents, who moved to Toronto to help with the extraordinary demands of an instant family. As it happens, there is research to suggest that helping to care for grandchildren could have benefits for brain health.

"The first couple of years here, it was almost nonstop. But absolutely it was good for me," said Muriel. She is also a determined walker. Anne-Marie's home is a mere five-minute drive away, but Muriel prefers to go on foot, even if offered a lift.

As the triplets grew older and the demands lessened, Muriel sought a new outlet for her energy, taking a course in counselling. Now, Muriel helps lead a healing prayer group through a church in Oakville, supporting those in need. "There's such a reward for doing it, when you see the difference it makes in people's lives, it's very encouraging."

For mother and daughter, brain health awareness may have come later in life, but they are both embracing it with vigour.

OCT 2019 | PRESENTED BY CIBC

FROM HER LIPS

(L-R) Lynn Posluns, Teresa Raponi, Sylvia Soyka, Kim Campbell, Jeanne Beker

THE RITZ-CARLTON | TORONTO

TO OUR EARS™

(L-R) Carly Picov, Robin Picov

BRAIN BUZZ

Support for WBHI and women's brain health continues

JAN 2020 | PRESENTED BY RBC | PETER PAN BISTRO

ENGAGING MILLENNIAL MINDS // THE HEALING POWER OF ART

(L-R Top Row) Laura Best, Matteo Tino, Katie Black, Laurie Piltz, Carly Picov (L-R Bottom Row) Vitina Blumenthal, Or Har-Gil, Jordan Rasberry

(L-R) Lynn Posluns, Sandy Gordon, Sean Jones, Gerry Throop, JoAnne Korten

(L-R) Gloria Salomon-Levy, Rosita Salomon

(L-R) Deborah Roberts, Tonya Lewis Lee, Zoe Buckman

NOV 2019 | NYC | LA GRENOUILLE

STAND AHEAD™ PRE-LAUNCH

Martha Stewart

(L-R) Alan Pepe, Lynn Posluns

Candace Bushnell

(L-R) Lauren Remington Platt, Laura Chau

Almond Butter & Jam Cauliflower Proats

SERVES 2 TIME: 5 MIN PREP (6+ HOURS)

INGREDIENTS

- 2/3 cup gluten-free old-fashioned rolled oats
- 1 cup frozen cauliflower rice (straight from the bag or pre-steamed and chilled or frozen)
- 2 Tbsp Nuzest Clean Lean Smooth Vanilla protein powder
- 2 Tbsp chia seeds
- 2 Tbsp unsweetened powdered almond butter
- 1 tsp pure almond extract
- 1 1/2 cups unsweetened almond milk
- 1/2 cup plain probiotic coconut yogurt or plain Greek yogurt
- Lakanto sugar-free monk fruit sweetener, pure stevia, or sweetener of choice, adjusted to taste

OPTIONAL TOPPINGS:

- homemade raspberry chia jam
- chopped nuts and/or seeds
- nut butter
- bee pollen
- granola
- cacao nibs or dark chocolate chips
- or toppings of choice

INSTRUCTIONS

1. Put all of the ingredients excluding toppings in a bowl or divide into single-serving mason jars. Stir well to combine.

2. Cover and refrigerate overnight or for a minimum of 6 hours.

3. In the morning, stir and add additional milk as needed for desired consistency.

Can be stored in an airtight container in the fridge for up to 5 days. Serve chilled with your choice of toppings.

Chia Seeds

Chia seeds are a great source of fibre and omega-3's, a good fat, to help reduce inflammation and support the health of your brain.

MEMORYMORSELS®

A WOMEN'S BRAIN HEALTH INITIATIVE

@DRTARASUNSHINE

This edition's recipes are courtesy of Dr. Tara Weir, doctor & mom of three turned recipe creator, blogger, and wellness consultant.

For more recipes, morsels, and the latest from our Featured Foodie, Dr. Tara Weir, visit **memorymorsels.org**.

Almond Banana Bread

MAKES 1 LOAF | TIME: 25 MIN PREP (90 MIN)

INGREDIENTS

- **3 pasture-raised eggs**
- **1/2 cup Lakanto Golden sugar-free monk fruit sweetener (or substitute coconut sugar)**
- **1/3 cup avocado oil or melted coconut oil**
- **4 medium ripe bananas, mashed**
- **1 1/2 tsp apple cider vinegar**
- **1 to 2 tsp pure almond extract***
- **1 1/2 cups almond flour**
- **1/3 cup arrowroot flour**
- **2 Tbsp coconut flour**
- **2 tsp ground Ceylon cinnamon**
- **1 tsp baking soda**
- **1/4 tsp sea salt**
- **1 cup well-chopped almonds (optional, or substitute chocolate chunks)**

INSTRUCTIONS

1. Preheat oven to 350F and grease an 8.5 x 4.5" standard loaf pan.

2. In a large bowl, using a hand mixer, beat together eggs, sweetener, and oil. Add mashed banana, apple cider vinegar, and almond extract, and blend well.

3. In a separate bowl, mix together almond flour, arrowroot flour, coconut flour, cinnamon, baking soda, and salt. Add to wet ingredients and stir until just combined. Fold in nuts.

4. Scrape the batter into prepared loaf pan. Bake for 45 to 50 minutes, or until top golden brown and a toothpick inserted into the middle of the cake comes out clean.

5. Cool in pan for 10 to 15 minutes, then remove to wire rack to finish cooling.

Can be stored in an airtight container at room temperature for 3 days, in the fridge for a week, or well-wrapped in the freezer for up to 2 months.

**Note: For a mild almond taste, use 1 tsp pure almond extract. Increase to 2 tsp (my preference) for a more pronounced marzipan flavour.*

Bananas

Bananas are packed with Vitamin B6 which can help to improve cognitive function.

Chia Seed Jam

MAKES 1.5 CUPS | TIME: 20 MIN

INGREDIENTS

- **2 cups fresh and/or frozen organic raspberries, blueberries, or mixed berries**
- **2 Tbsp water**
- **2 Tbsp chia seeds**

OPTIONAL:

- **1 tsp pure vanilla or almond extract, or a couple drops orange essential oils**
- **Lakanto Sugar-free Monk fruit Sweetener, Swerve sugar-free sweetener, raw honey, or sweetener of choice, adjusted to taste**

INSTRUCTIONS

1. Put berries and water in a pot over medium heat and cook until they start to break down and become syrupy, approximately 8 minutes.

2. Using a wooden spoon or potato masher, mash the fruit to desired consistency.

3. Remove from heat and stir in extract or essential oils if using. Sweeten to taste. Add chia seeds and stir until well combined.

4. Let stand 10 minutes or until thickened.

Enjoy now or transfer to a jar and cover and refrigerate. Jam will thicken further as it chills. Chia Seed Jam can be stored in an airtight container in the fridge for 2 weeks or frozen for up to 2 months.

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Women's Brain Health Initiative is a charitable non-profit organization that funds research and develops preventative health education programs to combat brain-aging diseases that affect women. We rely on philanthropic gifts to support these endeavours.

You can support Women's Brain Health Initiative and be a Champion for women and their brain health. Your charitable donation can further intensify our impact, allowing us to reach more and teach more.

CARE TO JOIN US?

WE ARE TRULY GRATEFUL TO

Fondation Brain Canada Foundation

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Brain Canada recognizes Women's Brain Health Initiative for its role in educating the public about the importance of women's brain health and the role of prevention, but is not responsible for the accuracy of the contents of this magazine.

Women's Brain Health Initiative

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