MIND OVER MATTER®

THE IMPACT OF SEX & GENDER ON BRAIN HEALTH

DRUGS IMPACT WOMEN DIFFERENTLY THAN THEY DO MEN

SPARKNOTES FROM A CAREGIVER

WHAT'S YOUR LONELINESS SCORE?

HOPE OR HYPE: WILL STEM CELLS CURE ALZHEIMER'S?

STRONG BODY, *STRONG MIND*

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

WITH GRATITUDE

THIS EDITION OF MIND OVER MATTER® WAS MADE POSSIBLE THANKS TO THE GENEROUS SUPPORT AND ENCOURAGEMENT OF INEZ JABALPURWALA, AND THE ONGOING GENEROSITY OF BRAIN CANADA FOUNDATION AND HEALTH CANADA.

The brain is the most critical organ in the body but the least understood – it has often been characterized as the last frontier in human science. As researchers delve deeper into our understanding of the brain and brain disorders, the complexity of the challenge increases, and so too does our need to join different disciplines and to pursue new thinking and new approaches.

Founded in 1998, the Brain Canada Foundation supports and advances transformative, original and outstanding brain research focused on outcomes that will benefit Canadians impacted by brain disorders and their families.

Since 2012, Brain Canada has awarded $183.9 million in new funding – with the financial support of Health Canada through the Canada Brain Research Fund and with funds from private donors and partner organizations – to support 188 projects involving more than 800 researchers at over 100 institutions across Canada.

In order to deliver on benefits for all Canadians, it is of critical importance to include sex and gender considerations in research. For example, although 70% of people experiencing chronic pain are women, only about 20% of the work being published in the field of pain research examines both male and female animal models, as stated by Dr. Jeffrey Mogil, a Brain Canada-funded researcher from McGill University.

Similarly, knowing that about 70% of all cases of dementia worldwide affect women, according to the Alzheimer's Society of Canada, it is important to ensure that sex and gender differences are taken into account in research. Brain Canada currently funds 23 projects totalling about $32 million in the area of Alzheimer's and dementia, and has started asking researchers to incorporate sex and gender considerations in their research in the early planning stages of their projects.

This sex and gender imbalance can be found across several other research areas, as was reported in an article published in *Nature* in 2010 that looked at over 2,000 published animal studies. In stroke research, for example, only 38% of animal studies included females despite the higher prevalence and poorer outcomes of stroke in women. In mental health research, fewer than 45% of studies focused on anxiety and depression included female animals, despite these diagnoses being twice as common in women.

Brain Canada also believes in the importance of encouraging young women and the next generation of researchers. Currently, 69% of the recipients of our capacity-building awards – which are awarded to graduate students, postdoctoral fellows and early career researchers – are women. Ensuring that women's voices are heard and celebrated in research is not only about equity; it is about excellence. Listening to diverse view points and making use of everyone's talents will help us solve the complex challenges related to understanding the brain and brain disorders, and will improve the health and quality of life of millions of Canadians.

Brain Canada is proud to once again partner with Women's Brain Health Initiative on this issue of *MIND OVER MATTER®*. On the occasion of Mother's Day, when we recognize all of the great women in our lives, we are proud to support WBHI's goals of increasing awareness of women's brain health issues, and of advocating for the inclusion of sex and gender considerations in research.

Inez Jabalpurwala
President and CEO, Brain Canada Foundation

EDITOR'S LETTER

"I am a mother, a daughter, and a woman who has curated a full career and a family life. I have done this with my mother as the angel on my shoulder, and my daughters as my inspirations. As I watch my daughters grow, I watch my mom shrink before us, and I feel the weight of that, and how it might impact my girls. There is much to be learned."

~ Susan Hodkinson
Chief Operating Officer and Human Resources Practice Group Leader, Crowe Soberman LLP

Every year, millions of mothers will disappear without ever leaving the room. In fact, over 70% of Alzheimer's disease patients are women, with the number of dementia sufferers expected to double by the year 2040.

The data is irrefutable that women heavily bear the burden of Alzheimer's, the most common cause of dementia. Women are twice as likely as men to succumb to dementia and depression, and are two-and-a-half times more likely to be providing care for someone else with a brain-aging disorder – not only for their own blood-relatives, but also for their partners' blood-relatives and loved ones – and too frequently women give up hard-fought successful careers in order to provide that care.

There is no question that the risk of developing Alzheimer's increases with age. This means that as Canadians live longer, the proportion of the population with Alzheimer's grows as well. Although women statistically live longer than men, longevity alone does not explain why far more females are likely to develop the disease and to decline more rapidly compared to their male counterparts.

LEARNING WHAT UNDERLIES SEX DIFFERENCES IS IMPORTANT NOT ONLY TO ENHANCE OUR UNDERSTANDING OF ALZHEIMER'S DISEASE AND OTHER BRAIN-AGING DISORDERS, BUT ALSO TO DEVELOP BETTER TREATMENTS AND PREVENTATIVE MEASURES.

To find answers for our daughters and granddaughters, Women's Brain Health Initiative (WBHI) invests in groundbreaking sex-based research, including funding for the first ever Research Chair in Women's Brain Health and Aging, awarded to Dr. Gillian Einstein at the University of Toronto. WBHI also supports the Canadian Consortium on Neurodegeneration in Aging (CCNA), a five-year research program involving Canada's best and brightest neuro-scientists, to ensure that brain-aging disease studies take sex and gender into account.

While we actively engage in scientific discovery for tomorrow, we want to share what the research findings are to date in order to give you access to the most current thinking on ways to stay cognitively healthy for as long as possible. With our latest issue of MIND OVER MATTER®, Women's Brain Health Initiative continues to provide you with the most cutting-edge research at your finger-tips. Mounting evidence indicates that maintaining a healthy life-style can delay or prevent some dementias and the earlier you start, the stronger the protective effect will be.

Together we can accelerate the pace of progress. Your generous support today will allow us to reach more, and teach more. I hope that you'll join us in our efforts to make a difference in the lives of women globally through our education initiatives and gender-focused research.

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

THINK ABOUT IT

HELPFUL THINKING

BETTER THINKING

CONTRIBUTORS

STEPHANIE HAHN | WRITER

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

MARGI OKSNER | WRITER

Margi is the principal of Margi Oksner & Associates, a full service consulting firm that offers strategic, creative and business planning in the philanthropic sector. "My mother's Alzheimer's journey gave me an insight into this horrific disease and the motivation to help others. Working with WBHI is my way of learning more and sharing that knowledge with others. Thank you Lynn Posluns for the opportunity to do both."

DILIA NARDUZZI | WRITER

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

RENI WALKER | WRITER

Reni Walker is a writer and media professional in Toronto. When she's not writing for some of Canada's largest media companies and brands, she's either working on producing her first documentary or managing a busy family of three teens and two dogs. In this issue, you can read her articles on the many causes of memory loss, foods that might prevent help dementia, and exciting developments in stem cell research.

SUSANNE GAGE | WRITER & CONTRIBUTING EDITOR

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."

VITINA BLUMENTHAL | WRITER & CREATIVE DIRECTOR

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

AMY CHAPLICK | CONTRIBUTING EDITOR

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

KRYSTAL & PATRICIA FAHIE | ON THE COVER

Dedicated to mind and body health, Patricia and Krystal are honoured to represent the Women's Brain Health community. Their relationship is built on unwavering support, deep respect and friendship; attributes passed down from Pat's own mother. Experiences of the past, present and future are the cornerstones to the memories they hope to cherish forever.

COVER PHOTO: JAYLYN TODD

STRONG BODY, **STRONG** MIND

Weight Train for Your Brain

WHAT IS RESISTANCE TRAINING?

Resistance training (also known as weight training or strength training) involves moving limbs against resistance to improve muscular strength and endurance. The resistance can be provided by weights, bands, or your own body weight and gravity.

WHAT IS AEROBIC EXERCISE?

Aerobic (or cardiovascular) exercise is any activity that stimulates an increase in heart rate and respiration, while using large muscle groups repetitively and rhythmically. Examples include walking, swimming, dancing, aerobic classes, cycling, and using cardio machines such as the treadmill and the elliptical.

Exercise is good for your entire body, including your brain. Much research has focused on the benefits of aerobic exercise for brain health, but more recently scientists have turned their attention to studying the effects of resistance training. Overall, resistance training appears to boost cognitive functioning, but its effects may vary depending on a variety of factors, including the cognitive task being tested, the exerciser's current cognitive state, and the frequency, duration, and intensity of the exercise. While a link has been established between cognitive function and resistance training, it remains unclear whether the cognitive »

improvements exhibited are a direct result of the resistance exercise or whether the two may share a common alternative cause.

RESEARCH HIGHLIGHTS LINKING RESISTANCE TRAINING & COGNITIVE HEALTH

A review of resistance training benefits by O'Connor et al., published in the September/October 2010 issue of the *American Journal of Lifestyle Medicine*, found seven randomized controlled trials that demonstrated that strength training on its own was associated with "small to moderate improvements in cognition among healthy older adults" and that memory tasks were improved the most.

A University of British Columbia-based experiment conducted by Liu-Ambrose et al. aimed to compare the effect of resistance training with "balance and tone" exercise training on the performance of executive cognitive functions in cognitively healthy women between the ages of 65 and 75.

THOSE WHO PARTICIPATED IN RESISTANCE TRAINING CLASSES ONCE OR TWICE A WEEK OVER THE COURSE OF TWELVE MONTHS EXPERIENCED SIGNIFICANTLY IMPROVED EXECUTIVE COGNITIVE FUNCTION IN THE AREAS OF SELECTIVE ATTENTION AND CONFLICT RESOLUTION,

compared with those who participated in the balance and tone training exercises. These results were published in the January, 2010 issue of *Archives of Internal Medicine*.

A later study conducted by the same research team, published in the April, 2012 issue of *Archives of Internal Medicine*, involved women between the ages of 70 and 80 with probable mild cognitive impairment (MCI) – a well-recognized risk factor for dementia. After only six months, the experimental group that participated in twice-weekly resistance training classes experienced significant cognitive improvement. In particular, they enjoyed "improved selective attention/conflict resolution, associative and spatial memory, and regional patterns of functional brain plasticity," compared with twice-weekly balance and tone exercises.

Additionally, six months of twice-weekly resistance training greatly improved associative memory performance, co-occurring with positive functional changes in hemodynamic activity (the circulation of blood) in regions involved in the memorization of associations. Impaired associative memory is a hallmark of early stages of Alzheimer's disease. Importantly, the study suggests that twice-weekly resistance training is a promising strategy to "alter the trajectory of cognitive decline in seniors with mild cognitive impairment."

WHAT IS MILD COGNITIVE IMPAIRMENT (MCI)?

MCI is a condition in which people experience a slight but noticeable decline in cognitive abilities, including memory and thinking skills. Individuals with MCI have an increased risk of developing Alzheimer's disease or another type of dementia.

In a more recent study involving Liu-Ambrose, published in the October 2015 issue of the *Journal of the American Geriatric Society,* researchers focused on 54 of the women from the above-noted study who had been found during magnetic resonance imaging (MRI) scans to have white matter lesions on their brains. Cognitive impairment and falls increase morbidity and mortality in older adults, and both syndromes are associated with white matter lesions.

Thus, interventions that prevent or slow the progression of white matter lesions may help preserve cognitive function and mobility in older adults. The participants were assigned to one of three groups for a period of twelve months: (1) once-weekly progressive resistance training; (2) twice-weekly progressive resistance training; or (3) the control group, which participated in twice-weekly balance and tone training. Upon completion of the trial, the women who engaged in twice-weekly resistance training had a significantly lower volume of white matter lesions than those in the control group.

There was no significant difference between the control group and the women who participated in resistance training once per week.

"THESE FINDING SUGGEST THAT WEIGHT TRAINING HAS THE POTENTIAL TO MODERATE DISEASE COURSE IN THE BRAIN,"

explained Dr. Teresa Liu-Ambrose, co-author of the study and professor of physical therapy at the University of British Columbia. However, in order to experience the benefits of resistance training, it appears that a minimum threshold of exercise is necessary (in this case, exercising at least twice a week).

Recent research from the University of Sydney also found that resistance training improves the cognitive function of older adults with mild cognitive impairment. The Study of Mental and Resistance Training (SMART) was a randomized, controlled trial involving 100 community-dwelling adults with MCI between the ages of 55 and 86. Participants assigned to the resistance training experimental group (doing high intensity training two to three days per week) showed significant improvements in "global cognitive function" at the end of the six-month intervention, and the benefits persisted even twelve months after the supervised exercise sessions ended.

These new findings are reinforced by research from the SMART trial published in the March 2016 issue of *Molecular Psychiatry* by Suo et al., wherein MRI scans of participants showed an expansion of grey matter in a particular part of the brain called the posterior cingulate cortex among those who took part in the resistance training program. Reduced function in this part of the brain is an early sign of dementia. Significantly, the expansion of grey matter was associated with improvement in cognition.

WHAT LEVEL OF INTENSITY IS BEST?

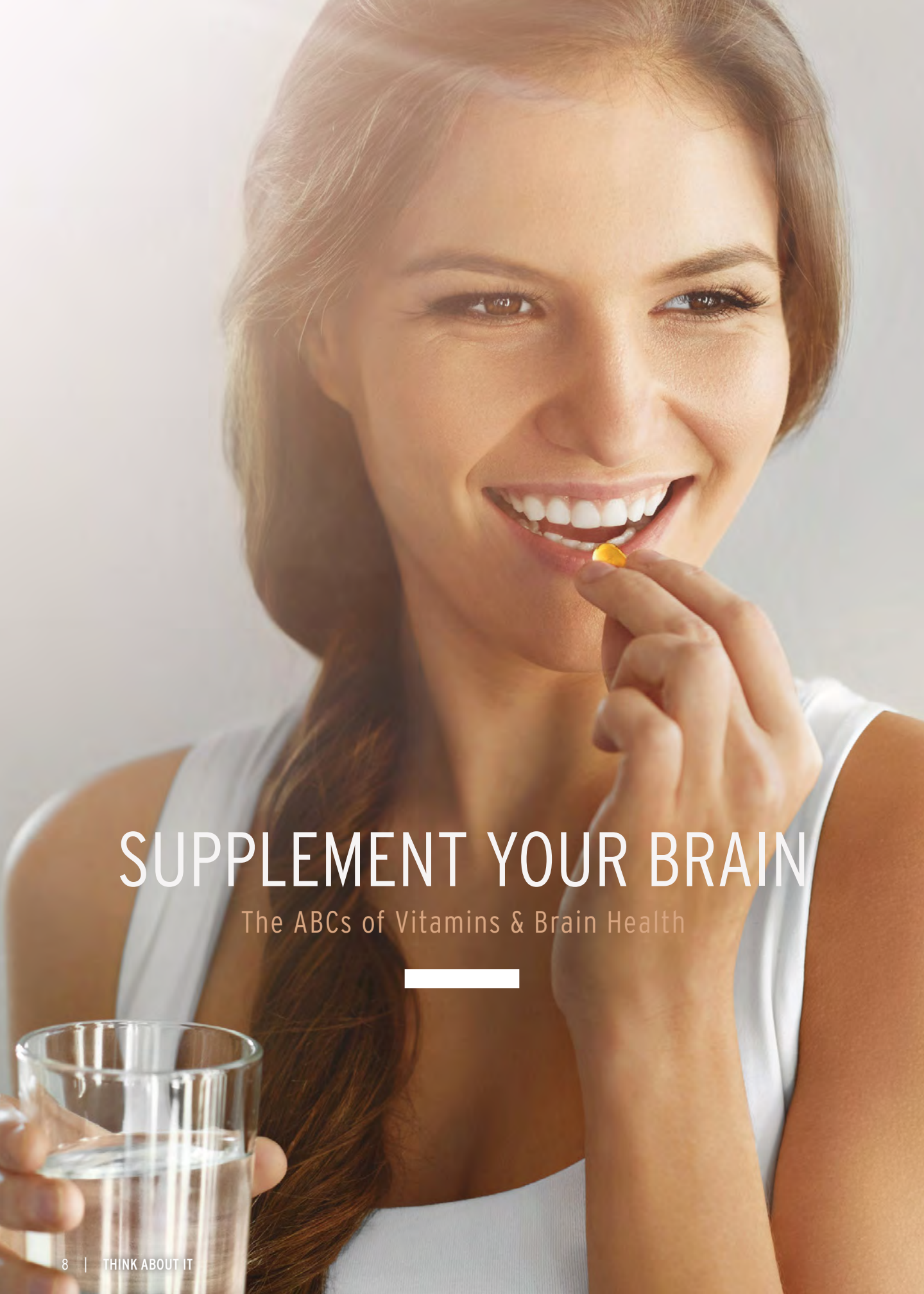
A study conducted by Cassilhas et al., published in the August 2007 issue of *Medicine & Science in Sports & Exercise*, assessed the impact of 24-week resistance training at two different intensities on cognitive functions in elderly, cognitively-intact men (between the ages of 65 and 75). Participants were divided into three groups: (1) resistance training at a moderate intensity; (2) resistance training at a high intensity; or (3) the control group. Researchers found that both of the exercise groups experienced more improvement in cognitive performance than the control group on several tests, supporting previous findings that resistance training helps improve cognitive functioning. Additionally, researchers found that moderate- and high-intensity resistance exercise programs had equally beneficial effects on cognitive functioning.

More recent research by Mavros et al., published in the *Journal of the American Geriatrics Society* in 2016, revealed that

WEIGHT TRAINING SHOULD BE CHALLENGING ENOUGH TO MAXIMIZE STRENGTH GAINS, BECAUSE THAT HAS THE LARGEST IMPACT ON AN INDIVIDUAL'S COGNITIVE HEALTH.

Older adults with mild cognitive impairment who participated in six months of high-intensity resistance training two or three times a week experienced significant improvements in cognitive function. These findings, which were part of the SMART trial, suggest that improvements in cognitive function are "directly related to gains in muscle strength." Dr. Yorgi Mavros, lead author of the study and a lecturer in the Faculty of Health Sciences at the University of Sydney, explained that "the stronger people became, the more cognitive benefit. So, the key is to do resistance training frequently – at least twice a week – and at a high intensity to maximize your strengths gains, thereby maximizing benefits for your brain."

As Dr. Liu-Ambrose has observed, resistance training tends to be an "underutilized type of exercise," particularly among senior women, despite being incredibly beneficial. Hopefully this growing body of research encourages you to get moving and, in particular, to weight train your brain.



SUPPLEMENT YOUR BRAIN

The ABCs of Vitamins & Brain Health

With the recent disappointing results of Alzheimer's and dementia-related drugs showing efficacy at trial, research on lifestyle and nutrition on brain health has been gaining momentum. Nutritional modifications have the advantage of being cost effective, easy to implement, generally safe and, in most cases, devoid of significant adverse effects. Many experts recommend getting your vitamins and minerals intake through a balanced, healthy diet. Along with engaging in mental and physical exercise,

WELL-BALANCED VITAMIN AND MINERAL CONSUMPTION "HELPS TO SLOW DOWN THE AGING PROCESS AND SLOW MENTAL DECLINE,"

says Dr. Weihong Song, a professor of psychiatry at the University of British Columbia and Canada Research Chair in Alzheimer's disease. The following is a summary of the most recent findings on vitamins and your brain health:

VITAMIN A

Vitamin A is primarily known for its ability to keep eyes and skin healthy. But does it have an effect on brain health, too? New research out of the University of British Columbia has found a link between *in utero* Vitamin A deficiency and an increased risk for developing Alzheimer's disease. Building on previous studies that linked low levels of Vitamin A with cognitive impairments in seniors, Dr. Song and his colleagues examined the effects of Vitamin A deprivation in the womb and infancy using genetically-engineered mice. The study, published online in *Acta Neuropathologica*, found that mice deprived of Vitamin A as fetuses developed more severe cognitive impairment and had increased production of amyloid beta – the protein that forms plaques that kill neurons in Alzheimer's patients. The researchers also found that these mice, when deprived of Vitamin A, performed worse as adults on a standard test of learning and memory. However, Dr. Song and his colleagues demonstrated that some reversal is possible. Mice who were deprived of Vitamin A *in utero* but were subsequently provided with supplements as newborns performed better on the tests than mice that did not receive such supplements.

Dr. Song notes that Vitamin A deficiency, though common in many low-income regions of the world where food choice is limited, is uncommon in North America. What's more, excess intake of the nutrient could be harmful to our systems and may cause liver damage, bone pain, and other health issues. It is also important to note that this study is not suggesting that Vitamin A can prevent or treat Alzheimer's disease, but rather "if you're lacking Vitamin A you have a higher chance of getting dementia or Alzheimer's-related dementia."

BETA-CAROTENE

Beta-carotene is an antioxidant – a molecule that helps to counteract the free radicals that damage cells in the body. The best sources of beta-carotene are yellow, orange, and green leafy fruits and vegetables (such as carrots, yam, spinach, sweet potatoes, and cantaloupe). In general, the more intense the colour of the fruit or vegetable, the more beta-carotene it contains. Some of the beta-carotene that we consume gets converted to Vitamin A in our bodies after we eat the fruits and vegetables that are rich in the antioxidant (this precursor form of Vitamin A is non-toxic). Research published in *The Journal of Alzheimer's Disease* in 2012 suggests that beta-carotene, along with Vitamin C, may help guard against the body's neurodegeneration (when neurons in the brain are damaged), which has been established as prevalent in individuals with dementia and Alzheimer's disease. Additionally, research out of the University of California, Los Angeles School of Medicine published in the *Journal of Gerontology* in 2006 examined data of seniors over a period of seven years and found that "among high-functioning older persons **antioxidants and beta-carotene in particular may offer protection from cognitive decline in persons with greater genetic susceptibility" to cognitive dysfunction**. Most health organizations suggest getting your beta-carotene from food sources instead of relying on supplements.

VITAMIN B

Vitamin B consists of eight different vitamins (thiamine (B_1), riboflavin (B_2), niacin (B_3), pantothenic acid (B_5), vitamin B_6, folate (B_9) and vitamin B_{12}) that each serve to support the nervous system. Research out of Oxford University, published in the *Proceedings of the National Academy of Sciences of the United States of America* in 2013, indicates that Vitamin B treatment could be used to prevent Alzheimer's disease. The researchers used a high-dose B-vitamin treatment (B_6, B_9, B_{12}) with participants who were over 70 years old and had mild cognitive impairment, and were considered to be at a higher risk of dementia. Those who received the Vitamin B treatment for two years (compared with those receiving a placebo), experienced a "slowing [in] the loss of grey matter in areas of the brain that are specifically affected by the Alzheimer's disease neurodegenerative process" as evidenced by magnetic resonance imaging (MRI) scans, says Dr. Gwenaëlle Douaud, one of the researchers on the study. While this news is exciting, this study was relatively small and more research needs to be conducted to determine whether Vitamin B supplementation is useful for the general population of older adults. >>

Like many of the other vitamins, supplementing with doses that are too high can be detrimental to one's health. Too much B_6, for instance, can damage nerves and too much B_3 can cause nausea, vomiting, and other symptoms.

VITAMIN C

Vitamin C is not only great for keeping a winter cold at bay, but also boosts immunity and can help curtail the development of many diseases. Research published in *The Journal of Alzheimer's Disease* in 2012 found that Vitamin C levels in individuals with mild dementia were "significantly lower" than in control persons even after adjusting for "school education, intake of dietary supplements, smoking habits, body mass index, and alcohol consumption." What's more, work published in the *American Journal of Alzheimer's Disease & Other Dementias* in 2013 suggests that since oxidative stress is believed to play a major role in the pathogenesis of Alzheimer's disease (those damaging free radicals at work again), Vitamin C's well-known antioxidant capabilities could impact these degenerative processes. No better reason to eat your dark, leafy greens and to snack on oranges!

CALCIUM AND MAGNESIUM

Calcium and magnesium are two of the most powerful minerals for a healthy brain. Of course, we know that we need calcium for healthy bones but "**the body also needs calcium for muscles to move and for nerves to carry messages between the brain and every body part**," according to the U.S. National Institutes of Health (NIH). Because the body stores calcium in the bones and draws upon it if needed, people usually are not deficient for the key bodily functions; however, as we age, the risk of developing osteoporosis increases. In addition to milk and yogurt, eat kale and broccoli for good sources of calcium.

Magnesium is needed to regulate muscle and nerve function, blood sugar levels, and blood pressure, and it helps make protein, bone, and DNA, according to the NIH. Research published in the journal Neuron in 2010 found that elderly rats experienced better working short- and long-term memory when given magnesium. Additionally, a 2016 PhD dissertation out of the Southern Illinois University at Carbondale found that magnesium helps rats with a traumatic brain injury to improve cognitive and motor functions. Green leafy veggies, nuts, and seeds, as well as some fortified foods, are good sources of magnesium.

CHOLINE

Choline is another vitamin that has been deemed necessary for brain health. In fact, the NIH says that "the availability of choline for the normal development of the brain is critical" and encourages pregnant women to eat choline-rich foods to ensure that their babies are getting enough of the vitamin. Research published in the 2011 issue of the *American Journal of Clinical Nutrition* studied individuals who did not have dementia and found that

THOSE WHO WERE GETTING ENOUGH CHOLINE THROUGH THEIR DIETS HAD BETTER COGNITIVE PERFORMANCE THAN THOSE WHO DID NOT.

Research published in the *Journal of Alzheimer's Disease* in 2012 found that choline, along with uridine and the fatty acid DHA, helps individuals in the early stages of Alzheimer's to improve their memory. More clinical trials are being conducted with this cocktail. Choline is found in eggs, liver, chicken, and soy and kidney beans.

VITAMIN D

Vitamin D has been long known to support bone health and can help stave off osteoporosis because it helps the body absorb calcium; however, this did not explain "why there were Vitamin D receptors throughout the brain," says Dr. David Llewellyn of the University of Exeter Medical School in the United Kingdom. Dr. Llewellyn and his colleagues published research in 2014 that shows that Vitamin D is linked to brain health and, more specifically, that people with low levels of Vitamin D experienced approximately a 60% increased risk of cognitive decline, and those who had dementia or Alzheimer's disease experienced approximately a 120% higher risk. Why is Vitamin D so important to brain health? Although more research needs to be conducted, Dr. Llewellyn points out that "it seems that **Vitamin D is protective in the brain in a number of ways, it is good for vascular health and may protect against stroke, which is one of the major risk factors for dementia**, and it may also protect against smaller vascular abnormalities that you see in the brain that have also been linked with a dementia risk." Dementia is also

associated with calcium dysregulation and "Vitamin D is a very potent regulator of calcium, so it might help there as well."

Many individuals living in developed countries are deficient in Vitamin D because one of the best ways to get it is by absorbing it through the skin from the sun – meaning that during the wintertime, or in places that are often cloudy, it becomes difficult to get enough of the vitamin. Oily fish is one of the best food sources of Vitamin D, says Dr. Llewellyn, but people do not consume enough of it to get the required amount. Vitamin D is one vitamin that you should consider supplementing if you know you are not getting enough of it, but first check your country-specific guidelines for dosage recommendations. Too much Vitamin D can lead to too-high calcium levels in the blood, which can cause bone pain and affect the organs – so more is not necessarily better.

VITAMIN E

Vitamin E is another antioxidant that protects our bodies from free radical damage. Research published in the *Journal of the American Medical Association* in 2013 found that "among patients with mild to moderate Alzheimer's disease, 2000 IU/day of alpha tocopherol [Vitamin E] compared with placebo resulted in slower functional decline." These findings suggest that those Alzheimer's patients getting an adequate amount of Vitamin E can maintain a higher quality of life for longer. More recent research published in the *Journal of Lipid Research* in 2015 compared zebrafish who received a diet deficient in Vitamin E with those who received adequate amounts. The researchers found that the Vitamin E-deficient fish had lower levels of very important brain-building fat phosphocholine with DHA, which is found in fatty fish like salmon.

"**If you don't have adequate Vitamin E, you aren't protecting the important fatty acid in your brain, DHA**, which is present in fish oils," says Dr. Maret Traber, a professor at the College of Public Health and Human Sciences at Oregon State University and lead author of the study.

The latest dietary guidelines suggest that 96% of women in the United States are deficient in Vitamin E, says Dr. Traber, and that this is because the foods that are high in the vitamin are not eaten frequently (foods like nuts, seeds, and more expensive oils like olive oil). As a result, a supplement or multivitamin may make sense. Be aware, however, that getting too much Vitamin E from supplements (rather than food) can cause blood hemorrhage, according to the NIH, and supplements can interact with several medications.

ZINC

Research about the relationship between zinc and Alzheimer's disease is currently inconsistent. A 2013 study out of the University of Wisconsin-Madison found that low zinc levels "may contribute to diseases like Alzheimer's and Parkinson's" because of zinc's role in creating proteins in the body and the brain. However, other studies published in 2014 have found that zinc levels did not matter when it came to Alzheimer's; rather, lower levels of zinc are simply indicative of the aging process in general. With many nutrients, more research is required, but we know that the body needs zinc because it increases immunity and some research suggests that it can help slow macular degeneration. Zinc is found in red meat, poultry, grains, and nuts.

While more long-term studies need to be conducted to determine exactly how particular vitamins may or may not impact Alzheimer's disease and other dementias, the foregoing research shows excellent promise for better understanding, preventing, and possibly treating the disease. Remember to check with your doctor before starting to take any kind of supplementation.

BENEFITS OF BILINGUALISM ON BRAIN HEALTH

Knowing More Than One Language Builds Cognitive Reserve

On June 30, 2016, Governor General David Johnston announced the new list of appointments to the Order of Canada. Among the recipients was Dr. Ellen Bialystok, O.C.

Admission into the Order of Canada is the second highest meritorious honour in the country's system of orders, decorations, and medals – second only to membership in the Order of Merit.

Dr. Ellen Bialystok, Toronto's York University Professor of Psychology and Rotman Research Institute Associate Scientist, was recently named an Officer of the Order of Canada (O.C.) for her contributions to our understanding of the "cognitive benefits of bilingualism, and for opening up new avenues of research in her field," according to the Governor General.

Dr. Bialystok believes that her admission into the O.C. will have a positive influence on education into the benefits of bilingualism.

"Canada is pretty sympathetic to bilingualism. But outside of Canada, there's great antipathy [towards bilingualism] and it's a constant battle ... to persuade people that bilingualism is a good thing. I see this award as being helpful in the education battle, as it gives credibility to [my work] and explains to people that these are big questions, and important issues regarding brain health."

Much of her current work focuses on neuroimaging and the neurological bases of bilingualism. "Our research shows that across the lifespan, **BILINGUALS ARE BETTER THAN MONOLINGUALS AT TASKS THAT REQUIRE CONTROLLING ATTENTION AND HOLDING SEVERAL GOALS IN MIND AT ONCE**. This includes things like multi-tasking, avoiding distraction while performing a task, and shifting between tasks. For adults, even if the tasks are performed to the same level of proficiency, monolinguals and bilinguals use different brain regions.

In other words, monolinguals and bilinguals are using their brains differently. One difference is that bilinguals need less brain 'activation' or energy to achieve the same levels as monolinguals. And in some studies, there is also evidence that the brains themselves are different, with bilingual brains having more density than monolingual brains."

Dr. Bialystok has spent decades investigating the cognition-bilingualism connection, initially focusing on children then shifting to older adults.

"I had been studying the effect of bilingualism on children for about 30 years. But at some point, for this research to really move forward, it needed to move into a different context and to include older adults and ultimately ... patients. Because there was no other way to put together a story that made sense across the whole lifespan," she says. "To make this a real study about brains and minds, it had to be recast in how we develop cognitive reserve.*"

Recent evidence shows that the "cognitive reserve" that accumulates from engagement in stimulating activities can not only boost cognitive performance throughout life, but also protect against symptoms of dementia in the presence of neuropathology such as Alzheimer's disease.

Does the additional cognitive effort required to manage two languages contribute to cognitive reserve? Ongoing research suggests that it does. On average, **LIFELONG BILINGUALS DIAGNOSED WITH DEMENTIA DEMONSTRATE SYMPTOMS OF THE DISEASE FOUR YEARS LATER THAN COMPARABLE MONOLINGUALS,** with a similar rate of decline for both groups after the diagnosis. This finding has dramatic implications for public health, and a growing body of research examines the emergence and decline of monolingual and bilingual patients with dementia in more detail.

** Cognitive reserve is the extra protection against cognitive decline afforded to people with greater intellectual enrichment.*

THE MANY CAUSES OF MEMORY LOSS

(That Aren't Alzheimer's)

It is understandable to worry when you experience bouts of forgetfulness. With an aging population, Alzheimer's disease has become increasingly prevalent and a growing concern for the general public. Before hitting the panic button, however, bear in mind that there are many potential causes of memory loss that have nothing to do with Alzheimer's.

Firstly, as we age, a little forgetfulness is to be expected. In fact, according to Associate Professor Morgan Barense at the University of Toronto, some memory loss is even a good thing. "People who have good memories are often really good forgetters," says Barense, a cognitive neuroscientist who studies how the brain forms memory. "This prioritization of remembering information that's relevant versus information that's irrelevant. That's a key part of having a good memory." One recent strand of research out of the University of California, Los Angeles, published in ***Developmental Psychology***, found that

WHILE YOUNGER INDIVIDUALS HAD GREATER MEMORY CAPACITY, OLDER ADULTS WERE BETTER AT DECIDING WHAT TO REMEMBER AMONGST THE CLUTTER.

However, in the event that you are past acceptable "senior's moments" and feel that something is awry, it is important to look first to what is happening in your life. Have you been experiencing a great deal of stress at home or suffering under an overbearing boss at work? In 2013, *Harvard Health Publications* described stress, anxiety, depression, and exhaustion as the "four horsemen of forgetfulness." While these causes can be linked to one another, they are quite distinct in terms of what they do to the body and how they lead to memory loss.

Stress and anxiety, for example, have been shown over the long term to have damaging effects on the brain and on memory in particular. In a study published in 2016 in *The Journal of* »

Neuroscience, a research team out of Ohio State University tested the effects of sustained stress on the memory of mice. They found that mice repeatedly exposed to larger, aggressive mice had difficulties locating an escape hole in a maze that they had been adept at navigating prior to the exposure. The cause of the memory loss, according to the researchers, was inflammation of the brain triggered by the immune system, which was itself activated by recurrent exposures to the alpha mice.

Depression could be another culprit. Severe depression can make even the most mundane cognitive processes, such as deciding what to eat for lunch, extremely difficult. An international consortium with the intriguing name of ENIGMA conducted a wide-scale study examining brain scans of approximately 9,000 men and women. The ENIGMA study, published in the 2016 issue of *Molecular Psychiatry*, found that

DEPRESSION ON A RECURRING BASIS ACTUALLY SHRINKS THE HIPPOCAMPUS — THE PART OF THE BRAIN RESPONSIBLE FOR FORMING MEMORIES.

The good news, according to one of the study's lead researchers, is that the hippocampus is one of the most regenerative areas of the brain and the effects of depression can be reversed.

Stress, anxiety, and depression are all associated with another potential cause of memory loss – sleep deprivation. As most people who have experienced life with a newborn can attest, exhaustion can sometimes make it hard to remember your own name, let alone much else. A recent study published in *eLife* sheds some light as to what is actually occurring inside of your brain when you are not getting enough sleep. Researchers from the University of Groningen in the Netherlands and the University of Pennsylvania conducted various sleep-loss experiments with mice and found that five hours of sleep deprivation can lead to a loss of connectivity between neurons in the hippocampus – a problem in terms of remembering things because memories are stored by ensembles of neurons that communicate across the brain.

A vitamin B_{12} deficiency may also cause memory loss, but can be reversed when properly treated. As a review and case report in the *Primary Care Companion to the Journal of Clinical Psychiatry* found in 2009, vitamin B_{12} - together with folic acid - is believed to ward off several disorders, including dementia. The richest sources of B_{12} are animal and fortified foods. There are various reasons why you may not be getting enough B_{12}, including the fact that as we age, many of us stop producing enough stomach acid to release B_{12} naturally from the food we eat. Vegans and vegetarians may also be B_{12} deficient, as well as individuals who have had surgery on their digestive systems to aid weight loss.

Memory loss may also be linked to urinary tract infections (UTIs). While UTIs impart many unpleasant symptoms upon the young, they can create an entirely different set of challenges for older adults (primarily because our immune system changes as we get older and we respond differently to various infections). Older adults with UTIs may not experience pain, and instead may show signs of confusion, agitation or withdrawal. This is a particular concern for individuals caring for a friend or family member with dementia, as these symptoms may be conflated with the condition or general decline.

Another potential cause of your forgetfulness may be residing in your medicine cabinet. A number of commonly prescribed drugs have been found to be associated with memory loss. These include drugs to combat anxiety (benzodiazepines), cholesterol (statins), depression (tricyclic antidepressants), seizures, Parkinson's disease (dopamine agonists), hypertension (beta-blockers), and incontinence (anticholinergies). Others include certain kinds of painkillers, sleeping aids, and antihistamines. Be sure to consult your doctor before reducing or eliminating any of your prescribed medications.

Finally, included among the possible causes of memory loss that are not Alzheimer's are injuries or chronic illness, which are usually irreversible. If either of these is the cause of your forgetfulness, you are likely well aware of the condition irrespective of its effect on your memory. These brain injuries may stem from violent sports, hydrocephalus or "water on the brain" (which is an excess or cerebrospinal fluid around the brain), brain tumours, subdural hematomas (blood clots caused by bruising), thyroid disease, vascular dementia, and a variety of degenerative diseases, including Parkinson's and Huntington's.

Regardless of what is causing your memory loss, catching symptoms early remains your best defence. "The brain is this exquisitely organized, complex machine and it's really hard to put such a machine back together once it's started to break down," says Professor Barense. "It's like reconstructing the Sistine Chapel from crayons. You just can't do it."

HOPE OR HYPE:

Will Stem Cells Cure Alzheimer's?

The discovery of stem cells has revolutionized medical practice, becoming an effective (albeit controversial) treatment for some of the most debilitating diseases. The final frontier for stem cells, however, will likely be the human brain. The central nervous system is one of the body's most fragile and complex systems with limited capacity to regenerate, either from injuries or neurodegenerative diseases such as Parkinson's disease (PD) or Alzheimer's disease (AD). This lack of regenerative capacity is one of the primary reasons why stem-cell-based therapies are so promising. »

While stem cells have incredible potential, there has been significant ethical dilemma surrounding their use. Embryonic stem cells (ESCs) come from five-day-old blastocysts (cell clusters that are the precursors to embryos) and their extraction effectively destroys the embryo. These cells are particularly valuable to researchers because they are pluripotent – meaning that they can generate any kind of cell in the body.

An important advancement in the field of stem cell research occurred in 2006 with the discovery of induced pluripotent stem cells (iPSCs) – adult stem cells that have been reprogrammed to the pluripotent state. The use of iPSCs eliminates problems with tissue rejection since the cells are directly from the patient.

While it was previously believed that iPSCs were similar to ESCs except for their inability to generate the cell layers necessary for producing and developing a complete embryo, scientists now believe that iPSCs might even possess these abilities. If iPSCs are in fact found to have full embryonic potential, this discovery may open the door to the potential of creating a clone, an exact genetic match of the human donor (perhaps an even greater ethical dilemma than the use of human embryos).

"Stem cells are unique from all other cell types in two fundamental ways," says Dr. Mick Bhatia, Director and Senior Scientist at McMaster's Stem Cell and Cancer Research Institute in Hamilton, Ontario. "Unlike other cells, stem cells have the ability to (1) produce mature cells that have very specific functions required for organs and tissues to work; and (2) make copies of themselves, a process called 'self-renewal' so that they are continuously producing mature cells required for tissue maintenance and/or regeneration."

Adding particular momentum to the medical research over the past decade is the ability to generate stem cells from a human patient. Dr. Bhatia notes that this process, called "reprogramming," enables scientists to take a blood cell from a patient suffering from a disorder and turn it into a stem cell that can produce neurons. "Studying these neurons from a specific patient," he explains, "allows us the opportunity to compare the proteins and genes from the patient's neurons to the neurons from someone without the disorder." Dr. Bhatia says that identifying the differences between those with and without the disorder helps to further our understanding of the disease process and how to stop its progression, or even reverse it.

"Disorders and diseases of the brain are complex," says Dr. Bhatia.

"THERE ARE MANY CELL TYPES THAT MAKE UP THE BRAIN, AND WE'RE ONLY NOW UNDERSTANDING HOW ALL OF THESE CELLS COME TOGETHER TO FUNCTION.

One way to understand this is to model this complex organ in a dish using specific cell types, one by one."

With the number of people worldwide living with dementia currently estimated at over 47 million (and Alzheimer's disease accounting for an estimated 60-80% of cases), scientists are endeavouring to find stem-cell therapies to reverse the damage caused by neurodegenerative diseases. In Canada alone, the Alzheimer Society of Canada indicates that the number of individuals diagnosed with dementia increases by 25,000 every year.

The Alzheimer Society Research Program (ASRP) has invested more than $50 million toward Canadian researchers in the field of Alzheimer's disease and other dementias. Dr. Andrea Leblanc, a neurology and neurosurgery professor at McGill University in Quebec, was one such researcher. She says that her research is a "bit like science fiction" but could eventually identify the early causes of Alzheimer's disease and thereby provide an early diagnosis.

Dr. Leblanc's team assessed 302 individuals clinically and cognitively through neuro-psychological testing and then collected human tissue samples. "We took peripheral blood mononuclear cells from patients and reprogrammed these cells into pluripotent stem cells, meaning we immortalized these cells so we can multiply them as much as we want."

The research team was then able to differentiate the cells to become neurons. "So if you took the blood from someone who has Alzheimer's disease versus someone who is cognitively normal, we're hoping that the neurons that we make from their blood cells will represent the Alzheimer neurons and the normal neurons. This will give us a cellular model to determine all the different things that could go wrong in a neuron that comes from an Alzheimer brain."

Dr. Leblanc notes that there were two overriding goals for the study. The first was to use these cells to identify the molecular mechanisms of disease in order to identify a therapeutic target to stop Alzheimer's from progressing, or even from being manifested if there is an early diagnosis.

The second goal was to test potential treatments on actual Alzheimer's neurons. "This is a big step because often we do research on animal models or just cell cultures in a dish that are not

even neurons, some are cancer cells or cells from different parts of the body. But neurons are highly specialized cell types that we need to study if we want to know what's going on with Alzheimer's patients."

"When we test drugs," Dr. Leblanc says, "we often test them on mice but when we go to humans, 95% of the time we fail.

SO THESE STEM CELLS FROM WHICH WE CAN DERIVE NEURONS WILL BECOME VERY USEFUL TO TEST CERTAIN DRUGS.

This way we can say, 'Okay, it worked on a human neuron, we know it can reverse a bad pathway or reestablish neuronal health so then there's a higher chance it will work when we go to the human body.'"

Dr. Gordon Glazner is another cutting-edge researcher who received funding from the ASRP. Dr. Glazner is a neurobiologist and Assistant Professor at the University of Manitoba and the Principal Investigator for the Division of Neurodegenerative Disorders at St. Boniface Research Centre in Winnipeg.

Dr. Glazner's team is currently investigating the relationship between diabetes and Alzheimer's. "We know that diabetes is a risk factor for Alzheimer's," he says, "and that in human brain tissue from Alzheimer's patients, the brain is insulin-resistant, so the brain is diabetic even if the person isn't."

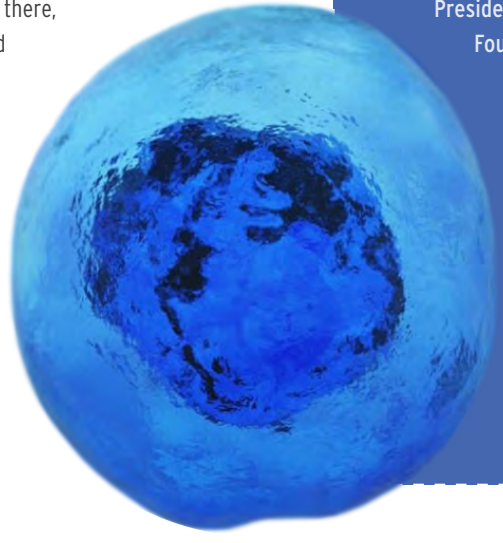
While previous research had established that the neurotrophic factor (a hormone found in the brain that essentially makes the brain healthy) is reduced in Alzheimer's patients, Dr. Glazner's lab discovered that this deficit is in fact related to the insulin system.

Dr. Glazner says, "we wanted to get the hormone into the brain and the best delivery system is to have stem cells overexpress it into the brain. Once there, stem cells turn into a brain cell and live just fine and because they've been genetically manipulated to make a lot of this neurotrophic factor, they start pumping it out."

Using rapid-aging mice as models, the stem cells were derived from the animal itself but eventually the stem cells would come from the patient, eliminating concerns about rejection. "What we're looking to see is, can we use stem cells as a delivery vehicle and actually improve symptoms."

"When you're looking at something like dementia, we don't know what the problem is, specifically, and it's almost certainly not the loss of a single thing that can be replaced. So as far as completely curing it, with the method that we're using right now, probably not. As a possible treatment that could keep the person alive longer, that could give them a better quality of life, that could treat it and make it a living disease like HIV? That's more likely."

Nevertheless, Dr. Glazner remains optimistic that a cure could be found. "Anything that we have put time and effort into studying to find a treatment for, we've been successful. This is science. It's not magic. If we put enough time into it and understand it well enough we will find a treatment for it and eventually a cure."



CANADA'S STEM CELL LEADERSHIP

Although stem cells were noted in scientific publications as far back as the mid-19th century, it was not until 1963 that two Canadian researchers proved that they exist. While performing various experiments on the bone marrow of mice, doctors James Till and Ernest McCulloch developed evidence that different blood cells come from a special class of cells—what eventually would be known as stem cells.

The discovery of the existence of stem cells joins the development of insulin and Pablum to vaccines for small pox, HIV and Ebola as landmark Canadian medical breakthroughs.

"Their discovery ranks right up there with James Watson and Francis Crick's double helix model of DNA in terms of altering the research landscape," says James Price, President and CEO of the Canadian Stem Cell Foundation.

Equally exciting, Canada has remained at the forefront in stem cell research and its applications for delivering new treatments. "We've made great strides in treating autoimmune diseases like MS, and Canadian-led clinical trials are testing new cell-based treatments for diabetes, septic shock, arthritis and heart attacks," says Price. "It's a very exciting time."

TECH TOOLS

Supporting Independence, Quality of Life & Safety

Dementia is a progressive disease that, over time, makes everyday activities increasingly difficult, and sometimes unsafe. Cognitive assistive technologies are devices or systems that help improve independence, safety and quality of life for individuals with cognitive difficulties. Although many assistive technology devices are electronic, the term encompasses both high-tech and low-tech options.

EXISTING TECHNOLOGY TO ASSIST WITH DAILY ACTIVITIES

As dementia progresses, a person's ability to keep track of time is often affected, leading to confusion and anxiety. A **digital clock** with large font is easier to read and understand than an analog clock. Even better are clocks designed specifically for dementia, which display the month and day of the week. Some clocks also show if it is morning, afternoon or night, to provide even more context to the day.

Adapted phones are available that are easier for someone with dementia to use. These typically have pre-programmable buttons for frequently called phone numbers. Some allow photographs to be placed on the pre-programmed buttons making it clear whom you are calling when you press each button.

There are a variety of tools available to provide **automated reminders or prompts** to individuals with dementia. Some are recorded verbal messages, sometimes in a caregiver's voice, while others are alarms or visual messages that pop up on a smart phone or tablet. These reminders can be programmed to play at a particular time (for instance, to remind someone to take medication) or can be played when a motion sensor is activated (for instance, a sensor located near the front door could provide a reminder to lock the door).

There are also several options for helping someone with dementia take the correct medications or vitamins at the right time each day. In the early stages of dementia, these **medication aids** can be simple, such as a pillbox with individual sections for days of the week and times of day. As the disease progresses, there are high-tech options that automate the pill dispensing process, such as an alarm that goes off when medication needs to be taken and the correct compartment opens. Some devices can send an alert to the designated caregiver if the medication is not taken or if the device has stopped working, requires new batteries, or needs to be refilled.

Some technology is designed to improve the safety of individuals with dementia, to help them maintain independence and live at home longer. Safety-focused devices include:

Motion-sensor lights that turn on and off automatically as a person enters and leaves a room can help prevent falls at night while eliminating the need to keep track of and use light switches, an overwhelming task for some individuals with dementia.

GPS (global positioning systems) locating devices designed specifically for individuals with dementia can provide support and safety when they are out walking alone. These devices come in different styles, including a phone-like device worn around the neck, lockable watch, and shoe insole. The exact services provided by each device vary but can include real-time location viewable on an online map, geofencing (pre-set safe zone and alerts sent to a caregiver if the person wearing the device wanders outside the boundary), two-way voice communication, and panic button. (See "The Road Less Traveled: The Impact of Dementia on Independent Mobility" in the third issue of MIND OVER MATTER® magazine for more information about GPS devices and dementia.)

To help prevent wandering, there are **movement sensors** – such as pressure mats in bed or on the floor, or socks with integrated sensors – that send alerts to caregivers when someone with dementia moves in a particular way. For example, these devices can send a warning to a caregiver via a mobile app when the person gets out of bed at night or steps on a mat placed by the front door indicating that he or she may be heading out. Another movement sensor is designed to detect if someone has fallen.

There are even devices that can **automatically shut off** a tap that has been left running, or a stove if it has been left on.

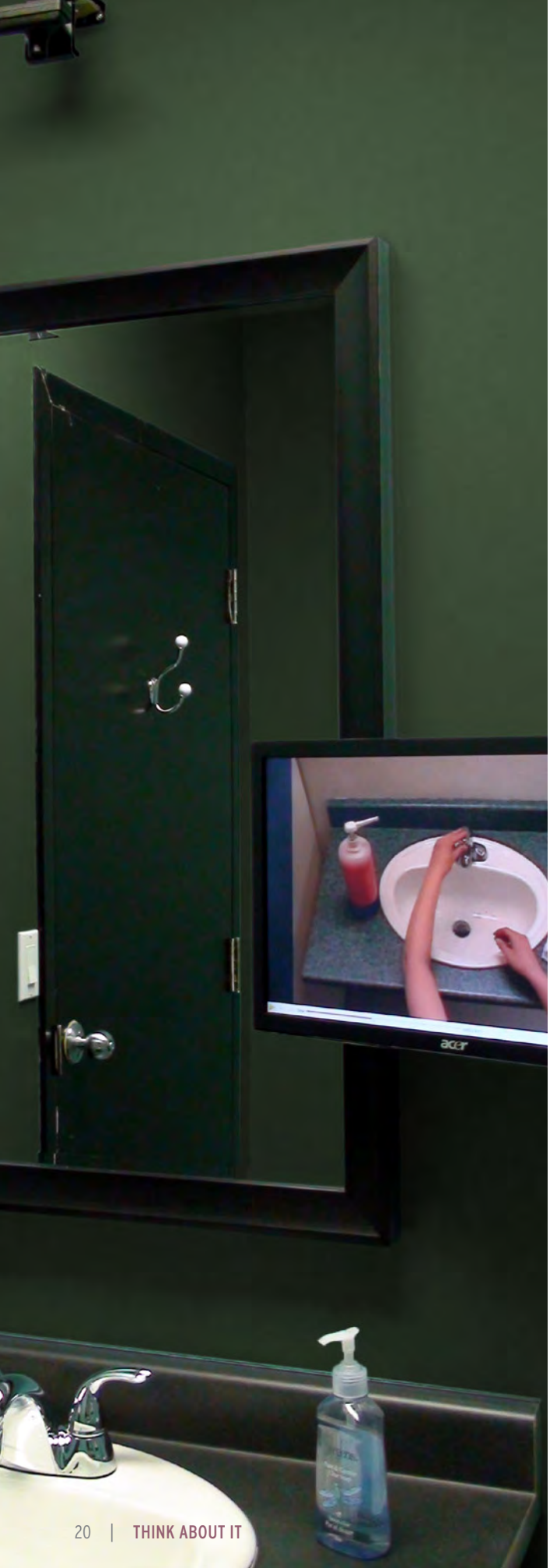
Assistive technology is also being used to enhance **social and leisure activities**, such as sensory and mental stimulation games and puzzles, digital photo frames for reminiscing, and video calling for maintaining relationships.

CHOOSING COGNITIVE ASSISTIVE TECHNOLOGY

There is no "one-size-fits-all" assistive technology for individuals with dementia. A good example is motion-sensor lights – these can be very helpful to some, yet alarming or frightening to others. Although dementias all involve a pattern of increasing mental decline over time, the impact varies significantly from person to person. Therefore, the technology that is suitable for one person may not work at all for another. In addition, what works for one person at a particular point in time is likely to change as the disease progresses.

Degree of memory loss is only one aspect that impacts the suitability of a given technology. Other considerations include the person with dementia's ability, confidence and interest in using a particular technology, as well as how much support will be required by caregivers for a certain tool to be effective and whether that support is available. Experience has demonstrated that the earlier an assistive device is introduced, the more likely it is to be successful.

Cognitive assistive technology should always be selected based on what is best for the person with dementia. When choosing assistive technology, be sure to involve the person with dementia in the decision-making process as much as possible. The tools selected should support the person, not restrict him or her. Assistive devices should not be used by caregivers to monitor individuals without their consent, or as a replacement for human interaction. >>



Given the potentially short span of usefulness and the cost (especially of some of the more high-tech devices), you may want to consider renting cognitive assistive technology if that option is available.

TECHNOLOGY IN DEVELOPMENT

Many research projects are underway that are focused on assistive technologies for older adults with dementia. At the University of Toronto's Intelligent Assistive Technology and Systems Lab (IATSL), for example, researchers from multiple disciplines are collaborating to develop technologies that will help those with dementia participate fully in their daily lives.

Dr. Alex Mihailidis is the Director of IATSL, an Associate Professor in the Department of Occupational Science and Occupational Therapy and Institute of Biomaterials and Biomedical Engineering at the University of Toronto, and the Principal Investigator and a joint Scientific Director of the AGE-WELL network. One of the projects Dr. Mihailidis's team is working on is known as COACH (Cognitive Orthosis for Assisting Activities in the Home). COACH uses computer vision and artificial intelligence techniques to provide reminders for common care activities.

"When the system is used to help with handwashing, the bathroom is equipped with sensors that can detect if important steps are missed, such as turning on or off the water, or using soap," explained Dr. Mihailidis. "Depending on what it detects, COACH can provide a low-guidance oral prompt, a high-guidance oral prompt, or if the person needs even more assistance it will provide an oral prompt along with a video demonstration on a screen positioned near the sink." Other potential COACH responses are to do nothing and continue to observe the user, or to call a caregiver to intervene. COACH may sound very futuristic and expensive but, as Dr. Mihailidis advised, this type of system "uses very little hardware and installation is not complicated, so it's realistic that this technology may be suitable for eventual use in a home environment."

"When developing technology to help individuals who have dementia, it is crucial that the end product be user-friendly," emphasized Dr. Mihailidis. "That means it must be unobtrusive, able to accommodate high levels of customization, and not require feedback such as a button press, since that cannot be reliably expected from someone with dementia."

IATSL is a unique place where researchers in engineering, computer science, occupational therapy, speech-language pathology, and gerontology are working together to create solutions, such as COACH, to improve the lives of those with dementia. Without a doubt, the collaboration of their time, resources and efforts, will go a long way to supporting independence, quality of life, and safety for dementia patients in both the short and long term.

BLOOD PRESSURE & YOUR BRAIN

A Relationship that Changes with Age

Hypertension – chronic high blood pressure – has been linked with decreased cognitive function and increased risk of developing dementia, but its influence on cognition appears to vary depending on your age.

MID-LIFE HYPERTENSION'S IMPACT ON THE BRAIN

According to a scientific statement published by the American Heart Association (AHA) in the 2016 issue of *Hypertension*, "There is consistent evidence that [hypertension] in mid-life is associated with **altered cognitive function** in both mid-life and late-life." While earlier studies primarily considered global cognitive outcomes, such as using tools like the Mini-Mental State Examination (MMSE), or composite measures that combined results from several cognitive tests, recent research has begun looking at specific domains of cognitive function, which may be affected differently by hypertension. Research has revealed "moderately strong evidence" that

> IMPAIRED AND DECLINING SPEED OF PROCESSING AND EXECUTIVE FUNCTION ARE THE MOST COMMON COGNITIVE CHANGES ASSOCIATED WITH HYPERTENSION.

An earlier review, published in 2009 in *Therapeutic Advances in Neurological Disorders*, sought to examine the link between blood pressure and dementia and achieved substantial benchmarks of evidence of mid-life high blood pressure increasing the risk of developing late-life dementia. By the time the AHA statement was >>

WHAT IS BLOOD PRESSURE?

Blood pressure is the pressure exerted by blood upon the walls of your blood vessels, especially the arteries. A blood pressure reading is expressed as two numbers:

1. The top number is a measure of "systolic" blood pressure, which is the pressure when your heart contracts and blood moves through the arteries; and
2. The bottom number is a measure of "diastolic" blood pressure, which indicates the pressure in your arteries between heartbeats, when your heart relaxes.

WHAT IS CONSIDERED NORMAL, HIGH AND LOW?

According to The Heart and Stroke Foundation of Canada, "low risk" blood pressure (**normal**) for most people is 120/80 (read as "120 over 80"), with 120 being the top number/systolic and 80 being the bottom number/diastolic. **High blood pressure** (also referred to as hypertension when experienced over a long period of time) is 140+/90+. The medium-risk category (**prehypertension**) is 121-139/80-89.

For individuals with diabetes, a reading of 130/80 or higher is considered high, and for individuals who are 80 and older, their systolic blood pressure should be less than 150 in order to be considered normal (in most cases).

Definitions of **low blood pressure** (also referred to as hypotension) vary. The Heart and Stroke Foundation of Canada does not publish a low blood pressure number but instead indicates that blood pressure below 120/80 may be considered normal unless you experience symptoms such as dizziness. The Mayo Clinic in the U.S. indicates that a reading of 90/60 or less is generally considered low blood pressure.

published in 2016, researchers had repeatedly reached the same conclusion: hypertension is "an important vascular risk factor and may influence the risk of MCI [mild cognitive impairment] or dementia."

Research conducted by Maillard et al., published in the November 2012 issue of *The Lancet Neurology*, further supports the conclusion that mid-life hypertension negatively impacts the brain. The researchers used magnetic resonance imaging (MRI) to gauge participants' brain health through measurements of white matter injury and grey matter volume. They found "accelerated brain aging among hypertensive and prehypertensive individuals in their 40s."

> THIS WAS THE FIRST STUDY TO DEMONSTRATE THAT ADULTS IN THE YOUNG-END OF MIDDLE AGE EXPERIENCE STRUCTURAL DAMAGE IN THEIR BRAINS AS A RESULT OF HIGH BLOOD PRESSURE.

While research to date strongly suggests an association between mid-life hypertension and negative impacts on the brain, the relationship between blood pressure and the brain becomes less clear when older individuals are studied.

LATE-LIFE HYPERTENSION'S IMPACT ON THE BRAIN

High blood pressure was previously thought to increase dementia risk for everyone, but emerging evidence suggests that the connection between hypertension and dementia changes with age, with the risk of cognitive decline due to high blood pressure likely decreasing as one gets older. New research by Corrado et al., published in February 2017 in *Alzheimer's & Dementia: The Journal of the Alzheimer's Association*, examined how the age of the onset of hypertension impacts the risk of dementia among the "oldest-old" (those aged 90 years and older). The researchers found that hypertension may actually be protective – rather than harmful – for individuals in that age group.

The findings suggest that when high blood pressure develops later in life, particularly at age 80 and older, there is a concomitant lower risk of dementia after the age of 90. More specifically, participants who reported hypertension onset between the ages of 80 and 89 years were found to be 42% less likely to develop dementia after age 90, compared to those who reported no history of high blood pressure. Participants with hypertension onset at age 90 and older were at an even lower risk; they were 63% less likely to develop dementia. Thus, this study suggests that hypertension is not a risk factor for dementia among the oldest-old, and that developing hypertension later in life is linked with a reduction in the risk of developing dementia.

It is important to note, though, that

> THE RELATIONSHIP BETWEEN HYPERTENSION AND COGNITIVE DECLINE IN LATE-LIFE REMAINS UNCLEAR,

with research revealing inconsistent results. Although some studies have found that high blood pressure may be potentially beneficial for the brains of older adults, others have found that high blood

ORTHOSTATIC HYPOTENSION & DEMENTIA RISK

There appears to be a link between sudden drops in blood pressure upon standing up (i.e. orthostatic hypotension) and increased risk of developing dementia, according to a study by Wolters et al. published in the October 2016 issue of *PLOS Medicine*. This study, of more than 6,000 Dutch participants over a period of 24 years, found that experiencing orthostatic hypotension "was associated with a 15% increase in long-term risk of dementia." The brief episodes of sudden drops in blood pressure may be leading to a lack of oxygen to the brain, negatively affecting brain tissue. Note, however, that most of the participants who developed dementia did not experience orthostatic hypotension.

pressure may be harmful to older adults' cognition. Clearly, more research is needed to fully understand the true association between hypertension and cognition in late-life.

LOW BLOOD PRESSURE'S IMPACT ON THE BRAIN

When treating high blood pressure, traditional practice used to presume that the lower one's blood pressure got the better, but research is revealing that this presumption may not be universally true. Recent research has identified low blood pressure (i.e. hypotension) as a risk factor for dementia, particularly among the elderly. It appears that both high and low blood pressure may play a role in brain atrophy (the shrinking of the brain caused by the loss of its cells, called neurons). While hypertension in midlife has been associated with more brain atrophy in later life, several studies have now shown that late-life hypotension is also associated with a greater progression of brain atrophy. Such findings suggest that lowering blood pressure excessively with medication may negatively impact cognition.

FLUCTUATING BLOOD PRESSURE'S IMPACT ON THE BRAIN

It appears that fluctuations in blood pressure may be a health concern as well. A study conducted by Qin et al., published in the May 2016 online issue of *Hypertension*, reported that higher "visit-to-visit variability" in blood pressure is associated with a faster rate of cognitive decline among older adults. The researchers stated that their findings are "consistent with previous studies suggesting that long-term [blood pressure] variability may be more informative than mean [blood pressure] in predicting cognitive function in older adults." Note, however, that it is common for blood pressure to fluctuate somewhat throughout the day (blood pressure typically follows a daily pattern, lowering during sleep and then rising throughout the day, peaking mid-afternoon, and then dropping again).

KEEPING YOUR BLOOD PRESSURE IN BALANCE

After considering the extensive (and sometimes conflicting) research findings about the relationship between blood pressure and cognition, it seems that the key to optimizing one's brain health is to maintain blood pressure at a healthy, "normal" level – in other words, neither too high or too low, nor fluctuating excessively. The Heart and Stroke Foundation of Canada suggests the following lifestyle changes to reduce your risk of high blood pressure:

- Limit your sodium intake to less than 2,300 mg per day;
- Eat a healthy, balanced diet – for instance, consider following the DASH (Dietary Approaches to Stopping Hypertension) eating plan, which can be found online at *www.heartandstroke.ca/get-healthy/healthy-eating/dash-diet;*
- Engage in moderate- to vigorous-intensity aerobic physical activity for a minimum of 150 minutes per week;
- Achieve and maintain a healthy body weight;
- Do not smoke cigarettes;
- Reduce, or eliminate, your alcohol consumption; and
- Discover healthy ways to cope with stress.

If these lifestyle changes are not successful at maintaining your blood pressure at a healthy level and your healthcare provider prescribes medication, be sure to take it as directed.

IMPACT OF HYPERTENSIVE MEDICATION ON BRAIN HEALTH

Given the link between mid-life hypertension and the risk of dementia, one might assume that antihypertensive medication (drugs to lower your blood pressure) would provide protection for your brain. However, research to date has found inconsistent results regarding the effect of hypertensive drugs on cognitive health and prevention of dementia. While some studies have found a reduction of risk, others have found no impact, and some have found increased risk in hypotensive individuals. It may be that certain types of antihypertensive drugs offer cognitive benefits while others do not.

PARKINSON'S DISEASE

There are Differences for Women

Parkinson's disease (PD) is a neurodegenerative disorder, meaning that it involves progressive loss of the structure or function of neurons (cells that transmit nerve impulses). It is the second most common neurodegenerative disorder after Alzheimer's disease and other dementias. PD is characterized by movement dysfunction—for instance, tremor, impaired balance, slowness and stiffness—as well as cognitive and other non-motor impairments such as dementia, depression, insomnia, problems with handwriting and constipation.

DIFFERENT PEOPLE WILL EXPERIENCE DIFFERENT SYMPTOMS, IN VARYING ORDER AND WITH VARYING INTENSITY.

The disease develops over many years, as the brain slowly stops producing dopamine, a neurotransmitter that carries signals between the brain's nerve cells. The disease itself is not fatal, and unfortunately there is currently no cure.

More men are diagnosed with Parkinson's disease than women. A large meta-analysis conducted by Elbaz et al. published in the *Journal of Clinical Epidemiology* in 2002 found that in any given time period, twice as many men have PD than women. This difference in prevalence rates is just the tip of the iceberg, though. There are many more differences between women and men when it comes to Parkinson's disease, including differences in age of onset, symptoms and treatment.

DIFFERENCES IN AGE OF ONSET & SYMPTOMS

The age of onset of Parkinson's disease tends to be about two years later in women than in men. Among women, tremor is usually the primary symptom evident when they are diagnosed, whereas in men, the dominant initial symptom is usually bradykinesia (slow or rigid movement).

Women are more likely than men to experience constipation, pain, dyskinesias (difficulty with voluntary movement), and difficulties with daily activities such as walking and getting dressed. Men, on the other hand, are more likely to experience daytime sleepiness, drooling, sex-related symptoms, rigidity, and rapid eye movement behaviour disorder (a sleep disorder in which the person physically acts out their dreams).

There are differences in cognitive symptoms as well, with men more likely to have deficits in verbal fluency and recognition of facial emotion, while

WOMEN ARE MORE LIKELY TO EXPERIENCE REDUCED VISUOSPATIAL COGNITION

–the skills that allow visual perception of objects and the spatial relationships between them.

Women and men also seem to differ in how they respond to living with Parkinson's disease. Men are more likely to exhibit challenging behaviours such as wandering, and physical or verbal abuse. Conversely, women tend to experience more distress because of their PD symptoms (i.e. they are more likely to be anxious or depressed).

Currently, there are two surgical treatments available for people living with Parkinson's disease – deep brain stimulation (DBS) and surgery performed to insert a tube in the small intestine, which delivers a gel formulation of carbidopa/levodopa (Duopa™), the drug used to treat the motor symptoms of PD.

DIFFERENCES IN TREATMENT

- Men with PD are more likely to be prescribed antipsychotic medication while women are more likely to be prescribed antidepressants – not surprising given their differing responses to PD as noted previously.
- Women and men appear to respond differently to PD medication. The effectiveness of PD drugs may vary between women and men, and of particular concern is evidence that suggests women are more susceptible to negative side effects such as dyskinesia.
- Women with PD are less likely than men to see a neurologist, despite studies showing that this can significantly improve care.
- When women do see a neurologist, they tend to do so after a longer period of time post-diagnosis than men.
- Women have surgery as part of their PD treatment less often than men, and they tend to have more severe symptoms by the time they undergo surgery.

WHY THESE DIFFERENCES EXIST

The primary focus of research into the major factors affecting sex differences in PD has been on the role of sex hormones, mostly looking at the potential neuroprotective effects of estrogen in females. Several studies suggest estrogen has a neuroprotective effect on dopamine systems and helps reduce the risk of PD.

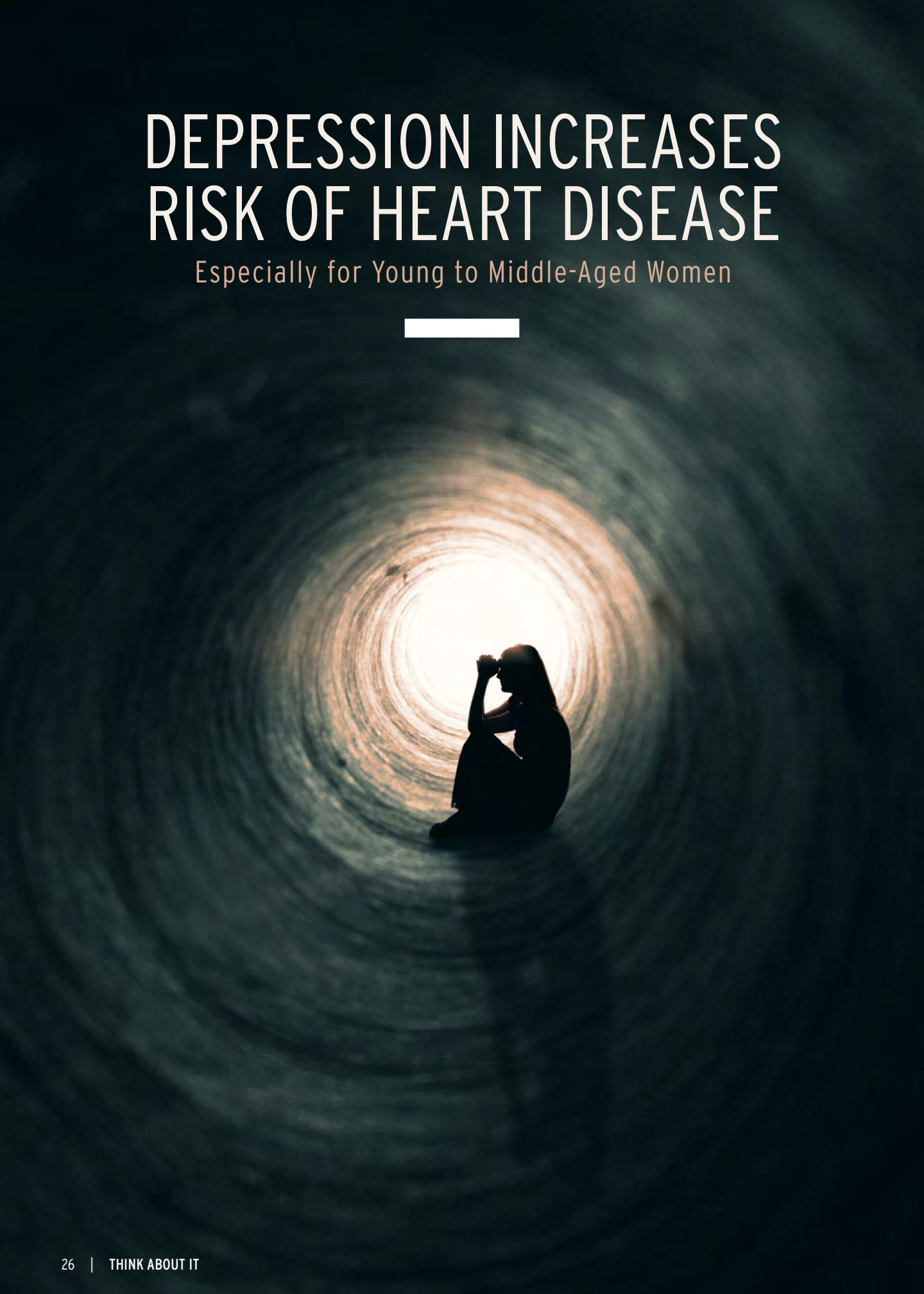
Lifestyle differences are also thought to contribute to men's apparent increased risk of developing Parkinson's disease. For instance, men may have increased risk because of exposure to toxicants (e.g., men are more likely to work with herbicides) or head trauma (which is more common in men).

Genetics, inflammation, and stress have also been suggested as factors that may also play a role in the sex differences noted with Parkinson's disease.

More research is needed to better understand why these female-male differences exist. In particular, more clinical studies involving female participants are required. Currently, men with PD are studied more often than women with PD, in numbers that are disproportionate to the male-to-female prevalence ratio for the disease. Research on sex differences is crucial because it can inform treatment and care of those living with PD, for instance by aiding in accurate early diagnosis in both women and men (even if their initial symptoms differ) and by developing effective, but perhaps differing, courses of treatment.

DEPRESSION INCREASES RISK OF HEART DISEASE

Especially for Young to Middle-Aged Women



It has been known for some time that depression increases the risk of developing heart disease. Meta-analyses—that statistically analyze multiple studies and pool the results—have reported that individuals with depressive symptoms or clinical depression are between 50% and 100% more likely than non-depressed individuals to develop cardiovascular disease. In 2008, the American Heart Association emphasized the significance of this link when it issued a scientific paper recommending that depression be formally considered a risk factor, like diabetes or hypertension, for increased heart disease risk.

But variability in the results of individual studies left some researchers wondering if depression's effect on the risk of heart disease might differ across demographic groups. In particular, they thought that there might be differences based on sex or age, and recent studies suggest that these researchers may be correct.

A study of more than 3,200 men and women with diagnosed or suspected coronary artery disease, published in *the Journal of the American Heart Association* in 2014, found that **women aged 55 or younger are twice as likely to suffer a heart attack, die at an early age, or require artery-opening procedures if they are moderately or severely depressed.** However, in men of any age and women aged 56 or over, symptoms of depression did not predict the presence of heart disease. "While depression is a risk factor for heart disease for everyone, our findings suggest that young to middle-aged women may be especially vulnerable to depression as a risk factor," said Dr. Amit Shah, lead author of the study and assistant professor of Epidemiology at Emory University in Atlanta.

More recently, a 2016 study from the Reading Hospital and Medical Center in Pennsylvania examined how the impact of depression on heart disease risk in women varies by age. After tracking almost 1,100 women over a period of ten years, the researchers discovered that depression was the only significant risk factor for coronary artery disease in women younger than 65 who had no history of heart disease at the inception of the study. Yet, among women aged 65 and over, they found that age was the only significant predictive factor for developing coronary artery disease. In other words, depression was not a significant predictive factor among women aged 65 and over.

WHY ARE DEPRESSION & HEART DISEASE LINKED?

Although scientists do not yet fully understand the correlation between depression and the risk of heart disease, the link could be related to the physical changes that result from depression such as increased production of stress hormones, low-level inflammation and activation of platelets making them more likely to form clots. Alternatively, the depression-heart disease link may be influenced by the behavioural tendencies of those who are depressed, who may find it difficult to make healthy behaviour choices such as exercising, eating well, avoiding the consumption of drugs and alcohol, and taking prescribed medication (which are each associated with staying "heart healthy").

DEPRESSION-HEART DISEASE LINK IS COMPLEX

While this article focuses on how depression increases the risk of heart disease, particularly among young to middle-aged women, the relationship between the two is more complex than that. Additional research indicates that individuals with heart disease are more likely than those without heart disease to be depressed, suggesting that heart disease may increase the risk of depression. Accordingly, depression is both a risk factor for developing heart disease and a potential outcome from having heart disease.

ARE YOU DEPRESSED?

According to depressionhurts.ca, feeling sad or having dark thoughts does not necessarily mean that you are experiencing depression. Depression symptoms can be emotional, physical, behavioural and cognitive. Watch for feelings of constant, persistent sadness; feelings of worthlessness, suicidal thoughts; loss of interest in favourite activities; low energy; insomnia or excessive sleeping; substantial weight loss or gain; restlessness; or difficulty making decisions or focusing. If you are experiencing some of these symptoms and they are impacting your life, see your doctor. "Everyone needs to take action if they suspect they may be experiencing depression, but this is especially true for young and middle-aged women," urged Dr. Shah. "Depression itself is reason enough to take action, but knowing that depression may increase the risk of heart disease and death should provide even more motivation to seek help."

WHY ARE WE TALKING ABOUT HEART DISEASE IN A MAGAZINE ABOUT BRAIN HEALTH?

As this article describes, depression is linked with heart disease. Likewise, research shows that heart disease is linked with dementia, and depression is linked with dementia (as explored in previous editions of *MIND OVER MATTER*®). Essentially, what is good for your heart is good for your brain, and the converse is also true: what is not good for your heart (i.e. depression) is not good for your brain.

ENGAGING MILLENNIAL MINDS

What Millennials Need To Know To Protect Their Brain Health

"The EMM series is extremely important as it is imperative for young people to develop healthy lifestyle choices so they are able to protect their brain now, not 40 years down the line. Topics such as exercise, healthy eating habits, and stress management need to be ingrained in a young person's life and the EMM series is able to reach Millennials in a fun and informative way.

As a young woman, who at the age of 29 had a massive stroke and underwent emergency brain surgery, I know that one of the reasons I was able to make such a miraculous recovery is that I had made healthy lifestyle choices and taken care of my brain and body much before the stroke.

I hope the EMM series grows so that even more young people learn about the lifestyle choices they need to make right now to protect their brains."
~ Dina Pestonji, Motivational Speaker and Coach

Millennials – those born between the years 1984 and 2000 – represent the largest demographic entering the work force since the baby boomers. They are a growing group of young professionals who have an interest in attending, creating, organizing and managing networking opportunities that are unique and informative as part of their volunteer and community engagement and personal growth.

Recent research shows that in order to prevent or delay the onset of dementia, individuals need to adopt healthy lifestyle behaviours in their 20s and 30s, such as regular exercise, proper diet, adequate sleep, stress reduction, mental stimulation and social interaction. Millennials need to be informed about the importance of looking after their brain health when they are young enough to make changes in their lifestyle to slow down any potential lifelong damage.

Founded by RBC Royal Bank, with generous support from Brain Canada and several philanthropists, Engaging Millennial Minds™ (EMM) is a series of interactive relationship-building educational events geared towards the Millennial demographic, focusing on key lifestyle choices necessary to take care of your brain. Each event in the first EMM series was dynamic and energizing, and overwhelmingly successful.

(L-R: RAN GOAL, VITINA BLUMENTHAL & JOY MCCARTHY)

NUTRITION: YOU ARE WHAT YOU EAT

Food that is good for the heart is good for the brain. You can help to keep your brain healthy by eating smart food and eliminating harmful choices from your diet (choices like sugar and salt).

Brain-healthy food groups include green leafy vegetables, other vegetables, nuts, berries, other fruit, beans, whole grains, fish, poultry, olive oil, and red wine (a glass, not the bottle!). Unhealthy food groups are those comprised of red meats, cheese, pastries and sweets, fried and fast food.

(L-R: VITINA BLUMENTHAL, JULIA HAMER & SHANNON GAUDET)

STRESS REDUCTION: CALM YOUR MIND

Experiencing anxiety, fear, and stress is considered a typical part of life when it is occasional and temporary, such as feeling anxious and stressed before an exam or a job interview. However, when those acute emotional reactions become more frequent or chronic, they can significantly interfere with one's daily activities such as work, school, and relationships, can wreak havoc on immune, metabolic and cardiovascular systems, and may lead to atrophy of the brain's hippocampus (crucial for long-term memory and spatial navigation).

Yoga's breathing and meditative exercises aim at calming the mind and body and keep distracting thoughts at bay while you focus on your body, posture, and breathing. These processes translate beyond yoga practice when you try to perform mental tasks or day-to-day activities, allowing you to focus mental resources, process information quickly and more accurately, and also learn to retain and update information more effectively.

(L-R: ABBY KASSAR, DR. BRYNN WINEGARD & LYNN POSLUNS)

MENTAL STIMULATION: YOUR MIND, USE IT OR LOSE IT

Mental exercise is just as critical as physical exercise in keeping your brain fit and healthy. Like your muscles, you have to exercise your brain or it shrinks. Additionally, becoming truly successful requires that you stimulate certain areas of your brain and not others. Using some areas preferentially can help you build a brain that is better at business, making financial decisions, and planning ahead.

(L-R: DR. VALERIE TAYLOR, JORDAN RASBERRY & NICOLE CAMPBELL)

SOCIAL ENGAGEMENT: STAY CONNECTED

Social engagement means mental engagement. Talking or just being around others requires focus and attention to detail, while combatting loneliness (which is a well-established risk factor for dementia), and some research suggests that even brief but regular social engagement bolsters memory, self-awareness, and the ability to not be easily distracted. Staying socially engaged keeps you brain healthy by providing emotional and mental stimulation. Individuals with strong social ties also tend to live longer.

(L-R: NAZEEFAH LAHER & DR. NASREEN KHATRI)

SLEEP: REST WELL

We grow and repair cells at a faster rate while sleeping, and neurons in our brain reconnect or make new connections, which helps consolidate memory and improves focus. Research shows that your brain "clears" itself of "garbage" (or bad toxins that accumulate over time) when you sleep, helps your brain stay sharper and boosts your power of recall, and improves our mood and immune system.

(L-R: DR. JENNIFER HEISZ, TONY MARK & JENNIFER MOONEY)

EXERCISE: PUMP UP YOUR BRAIN

Exercise tones the legs, builds bigger biceps, and strengthens the heart. But of all the body parts that benefit from a good workout, the brain may be the big winner. Physical fitness directly affects our mind and plays a crucial role in the way the brain develops and functions. Exercise is linked to brain changes throughout all stages of life, beginning in infancy and lasting through old age.

With broad benefits on cognition, particularly executive functioning, including improvements in attention, working memory and the ability to multitask, a combination of different exercise (aerobic, strength, balance and flexibility) is best. Exercise daily to boost your brainpower.

For more information, please visit http://womensbrainhealth.org/millennial-minds.

DOES IT HURT?

Perception, Assessment & Treatment for Dementia Patients

As people grow older, their risk of experiencing pain increases. The oldest population is hit the hardest, with pain prevalence rates of 72% among those aged 85 years and older. Given that dementia largely affects older adults, it makes sense that many individuals with dementia would experience pain, and it turns out that many of them do, despite not always being able to express their pain. One large study of more than 5,000 home-care patients found that there was no difference in the prevalence of pain among patients with or without dementia.

The article "Pain Management in Patients with Dementia" by Achterberg et al., published in 2013 in *Clinical Interventions in Aging*, reports that approximately 50% of people with dementia regularly experience pain. It further indicates that among individuals with dementia who reside in care homes, 60 - 80% regularly experience pain, "most commonly related to musculoskeletal, gastrointestinal and cardiac conditions, genitourinary infections, and pressure ulcers."

THE IDEA THAT DAMAGE IN THE BRAIN PREVENTS INDIVIDUALS WITH DEMENTIA FROM EXPERIENCING PAIN IS A TRAGIC MYTH.

A study in Australia used functional Magnetic Resonance Imaging (fMRI) to scan the brains of 14 individuals with mild to moderate Alzheimer's disease (AD) and 15 age-matched individuals without AD (the control group) as they experienced pressure applied to the thumbnail of their right hands to induce varying levels of pain. The brain scans showed that pain-related brain activity was just as strong in the AD participants as in the control group. Although both groups experienced similar strength of pain-related brain activity, the pain activity lasted longer for those with AD.

DIFFERENCES IN PAIN PERCEPTION

While we know from fMRI scans that the brains of individuals with dementia experience pain in the usual ways, other research suggests that there are differences in how those with dementia perceive pain. A Vanderbilt University study—published in *BMC Medicine* in 2016—examined pain responses in two groups of older adults (aged 65 and over): (1) healthy individuals and (2) people with Alzheimer's disease who were able to communicate verbally. Both groups were exposed to different heat sensations and asked to report their pain levels. Participants with Alzheimer's disease demonstrated a reduced ability to detect pain. In other words, it required higher temperatures for them to report sensing warmth, or to experience mild or moderate pain, as compared to the healthy individuals. However, there was no evidence that those with AD were less distressed by pain or that the experience was less unpleasant for them. Key questions remain such as are those with AD not as capable of perceiving pain, or do they perceive the pain but do not recognize and report it as pain?

PAIN PERCEPTION VARIES BY TYPE OF COGNITIVE IMPAIRMENT

A review of research literature about the pain responses of individuals with cognitive impairment, conducted by Defrin et al. and published in the journal *PAIN* in 2015, found that in general, people with cognitive impairment, may be more sensitive to pain than cognitively-intact individuals, and the differences vary depending on the type of cognitive impairment. For example, the literature repeatedly indicated that **the experience of pain is elevated in those with mild to moderate Alzheimer's disease, but pain sensitivity in a late stage of the disease is not clear.** Pain responses also appear to be increased in people with Parkinson's disease, but decreased in those with frontotemporal dementia and Huntington's disease. The authors point out, though, that our current understanding of why these differences exist is limited.

PAIN IS UNDER-ASSESSED & UNDER-TREATED

Pain is often under-assessed and under-treated in people with dementia, likely because of their altered pain experience and inability to self-report the pain (particularly in later stages of the disease). When their pain is not noticed or goes untreated, not only do they suffer unnecessarily, but it can also lead to other problems, including:

- Behavioural changes, some of which make caregiving more challenging. Pain is considered a frequent cause of behavioural and psychological symptoms of dementia (BPSD), such as agitation and aggression. This can lead to the prescription of inappropriate medication such as anti-psychotics or antidepressants;
- Decreased mobility, leading to less independence and increased risk of falling;
- Missed opportunity to diagnose underlying health issues that could be causing the pain, such as urinary tract infection; and
- Hastening deterioration of cognitive function. Studies have found that when people live with chronic pain, the volume of grey matter in their brains declines and the white matter is affected as well; **the longer and more intense the pain, the more dramatic the changes to the brain.** These changes may lead to faster declines in mental function.

HOW TO RECOGNIZE SIGNS OF PAIN IN PEOPLE WITH DEMENTIA

Do not wait for individuals with dementia to mention that they are in pain; rather, ask them if they are. Many people with dementia, >>

especially those in mild or moderate stages, can accurately self-report their perception of pain. As dementia progresses, however, the ability to self-report pain generally declines. Patients who score below 15 on the Mini-Mental State Exam are generally considered too impaired to fully understand self-reporting pain scales. So, in later stages of dementia, observation is used to detect pain.

"For those who are nonverbal, you can watch for behaviours and signs that can indicate pain," explained Dr. Cary Brown, a professor in the department of Occupational Therapy at the University of Alberta, and co-presenter of an online workshop about pain and dementia for family members of persons with dementia (www.painanddementia.ualberta.ca). Dr. Brown suggests using a simple tool called PAINAD (Pain Assessment in Advanced Dementia) to track your loved one's potential signs of pain.

The tool, available on the website, is a checklist with five items:

1. **Breathing;**
2. **Negative vocalization;**
3. **Facial expression;**
4. **Body language; and**
5. **Consolability.**

After observing your loved one for a short time, you simply mark off where your loved one falls on a continuum, scoring between zero and two for each item, then add up the total score out of ten. For example, under facial expressions, "smiling or inexpressive" gets a score of 0, while "sad, frightened or frowning" scores one, and "facial grimacing" scores two.

PAIN ASSESSMENT IN ADVANCED DEMENTIA- PAINAD (WARDEN, HURLEY, VOLICER, 2003)

ITEMS	0	1	2	SCORE
Breathing independent of vocalization	Normal	Occasional labored breathing. Short period of hyperventilation.	Noisy labored breathing. Long period of hyperventilation. Cheyne-stokes respirations.	
Negative vocalization	None	Occasional moan or groan. Low-level of speech with a negative or disapproving quality.	Repeated troubled calling out. Loud moaning or groaning. Crying.	
Facial expression	Smiling or inexpressive	Sad, frightened, frown.	Facial grimacing.	
Body language	Relaxed	Tense. Distressed pacing. Fidgeting.	Rigid. Fists clenched. Knees pulled up. Pulling or pushing away. Striking out.	
Consolability	No need to console	Distracted or reassured by voice or touch.	Unable to console, distract or reassure.	
			TOTAL*:	

***Total scores range from 0 to 10 (based on a scale of 0 to 2 for five items), with a higher score indicating more severe pain (0="no pain" to 10="severe pain").**

INSTRUCTIONS: Observe the older person both at rest and during activity/with movement. For each of the items included in the PAINAD, select the score (0, 1, or 2) that reflects the current state of the person's behavior. Add the score for each item to achieve a total score. Monitor changes in the total score over time and in response to treatment to determine changes in pain. Higher scores suggest greater pain severity.

NOTE: Behavior observation scores should be considered in conjunction with knowledge of existing painful conditions and report from an individual knowledgeable of the person and his or her pain behaviors. Remember that some individuals may not demonstrate obvious pain behaviors or cues.

Reference: Warden, V, Hurley AC, Volicer, V. (2003). Development and psychometric evaluation of the Pain Assessment in Advanced Dementia (PAINAD) Scale. J Am Med Dir Assoc, 4:9-15. Developed at the New England Geriatric Research Education & Clinical Center, Bedford VAMC, MA. Reprinted with permission from Elsevier.

"It is important to note that the PAINAD tool only helps identify the potential presence of pain. The final score should not be interpreted as an indicator of the severity of pain," warned Dr. Brown. "The tool helps caregivers observe behaviours in an organized way and, if recorded in a pain journal, can highlight changes in one individual over time."

If you believe that your loved one with dementia is experiencing pain, advocate for his or her comfort by sharing your observations with his or her health care team. Continue with periodic observations and watch for changes in response to pain treatments or shifts occurring over time due to advancing age and disease. The health professionals will be using their own approaches and tools to assess pain, but no one knows your loved one like you do, and your supplemental observations can be very helpful as part of an overall pain management effort.

TREATING PAIN

"When family members believe that their loved one with dementia is showing signs of pain, there are several steps they can take immediately," explained Dr. Brown. "First, look for and address any potential underlying causes of pain. For example, are their clothes comfortable or are seams perhaps rubbing on their skin? Are their shoes giving them blisters or corns? Do their glasses fit comfortably? Might they be experiencing some dental pain?"

Family members can also try non-drug therapies to help alleviate pain such as gentle massage, applying hot or cold packs, gentle movement of the limbs, and relaxation. "These activities are safe to do even if someone is taking pain medication as well," said Dr. Brown.

Be sure to consult with a doctor to determine the best treatment approach for addressing your loved one's pain. The doctor may identify and treat an underlying medical issue that is causing the pain, provide a referral for physiotherapy or acupuncture, or prescribe pain medication.

When choosing pain medication for someone with dementia, a doctor must carefully consider the balance between benefits and risks. For example, some medications may interact with other drugs the person already takes, may negatively impact other health problems the person has, or may increase the risk of falling. The dosage may need to be higher than what a cognitively-healthy adult would take because some dementia-related changes in the brain can impact one's response to analgesics. To add further complexity, doctors need to consider the ways in which pain medications affect the sexes differently. We already know that women and men can experience varying impacts and side effects when taking pain medication, but more women-focused research is needed to explore differences among women (i.e. if responses to pain medication vary depending on a woman's age and whether she is pre-, peri-, or post-menopausal).

WOMEN EXPERIENCE PAIN DIFFERENTLY THAN MEN

In recent years, there has been much interest and research into the differences between women and men when it comes to pain. Each new study provides a piece of the complex puzzle, but a complete picture has not yet emerged. A 2013 review paper entitled "Sex differences in pain: a brief review of clinical and experimental findings," published in the July 2013 issue of *British Journal of Anaesthesia (BJA)*, provides a recent snapshot into what has been learned so far. It reports that the literature "clearly suggests that men and women differ in their responses to pain." For example, women tend to exhibit increased pain sensitivity. When exposed to an increasingly painful stimulus in an experimental setting, women usually ask the researchers to stop sooner than men do. The paper also mentions that women are at higher risk for experiencing pain.

Research by Ruau et al., published in the March 2012 issue of *Journal of Pain*, is an example of a study that found sex differences in reported pain. This innovative research made use of a vast collection of electronic medical records. Researchers analyzed over 160,000 pain scores reported for more than 72,000 adult patients at Stanford Hospital and Clinics and discovered that women reported feeling more intense pain than men, with almost every type of disease.

Brain scans have shown that different parts of the brain respond to pain, depending on whether you are a woman or man. A University of California, Los Angeles study published in *Gastroenterology* in 2003, involving 26 women and 24 men with irritable bowel syndrome, looked at positron emission tomography (PET) brain scans during mild pain stimuli. While there was some overlap in the areas of brain activation seen in the women and men, there were several areas of differentiation. The female brain was more active in limbic regions (emotion-based centres) while the male brain was more active in the cognitive/analytical regions. The researchers point out that there are unique advantages to each type of response and neither is better than the other.

Why women are more likely to experience pain, and tend to feel pain more intensely than men, is not entirely clear. Sex hormones, as well as psychological and cultural influences, are thought to be potential reasons. Another potential influence was cited in a study conducted by Bradon Wilhemli, described in the October 2005 edition of *Plastic and Reconstructive Surgery*. Dr. Wilhemli discovered a difference in the number of nerve receptors (which pick up on sensation) in women versus men. While women had on average 34 nerve fibers per square centimetre of facial skin, men had only 17. Although this study provided important insight into why women experience pain more powerfully, there is certainly more to learn in order to fully understand what makes a woman's experience of pain different from a man's.

DRUGS IMPACT WOMEN DIFFERENTLY THAN THEY DO MEN

What You Need To Know

In the last few decades, medical research has begun to show that drugs can impact women and men differently. This matters whether you are a younger woman who is taking an oral contraceptive or an anti-anxiety drug, or you are an older woman who may need a sleeping pill or high blood pressure medication. "Drug regulatory agencies recommended that women of childbearing years not be included in drug trials from the 1960s to the 1980s," says Dr. Cara Tannenbaum, Scientific Director of the Institute of Gender and Health for the Canadian Institutes of Health Research (CIHR). Although that decision was "probably

well-intended after the Thalidomide and DES (Diethylstilbestrol) scares" of the 1950s and 1960s, says Dr. Tannenbaum, that has left us in a situation where many "scientists who were trained in the 1970s and 1980s, who are among the smartest in the world working today, were trained only using male animals" and then only males in clinical trials.

Dr. Marianne Legato of The Foundation for Gender-Specific Medicine based in New York City echoes this sentiment, noting that "women were seen as more vulnerable than men in terms of possible injury to their reproductive potential, and furthermore they were seen as less stable physiologically because of the monthly fluctuations in their hormones. So the exclusion of women was not malicious." However, by 1993, after the mobilization of feminists concerned with women's health, the National Institutes of Health (NIH) in the United States mandated that women "be included wherever possible in clinical studies," says Dr. Legato.

CHANGE CAN BE SLOW, BUT IT IS HAPPENING

Change occurs slowly in a research culture and therefore female mice still appear in smaller numbers than male mice in drug development experiments, according to an article published in the science journal *Nature* in 2010, which means that at the very beginning levels of research, females are excluded. To counter this, the NIH recently developed new policies requiring scientists to report "their plans for the balance of male and female animals in preclinical studies." Likewise, Canada's health funding organization, the CIHR, started providing financial incentives to researchers "to broaden the habit they've had of doing research only in male animals," says Dr. Tannenbaum. The CIHR also has training modules on its website for researchers to learn more about sex differences (www.discoversexandgender.ca).

Importantly, major medical journals are beginning to encourage scientists to report sex-related differences in trial outcomes. However, a commentary published in *The Lancet* in late 2016 found that while women are being included more frequently in trials,

"ANY DIFFERING OUTCOMES BETWEEN MALE AND FEMALE PARTICIPANTS ARE NOT BEING APPROPRIATELY ANALYSED AND REPORTED."

We know that acknowledging sex-based differences is important because contemporary research has found significant differences in how men and women metabolize, utilize, and excrete drugs. For instance, a study published in the *American Family Physician* in 2009 reported that the Digoxin drug class (used with heart failure) has "increased mortality in women" and that women should be receiving a lower dose than men. The commonly held belief that an Aspirin a day will help prevent heart attacks is actually only true for men but that same Aspirin provides women with some protection against stroke.

And research in *U.S. Pharmacist* published in 2014 concluded that while men and women react differently to drugs, sex-specific dosing rarely exists. These examples are just scratching the surface of the differences that researchers are finding. A 2016 article published in the journal *Scientific Reports* found that

"AMONG 668 DRUGS OF THE MOST FREQUENT 20 TREATMENT REGIMENS IN THE UNITED STATES, 307 DRUGS HAVE SEX DIFFERENCES IN ADVERSE DRUG EVENTS." SOMETIMES THESE SEX DIFFERENCES IN THE BODY'S ABILITY TO USE DRUGS CAN BE FATAL.

"An audit published in the United States found that out of ten drugs withdrawn from the market, eight had potentially fatal side effects such as heart arrhythmias, more commonly found in women, or that more women took the culprit drugs, like appetite suppressants," says Dr. Tannenbaum.

WHY DO WOMEN REACT DIFFERENTLY?

There are a variety of different reasons why drugs impact women and men differently, including body size, fat distribution, and organ sizes. Some drugs are more likely to dissolve in fat, and because women have more fat than men due to evolutionary reasons (women carry children), these types of drugs will remain in women's bodies longer, says Dr. Tannenbaum. In addition, drugs that are eliminated through the kidneys are eliminated more slowly in women because women's kidneys are on average 20% smaller than men's. Some differences are explained by "basic physiology; for example, a woman's heart rate is slightly different than a man's because of the effects of estrogen on the heart," and this will vary depending on what stage of life a woman is at (such as in her reproductive years or in menopause). If a younger woman is taking an oral contraceptive, that affects how "the liver metabolizes and activates other medications," says Dr. Tannenbaum. Researchers are continuing to discover these sex differences and it is certainly a popular topic in medicine.

Doctors like Dr. Tannenbaum and Dr. Legato are innovators when it comes to research that takes into account sex and gender-specific differences in medicine. >>

BUT THE NEWEST INFORMATION DOES NOT ALWAYS FILTER DOWN INTO YOUR DOCTOR'S OFFICE AS QUICKLY AS YOU WOULD HOPE.

Part of this is due to the fact that Canadian physicians rely on the Canadian Medical Association (CMA) to post clinical practice guidelines – the recommendations to physicians, nurses, and pharmacists about how to treat patients with a range of illnesses. For instance, the recommendations for asthma, stroke, high blood pressure, or insomnia need to do a better job of accounting for sex differences in treatment options. "We did a review of all the clinical practice guidelines posted by the CMA between 2013 and 2015 and we found that only 25% specifically included recommendations that targeted men and women differently," says Dr. Tannenbaum. Doctors can be conflicted as well, Dr. Tannenbaum explains, because they "can only deliver care based on evidence, and if there's been a lag in the development of evidence, they don't know exactly what to do and they can't just guess."

To date, Health Canada has only issued one warning for prescribing a different dose of a medication, the sedative Sublinox (Zolpidem), where women should be receiving a smaller dose than men because the drug "accumulates in their blood and they have a 40% higher level the next morning than do men, which can affect their brain and impair their driving," says Dr. Tannenbaum. In 25 years, it is expected that dosing by sex will become more common.

BEING PROACTIVE

What should you do then, if you are a woman taking any kind of medication? The answer is to start by simply asking your doctor if the drugs you are taking have been tested in women like you. "If enough women start asking their doctors, the doctors will make more of an effort to look it up," says Dr. Tannenbaum. That is how change starts to happen. You can also look at the U.S. Food and Drug Administration's "drug trials snapshots" page and insert a new drug name to find out how many women were included in a drug trial. It would be useful for Canadians if Health Canada created a drug safety website so that Canadian women could be better informed about the medications they are taking, and the specific effects in women. Unfortunately, this resource does not yet exist.

HOW THIS LINKS TO BRAIN HEALTH

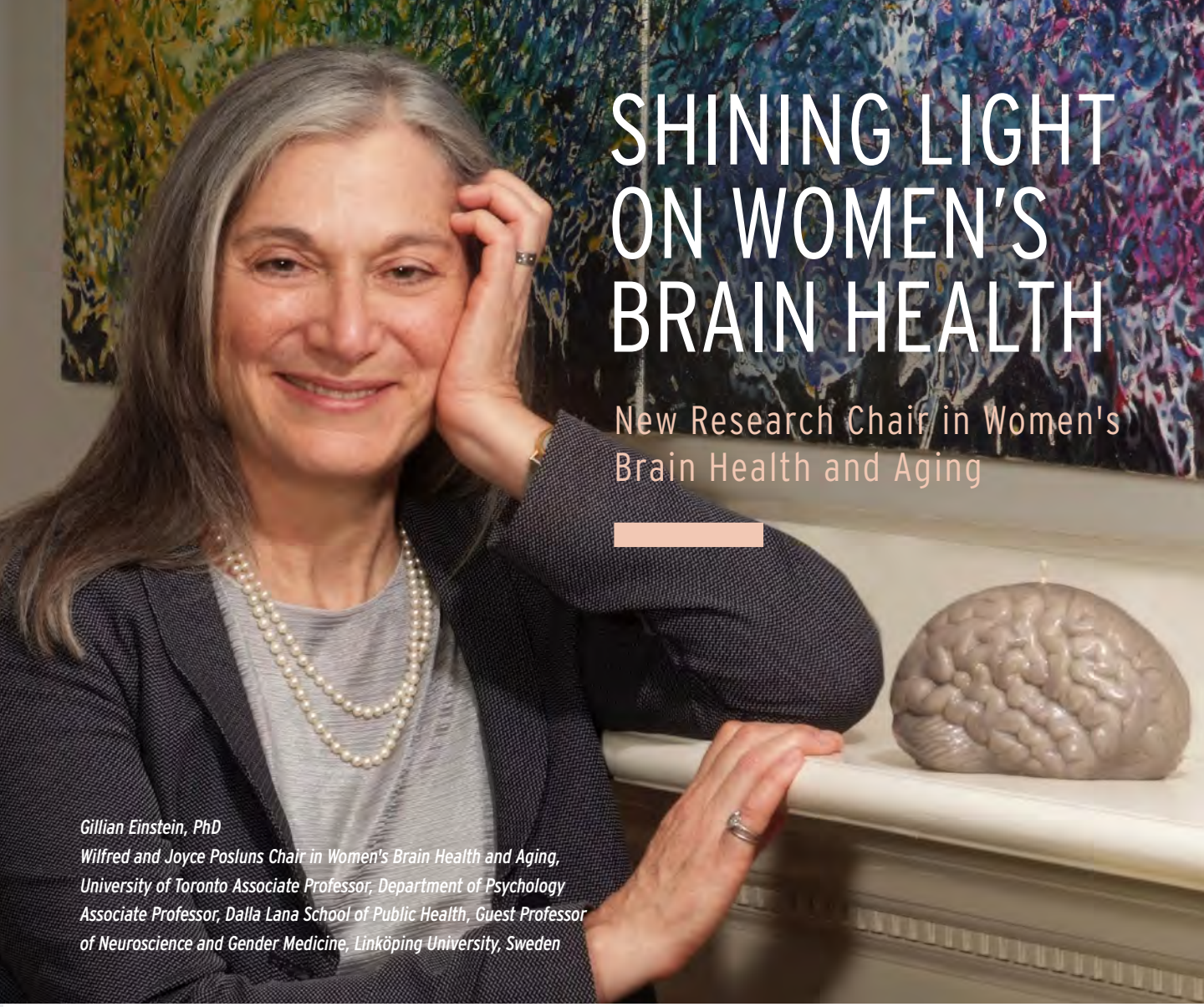
Being aware of the effects of the drugs you are taking can help in the fight against women's brain aging disorders – and that goes for anything from insomnia medication to antihistamines – because many drugs on the market "are designed to affect the brain," says Dr. Tannenbaum. A preliminary study published in *The BMJ (British Medical Journal)* in 2014, and conducted in part by researchers out of the University of Montreal, studied nearly 9,000 elderly people and found that those who used benzodiazepine drugs (commonly prescribed for anxiety, depression, and insomnia) had a 43% - 51% increase in the risk of developing Alzheimer's. Considering that "some sleeping pills stay in women's bodies longer," says Dr. Tannenbaum, this early research may eventually prove to be more detrimental to women and their health.

More recently, research published in *JAMA Internal Medicine* found that anticholinergic medications (such as Gravol, allergy medications like Benadryl, and overactive bladder medications) have also been proven to affect memory, while some pain medications "depress the nerves in your brain," says Dr. Tannenbaum. If these drugs are accumulating in the fat tissues and building up in the blood more so in women than they are in men, then "more of it may be getting into the brain and placing women at greater risk for harm."

Overwhelmed? One thing women can consider is whether it is completely necessary to be taking all of the medications that they are taking, says Dr. Tannenbaum. The Canadian Deprescribing Network (deprescribing.org) helps older Canadians lower doses of medications that are "too high" or completely stop taking those "that are no longer needed." Look to the Canadian Deprescribing Network for resources on how you can safely withdraw medications that you no longer require with the help of your doctors and pharmacists. It is a significant step to long-term health.

SHINING LIGHT ON WOMEN'S BRAIN HEALTH

New Research Chair in Women's Brain Health and Aging



Gillian Einstein, PhD
Wilfred and Joyce Posluns Chair in Women's Brain Health and Aging, University of Toronto Associate Professor, Department of Psychology Associate Professor, Dalla Lana School of Public Health, Guest Professor of Neuroscience and Gender Medicine, Linköping University, Sweden

The new Wilfred and Joyce Posluns Research Chair in Women's Brain Health and Aging will be a leader in developing quantitative knowledge on the subject of brain health. This Chair supports an exceptional researcher working to enhance women's brain health through the study of cognitive aging and associated disorders. More specifically, this initiative builds capacity in research that accounts for gender and sex – that is, social and biological influences – on brain health and aging for women. The Chair holder works to translate the research results into gender and sex-sensitive policies and interventions that improve brain health and promote wellness in aging.

We had the pleasure of talking with Dr. Gillian Einstein, the first recipient of the Chair and an Associate Professor of Psychology at the University of Toronto.

WBHI: First, let me congratulate you on being selected the first Wilfred and Joyce Posluns Research Chair in Women's Brain Health and Aging.

GE: Thank you. This is an exceptional honour and opportunity. Not just for me, but for the entire scientific community. The establishment of this Chair gives visibility to the whole issue of women's brain health and aging. As the first of its kind in the world, it has positioned Canada at the forefront of brain research on the global stage. We must thank and credit the Posluns Family, together with their partners at the Canadian Institutes of Health Research (CIHR), the Alzheimer's Society, and the Ontario Brain Institute (OBI), for their leadership and vision.

WBHI: What will this initiative investigate that isn't currently being done?

GE: We are going to look at the brain from not only the scientific >>

perspective, but also cultural and environmental. The Chair's program will operate according to three principles:

1. Biological differences (sex) and social position (gender) both affect brain health, requiring integrated approaches transcending the historic divide between biological science (focused on sex) and humanities/social sciences (focused on gender).

2. The brain is neither autonomous nor dictatorial; rather, it responds to and integrates other body processes and signals, which are in turn sensitive to the world outside the body, including to changes induced by cultural (gendered) practices.

3. Brain health, from embryonic development to aging, is the accumulated result of diverse interacting processes. To ensure brain health, outcomes must be studied in the context of life-long trajectories; interventions may need to be in early stages of women's lived lives.

BY USING A MIX OF APPROACHES FROM DIFFERENT DISCIPLINES, WE CAN MORE EFFECTIVELY STUDY BOTH THE BIOLOGICAL AND SOCIAL ASPECTS OF BRAIN HEALTH.

Our research will draw from different disciplinary approaches – most rooted in cognitive neuroscience, but with others rooted in the social sciences and humanities – in order to obtain a fuller understanding of women's brain health. We believe that having all of these perspectives represented equally will provide unique insights into women's brain health over the life span.

WBHI: How will these funds change the conversation?

GE: This funding is giving us the opportunity to increase sex and gender awareness through research, mentorship, education, and knowledge translation. We really haven't been able to engage fully in all these activities before but by doing so we should be able to study women's brains from the perspective of different disciplines focusing on the same issues and training young people to do the same. For example, $10,000/year will top up the research allowance of graduate psychology and neuroscience graduate students who want to add a sex or gender dimension to their research.

For the main Chair's project, to understand how memory changes after ovarian removal in young women, the security this funding provides allows us to add new components to this particular project over an extended period of time.

It's also giving us the time and space to go out into the world to meet and work with global colleagues. I've already been able to plan three different international symposia – something I could not have done without the support of this Chair.

WBHI: What is the ideal outcome at the end of the first of two five-year terms of this Chair?

GE: It would be wonderful if we had a better understanding of the brain's response to estrogen withdrawl in terms of what that change signifies, what is the timing of that change, what is the most important intervention we can provide and when. If we can find some answers that can then be taken to clinical trials, we would have made enormous strides in our quest for understanding how estrogen contributes to young women's brain health, as well as what is happening in women's brains over the life span.

Additionally, if we could encourage other fields to investigate the importance of ovaries beyond reproduction and on their impact on the whole body, we will have made enormous strides. We need to be looking at methodologies for imaging ovaries so that we can catch ovarian cancer much earlier and once these are developed, perhaps they could be applied to other difficult areas of imaging like pancreatic cancers.

We know the brain is not just the CEO of the body, but also other body functions have an impact on the brain. For example, dysregulation of the immune system (inflammation) is thought to play a role in Alzheimer's disease. How does estrogen withdrawal affect the immune system and influence memory decline? Lack of sleep is thought to play a role in cognitive decline as well. How does estrogen withdrawal affect sleep and therefore affect memory? These are all questions that need to be addressed.

WBHI: Any final thoughts you'd like to share?

GE: It is inspiring to be the spokesperson and ambassador for this initiative. On a basic level, I want to bring the Chair's key project to the point that we have answers about the effect of ovarian removal on memory in younger women and how those cognitive and brain changes progress over time. On a broader level, I want to get the news out from our research, hosting a public exhibition of women's own stories, drawings, and poems about their memory. I also want the project to come to the point of measuring biomarkers for Alzheimer's disease and begin clinical trials of some interventions. Overall, I hope that I will make the strides that need to be made so that this Chair will become an acknowledged platform for continued great research and advancements in women's brain health and aging.

CAN LONELINESS AFFECT YOUR COGNITIVE HEALTH?

No matter at what age, we have all experienced a sense of isolation and the sinking feeling of loneliness – whether you were not invited to go out with work colleagues for drinks, or you were not included in a group game of bridge or mahjong, or you spent a holiday alone with no one to celebrate with.

While we know that loneliness and social isolation can deprive us of happiness, several studies have shown that experiencing loneliness can also negatively impact our brain health.

Living alone, suffering from isolation, or even living with others but feeling like you do not have someone to talk to can lead to depression, which can have serious implications for both your physical and mental well-being. In fact, an Amsterdam-based study of the elderly, reported in the *Journal of Neurology, Neurosurgery & Psychiatry* in 2013, found that

"LONELINESS INCREASES THE RISK OF DEMENTIA IN OLDER ADULTS BY AS MUCH AS 64%".

"Research conducted over three years on more than 2,000 seniors living outside of a long-term care setting determined that loneliness was a significant factor when predicting an individual's odds of developing dementia. Even after adjusting the findings for other factors such as age, initial cognitive functioning and socioeconomic status, the researchers found that lonely seniors were more likely to develop dementia than those who did not have these feelings." >>

CONTRIBUTING FACTORS OF SOCIAL ISOLATION & LONELINESS

As we get older, our social options often get smaller, yet our pattern of dependency increases. For example, an older neighbour who is homebound (particularly during the wintertime) may lack interactions with others who could help oversee his or her daily routine and raise any necessary flags (such as ensuring that he or she is properly taking his or her medications). This is becoming a growing concern since some of the contributing factors of social isolation are the result of today's rising trend of changing neighbourhoods – very different from the days when everyone knew their neighbours, church members, and even the mail carrier and together they would notice activity (or lack thereof) of people on their streets.

On the other hand, there are individuals who become fiercely independent as they age, and do not like asking others for help or revealing their weaknesses for needing support, thereby pushing themselves into isolation and generating feelings of loneliness.

Declines in mobility and physical limitations can also contribute to social isolation and loneliness.

SOME OF THE SCIENCE

Research has shown that healthy seniors with elevated brain levels of amyloid (a type of protein fragment associated with Alzheimer's disease) seem more likely to feel lonely than those with lower levels of amyloid. More specifically, "for people who have high levels of amyloid – the people truly at high risk for Alzheimer's – they were 7.5 times more likely to be lonely than non-lonely," said lead researcher Dr. Nancy Donovan, director of the Center for Alzheimer Research and Treatment at Brigham and Women's Hospital in Boston.

Dr. Donovan also speculates that "the psychosocial stress of loneliness may cause inflammation that is harmful to the brain." Dr. Donovan and her colleagues studied 8,300 men and women aged 65 and over and found that "those who reported feeling the loneliest had a 20% faster decline in mental ability than those who said they weren't lonely. Depression also accelerated the decline. Interestingly, problems with memory did not predict loneliness, which implies that

BEING LONELY MAY BE CAUSING MEMORY PROBLEMS BUT MEMORY PROBLEMS DON'T NECESSARILY CAUSE LONELINESS."

PREVENTING LONELINESS & ISOLATION

There are a number of ways to avoid isolation and help support those individuals that you think may be at risk.

Focus on Feelings: Surprisingly, living with other people does not prevent loneliness. In fact, the aforementioned Amsterdam-based study revealed that "older adults who reported feeling lonely were 250% more likely to have developed dementia over the course of the study than their non-lonely peers, no matter their living conditions. These results suggest that feelings of loneliness independently contribute to the risk of dementia in later life. Interestingly, the fact that 'feeling lonely' rather than 'being alone' was associated with dementia onset suggests that it is not the objective situation, but, rather, the perceived absence of social attachments that increases the risk of cognitive decline."

Take Up a Hobby: Keeping yourself busy and engaging in brain-stimulating activities such as painting, gardening or cooking can be incredibly beneficial, particularly if such activities are shared with another person. Enjoying more time outdoors for walks can also help break up the monotony of a quiet day or routine (not to mention the fresh air is great for your health and mind and can vastly improve your emotional state). Individuals can also consider owning a pet to encourage companionship, conversation, and comfort. Pet options can vary in responsibility from a dog or a cat to even a bird or fish.

Some Ways to Help Reconnect: If you are concerned that someone you know is suffering from isolation, there are a number of ideas and resources available:

- **Check with the local senior center.** For individuals already living in senior living communities, participation in activities should be encouraged.
- **Register for drop-in services** such as "Meals on Wheels."
- **Participate in local mall walking clubs.**
- **Engage in social media.** Many senior centers today have initiatives to help individuals understand the benefits of technology and teach the joys and simplicity of connecting with relatives (most often grandchildren and great grandchildren) through FaceTime, Facebook, Instagram, and texting. This basic social media training keeps individuals connected to their family and friends. Note, however, that it is critical to achieve the right balance of social media engagement because technology can also lead to social isolation (particularly amongst teenagers and younger adults – just ask their parents!).
- **Encourage volunteer opportunities.** Join a club or take a class to connect with other like-minded individuals.
- **Make plans.** Run errands with a friend, cook a recipe together, take time to fit social events into your schedule.

WORKING ON EXPANDING YOUR SOCIAL NETWORKS WILL CONTRIBUTE TO INCREASED ACTIVITY, MENTAL STIMULATION, AND IMPROVE OVERALL BRAIN HEALTH,

and making those additional efforts when you are younger will be beneficial in later years.

Another valuable resource comes from the UK where a national campaign to end loneliness was launched in 2011 (www.campaigntoendloneliness.org). The campaign, which is based on the premise that ending loneliness can create change, seeks to inspire "thousands of organisations and people to do more to tackle the health threat of loneliness in older age. The Campaign to End Loneliness is a network of national, regional and local organisations and people working together through community action, good practice, research and policy to ensure that loneliness is acted upon as a public health priority at national and local levels."

"LONELINESS AND THE FEELING OF BEING UNWANTED IS THE MOST TERRIBLE POVERTY."

~Mother Teresa

HOW DO YOU KNOW IF YOU ARE AT RISK?

There is a recognized assessment tool that helps to measure an individual's social support network, including family, friends and neighbours, called the Lubben Social Network Scale (LSNS). The LSNS consists of an equally weighted sum of ten items used to measure size, closeness, and frequency of contacts of a respondent's social network, which typically takes five to ten minutes to complete. It was originally developed in 1988 and was revised in 2002 (LSNS-R), along with an abbreviated version (LSNS-6) to meet clinicians' needs for brevity, and an expanded version (LSNS-18) for basic social and health science research-oriented purposes.

Dr. Lubben is a leading expert in social gerontology who focuses on social support networks among older populations. Dr. Lubben is the director of the Center of Excellence in Geriatric Social Work and the founding director for the Institute on Aging at Boston College. His research considers "social isolation as a behavioural health risk among older adults."

The LSNS is most often used with older adults, as well as caregivers in various settings (such as assisted living, doctors' offices, hospitals, and community centers). The assessment tool has been translated into multiple languages and has been an integral part of studies across the globe.

WHAT IS YOUR LSNS SCORE?

LUBBEN SOCIAL NETWORK SCALE – 6 (LSNS-6)

SCORING:
The total score is calculated by finding the sum of all the items. For the LSNS-6, the score ranges between 0 and 30, with a higher score indicating more social engagement.

FAMILY: Considering the people you are related to by birth, marriage, adoption, etc.

1. How many relatives do you see or hear from at least once a month?
0 = none; 1 = one; 2 = two; 3 = three or four; 4 = five through eight; 5 = nine or more

2. How many relatives do you feel at ease with that you can talk about private matters?
0 = none; 1 = one; 2 = two; 3 = three or four; 4 = five through eight; 5 = nine or more

3. How many relatives do you feel close to such that you could call on them for help?
0 = none; 1 = one; 2 = two; 3 = three or four; 4 = five through eight; 5 = nine or more

FRIENDSHIPS: Considering all of your friends including those who live in your neighborhood

4. How many of your friends do you see or hear from at least once a month?
0 = none; 1 = one; 2 = two; 3 = three or four; 4 = five through eight; 5 = nine or more

5. How many friends do you feel at ease with that you can talk about private matters?
0 = none; 1 = one; 2 = two; 3 = three or four; 4 = five through eight; 5 = nine or more

6. How many friends do you feel close to such that you could call on them for help?
0 = none; 1 = one; 2 = two; 3 = three or four; 4 = five through eight; 5 = nine or more

Loneliness and social isolation do not have to be an inevitable part of growing older. As research continues to emphasize the important link between one's social network and physical and mental health, new resources are being made available to the public, and the conversation continues to grow. It is encouraging to know that we will not have to face these challenges alone.

THE IMPACT OF SEX AND GENDER ON BRAIN HEALTH

Better Health Outcomes for Women & Men

WHO'S LOOKING?

The Women, Gender, Sex and Dementia (WGSD) program plays an important role in the Canadian Consortium on Neurodegeneration in Aging (CCNA). CCNA is a national network of researchers, clinicians and students across Canada that conduct research on the prevention and treatment of age-related neurodegenerative disorders such as Alzheimer's disease.

The goal of the WGSD is to ensure that sex and gender are considered in all research projects within the CCNA.

Ultimately, these types of investigations will help uncover important sex and gender differences in the risk, etiology and progression of dementia disorders. These differences could be due to a variety of factors, including environmental factors, hormones, social roles, or other life experiences. Identifying where and why sex differences in dementia exist will provide critical insight for treatment development and disease management.

"YOU DON'T FIND IF YOU DON'T LOOK."

~Dr. Howard Chertkow,

Scientific Director, Canadian Consortium on Neurodegeneration in Aging, Director, Bloomfield Centre for Research in Aging, Lady Davis Institute

The WGSD program is led by Dr. Mary Tierney, Professor and Clinician Scientist at the University of Toronto and Director

of the Primary Care Research Unit at Sunnybrook Health Sciences Centre in Toronto, and assisted by post-doctoral fellow and program coordinator Ashley Curtis. They consult with and advise CCNA researchers on ways to incorporate sex and gender questions into their work and collaborate on projects that directly investigate sex and gender differences in various types of research on neurodegeneration. The CCNA provides funding to the WGSD through a grant from the Canadian Institute of Health Research (CIHR), along with additional support from several partners. Women's Brain Health Initiative and the CIHR Institute of Gender and Health are two of the partners heavily involved with WGSD.

CURRENT WORK AND RECENT FINDINGS

The WGSD program has observed a steady rise in the number of CCNA projects that are researching sex and gender differences.

The program collaborated with Dr. Gary Naglie at Baycrest in Toronto and Dr. Mark Rapoport at Sunnybrook Research Institute on a recently published study that looked at whether there are differences in the numbers of men and women with dementia that stop driving. They found that women with dementia stopped driving sooner than men. This information has important implications for the design of driving cessation support programs – a much-needed resource that will help alleviate the negative psychological and physical consequences of driving cessation in older adults with dementia.

Dr. Tierney and Ashley Curtis of the WGSD program, in collaboration with Dr. Mario Masellis (Sunnybrook Research Institute), Dr. Ekaterina Rogaeva (University of Toronto), Dr. Ian MacKenzie (University of Waterloo), and Dr. Ging-Yuek Robin Hsiung (University of British Columbia), are also completing a study that examines sex differences in the cause of two rare neurodegenerative disorders: frontotemporal dementia (FTD) and amyotrophic lateral sclerosis (ALS). There are no effective treatments for these disorders, which usually affect middle-aged individuals and lead to death within a few years of onset. Their findings of sex differences in genes that cause these disorders may help us better understand risk factors and disease mechanisms.

McMaster University's Dr. Margaret Fahnestock's team conducted a study on mice with Alzheimer's disease and found that

FEMALE MICE SHOW A HIGHER LEVEL OF A BIOLOGICAL MARKER FOR ALZHEIMER'S DISEASE, COMPARED TO MALE MICE. >>

Given the known sex differences in the risk of developing Alzheimer's disease, with women showing a higher risk, Dr. Fahnestock's results could provide important information about the cause of this increased female risk. Her team will continue to investigate possible sex differences in this important biological marker in human patients in the upcoming clinical trials within the CCNA.

University of Toronto's Dr. Angela Colantonio's team studied sex differences in dementia caregivers regarding the use of technology-based interventions aimed at reducing caregiver burden. Her team found that relative to men, women benefitted more from technology in terms of reducing this burden.

Mount Sinai Hospital's Dr. Joel Sadavoy's team also conducted research on dementia caregivers. They investigated differences between men and women in their experiences of being a caregiver and whether this was associated with any conflict in their work or lives in general. They found that

FEMALE GENDER WAS ASSOCIATED WITH A GREATER DEGREE OF WORK AND LIFE CONFLICT AND A MORE NEGATIVE CAREGIVER EXPERIENCE.

This information will help inform future therapeutic interventions for dementia caregivers that take into account gender role identity and its differential impact on caregiver experience.

Dr. Kristen Jacklin (Laurentian University in Sudbury) and Dr. Carrie Bourassa (University of Regina) are leading a project that examines gender perspectives in dementia healthcare in Indigenous populations. Their preliminary observations show that men are more likely to be diagnosed with dementia, whereas Indigenous women are more likely to be caregivers. They are continuing research that will specifically investigate whether Indigenous men and women differ in their opinions on access to healthcare, cultural approaches to health and wellbeing, use of supportive technology, and other related outcomes.

Dr. Claudio Cuello (McMaster University) and his team will also investigate sex differences in Alzheimer's disease, particularly whether there are differences in the amount and progression of a recently discovered early biomarker of the disease.

University of Ottawa's Dr. Dale Corbett and his team will conduct research on vascular dementia and examine whether there are sex differences in the brains of rats with the disorder. Another study led by Dr. Dallas Seitz (Queen's University) and his team will be investigating usage of commonly prescribed medications for psychiatric disturbances in dementia patients living in long-term care facilities. These medications have numerous side effects, and Dr. Seitz's team will investigate sex or gender-related factors that influence when these medications are prescribed, and when they are discontinued.

Dr. Tierney and Ashley Curtis of the WGSD program, in collaboration with Dr. Richard Camicioli (University of Alberta) and Dr. Mario Masellis (Sunnybrook Research Institute), have also recently begun work looking at sex differences in the second most common neurodegenerative disorder, Parkinson's disease. This disease is more prevalent in men, but sex differences in the clinical symptoms, particularly cognitive decline, are largely unknown. The group team will review the research literature to examine whether men and women differ in their cognitive symptoms across various stages of Parkinson's disease. This information will help improve our understanding of the factors that affect the disease course and provide insight into the management of the disorder.

From cell to bedside, the more scientists take sex and gender into account, the greater the likelihood there will be better answers and healthier outcomes for both women and men. Women's Brain Health Initiative is proud to provide funding to support this important research.

Prepared by Ashley Curtis and Dr. Mary Tierney

RECENTLY INITIATED PROJECTS

Sex and gender research within the CCNA is growing, and four new projects were recently initiated.

Dr. Robert Bartha's team (in London, Ontario of the Robarts Research Institute) will be researching sex differences in the development of amyloid deposits in the brain, which are associated with cognitive decline in Alzheimer's disease.

WHAT YOU CAN EXPECT

Caregiving Through the Stages of Dementia

When someone is diagnosed with dementia, it can be devastating not just for the person receiving the diagnosis, but also for his or her family and friends. Everyone involved realizes that the person with dementia is about to change significantly, in ways that will reduce that individual's independence and will require substantial support from others.

The role of caregiver is often undertaken, at least in part, by family members who may know little or nothing about the disease and its effects. Although the course dementia takes can vary widely between individuals – with each person experiencing different symptoms and exhibiting diverse behaviours over varying lengths of time – dementia typically progresses slowly through three general stages.

EARLY-STAGE (MILD) DEMENTIA

During the early stage of dementia, most people are functioning independently in many ways. The person with dementia may be struggling with certain aspects of memory, learning and planning, but he or she is likely competent with self-care activities (such as bathing and dressing), and could still be participating in social activities, volunteering, managing the household, and perhaps even working and driving. According to the Alzheimer's Association,

YOUR ROLE IN THIS EARLY STAGE OF DEMENTIA IS MORE AKIN TO A "CARE PARTNER" THAN A "CAREGIVER"

since at this stage of the development someone may not require much assistance.

Provide emotional support and help with planning for the future

At this stage, the person with dementia most likely needs emotional support and companionship as he or she works through the complex emotions of processing his or her diagnosis – possibly sadness, fear, anxiety, depression – and assistance with making plans for the future, including legal, financial, long-term care and end-of-life planning.

Balance help with independence

One of the biggest challenges for the care partner during this stage is determining how and when to help. Indeed, finding an >>

appropriate balance between providing support when necessary and allowing your loved one to maintain a sense of independence can be quite arduous. Tasks that the person with dementia may find difficult include managing a daily schedule (e.g. remembering appointments and to take medication) and managing the household budget (e.g. dealing with money). Watch for areas your loved one is struggling with, and ask him or her directly what he or she needs.

Encourage healthy lifestyle choices

To help your loved one stay healthy for as long as possible, encourage healthy lifestyle choices such as engaging in regular physical activity, maintaining a balanced diet, getting adequate sleep, socializing with others, and reducing stress.

MIDDLE-STAGE (MODERATE) DEMENTIA

During the middle stage of dementia, progressive damage in the brain can affect judgement, the ability to express thoughts, and perform routine tasks. You may notice your loved one jumbling words or using inappropriate language, struggling to get dressed, forgetting about personal hygiene, wandering, or having verbal and physical outbursts to express anger or frustration. Memory problems become more pronounced: your loved one may remember his or her own name but not address or phone number, he or she may have difficulty identifying family and friends but can still recognize familiar faces, and he or she may lose or misplace possessions and take things belonging to others. **As the disease progresses, you will notice a need for ever-increasing levels of care**.

This stage is usually the longest, sometimes lasting for many years. Key attributes for a caregiver at this stage include flexibility and patience. Do what you can to provide structure but be willing to adapt as you go, since each new day will be different than the last.

Understand BPSD

In addition to cognitive symptoms such as memory loss and confusion, behavioural and psychological symptoms of dementia (known as "BPSD") affect one's personality, conduct and emotions – often making the individual with dementia much more challenging for a caregiver to handle. BPSD include depression, hallucinations, delusions, aggression, agitation, and sleep or appetite changes. These symptoms cause considerable levels of distress both in dementia sufferers and their caregivers, and frustration is often the breaking point prior to institutionalization in long-term care facilities. When your loved one exhibits BPSD, remember that he or she is ill and try not to take the behaviour personally. Observe your loved one's behaviours over time and watch for patterns and triggers so that you can adapt your caregiving strategies to try to avoid outbursts or problems. For more tips on how to manage BPSD in a positive way, check out the article "When Mom is Difficult: Dementia May Cause Challenging Behaviours" in the third issue of *MIND OVER MATTER*® magazine.

Adapt to communication changes

In this middle stage, people with dementia have trouble finding words to express their thoughts, and struggle to follow conversations and understand what others are saying. You may notice your loved one repeating himself or herself, losing his or her train of thought or relying on non-verbal communication. To help improve communication between the two of you, be sure to speak slowly and clearly, in a gentle tone. Use straightforward, simple sentences and resist the temptation to correct him or her when she is confused about reality. It is fine if your loved one believes certain things that are not true such as believing that his or her father is still alive when, in actuality, he has been deceased for decades – there is no harm in your loved one believing that, and trying to correct him or her is likely to be ineffective and cause distress.

Assist with daily care needs

Since basic daily activities such as eating, dressing and grooming are increasingly challenging for someone with dementia at this stage of the disease, expect to be needed to provide assistance with these tasks. Be sensitive to the fact that helping your loved one with these personal activities may be especially difficult for him or her, since such assistance represents a loss of both independence and privacy. Encourage your loved one to perform as many of these daily care activities as possible, but provide support as needed.

Take steps to ensure safety

During the mild-dementia stage, and the beginning of the moderate stage, there may be steps that you can take to help your loved one stay safe while living independently, such as having a tea kettle that automatically shuts off and using a global positioning system (GPS) device to prevent him or her from getting lost (see "Tech Tools" starting on page 18 for a discussion about technology that helps individuals with dementia stay independent longer). At some point in the middle stage, however, it will likely become evident that it is no longer safe for the person with dementia to be left alone. Consequently, you will need to look for a new, safe living arrangement—whether that means moving your loved one in with relatives or into a residential care home.

Address driving, if necessary

If your loved one is still driving, he or she will need to stop at some point during this middle stage. Convincing someone with dementia to give up his or her keys is often very difficult. Many people associate driving with self-reliance and freedom; the loss of driving privileges and the inherent loss of independence is likely to be upsetting. However, for everyone's safety, it is an absolute necessity. When it becomes evident that driving is no longer safe, try to involve the person with dementia in discussions and decisions about when to stop. It will also help if you reassure your loved one that you will get him or her where he or she needs to go by providing, or arranging for, transportation. For information

about how to know when it is time for an individual with dementia to stop driving, and how to help with the transition from driver to passenger, see "The Road Less Travelled" article in the third issue of *MIND OVER MATTER®* magazine.

LATE-STAGE (SEVERE) DEMENTIA

With late-stage dementia, there can be extensive memory loss, limited to no mobility, and increased vulnerability to infections such as pneumonia. You may notice the person with dementia has trouble eating and swallowing, can no longer communicate with words, and experiences incontinence. This stage can last from several weeks to several years.

Provide intensive assistance with basic activities

Around-the-clock care is usually necessary during this stage. In particular, your loved one is likely to need help with all of his or her personal care activities, including maintaining oral hygiene, bathing, dressing, and using the washroom. You are also likely to be needed to assist with eating and ensuring that he or she consumes an adequate amount of food and fluids. Also, watch for and address any signs of pain – see the article "Does It Hurt?" starting on page 30 for information about pain and dementia.

Stay connected

At this stage, the person with dementia primarily experiences the world through his or her senses. Even though your loved one can no longer talk or directly express his or her needs,

YOU CAN STILL CONNECT WITH YOUR LOVED ONE AND EXPRESS YOUR LOVE THROUGH TOUCH, SOUND, SIGHT, TASTE, AND SMELL.

Some ideas for staying connected include:

- Listen to his or her favourite music together – check out the article "If Music Be the Food of Life, Play On" in the second issue of *Mind Over Matter®* magazine for details about the power of music during dementia.
- Read aloud from a favourite book.
- Reminisce together by looking at photographs.
- Prepare and share favourite foods.
- Provide gentle, caring touch (such as massaging his or her hands and arms with lotion, brushing his or her hair). Touch is especially beneficial; it can ease anxiety and stress, reduce agitation and promote sleep while enhancing the emotional connection between the two of you.

ADVICE FOR ALL THE STAGES

Some tips to keep in mind as your loved one progresses through all three stages of dementia:

Accept or ask for help. If someone offers to help, say yes! If no one offers, be sure to ask. Family and friends are often willing to pitch in; they just need to know how they can be of assistance. Caring for someone with dementia is too big of a responsibility for one person to handle alone.

Take care of yourself, too. It is more important than ever to make time to care for your own emotional and physical well-being. Be sure to make healthy lifestyle choices yourself (e.g. eat well, get enough sleep, and exercise), and use tools for managing stress such as meditation and yoga.

Remember that it is impossible to be a "perfect" caregiver. There will be good days and bad. You will experience a wide range of difficult emotions. Do your best, and forgive yourself for any moments of "imperfection."

Know that you are not alone and seek out support. Avoid isolation and loneliness by keeping up with social activities and contact with others as much as possible. Join a caregiver support group or attend caregiver-training workshops to connect with others living with the day-to-day issues of Alzheimer's disease and facing practical challenges, grief and loss. A good place to start when looking for support is contacting your local Alzheimer's Association chapter (i.e. Alzheimer Society of Canada, Alzheimer's Association in the U.S., and Alzheimer's Society in the U.K.).

ALZHEIMER'S DRUGS

What's Available & What's in Development

Currently, there are no drugs available to cure Alzheimer's disease (AD) or to stop its progression. However, there are two types of medication available—cholinesterase inhibitors and memantine—that can help manage symptoms, such as memory loss and confusion, in some patients for a limited time.

While scientists do not fully understand how cholinesterase inhibitors work to treat AD, research suggests that they prevent the breakdown of acetylcholine, a neurotransmitter (chemical messenger in the brain) that is important for memory, thinking and judgement. Alzheimer's is associated with inadequate levels of acetylcholine.

Three cholinesterase inhibitors are commonly prescribed:

1. Galantamine (brand names: Reminyl® or Razadyne®);
2. Rivastigmine (brand name: Exelon®); and
3. Donepezil (brand name: Aricept®).

All three of the cholinesterase inhibitors are approved to treat symptoms in those with mild to moderate AD.

There are two options for treating the symptoms of moderate to advanced Alzheimer's: Memantine, as well as one of the cholinesterase inhibitors, Donepezil. Memantine shields brain cells from overexposure to glutamate, a neurotransmitter associated with brain cell death when it is present at excess levels, which happens as Alzheimer's progresses. Memantine is available in Canada under the brand name Ebixa® and in the U.S. under the brand name Namenda®.

ALL OF THE DRUGS CURRENTLY AVAILABLE TO MANAGE THE SYMPTOMS OF AD HAVE MODEST, SHORT-TERM EFFECTS THAT ONLY SOME PEOPLE EXPERIENCE,

and at least half do not respond at all. Although the cholinesterase inhibitors are generally well tolerated, common side effects can include nausea, loss of appetite, vomiting, and diarrhea. The potential side effects of Memantine include headache, constipation, confusion, and dizziness. Given the limited effectiveness of the drugs currently available, there is clearly an urgent need for new treatments. In fact, a 2016 research paper published in *The Lancet Neurology*, written by 34 prominent Alzheimer's experts from around the world, declared that an effective therapy for Alzheimer's disease is "perhaps the greatest unmet need facing modern medicine."

DRUGS IN DEVELOPMENT

According to the article "Alzheimer's drug-development pipeline: 2016," published in *Alzheimer's & Dementia: Translational Research & Clinical Interventions*, there were 93 agents (chemical substances) in phases 1 through 3 of clinical trials: 24 in phase 1, 45 in phase 2, and 24 in phase 3 (as of January 4, 2016). The lead author of the article, Dr. Jeffrey Cummings from the Cleveland Clinic Lou Ruvo Center for Brain Health in Las Vegas, explained that "those numbers are based on a review of all trials registered in clinicaltrials.gov, a U.S. government website that includes all U.S. clinical trials and most global ones as well. Although the list is quite thorough, it is not exhaustive."

Drugs that target **amyloid beta (Aβ)** are the major focus of current research. Aβ is the main component of brain plaques that are present in most people with Alzheimer's disease. Researchers are investigating various drugs that target Aβ in different ways, for instance by trying to block production, prevent Aβ fragments from clumping into plaques, and/or clear Aβ from the brain.

Solanezumab® is an example of a drug that targets Aβ; it is a monoclonal antibody that binds to Aβ, preventing plaques from forming and perhaps helping to clear excess Aβ from the brain as well. Note, however, that Solanezumab® did not perform well in clinical trials involving individuals who already displayed symptoms of Alzheimer's disease and is now being tested as a potential preventive medicine with at-risk individuals who are not yet symptomatic (for more information about the shift toward drug testing earlier in the disease process, see the article "Trying to Find the Cure for Alzheimer's" published in the third issue of *MIND OVER MATTER*® magazine).

Amyloid beta is a protein fragment clipped from its parent compound, amyloid precursor protein, by two enzymes – beta - secretase (BACE) and gamma-secretase. Some drugs, BACE inhibitors, aim to prevent the "clipping" process in an attempt to block the production of Aβ. Verubecestat is one BACE inhibitor being studied and is currently in phase 3 clinical trials.

Tau is another target being studied, but not nearly as extensively as amyloid beta. As Dr. Cummings noted, "tau is a relatively unexploited target, with only four drugs being researched at the time of our review." Alzheimer's disease is characterized by two abnormal structures in the brain – amyloid beta plaques along with tau protein tangles. The tau tangles destroy a vital cell transport system in the brain. AADvac1 is one of the drugs that targets tau protein; it is a vaccine in phase 2 testing that stimulates the immune system to go after an abnormal form of tau in an attempt to prevent the tangles from forming.

The 5HT6 receptor is also being targeted in Alzheimer's drug research. This receptor is found on some brain cells and it locks in neurotransmitters, thereby decreasing the amount of these brain chemicals available for communication between neurons. Blocking the 5HT6 receptor may help maintain healthy communication between nerve cells in the brain by increasing the amount of available acetylcholine, the same neurotransmitter targeted by current cholinesterase inhibitor drugs. Intepirdine is a 5HT6 receptor antagonist, which means that it prevents the receptor from decreasing acetylcholine levels, and it is currently being used in a phase 3 clinical trial.

Inflammation is yet another target for AD research because it is known to play a role in Alzheimer's disease. Amyloid beta plaques and tau tangles both elicit an immune response in the brain. Microglial cells respond to their presence, trying to clear them from the brain, but can overreact and end up damaging nearby cells. An example of a drug currently being researched that targets inflammation is CSP-1103 or CHF 5074 (it is a microglial modulator in phase 3 testing). >>

IN THE FUTURE, IT IS POSSIBLE THAT SUCCESSFUL TREATMENT FOR AD PATIENTS WILL INVOLVE A "COCKTAIL" OF MULTIPLE MEDICATIONS THAT ADDRESS SEVERAL DIFFERENT TARGETS,

as is the case with treatments for many cancers as well as AIDS. Indeed, "a small number of trials are underway looking at the impact of combinations of more than one drug," said Dr. Cummings.

Considering the dire need for effective AD treatments, the number of drugs currently in phase 1 to 3 clinical trials is very low. "The small number of agents currently being tested in phase 1 trials is especially concerning since that is the phase that will be the source of innovative, new drugs that could move forward to phases 2 and 3 through to approval," warned Dr. Cummings.

CHALLENGES

Why are there so few approved drugs for Alzheimer's disease and so few drugs in the development pipeline? There are a wide range of challenges affecting Alzheimer's drug development, some of the biggest include:

- **High failure rate.** The track record of success for Alzheimer's drugs is extremely poor. A review of AD trials performed between 2002 and 2012 revealed that only 0.4% of the drugs tested were successful; in other words, 99.6% of the 413 clinical trials failed. There were 244 compounds tested in those trials, and only one of them was approved. By comparison, cancer trials have an average failure rate of 81%.

- **Alzheimer's drug testing takes a long time.** There is minimal financial incentive for drug companies to invest in long, costly trials of drugs that will have little to no patent protection left by the time the drug is approved, especially if there is an extremely low likelihood of success. The cost of developing a disease-modifying treatment for AD is currently estimated to be US$5.7 billion, including the cost of failures.

- **Difficulty recruiting trial participants**. Finding participants, particularly for Phase 3 studies that often require over 1,000 participants, is the most time-consuming component of the clinical trials, slowing down the process and increasing costs.

DRUG APPROVAL PROCESS

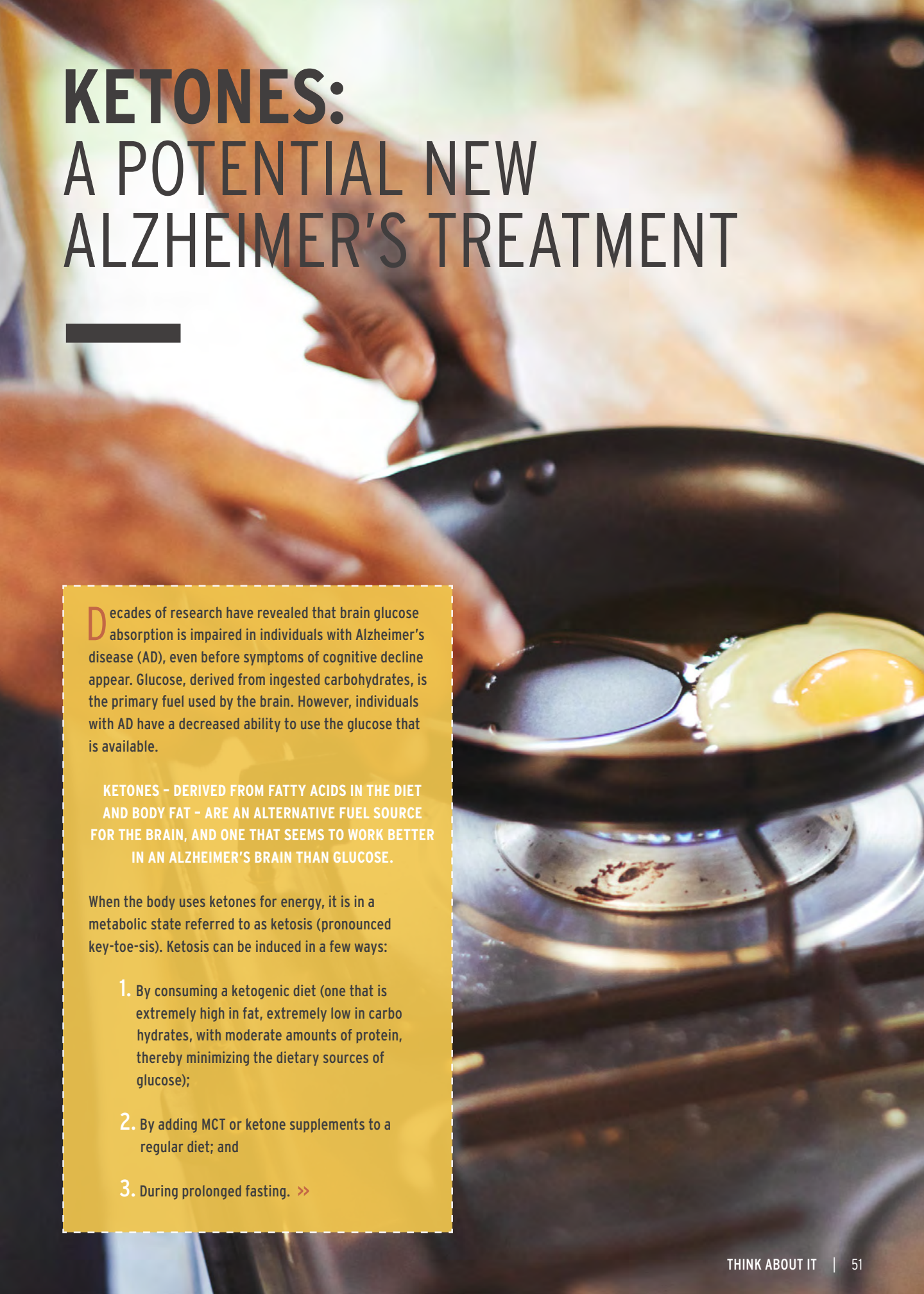
According to Alzheimer's Disease International (the worldwide federation of Alzheimer associations), the drug development process takes an average of 13 years. The process begins with preclinical testing in the laboratory using tissue cultures and animals to see if it has the potential to treat the disease. If it does, testing with people begins and moves through three phases of clinical trials: (1) to test safety (i.e. can people tolerate the drug); (2) to begin testing effectiveness at treating Alzheimer's disease; and (3) to confirm effectiveness in a large number of people, often as compared to a placebo. If a drug proves successful in phase 3, health regulatory authorities review the results and decide whether to approve the drug. Even after a drug is approved and is being used as a treatment, it often continues to be studied in phase 4 trials to see if any uncommon side effects surface as the drug is administered in greater numbers of people.

GLOBAL GOALS

The good news is that Alzheimer's disease research is being recognized as an urgent priority around the world. Governments are realizing the huge economic and social burden of the disease, and recognizing that coordinated action is needed. A G8 Summit on Dementia was held in London, England in December 2013. Ministers from each of the G8 countries agreed to the goal of identifying a cure or disease-modifying therapy for dementia by 2025. To meet that goal, the Ministers further agreed to significantly increase the amount spent on dementia research and to increase the number of people involved in clinical trials and studies. To accelerate drug development, they also agreed to encourage sharing of data and results among researchers, particularly for publicly-funded dementia research.

"The 2025 deadline was initiated by politicians and may not reflect the realities of drug development," explained Dr. Cummings, "but nonetheless it was an important step because it has become a rallying cry for researchers." Realistic or not, the 2025 deadline has helped boost Alzheimer's drug research, but even more must be done to accelerate this essential work. Dr. Cummings emphasized, "There is a great need to take steps to reduce the time and risk of AD drug development if we are to reach the 2025 goal."

KETONES: A POTENTIAL NEW ALZHEIMER'S TREATMENT



Decades of research have revealed that brain glucose absorption is impaired in individuals with Alzheimer's disease (AD), even before symptoms of cognitive decline appear. Glucose, derived from ingested carbohydrates, is the primary fuel used by the brain. However, individuals with AD have a decreased ability to use the glucose that is available.

KETONES – DERIVED FROM FATTY ACIDS IN THE DIET AND BODY FAT – ARE AN ALTERNATIVE FUEL SOURCE FOR THE BRAIN, AND ONE THAT SEEMS TO WORK BETTER IN AN ALZHEIMER'S BRAIN THAN GLUCOSE.

When the body uses ketones for energy, it is in a metabolic state referred to as ketosis (pronounced key-toe-sis). Ketosis can be induced in a few ways:

1. By consuming a ketogenic diet (one that is extremely high in fat, extremely low in carbo hydrates, with moderate amounts of protein, thereby minimizing the dietary sources of glucose);

2. By adding MCT or ketone supplements to a regular diet; and

3. During prolonged fasting. »

WHAT IS MCT?

Medium chain triglycerides (MCT) are fatty acids of a particular length (i.e. medium). These fats are unique because they are processed in the liver, rather than being metabolized through the digestive system like most other foods. MCT oil occurs naturally in certain foods, including coconut and palm oil, but can also be consumed as a concentrated MCT oil (which is typically extracted from coconut or palm oil).

Ketogenic diets have been used since the 1920s to successfully treat symptoms of epilepsy, so it is not surprising that ketosis is now being explored as a potential treatment for other neurological disorders, including AD. Research conducted to date suggests that ketosis may indeed have beneficial effects in individuals with mild cognitive impairment (MCI) or AD.

KETONE AND DEMENTIA RESEARCH HIGHLIGHTS

A single dose of MCT improves memory in individuals with mild-to-moderate Alzheimer's disease.

A 2004 study by Reger et al., published in *Neurobiology of Aging*, involved 20 individuals with AD or mild cognitive impairment who consumed a drink containing emulsified medium chain triglycerides (MCTs) or a placebo. Ninety minutes later, those who drank the MCT beverage experienced significant increases in ketones, as well as greater improvement in paragraph recall (a measure of memory), compared to the control group.

A ketogenic supplement taken over a 90-day period boosts cognitive scores in mild-to-moderate AD patients.

In a study conducted by Henderson et al., published in the August 2009 issue of *Nutrition & Metabolism*, 152 individuals who had been diagnosed with mild-to-moderate AD were given either an oral ketogenic compound (AC-1202, which is a MCT supplement) or a placebo while eating as they normally would. AC-1202 was found to quickly elevate the participants' ketone levels and induce a mild level of ketosis. By the end of the 90-day trial, those who took the MCT supplement experienced significant improvements in their cognitive scores, compared to the placebo group.

Low-carb diet improves memory among small group of older adults with MCI.

A more recent study conducted by Krikorian et al., published in the February 2012 issue of *Neurobiology of Aging*, involved 23 older adults with mild cognitive impairment who ate either a high carbohydrate or very low carbohydrate diet over a six-week period. The very low carbohydrate diet was designed to induce ketone metabolism. The results showed that ketone levels were "positively correlated with memory performance." In other words, very low carbohydrate consumption, and the accompanying increase in ketone levels, was found to improve memory function in a short period of time.

Ketone ester proves effective in a single case study of a man with Alzheimer's disease.

A 2014 case study conducted by Newport et al., published in *Alzheimer's & Dementia*, shared the results of administering a ketone ester (a synthetically-made supplement to induce ketosis) to one individual with younger-onset AD. The study participant maintained his usual diet and continued with the MCT/coconut oil supplementation he had been taking since 2008. During the 20-month study period, improvements were noted in his behaviour, as well as cognitive and daily-activity performance, leading the researchers to conclude that the ketone ester treatment was "robust, convenient and safe."

THE LIMITED RESEARCH TO DATE SUGGESTS THAT MANY DIFFERENT KINDS OF KETOGENIC INTERVENTION OFFER NEUROLOGICAL AND COGNITIVE BENEFITS.

Improvements seem to occur regardless of whether ketosis is achieved through prolonged fasting or a very high-fat ketogenic diet (both of which are difficult to adhere to, especially for individuals with cognitive impairment), or whether ketosis is induced by taking MCT or ketone supplements while maintaining a regular diet.

It is important to note, though, that the mechanisms through which ketosis boosts cognitive function are not fully understood at this early stage in the research. Ketosis has not been rigorously studied in large-scale or controlled clinical trials, so there is a lot that remains unknown. For example, the positive effects of ketosis may not apply to everyone, and it is uncertain whether there are any long-term side effects to the various ketogenic treatments. Nevertheless, the research to date is certainly promising, and suggests that further investigations would be valuable to determine whether ketosis could be the cure or effective treatment that we have been hoping for.

WHAT IS A PLACEBO?

A placebo is a harmless substance that has no therapeutic effect. Placebos are used as a control when testing new drugs to assess whether there is a psychological impact of simply being treated (i.e. in the absence of any real physiological effect).

FOR A HEALTHIER BRAIN AS YOU AGE,

Try a Little Naughty with that Nice

Have an apple a day; eat your vegetables; cut out the junk food – these well-established nutritional tips from your parents have stood the test of time and peer review. However, as it turns out, it seems that what we should and should not eat may be less restrictive than we once thought, particularly when it comes to brain health. For instance, while you may never have been told to drink wine to ward off dementia, research from Loyola University Chicago's Stritch School of Medicine has suggested that moderate social drinking significantly reduces the risk of dementia and cognitive impairment.

The research team's findings, published in the 2011 issue of *Neuropsychiatric Disease and Treatment*, indicate that moderate drinkers (defined as a maximum of one drink a day for women and one to two for men) were 23% less likely to develop Alzheimer's disease or exhibit signs of serious memory problems than non-drinkers. Both light and moderate drinking »

EATING FOR A HEALTHIER MIND

FOODS TO EAT

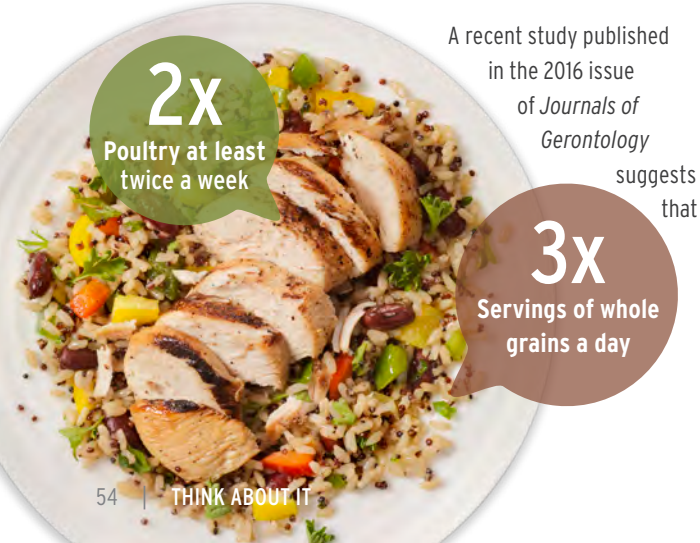
- Vegetables (and green leafy vegetables)
- Nuts
- Blueberries & strawberries
- Beans
- Whole grains
- Fish
- Poultry
- Olive oil
- Wine

FOODS TO AVOID

- X Red meats
- X Butter or margarine (less than 1tbsp a week)
- X Cheese (less than once a week)
- X Fried or fast food (less than once a week)
- X Pastries and sweets (less than once a week)

provided a similar benefit, but heavy drinking was associated with significantly higher cognitive risk for dementia and cognitive impairment (and is, of course, also associated with a host of other health issues).

A more recent study, published in *Neurology* in February 2015, focused on the potential benefits of resveratrol – a compound found in some red wines, dark chocolate, and raspberries. The study suggests that resveratrol, taken in highly concentrated doses, could stabilize levels of a biomarker that declines in individuals with Alzheimer's, thereby slowing the progression of the disease. During the clinical trial, half of the participants consumed a pure synthetic form of resveratrol while the other half received a placebo. The highest dose tested was one gram twice daily – the equivalent to the resveratrol contained in approximately 1,000 bottles of red wine! Since drinking alcoholic beverages is best in moderation, it may be difficult to get a sufficient dose of resveratrol from wine consumption alone.



A recent study published in the 2016 issue of *Journals of Gerontology* suggests that drinking three cups of coffee a day reduces the risk of Alzheimer's in older women. The study involved nearly 6,500 women aged 65 and over who drank caffeinated beverages daily. Those who drank at least two to three cups of coffee (more than 261 milligrams of caffeine per day) showed a lower risk of developing dementia or cognitive impairment ten years later than those who consumed less coffee.

It also turns out that a diet of foods rich in extra virgin olive oil, together with plenty of fruits and vegetables and a little red wine, seems to lower the risk of developing Alzheimer's and other forms of dementia. While Alzheimer's affects approximately 30 million people worldwide, the prevalence of the disease is lower in Mediterranean countries. Scientists previously attributed this to the high concentration of healthful monounsaturated fats in olive oil – consumed in large quantities in the Mediterranean diet. However, more recent research has suggested that the actual protective agent may be a substance called oleocanthal, which has effects that protect nerve cells from the kind of damage that occurs in Alzheimer's.

To find out why, researchers from the University of Louisiana at Monroe's College of Pharmacy sought evidence on whether oleocanthal helps decrease the accumulation of beta-amyloid (Aβ) in the brain – the toxic protein that builds up in the brains of individuals with Alzheimer's. Their study, which appeared in the 2013 issue of *ACS Chemical Neuroscience*, found that oleocanthal appears to help speed up the removal of beta-amyloid from the brains of laboratory mice. While further studies in humans are necessary to confirm this effect, the good thing about extra virgin olive oil is that it is both safe and easy to incorporate into our everyday diets.

Two years ago, a research team at Rush University in Chicago led by Dr. Martha Clare Morris, a nutritional epidemiologist at Rush, developed the MIND diet – a hybrid of the Mediterranean and DASH (Dietary Approaches to Stop Hypertension) diets. Dr. Morris and her colleagues believe that

THE MIND DIET OFFERS THE BEST-KNOWN DEFENCE AGAINST BRAIN DEGENERATION.

In two observational studies, the MIND diet was impressively

effective. In those participants who adhered to the diet rigorously, the risk of developing Alzheimer's was lowered by as much as 53%, while those who followed the diet moderately saw their risk reduced by approximately 35%. The MIND diet is also easier to follow than the Mediterranean diet, which requires you to consume copious amounts of fish, as well as three to four servings of both fruits and vegetables daily.

"Alzheimer's is a disease of aging," says Dr. Morris, "and it's not declining because our population is getting older. It's a very costly disease and it's a very devastating disease. Right now there are no treatments and there are no cures so it's a very important public health problem."

"Though we know that there is a strong link between what a person eats and health, dietary intervention trials to examine whether a change in diet will help prevent Alzheimer's disease and other dementias have been largely neglected," Dr. Morris notes.

In an effort to better understand the relationship between nutrition and brain health, Dr. Morris and her team began conducting a randomized trial in February 2017 to examine why the MIND diet is so successful. Over the course of five years, the researchers will study 600 individuals aged 65 years and over who are overweight and have less-than-ideal diets – factors that make them vulnerable to developing Alzheimer's disease.

"The results of this study should help us to improve brain health by developing new dietary guidelines for clinical use and for public health education," Dr. Morris says.

"IT'S UNFORTUNATE THAT THE FIELD OF NEUROLOGY HAS BEEN VERY STUBBORN TO BELIEVE THAT DIET COULD HAVE SOMETHING TO DO WITH NEURODEGENERATIVE DISEASES."

Dr. Morris further notes that to date, there has not been a study "that has targeted people who have marginal levels of a nutrient and then supplemented them to see if it had a positive benefit on their cognition. Hopefully this trial will have a positive finding and then it should be even better."

Dr. Morris's work exemplifies another age-old pearl of health wisdom – an ounce of prevention is worth a pound of cure. "There's been a 99.6% failure rate for drug trials for treatment of Alzheimer's Disease," says Dr. Morris. "That is not the case at all for the prevention trials. They have actually been very successful, in particular for cognitive activity and physical activity and their ability to slow cognitive decline."

A sign that an aging family member may require more support could be a fridge full of uneaten food. While it is normal for us to eat less as we get older, aging bodies still have important nutritional needs – especially when it comes to the mind.

According to a 2012 report by the Dietitians of Canada entitled "The Role of Nutrition in Mental Health Promotion and Prevention," because neurocognitive disorders tend to occur more frequently in older adults, it is believed that the link between nutrition and brain health may be related to consuming less food just when better nutrition is needed.

Numerous studies have shown that older adults have higher rates of nutritional deficiencies than younger age groups, particularly in the B-vitamins and Vitamin E. Vitamin B12, for example, affects neurocognitive development so deficiencies in this vitamin could lead to cognitive decline. Vitamin E may reduce brain amyloid beta peptide accumulation, which is known to be relevant in Alzheimer's disease.

"Cognitive decline may be accelerated if nutritional deficiencies are not addressed," the report indicates.

SPARKNOTES FROM A CAREGIVER

Care partner. Caregiver. Who Really Cares. Call us whatever makes you feel better. It doesn't change what we do.

We've all cared for loved ones who are ill but never thought of ourselves as caregivers. We are wives and husbands, adult children, significant others, even grandchildren. But it is the years on the job that define you.

People ask me "Would your husband have done the same for you?" Given up his career. Devoted himself to your care and comfort and kept you at home. Ladies, what do you think?

My bookshelf is lined with tomes on dementia care, yet the page I need always seems to be missing. Each brain unravels in its own quirky and idiosyncratic way.

I care for my husband in our library and my mother's been ensconced in our dining room for more than a decade after reporting me to social services for holding her "against her will" in a penthouse apartment in a new, swinging singles building. This proud woman with a walker didn't like the "idea of living with old people."

I've been a caregiver for close to 21 years – first for my husband with early-onset Alzheimer's at age 57 and then for my mother, as well at age 85. She'll turn 97 this year. She didn't like my husband when she was well and he was a Jewish doctor. Can you imagine her in dementia?

I have spent close to two decades trying to decipher what's going on in my husband's head. No new short-term memories stick: his internal navigational compass has shut down. His disease is my puzzle.

I am not here to tell you that I am a good example to follow. No one who has ever been on the front lines of care ever questions when someone says "I can't do this anymore." And quite frankly, having no guilt about my choices has come with too high a price. No disease deserves to take down the well spouse too.

We must be sensitive not to insult our parents' generation with the idea that behavior modification in lifestyle and diet might have saved them from Alzheimer's. It couldn't save them and there's no guarantee it can save us. Right now that's all we have.

People ask "How have you survived"? Well I lived forward from crisis to crisis, never looking back at what was happening to me or my life. I never complain because I see pain everywhere.

Women progress faster into Alzheimer's than men, and the latest research shows that cognitive decline begins to occur earlier in women than men who have a protective gene. And for those of us who complain about a few extra pounds (don't we all), researchers call it a "power pack" needed to fuel our brains as we age. Now we've got our excuse.

This is our generation's battle. Our weapons are research and advocacy. By any measure, it is worth the fight. So when asked why I fight, the answer is simple: it is all about the pain.

I fight because I never want my great grandchildren to ask their parents as one of my grandsons did to me, "Nana, how could Gigi ever forget me?" I will never forget his little face, those words and that I had no storybook ending to tell.

Was I too stubborn? I still do 12-hour shifts each day to stow the financial bleed. Two adults in their prime out of work; no long- term care insurance. I am our sole support. What will happen to me? My advice to women: protect yourself.

Caring for a loved one with Alzheimer's either strengthens family ties or divides and destroys. I call my three precious grandchildren "my anti-depressant of choice."

If you have cancer, 90% of doctors will give you a diagnosis. If it's Alzheimer's more than 50% of doctors won't tell you because they have nothing to offer and don't want to depress the patient. As a result, couples are often torn apart by inappropriate behaviors, or what I call the "garden variety" grounds for divorce. The disease slips over you as you fight for control. Let's end paternalism in medicine. Just tell it to us straight.

Alzheimer's disease is not the legacy we want for our children or the way anyone wishes to be remembered.

As baby boomers, our generation is in denial. We're into "use it or lose it mode" exercise cross-word puzzles learn a new language books on 101 nights of great sex after 60 go for it – can't hurt, but watch your back.

Meryl Comer,
President and CEO,
Geoffrey Beene Foundation
Alzheimer Initiative and
21st Century BrainTrust

MIND YOUR STRESS

Live Your Life With Less Stress & More Balance

Stress is an inevitable part of life, but can be detrimental to your health when it is at chronic levels for long periods of time. The good news is that there is never a bad time to start learning new techniques to help put your mind at ease.

WHAT IS MINDFULNESS PRACTICE?

A mindfulness practice doesn't necessarily mean that life is full of blissful moments. The concept involves practicing mindful techniques to help you navigate through your life in a more fluid way, rather than resisting or dwelling on negative situations. There are many benefits to incorporating this into your lifestyle, including regulating mood, reducing depressive symptoms, improving focus and attention, and reducing your stress and anxiety.

PRACTICING BALANCING POSES, such as Tree Pose (Vrksasana), is a great way to regain focus and bring yourself back to the present moment.

Vitina Blumenthal
Founder of WanderfulSoul,
Co-Founder of Wander Well

PHOTO BY ALEN PALANDER

5 TIPS TO BEGIN MINDFULNESS PRACTICE:

1. WRITE IT DOWN

Journaling is a great ritual to start or end your day. Your journal is a place to run free with your thoughts. There are no right or wrong topics to write about. Here are a few ideas if you are unsure of how or where to start:

- Ask yourself how you are feeling in the moment.
- Is there a current situation that is consuming your mental energy?
- Keep notes and write down any self-sabotaging thoughts, no matter how silly you think they are (for example, "I am not good at ____", "I can't do _____").
- If you are stressed about making a decision, write down a list of your life's desires. Seeing how your choice aligns with this list tends to make the decision much easier.
- Reflect on what you are grateful for in life.

2. FLOWING

Flowing refers to a style of yoga where the practitioner moves gracefully from one pose to the next and the practice becomes almost like a dance. Generally, each movement in to or out of a

posture is made on an inhalation or exhalation, so the yoga unites the breath with the movement in a choreographed sequence. There is a lot to learn about yourself in the physical practice of yoga. The process of connecting to your body is a great tool to help you focus on the present moment. Not only will you see physical benefits, but also there are many emotional and mental perks as well. What happens on the yoga mat is often a reflection of what happens in your everyday life.

Some realizations include overcoming fears, being patient with yourself, letting go of expectations, recognizing when you are comparing yourself to others around you.

KEEP IN MIND THAT THE SUCCESS OF YOGA IS NOT IN PERFORMING POSES; RATHER, THE SUCCESS OF YOGA LIES IN HOW IT POSITIVELY CHANGES YOUR LIFE AND RELATIONSHIPS.

There are many different types of yoga. If you have never tried a class, or you have attended one class but decided that it wasn't for you, take more than one class to try various styles.

3. CONTROL YOUR BREATHING

Think about when you are scared or when you are running late for work. Your breathing is quite fast. Your heart races. Now, imagine yourself at the spa. Your breathing usually consists of a shorter inhale and a longer exhale. Controlled breathing can calm the nervous system, increase focus, and reduce stress.

4. COME BACK TO THE PRESENT MOMENT

Do you tend to live life in the past or in the future? A very simple technique to help bring yourself back to the present moment is focusing on the senses.

"What do I see? What do I feel? What do I smell? What do I taste? What do I hear?"

Anchors such as mantras, sound and breath, as well as focusing on what is happening around you, are helpful tools to bring you back to the present moment. You can incorporate and practice this technique in your daily routine, whether you are brushing your teeth, eating, or going for a walk and enjoying the nature around you.

5. CREATE A MEDITATION HABIT

Much like adopting a healthy physical lifestyle, meditation is a healthy habit to incorporate into your everyday life. Just like any habit or routine, the mind can be trained. Think of meditation as push-ups for the brain.

Similar to setting goals for your physical practice, it is beneficial to know why you are meditating. It may be to connect to yourself, ground yourself, calm your mind, or manage your emotions better. Use the benefits that are most important to you as a motivator.

The best piece of advice that I have received about practicing meditation is that

IT IS BETTER TO MEDITATE FOR TWO MINUTES EVERYDAY THAN FOR THIRTY MINUTES ONCE A WEEK.

Find time in your daily routine, perhaps after you brush your teeth or while sitting in your parked car before heading to work, to practice just two minutes of meditation. You will reap the benefits of this simple, yet powerful, daily habit.

Be consistent and have fun playing with mindfulness. Different techniques and tools may work better than others for you, so just keep exploring and see where it takes you.

Mindfulness is being patient, calm, letting go of expectations, and being present. It's all about being grateful for the path that you are on and enjoying the journey!

2-1-4: STRESS RELIEF BREATHING | STEP-BY-STEP INSTRUCTIONS

1. Set a timer for a minimum of five minutes.
2. To begin, sit still and tall somewhere comfortable.
3. Close your eyes and begin breathing in and out through your nose in a natural rhythm to get comfortable.
4. Begin by inhaling for a count of two... hold the breath in for a count of one... exhale gently, counting out for four... and finish by holding the breath out for a count of one. Keep your breathing even and smooth.
5. Continue with this breathing pattern until the timer goes off.
6. Sit for a few moments afterwards, noticing how you feel.

Mixed Green Salad with Mango, Seasame Seeds & Ginger Yogurt Dressing

SERVES 4 - PREP TIME: 10 MIN

SALAD INGREDIENTS

5 oz. (5 cups) mixed baby greens
1 mango, cubed
2 Tbs. lightly toasted sesame seeds

DRESSING INGREDIENTS

1-1/2 Tbs. apple cider vinegar
1 Tbs. finely chopped shallot
2 tsp. freshly grated ginger
2 tsp. thinly sliced mint leaves
Kosher salt and freshly ground black pepper
1/3 cup plain full fat yogurt
1 Tbs. extra-virgin olive oil

INSTRUCTIONS

1. In a small bowl, combine the vinegar, shallot, ginger, mint, 1/8 tsp. salt, and a few grinds of pepper.

2. Stir in the yogurt and olive oil.

3. In a large bowl, season the greens and mangoes with a pinch of salt and a few grinds of pepper and toss with enough dressing to lightly coat. Toss with the sesame seeds and serve.

Mango

Mangoes are packed with Vitamin B6, which is essential for maintaining, if not improving, brain function.

MEMORYMORSELS®

A WOMEN'S BRAIN HEALTH INITIATIVE

You likely know that diet impacts heart health, but you may not realize that your brain is also affected by what you eat.

Research has shown that one of the best ways to keep your brain working the way you want is to eat right. Diet has a significant impact on your brain health, and as you age chronologically, you can keep your brain healthy by adding smart foods and eliminating harmful choices from your diet. A healthy diet and a healthy brain go hand-in-hand, and can knock years off your "brain age".

Memory Morsels®, a Women's Brain Health Initiative, is a website dedicated to delicious, brain healthy recipes, brain health tips (our morsels) and great information to help keep your brain functioning the way you want.

Tuna Stuffed Avocado

SERVES 2 - PREP TIME: 10 MIN

INGREDIENTS

1 avocado, halved and pitted
1 (4.5 oz) can tuna, drained
1/4 cup diced red bell pepper
2 tablespoons finely chopped celery
1/4 cup cilantro leaves, roughly chopped
1 tablespoon lime juice
salt and pepper (to taste)

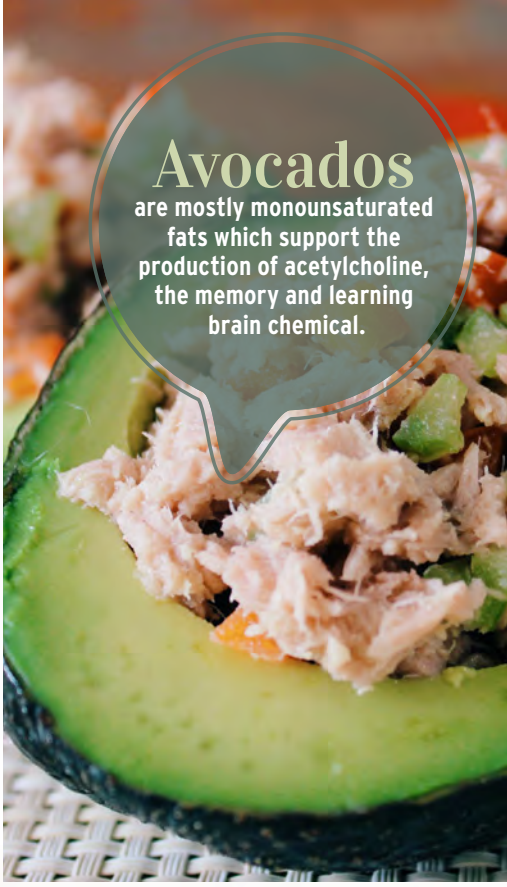
INSTRUCTIONS

1. To create an avocado "bowl", scoop out some of the avocado from the pitted area to widen the space to fill with stuffing. Place the scooped avocado into a medium-size mixing bowl. Mash it with a fork.

2. In a separate mixing bowl, add the tuna, bell pepper, celery, and cilantro. Pour lime juice over. Stir it all together until everything is well mixed.

3. Scoop the tuna into the avocado bowls. Season with salt and pepper.

For more recipes, morsels and the latest from our *Founding Foodie* Nora DeBora, visit memorymorsels.org



Avocados

are mostly monounsaturated fats which support the production of acetylcholine, the memory and learning brain chemical.

Raspberry Maca Smoothie Bowl

SERVES 2 - PREP TIME: 2 MIN

SMOOTHIE BOWL INGREDIENTS

1 frozen banana
1/2 cup fresh raspberries
1.5 cups of almond milk
1 scoop vanilla plant based protein powder
1 heaping tsp maca powder*
1 tbsp ground chia seeds

TOPPINGS

1/4 cup fresh raspberries
1/2 chopped banana
2 tbsp coconut flakes
2 tbsp gogi berries

INSTRUCTIONS

1. Blend smoothie base and pour into two separate medium bowls with at least 1.5 inches of room at the top of the bowl

2. Top with fresh raspberries, chopped banana, coconut flakes and gogi berries

**Maca is a Peruvian root vegetable; maca powder is available in most health food stores.*

Maca Powder

This stress buster improves energy and focus, balances hormones and mood, and boosts your brain health.

NOVEMBER 2016 | **TD PRESENTS:**

MILLENNIAL MINDS VS. BOOMER BRAINS BATTLE OF THE BANDS

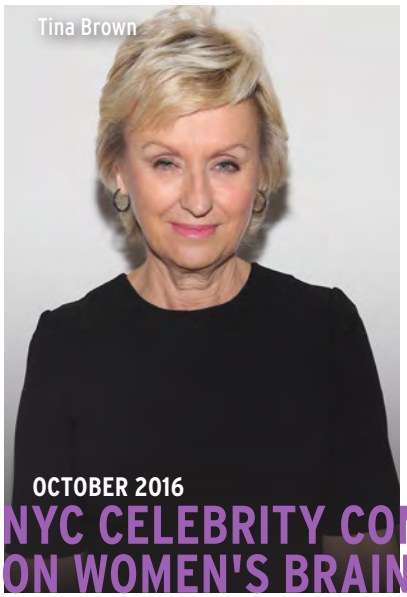
BRAIN BUZZ

Support for WBHI and women's brain health continues at events in Canada and the U.S.

(L-R) Lynn Posluns, MC - Jeanne Beker, Battle Judges - Traci Melchor, Divine Brown, Fefe Dobson, Dave Wanless and Marc Jordan

Candace Bushnell

Naomi Campbell & Lynn Posluns



Tina Brown

OCTOBER 2016

NYC CELEBRITY CONVERSATION ON WOMEN'S BRAIN HEALTH

Mamie Gummer

Lauren Hutton & Mark Lash

Dr. Samantha Boardman

Indigo's Heather Reisman & Kimberly Williams-Paisley

OCTOBER 2016 | **CIBC PRESENTS**

FROM HER LIPS TO OUR EARS

CIBC's Sarah Widmeyer & Lynn Posluns

WOMEN'S BRAIN HEALTH INITIATIVE HONOURARY BOARD

Jeanne Beker
Journalist, Author & Fashion Entrepreneur

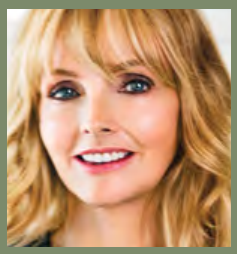
Catherine Delaney
President, C.A. Delaney Capital Management Ltd.

Arlene Dickinson
CEO, Venture Communications

Jordan Fogle
Founder, The Mint Agency

Heather Reisman
Founder, Chair & CEO, Indigo

Fran Sonshine
National Chair, Canadian Society for Yad Vashem



Kirstine Stewart
Chief Strategy Officer, Diply

Hon. Michael Wilson
Chairman, Barclays Capital Canada, Inc.

WOMEN'S BRAIN HEALTH INITIATIVE OFFICERS & BOARD OF DIRECTORS

Ken Aber
Founding Partner, Blueprint Business Architecture

Jane Allen
Senior Vice President, Strategy & Innovation, Hydro One

Lisa Borsook
Executive Partner, WeirFoulds LLP

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

Mark Girard
Chief Financial Officer, Cedarpoint Investments

Eileen Greene
Vice President & Partner, Hub International

JoAnne Korten
Executive Director, WBHI

Mark Lash
Founder & President, Mark Lash

Heather Masterson
President & CEO, Travelers Canada

Lynn Posluns
Managing Director, Cedarpoint Investments

Ellen Rachlin
Managing Director, J.P. Morgan

Mark Raynes Roberts
Crystal Artist & Designer

Sarah Widmeyer
Managing Director & Head Wealth Advisory Services Group, CIBC

SUPPORT THE INITIATIVE. WEAR A HOPE-KNOT.

The Hope-Knot was created to remind us all of the importance of our thoughts and memories, and the interwoven connections that make life meaningful. **This Mother's Day and every day**, celebrate the women in your life – your mother, wife, daughter, sister or best friend - with a gift of brain health.

Proceeds from each Hope-Knot sold support gender-based brain-aging disease research.

Stainless or Sterling Pin
$10 | $130

Sterling Pendant & Chain
$180

Sterling Cufflinks
$295

WILL YOU FORGET?
WE HOPE-KNOT

Order yours at **HOPKNOT.ORG**
or **1-888-927-2011**

OUR GREY MATTER MATTERS

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

Together we can accelerate the pace of progress. Your generous support today will allow us to reach more, and teach more.

DONATE NOW

We are truly grateful to:

Brain Canada Foundation

and all those who generously supported this publication:

Gay Berger, Berkhold Family Foundation, Bloom Lanys Professional Corp., Brain Canada, Joy Cherry, Sylvia Chrominska, Ken Crystal, Shirley Diamond, Evelyn Ernest, Susan Fenwick, Linda Frum, Gitta Ganz, Miriam Gee, Gillespie Foundation, Lynn Glazer, Carole Grafstein, Robyn Greenspan, Sandra Herlick, Michael Kallas, Debbie Kimel, JoAnne Korten, Jordanna & Earl Lipson, Sharon London Liss, Judith Megow-Rose, Valerie Melman, Myra Merkur, Milli Ltd., William Moir, Ellen Morris, Margaret Nightingale, Diane Nusbaum, Margi Oksner, Lynn Posluns, Sandy Posluns, Lionel & Helaine Robins, Royal Bank of Canada, Judy & David Schwartz, Lyla Schwartz, Doreen Scolnick, Sylvia Soyka, Barbara Sugar, Carole Tanenbaum, The Citrine Foundation of Canada, Karen Weinstein, Myrna Weinstein, Linda Williams Education Fund, Carole Winberg.

Women's Brain Health Initiative

Yes! I'd like to support Women's Brain Health Initiative now with my gift of:

☐ $2,000 ☐ $1,000 ☐ $500
☐ $250 ☐ $100 Other $ _____

☐ I have enclosed a cheque payable to Women's Brain Health Initiative

☐ I prefer to use my credit card

You can also donate online at ***womensbrainhealth.org/donate***

DONOR NAME

ADDRESS

ADDRESS

CREDIT CARD NUMBER

EXPIRY DATE: MM/YY

CVD

NAME ON CREDIT CARD

PHONE NUMBER

E-MAIL

SIGNATURE

30 St. Clair Avenue W, Suite 900 | Toronto, Ontario | M4V 3A1 | 1-888-927-2011 | info@womensbrainhealth.org

CHARITABLE NO: 80099 3206 RR0001 | 501(C)(3) TAX-EXEMPT ORGANIZATION | A charitable receipt for maximum amount allowed by law will be given for donations over $20.

BRAIN HEALTH IS A WOMAN'S ISSUE

TWO-THIRDS OF ALZHEIMER'S SUFFERERS ARE WOMEN, AND TWO-THIRDS OF CAREGIVERS ARE WOMEN.

Let's do more for the women in our lives.

Women's Brain Health Initiative is a national charitable foundation raising funds for research and education to combat brain-aging diseases that affect women.

CARE TO JOIN US?

womenbrainshealth.org | 1-888-927-2011

Women's Brain Health Initiative

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