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HELPING YOU PROTECT YOUR BRAIN HEALTH

Anxiety Disorders

Telltale Sign

Rewiring the Brain

> Secondary *Traumatic* Stress

Unlocking Vitality

Sounds Only You Can Hear



Boost Your Brain Awareness.

"It is critical to support research that examines health differences between men, women, and gender-diverse individuals. Time and time again, studies have shown that significant differences do, in fact, exist between males and females in many areas of health care."

> Dr. Viviane Poupon President & CEO, Brain Canada





braincanada.ca

Editor-in-Chief

e all share a universal desire: to lead longer lives. Yet, let's be honest, none of us relishes the idea of growing old. The inexorable march of time affects us all, marking its passage with undeniable changes in our bodies and minds.

However, aging doesn't necessarily mean slowing down. Recent research and mounting evidence have uncovered advancements in lowering our risk of developing cognitive impairment and dementia through lifestyle choices and reinforcing the Six Pillars of Brain Health: exercise, nutrition, sleep, social activity, stress management, and mental stimulation.

Studies have shown that a healthy lifestyle is associated with slower memory decline, even in the presence of the Alzheimer's APOE ϵ 4 allele risk gene.

Among older adults, more time spent in sedentary behaviours was associated with a higher risk of incident all-cause dementia.

Middle-aged women on the DASH diet, aimed at lowering blood pressure, were 17% less likely to experience cognitive decline in their later years.

The strongest evidence to date is that adhering to the Mediterranean diet as you age reduces the risk of cognitive decline, as confirmed by using more accurate dietary assessment methodologies.

Volunteering in late life may protect the brain against cognitive decline and dementia. Older adults who volunteer have better memory and executive function.

Practicing and listening to music can help fight cognitive decline in healthy seniors by stimulating the production of grey matter.

Lifelong learning improves cognitive abilities in older adulthood.

An elevated level of perceived stress (i.e., low stress vs. elevated stress) is associated with 1.37 times higher odds of poor cognition.

Regular walks strengthen connections in and between brain networks, adding to growing evidence that links exercise with slowing the onset of Alzheimer's (AD).

A short but intense bout of exercise could protect the brain from age-related cognitive decline.

Increased omega-3 fatty acids are associated with better memory, processing speed, and structural brain measures among healthy, cognitively older adults.

Each percentage decrease in slow-wave-sleep (often referred to as deep sleep) per year is associated with a 27% increase in the risk of dementia.

In addition to funding research that better meets women's unique needs, the second reason I founded Women's Brain Health Initiative was to empower you with this new knowledge through initiatives like Mind Over Matter® magazine, thanks to our partner Brain Canada.

We also strive to provide you with the tools, such as the free app BrainFit - Habit Tracker, to proactively modify your behaviours today to get ahead of diseases like AD, thereby influencing the trajectory of your brain health in the future.

At Women's Brain Health Initiative, we are committed to ensuring that you maintain your cognitive prowess for as long as possible. Our mission is to grant you the freedom to navigate life on your own terms, make your own choices, and secure your financial future in a way that aligns with your unique needs and desires.

Founded on the principle of empowering women with knowledge and tools to proactively modify behaviours, we aim to influence the trajectory of brain health for the better. Possessing the AD risk gene doesn't guarantee you'll succumb to this illness, and conversely, not having the risk gene doesn't guarantee immunity from it. The differentiating factor lies in the lifestyle choices we make.

While the exact causes of AD remain elusive, embracing a healthy lifestyle can significantly diminish associated risks. Join us in this transformative journey because at Women's Brain Health Initiative, we're not just improving lives, we're safeguarding the essence of who you are. Your brain, your power, your future, your independence – we're here to make it brilliantly compelling.

Wishing you and yours good health. 🛞

un

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

CONTENTS

- **6** Sounds Only You Can Hear
- **11** Mind Your Tongue
- 15 Women & Urinary Tract Infections
- **19** Mild Behavioural Impairment
- 23 You've Got to Have Faith
- 26 Into the Blue
- **29** Decision Fatigue
- 32 On the Cover
- 34 Unlocking Vitality

36 CPTSD

- **39** Rewiring the Brain
- **43** Secondary Traumatic Stress
- 48 Anxiety Disorders
- 51 Telltale Sign

56 AgeTech

- 59 How Old Are You Now?
- 62 All By Myself
- 64 Memory Morsels
- 66 Brain Buzz
- **67** Board of Directors & Supporting the Initiative

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Alex Mlynek is a Toronto-based journalist who has worked as an editor for *Today's Parent* and *Canadian Business* magazines. Her writing has appeared in a number of publications, including *Reader's Digest*, *Broadview, Chatelaine, Best Health, The Walrus* and *Report on Business*. She loves telling a good story and making copy entertaining and accurate. When she isn't hanging out with her husband and two kids, you will likely find Alex in her garden or with her nose in a book.

WENDY HAAF // WRITER

Wendy is a freelance health writer based in London, Ontario. As a longtime contributor to a Canadian retirement magazine, she has regularly covered topics related to healthy aging. A mother of three, including two adult daughters, and grandmother to a new granddaughter, she is particularly interested in providing women with evidence-based information about what they can do to protect and maintain their brain health throughout life.

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."

JANE LANGILLE // WRITER

Jane is a health and medical writer living in Richmond Hill, Ontario, who writes for healthcare organizations, hospitals, and academic health research institutions in Canada and the United States. Having seen close family members deal with progressive supranuclear palsy and Parkinson's disease, she enjoys interviewing experts to learn about the latest advances in women's brain health and sharing evidence-based insights.

ILIMA LOOMIS // WRITER

Vancouver-based Ilima Loomis is a freelance science writer whose work has appeared in publications like *Science, Popular Science, and Discover.* Having seen close family members cope with neurodegenerative conditions like Parkinson's disease and dementia, she is always eager to learn more about brain health, speak with experts, and share information with other women.

SEAN MALLEN // WRITER

Sean is a Toronto-based communications consultant, media trainer, and writer. Having seen close family members deal with dementia, he is a passionate supporter of WBHI's mission and is inspired by telling the stories of researchers who are expanding our knowledge of women's brain health. Sean's first book, *Falling for London: A Cautionary Tale* from Dundurn Press, is widely available across North America and the United Kingdom.

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Subha is a director and research consultant for Atmoco Ltd., specializing in health promotion through physical activity. With a PhD in public health, Subha helps non-profits collect relevant information, make research findings understandable, and put recommendations into action. She also teaches a university course in sustainable happiness. Writing for Mind Over Matter[®] unites Subha's knowledge, skills, and desire to share information and strategies that enhance brain health and overall well-being.













VITINA BLUMENTHAL // CREATIVE DIRECTOR

For over a decade, Vitina has lent her branding and design expertise to support WBHI's mission. Her passion for mindful living aligns seamlessly with the organization's mission to safeguard the mental and brain health of women, caregivers, and their families.



GREGORY CIRA // CREATIVE DESIGNER

Gregory is an established design entrepreneur with an acuity for information design and understands the importance of communicating clearly. Having had family members who suffered from dementia, he has been inspired to raise awareness of the importance of brain health and uses his visual communication skills to help bring that awareness to others.



LORI HICKEY & CHERYL HICKEY // ON THE COVER

As the former ET Canada co-host told Mind Over Matter® in our cover story, her parents shared many life lessons that have sustained her through a long career in broadcasting. "Mom always taught me that when bad things happen, as they do, you also have to give the same attention to things that were good," said Cheryl. Both mother and daughter have embraced mindfulness as a means of managing stress, along with exercise and healthy eating. Sharing a photo shoot for the cover was a unique treat. "That's kind of Cheryl's thing," said Lori. "But it was lovely. I loved spending the day with her. And it's an important cause."

WE ARE TRULY GRATEFUL TO:

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Sounds Only You Can Hear

TINNITUS & BRAIN HEALTH

Barbra Streisand, the famous singer, has heard phantom sounds since childhood. In grade six, she feared the strange noises and tried to block them with scarves around her head.

Millions of people in North America hear sounds that have no external source. This condition, called tinnitus, comes from the Latin verb "tinnire," which means "to ring." Experts pronounce it as TINN-it-is, but you may also hear tin-AYE-tis.

People living with tinnitus describe the noises they perceive as ringing, buzzing, grinding, roaring, hissing, whooshing, or similar to the sounds cicadas or crickets make or a kettle releasing steam.

These phantom sounds may last a short time or become constant. They may be barely noticeable or bothersome enough to disrupt daily life and sleep and cause stress, anxiety, and depression. Severe tinnitus can be debilitating and lead to suicidal ideation, although additional mental health issues may be involved with the latter.

Streisand is one of several celebrities who shared how tinnitus affects them in an awareness campaign by the Hearing Health Foundation. Others included actors William Shatner and Halle Berry, and Chris Martin, the lead singer of the band Coldplay.

Mind Over Matter® spoke with leading North American experts to learn more about tinnitus, how it affects brain health, current treatment options, and an innovative treatment strategy on the horizon.

TINNITUS CAUSES

Is tinnitus all in your head? Yes, but you're not imagining things. Your auditory system is producing sounds only you can hear.

Tinnitus is a symptom of a problem in the auditory system, which includes the ear, the auditory nerve that connects the inner ear to the brain, and the parts of the brain that process sound, according to the National Institute on Deafness and Other Communication Disorders (NIDCD).

"Most tinnitus is associated with damage to sensory cells in the inner-ear structure called the cochlea," explained Dr. Susan Shore, professor emerita of the Department of Otolaryngology-Head and Neck Surgery at Michigan Medicine's Kresge Hearing Research Institute.

"When the damaged cells send less input to the brain, certain cells in an area of the brain called the cochlear nucleus become hyperactive and fire, trying to compensate for the missing input."

"Tinnitus is almost always experienced alongside some level of hearing loss and frequently triggered by age-related or noise-induced hearing loss," said Dany Pineault, Doctor of Audiology, research advisor for Statistics Canada and adjunct assistant professor of the Post-Professional Doctor of Audiology Program at the A.T. Still University-Arizona School of Health Sciences.

I EXPLAIN TO MY PATIENTS THAT THE RINGING OR BUZZING INDICATES THE BRAIN IS WORKING HARDER IN AN EFFORT TO COMPENSATE FOR MISSING SOUNDS. THE INCREASED EFFORT IS PERCEIVED AS NOISE, LIKE A CAR'S ENGINE GROWING LOUDER AS IT ACCELERATES.

An estimated 15% of adults experience tinnitus, and only 10% of that group report it as debilitating. William Shatner's severe tinnitus was caused by noise-induced hearing loss: He was standing too close to a special effects explosion while filming a Star Trek episode. "There were days when I didn't know whether I would survive the agony; I was so tormented by the screeching in my head," he told the American Tinnitus Association.

Some people with tinnitus have normal hearing. However, a recent study by investigators from Massachusetts Eye and Ear, a treatment and research centre and teaching hospital of Harvard Medical School, found that despite having normal hearing, these individuals still had some degree of damage to their auditory nerve and hyperactivity in the brainstem. About half of the study participants were women. Their study was published in *Scientific Reports* in November 2023.

Certain medications have been linked to a higher risk of tinnitus, according to a longitudinal study by researchers at Brigham and Women's Hospital published in February 2022 in *Journal of General Internal Medicine*.

The investigators found that women who frequently used non-steroidal antiinflammatory drugs, such as ibuprofen or naproxen, had an almost 20% higher risk of developing persistent tinnitus.

Those who regularly used COX-2 inhibitors had a 21% higher risk of developing this condition. The study also revealed that frequent use of moderate-dose aspirin was associated \bigcirc

with a 16% higher risk of tinnitus in women under 60, but frequent use of low-dose aspirin did not affect risk.

Other medications linked to an increased risk of developing tinnitus include some antibiotics, antidepressants, and anti-cancer and anti-malaria drugs, according to the NIDCD.

Tinnitus may also be caused by other health issues, including Ménière's disease, acoustic neuroma, head and neck injury, jaw joint problems, high blood pressure, atherosclerosis, chronic diabetes, migraines, thyroid disorders, lupus, and multiple sclerosis.

SEX DIFFERENCES

"The evidence is mixed on whether more women or men experience tinnitus. It depends on what study you read," advised Dr. Shore. "Some say men are likelier to develop tinnitus since they work more often in noisy environments. Others say women are more likely to experience stress and anxiety, which can be contributing factors, but that's a chicken-or-egg situation. We don't know which issue arises first and contributes to the others." According to a recent study by researchers in Europe, there were no differences in reported loudness, duration, or location of the tinnitus between women and men.

Women, however, more often reported sudden onset tinnitus, headache, dizziness, and a lower tolerance for sounds, called hyperacusis, as well as experiencing depression, anxiety, and worries.

Men, on the other hand, more often reported a higher need to control their thoughts and more trouble coping with increasing distress related to tinnitus. The study was published in the journal *Frontiers in Neuroscience* in July 2020.

LINK TO BRAIN DISEASES?

The evidence is also mixed on whether individuals with tinnitus have a higher risk of developing neurodegenerative diseases.

Investigators in Taiwan recently analyzed ten years of data from their country's medical claims database to see if the risk of Alzheimer's disease and Parkinson's disease was higher in adults who developed tinnitus. In this study, published in July 2020 in *Scientific Reports*, 52% of the data was from women.

The analysis found that people with tinnitus were 1.54 times more likely to develop Alzheimer's and 1.56 times more likely to develop Parkinson's than people who did not have tinnitus. The authors concluded further studies are needed to confirm any biological connection. Still, they speculated that inflammation might explain these results since it is a common factor that triggers ringing in the ears and contributes to neurodegeneration.

On the other hand, researchers at the Center for Hearing Research at the University of California, Irvine, found that tinnitus was associated with improved cognitive performance in adults over 60 with hearing loss compared to those without hearing loss. The authors also said more work is needed to understand the underlying mechanisms. Their paper was published in October 2021 in *Frontiers in Neuroscience*.

CURRENT TREATMENTS

"One of the biggest myths about tinnitus is that there are no effective treatment options," said Mr. Pineault. "The technologies for hearing aids have advanced greatly in the past ten years. We have many options for providing people with relief from tinnitus and improving their quality of life."

The primary treatment for tinnitus is treating the associated hearing loss.

"It's important for people to know that's the case so they're not surprised when their audiologist recommends hearing aids," he said.

According to the NIDCD, only about 16% of adults aged 20 to 69 and about 30% of adults over 70 who could benefit from hearing aids have never used them. By contrast, the Vision Council reports that 64% of adults requiring vision correction choose corrective eyeglasses. "Awareness of the importance of good hearing health is slowly increasing, but there's still much room for improvement," Mr. Pineault said.

Hearing aids can be programmed to address each individual's hearing issues. "Patients with high-pitched tinnitus likely have hearing loss in that specific frequency," Mr. Pineault advised. "Many hearing aids come with tinnitus relief features, including a programmable app that an audiologist can calibrate to match a patient's tinnitus frequency. They also include sound therapy apps that provide relaxing sounds, such as ocean waves or rain."

A SOUND-ENRICHED ENVIRONMENT CAN GIVE AN OVEREXCITED AUDITORY SYSTEM SOMETHING ELSE TO FOCUS ON.

"Silence is not golden," Mr. Pineault said. "I can't start working on my computer until I have some low-level background music playing to support my hearing." He prefers jazz but says the type of music doesn't matter as long as you find it soothing.

If you or a loved one are bothered by tinnitus lasting longer than six months, Mr. Pineault advised it's best to consult an audiologist for an accurate diagnosis and discuss the best treatment options. He notes that accredited audiologists use evidence-based methods for diagnosing and treating tinnitus according to the American Academy of Otolaryngology-Head and Neck Surgery Foundation's clinical practice guidelines.

William Shatner found significant relief when an audiologist matched the tone of his tinnitus. He reported he's no longer bothered by it and doesn't think about it unless asked.

Cognitive behavioural therapy (CBT) teaches individuals how to identify negative thoughts about tinnitus that cause distress, change their responses, and focus on positive ways to reduce the impact of tinnitus on daily life. Mr. Pineault

TINNITUS & MEDICATIONS

There are no FDA-approved drugs for treating tinnitus, according to the American Tinnitus Association (ATA).

The National Institute on Deafness and Other Communication Disorders advises, "There are no medications specifically for treating tinnitus, but your doctor may prescribe antidepressants or antianxiety medications to improve your mood or help you sleep. While certain vitamins, herbal extracts, and dietary supplements are commonly advertised as cures for the condition, none of these has proven to be effective."

A recent survey by investigators at the University of lowa found that almost one-quarter of individuals with tinnitus reported taking a dietary supplement to address it – and none said they were effective. The most common supplements were ginkgo biloba, zinc, vitamin B12, melatonin, magnesium, and lipoflavinoid, a combination of vitamins and a phytonutrient found in lemon peels. The study authors concluded some of these supplements may help improve sleep, but they should not be recommended for treating tinnitus.

"The internet is rife with promises of a quick fix for tinnitus, but there's no proven cure yet," Mr. Pineault said. "I've seen many patients who spent a lot of money on unproven treatments and became even more distressed when they didn't work."

The ATA also points out that dietary supplements are regulated as food, not drugs, so manufacturers do not have to prove the products are safe or effective before selling them. Many contain powerful active ingredients that can result in unwanted side effects, depending on what other medications you're taking and your health history.

said CBT is a proven and highly effective treatment option, especially for those who experience unhelpful thinking patterns, heightened anxiety, or who avoid social situations to minimize noise exposure.

Tinnitus retraining therapy (TRT) combines psychological counselling with sound therapy. Counselling helps change \bigcirc

negative thinking patterns, emotional reactions, and sound hypersensitivity. Sound therapy decreases the contrast between the tinnitus and external sounds to get the brain more used to the tinnitus sounds. According to Hear Canada, more than 100 studies have shown that 80% of people have improved their tinnitus with TRT.

A PROMISING NEW TREATMENT ON THE HORIZON

A new device for treating tinnitus may soon be available for individuals who have tinnitus they can modulate with head or neck movements, such as tilting their head or moving their jawbone. About 70% of people with tinnitus have this type of tinnitus, called somatic tinnitus.

Several years ago, Dr. Shore and members of her lab made a critical discovery using guinea pigs.

"We found that in addition to auditory nerves, other nerves from touch-sensitive places in the body, called somatosensory nerves, provide input into the cochlear nucleus in the brain," said Dr. Shore. "We also discovered we could turn down the excitability of tinnitus-creating cells in the cochlear nucleus by combining input from the somatosensory and the auditory systems with a precise order and timing."

To translate this insight to human studies, they developed a prototype device that delivers both types of stimulation via an in-ear headphone and two electrodes that attach to the skin on the neck or cheek. The level of stimulation is calibrated for each user's tinnitus. The ground-breaking results of their first clinical trial were published in *Science Translational Medicine in* 2018, followed by a larger study published in *JAMA Network Open* in June 2023.

In the larger trial, 99 people with bothersome tinnitus used the device at home for 30 minutes daily for six weeks. Half of the participants received the bi-sensory treatment, and the other half received sound treatment only. None of the participants knew which treatment they received since the electrical stimulation from the active device was not noticeable.

MORE THAN 60% OF PEOPLE IN THE BI-SENSORY TREATMENT GROUP EXPERIENCED SIGNIFICANT DECREASES IN TINNITUS SYMPTOMS, YET THE SOUND-ONLY GROUP EXPERIENCED ONLY SMALL CHANGES.

Even during a following six-week break, people in the bi-sensory group continued to report improvements that lasted up to 36 weeks. They consistently reported an improved quality of life, handicap scores, and lower tinnitus volume.

PROTECT YOUR HEARING

Sound is measured in decibels (dB). A whisper is about 30 dB, and everyday conversation is about 60 dB. But noise that's 70 dB or louder over a prolonged period can damage your hearing.

According to the U.S. Centers for Disease Control and Prevention:

- two hours of exposure to gas-powered lawnmowers or leaf blowers (80 to 85 dB) may cause hearing damage;
- 15 minutes of exposure to noise at a football game (100 dB) may cause hearing loss; and
- less than five minutes of loud music on personal headphones at maximum volume or a rock concert (105-110 dB) may cause hearing loss.

Learn more about tinnitus from these reputable organizations:

- HearCANADA hearcanada.com/en-ca/hearing-services/ tinnitus-management
- The National Institute on Deafness and Other Communication Disorders nidcd.nih.gov/health/tinnitus

The American Tinnitus Association ata.org

"Our results were very encouraging," said Dr. Shore, who has formed the company Auricle with two colleagues. "We are now working toward gaining regulatory clearance for the device. If our submissions are successful, we plan to commercialize the device as soon as possible so that it may be available to help the many people who struggle with tinnitus."

In the meantime, if you suffer from ringing, buzzing, or screeching noises that aren't really there, know that you're not alone. Your best bet for finding relief is to consult an audiologist about proven effective treatment options and speak to your healthcare provider to learn whether medications for improving mood or sleep are right for you.

Mind Your Tongue

AN UNDERAPPRECIATED BODY PART

CAN HELP WITH STRESS MANAGEMENT

22

ou probably don't give your tongue much thought. However, what would come to mind if you stopped now and turned your attention to your tongue and its purpose?

You'd probably think about how it helps you taste, swallow, and speak. It actually does much more than that, though - for example, playing a role in breathing, chewing, and digestion and having effects on other parts of the body seemingly unrelated to the oral cavity, such as lower limb muscle strength and posture.

The tongue influences and interacts with the entire body through its muscular actions and role in releasing chemical messengers.

Many people hold a lot of tension in the tongue, and given its interconnectedness with the rest of the body, that tension tends to spread to other body parts such as your jaw, face, throat, and neck.

The tongue is part of the involuntary (autonomic) nervous system, which means it handles its various functions on autopilot, so we are typically unaware of the tension we hold there. Interestingly, the tongue is also part of our voluntary nervous system, which means we can consciously control it as well. It is possible to become aware of the tension we hold in the tongue and practice releasing it on purpose.

BENEFITS OF RELAXING THE TONGUE

Relaxing the tongue is a technique that yogis have practiced for a long time. Ancient yogis discovered that consciously relaxing the tongue helps to spread relaxation throughout the body while also quieting the mind.

The resulting widespread physical relaxation and quiet mind support brain health by helping reduce stress's physiological and psychological effects. (Stress management is one of the Six Pillars of Brain Health.)



Scan this QR code to listen to one of Ms. Miller's guided meditations on relaxing the tongue. It's ten minutes long and free.

https://www.sallymilleryoga.com/ offers/8KntF7iq/checkout

BY REDUCING BODY-WIDE MUSCLE TENSION, RELAXING THE TONGUE CAN HELP ALLEVIATE MANY ISSUES THROUGHOUT THE BODY, INCLUDING HEADACHES, JAW PAIN, AND EVEN DIGESTIVE ISSUES. ALSO, A QUIET MIND CAN ENHANCE FOCUS AND CLARITY.

Sally Miller is an experienced yoga and meditation teacher based in the United States who has been personally practicing and teaching others to relax the tongue for about 20 years. She first learned the practice from her teacher, Yogini Adept Parvathi Nanda Nath Saraswati, who had learned it at a young age in India from her teachers. (Yoga has a long history of oral teachings through various lineages.)

Ms. Miller's modern-day experience with relaxing the tongue aligns with what the ancient yogis discovered. She has found it to be an extremely helpful technique that works very quickly. "For me, it feels like a switch," she explained. "Once I relax my tongue, I can feel my whole body begin to relax. I get out of my head. I feel more spacious, open, and at ease. Many of my students have similar experiences."

HOW TO RELAX YOUR TONGUE DURING MEDITATION

Relaxing your tongue might sound like a simple task, but it can be surprisingly hard in practice. Here are the basic steps:

- Find a comfortable seated position. Relaxing the tongue works best when seated rather than lying down, particularly if you're new to the practice. You can be sitting in any meditation posture on the floor or in a chair with your spine upright and feet flat on the floor.
- Bring awareness to the tongue. Close your eyes (or allow them to soften and shift your gaze downward), turning your attention inward. Notice where your tongue is positioned and whether it feels tight or tense in any way. Notice the current state of your tongue for now, without trying to change anything yet.
- Soften the tongue. Now, consciously relax the tongue, allowing the entire tongue to go down to the bottom palate of your mouth and spread out there. As you do this, you might find your jaw releases, and you start to salivate more. This is common and a good sign.

If you find it hard to rest your tongue down in the bottom palate, you could see if it will float in the middle of your mouth instead. Regardless of whether the tongue rests at the bottom or floats in the middle, the key is to soften.

- Breathe deeply and slowly, relaxing the tongue even more. With each breath out, release any remaining tension in the tongue and allow that feeling of deep relaxation to spread through the rest of your body.
- Maintain awareness. Throughout your meditation, keep your attention on the tongue, noticing how it feels now that it's resting in a relaxed state in your mouth. Concentrated focus on the tongue will be like an anchor that helps ground your attention in the present moment. Any time you notice your attention has drifted to something else, bring your focus back to the tongue again.

The exact techniques used to relax the tongue can vary and may sometimes be more nuanced or complex than what's just been described.

"With repeated practice, relaxing your tongue during meditation usually gets easier and begins to feel more natural. However, every day is different, and some days may still be challenging, even for experienced meditators. But the end result is well worth the effort," said Ms. Miller. "Relaxing the tongue has been so helpful for me and my students. Most people say the practice is absolutely life changing."

RECOMMENDED EVERYDAY TONGUE RESTING POSITION

Contrary to what has just been described for a relaxed tongue position during meditation, your dental professional may have told you that the bottom of the mouth is not where you should typically rest your tongue daily.

That's because many dental professionals offer myofunctional therapy – an exercise program for the tongue, mouth, and face to correct any improper function – and myofunctional therapy recommends resting the tongue gently against the roof of the mouth without pressing against the teeth.

"In myofunctional therapy, we advise a tongue-up resting position. Keeping the tongue positioned gently against the upper palate, with the tip of the tongue resting just behind the top front teeth, helps prevent mouth breathing and snoring. It also supports a functional swallow and encourages optimal palate shape and teeth positioning," explained Kelly Durst, an Ontario-based dental hygienist and myofunctional therapist.

"In contrast, habitually resting the tongue in a low position in the mouth or pressing against the teeth is associated with a myriad of negative side effects throughout the body, including mouth infections such as tonsillitis, digestive issues, postural issues, jaw and neck pain, headaches, and sleep issues including sleep apnea."

Interestingly, a tongue-up resting position can help with stress management.

- Encouraging nasal breathing instead of mouth breathing activates the parasympathetic nervous system, which is our "rest-and-digest" response - the state it's ideal to be in unless you're facing a sudden stressful situation that requires the "fight-or-flight" response activated by the sympathetic nervous system.
- Resting the tip of the tongue against what is called "the spot" in myofunctional therapy - just behind the top front teeth - helps to stimulate the vagus nerve, which has endings in that area. The vagus nerve (also called vagal nerves) is the heart of your parasympathetic nervous system, which controls involuntary bodily functions like digestion and heart rate. As mentioned in the previous bullet, this is the nervous system state we want to be in as much as possible.

The key is learning to rest the tongue up, but in a relaxed way. Rather than using a lot of muscular force to press the tongue up firmly, you can use gentle suction and keep the tongue fairly soft as it indeed "rests" against the upper palate.

"Learning to change where the tongue rests naturally takes practice. To learn about optimal tongue position and the exercises you can do to train your tongue to rest there, go see a myofunctional therapist," said Ms. Durst. "In just a few appointments, you may discover an unexpected tool for addressing health challenges that perhaps you've been struggling for years to address, challenges that may seem like they'd have nothing to do with your tongue!"

WHY DOES RELAXING THE TONGUE HELP QUIET THE MIND?

"The tongue is connected to the thoughts. When we relax our tongue, we relax our thoughts and find more space between the thoughts," explained Ms. Miller. "When the tongue is pushing firmly on the roof of the mouth or the back of the teeth (instead of being relaxed), you might notice that you're overthinking or stuck in a habitual thought loop."

What's behind the connection between thoughts and the tongue?

A busy mind creates tension in the tongue because, for most people, thinking involves mentally talking to ourselves.

This internal verbalization is referred to as sub-vocalization. We may not even be aware of this running commentary going on in the mind, but the tongue is aware.

It tends to engage in tiny movements, as the tongue is essentially "saying" the words of our inner monologue. So, when we consciously relax the tongue, that inner monologue stops, and we unhook from the thoughts.

Beyond quieting subvocalization, relaxing the tongue also helps quiet the mind simply because it is a form of mindfulness practice. Relaxing the tongue during meditation requires focused concentration, and mindful focus on the tongue helps to displace thoughts.

It gives you something else to think about, i.e., relaxing the tongue and noticing how it feels without judgement. Returning to that focus again and again any time you notice your mind has wandered helps to keep the mind quiet.

WHY DOES RELAXING THE TONGUE HELP RELAX THE WHOLE BODY?

The tongue is located deep in the centre of the head and neck area and is a powerful muscular organ. Because of the interconnectedness of body parts, relaxing the tongue has a ripple effect on the body, spreading relaxation from the tongue to the jaw, face, head, neck, throat, shoulders, chest, and beyond. It is a form of relaxing from the inside out.

Relaxing the tongue during meditation promotes mind-body connection, helping build somatic awareness. Placing your

Somatic awareness involves paying mindful attention to bodily sensations.

attention on any part of your body and noticing how it feels can be a helpful practice.

It doesn't have to be the tongue. Still, the tongue, in particular, does seem to hold some special "magic," according to people who regularly practice relaxing the tongue as a form of meditation.

Any time you pay attention to a particular part of the body, whether that's the tongue or another body part, and deeply focus on feeling that part, it's so helpful," explained Ms. Miller.

"It wakes up interoception, helping you develop a better connection with your body signals overall. For example, it helps you be more in tune with when you feel full, thirsty, or sleepy. Many of us are quite disconnected from our bodies and bodily signals, from spending so much time immersed in thought."

So, the next time you sit down to meditate, mind your tongue and embrace its hidden potential for relaxation. By incorporating this "relax your tongue" technique into your meditation practice, you can experience widespread relaxation and a quiet mind and help support your brain health in the process.

Interoception refers to physiological/physical sensations in the body that provide internal signals, such as hunger, thirst, and needing to go to the bathroom. While anyone can struggle with interoception, conditions that have been linked to interoception difficulties include autism, ADHD, trauma disorders, anxiety, depression, and eating disorders.

Women & Urinary Tract Infections

HOW UTIS CAN AFFECT BRAIN HEALTH

an was sharp as a tack, well into her 90s. She seemed to forget nothing and no one," said Dana Dinerman, an editor who lives in New Jersey. "I'd often wonder how she kept track of all the little details about so many people. She'd always follow up on everything going on in my family's life and remembered to ask about my friends, too."

But one time, Dinerman noticed her grandmother was confused about things that didn't usually trip her up. "I wondered if she was showing early symptoms of Alzheimer's disease, as her father had it," she said. Dinerman was surprised to learn her grandmother's confusion was caused by a urinary tract infection (UTI), as she had not mentioned any other symptoms. "It was a relief when she returned to her usual self after the UTI resolved."

Mind Over Matter[®] spoke with leading experts and rounded up the latest evidence on how UTIs affect brain health, the importance of accurate diagnosis and treatment, challenges with existing treatments, and an innovative sublingual vaccine that holds promise for reducing the number of recurrent infections. \bigcirc

UTIs IN WOMEN

Most UTIs are infections of the bladder and the urethra, the tube that carries urine from the bladder to outside the body. UTIs are caused by bacteria that enter via the urethra aspread in the cells lining these parts of the lower urinary system. One of the main culprits is *Escherichia coli* (E. coli), which is commonly found in the gastrointestinal tract.

UTIs are a leading cause of bacterial infections in women.

MORE THAN 50% OF WOMEN WILL HAVE A UTI IN THEIR LIFETIME, AND FIVE TO 10% OF WOMEN WILL SUFFER FROM RECURRENT UTIS, DEFINED AS THREE OR MORE IN A YEAR OR TWO OR MORE WITHIN SIX MONTHS.

If a UTI extends higher up from the bladder, it can cause a kidney infection, which can be severe, but that only happens in about one out of 30 cases, according to the American Urological Association.

Women are more likely to develop UTIs than men for several reasons. Anatomically speaking, women have shorter urethras. Sexual intercourse and the use of contraceptive spermicides and diaphragms are additional risk factors. In post-menopausal women, lower estrogen levels thin the cells lining the urinary tract, increasing the susceptibility to infection.

According to Dr. Kalpana Gupta, Chief of the Section of Infectious Diseases at the Veterans Administration Boston Healthcare System and Professor of Medicine at the Chobanian and Avedisian School of Medicine,

56

IT'S OFTEN INCORRECTLY ASSUMED WOMEN ARE AT FAULT FOR CONTRACTING UTIS, AND IT'S SO UNFORTUNATE THIS STIGMA EXISTS. I'VE HAD WOMEN TELL ME THEY BATHE BEFORE AND AFTER INTERCOURSE IN AN ATTEMPT TO 'STAY CLEAN.'

But UTIs are not due to women being "unclean" or doing things incorrectly, like wiping in the wrong direction or the way they have sex. Bacteria are always present on and in our bodies. UTIs occur when certain bacteria colonize and spread in the mucosal lining of the urinary tract. Wiping differently or bathing more often does not make a difference."

Common UTI symptoms may include a burning sensation when urinating, a persistent, strong urge to pee, passing cloudy, red, bright-pink or cola-coloured urine, and pain in the centre of the pelvis and around the pubic bone area.

OLDER WOMEN DEVELOPING A UTI MAY NOT HAVE ANY OF THE MORE COMMON SYMPTOMS.

Instead, they may experience delirium, low blood pressure, an irregularly elevated heart rate, or fever. If they also have dementia as a pre-existing condition, the UTI may cause heightened confusion and agitation without them realizing why or being able to tell others they're not feeling well.

HOW UTIS AFFECT THE BRAIN

It's no wonder Dinerman was concerned about her grandmother's unexpected forgetfulness, because it's not widely known that UTIs can affect the brain in older women.

"Having an infection can certainly affect cognition, especially in older individuals, but dementia and delirium are two different syndromes," said Dr. Gupta. "Delirium is a sudden onset of confusion that waxes and wanes and typically lasts a few hours or days. Dementia is a much slower and ongoing process related to a neurodegenerative disease, such as Alzheimer's or Parkinson's disease, that doesn't resolve and occurs over many years."

Symptoms of delirium may include delusions, hallucinations, altered mood, dramatically reduced responsiveness, or paradoxically, increased agitation and hypervigilance. Old age, frailty, and existing cognitive impairment can raise the risk of experiencing delirium when an additional stressor, like an infection, gets added to the mix.

SCIENTISTS DON'T KNOW YET EXACTLY HOW A BACTERIAL INFECTION IN THE URINARY TRACT CAUSES DELIRIUM IN OLDER ADULTS.

One hypothesis is that increasing age makes the brain more susceptible to circulating inflammatory substances the body produces in response to infections.

UTIs negatively affect brain health in younger women, too. "Families, friends, and bosses at work tend to think UTIs are a nuisance easily treated with antibiotics," said Dr. J. Curtis Nickel, professor emeritus in the Department of Urology at Queen's University, clinician scientist at Kingston General Health Research Institute in Kingston, Ontario, and former Canada Research Chair in Urologic Pain and Inflammation, Tier 1.

THE TRUTH IS RECURRENT UTIS HAVE A SIGNIFICANT NEGATIVE IMPACT NOT ONLY ON WOMEN'S PHYSICAL HEALTH, BUT ALSO ON THEIR MENTAL HEALTH, CAUSING ANXIETY, DEPRESSION, AND STRESS. Recurrent UTIs reduce women's quality of life, self-esteem, ability to work or perform daily activities, and the quality of social relationships, according to a large review of the published literature.

The analysis, published in March 2022 in the journal *GMS Infectious Diseases*, also found that one-third of women with recurrent UTIs experienced them very often or often after sexual intercourse, and more than half reported their sexual relations were negatively influenced as a result.

ACCURATE DIAGNOSIS IS ESSENTIAL

An accurate diagnosis matters for both delirium and UTIs. For individuals experiencing delirium, pinpointing the cause is essential because episodes can have long-term negative consequences on brain health. Delirium can also accelerate cognitive decline in individuals living with Alzheimer's disease.

The United Kingdom National Health Service shows UTIs at the top of their list of common causes of delirium in older adults and individuals with dementia. They also include a stroke or mini-stroke, low blood sugar level in people with diabetes, head injury, taking drugs, carbon monoxide poisoning, a severe asthma attack, and epileptic seizures as other potential causes.

WHEN IT COMES TO DIAGNOSING A UTI, ACCURACY IS ESSENTIAL FOR DETERMINING THE BEST TREATMENT APPROACH.

HELPFUL TIPS FOR PREVENTING UTIs

The Mayo Clinic recommends the following tips for lowering your risk of developing a UTI:

- drink plenty of fluids, especially water, to dvilute your urine and lower the concentration of bacteria in your bladder;
- empty your bladder often. It's normal to pee four to eight times daily;
- urinate soon after sex. Voiding after intercourse removes some of the bacteria close to your urethra opening; and
- drink cranberry juice. A recently updated meta-analysis published in the Cochrane Database of Systematic Reviews in April 2023 found that cranberry juice or capsules probably reduced symptomatic, confirmed UTIs in women with a history of recurrent UTIs by 26%.

A test-strip urinalysis done at the doctor's office or at home only provides a yes-no answer on whether white blood cells are present. Only a urine culture test performed by a medical lab can identify the specific strains and bacterial species causing a UTI, enabling your healthcare provider to prescribe the right antibiotic to clear the infection.

You may be surprised to learn that cloudy, discoloured, or foul-smelling urine does not necessarily indicate the presence of an infection. In fact, there are public health campaigns with the tagline "Symptom-free pee, LET IT BE," encouraging healthcare providers not to prescribe antibiotics indiscriminately.

CHALLENGES WITH EXISTING TREATMENTS

Since the discovery of penicillin in 1928, antibiotics have cured many infectious diseases, prevented many postoperative infections, and saved countless lives. But globally, antibiotic drug development has slowed to a crawl, and at the same time, more bacteria are becoming superbugs, developing multiple ways to resist the antibiotics we have left.

Many women are prescribed antibiotics when they have bacteria in their urine without symptoms, known as asymptomatic bacteriuria, according to an extensive review of the published medical literature by researchers at the California Institute of Behavioral Neurosciences & Psychology.

The authors noted this practice increases the risk of antibiotic resistance and also accelerates the development of delirium. Their review was published in December 2022 in the journal *Cureus*.

Keep in mind that about one-third of women recover from uncomplicated UTIs without antibiotics. But UTI symptoms, such as fiery pain on urination, can be exceedingly uncomfortable while waiting a day or two for urine culture test results to come back.

As a result, many women with UTI symptoms are prescribed the wrong antibiotic, such as a broad-spectrum drug, when a targeted drug better matched to the bacterial strain would be more effective.

A recent study published in *Open Forum Infectious Diseases* found that almost half of about 670,000 women diagnosed with uncomplicated UTIs were prescribed an inappropriate antibiotic, and more than 75% were prescribed antibiotics for a longer period than necessary.

Dr. Gupta has spent more than a decade investigating how \ominus

to optimize treatment and prevention strategies for UTIs in women. In 2010, she was Chair of the Infectious Diseases Society of America (IDSA) UTI Guideline Update Committee, and is a current member of the IDSA committee working on an update in progress.

"Our research has shown the presence of healthy flora is essential for keeping infection at bay in the mucosa lining of the urethra and bladder," said Dr. Gupta.

ANTIBIOTICS WIPE OUT HEALTHY FLORA THROUGHOUT YOUR BODY, INCLUDING YOUR INTESTINE, VAGINA, AND URINARY TRACT, INCREASING THE RISK OF FUTURE UTIS.

"Each individual's flora is distinct, so access to historical urine culture results can be incredibly helpful for choosing the best antibiotic if results are not available yet for a present episode, especially if patients change healthcare providers," said Dr Gupta.

"Women should keep track of their UTI history, including symptoms, lab culture results, antibiotics prescribed and whether the medications resolved their infections."

RESEARCHERS CONTINUE INVESTIGATING WAYS TO OPTIMIZE ANTIBIOTIC TREATMENTS FOR UTIS WHILE LESSENING THE RISKS OF COMMON, UNWANTED SIDE EFFECTS, SUCH AS HEADACHES AND GASTROINTESTINAL UPSET.

For example, Dr. Gupta led a study that found five days of nitrofurantoin (Macrobid), a common drug for treating UTIs, was as effective as three days of trimethoprim-sulfamethoxazole (Bactrim), the gold standard treatment at the time.

"The IDSA treatment guidelines now recommend five days of Macrobid instead of seven, which greatly benefits patients. They experience fewer side effects and get back to what they need to do sooner," she said.

As a final plot twist, be aware that many antibiotics are associated with delirium, according to a recent study. Researchers at the University of South Carolina and the University of Texas at Austin analyzed 15 years of records in the reported adverse events database collected by the United States Food and Drug Administration (FDA).

They found statistically higher rates of delirium were reported with the use of 16 common antibiotics, some of which are prescribed for treating UTIs. Their study was published in *Drugs Real World Outcomes* in March 2022.

A NOVEL VACCINE

An innovative vaccine for reducing the number of recurrent UTIs in women is already approved and available for use under special access programs in 26 countries, such as Spain, the U.K., and New Zealand - but not yet in North America.

Known as Uromune, the vaccine is sprayed under the tongue. It contains inactivated strains of four bacterial species that most commonly cause UTIs - *E. coli, Klebsiella pneumoniae, Enterococcus faecalis,* and *Proteus vulgaris.*

THE VACCINE ENCOURAGES THE BODY TO BUILD IMMUNITY AGAINST THESE BACTERIA IN THE MUCOSAL LINING OF THE URINARY TRACT WITHOUT GASTRIC SIDE EFFECTS AND WITHOUT WIPING OUT HEALTHY FLORA IN THE GUT, URINARY TRACT, OR OTHER AREAS OF THE BODY.

Dr. Nickel recently led the first North American clinical trial of Uromune in Kingston and Toronto. A total of 67 women ages 18 to 80 who experienced more than three UTIs in the previous year participated in the study between 2019 and 2022. They used the vaccine twice daily for three months, and researchers followed them for an additional nine months.

Uromune significantly reduced the average number of UTIs for the group from 6.8 to 1.7 per year - a 75% reduction - and 40% of women in the study had zero UTIs in the nine-month follow-up period.

The results, published in October 2023 in the *Canadian Urological Association Journal*, demonstrated that the vaccine is safe and effective for reducing recurrent UTIs in women. The vaccine manufacturer has applied for approval in Canada, and time will tell whether the company files for FDA approval in the United States.

Dr. Nickel, who has no financial interest in the company that makes Uromune, said,

AN ANTIBIOTIC-FREE, EFFECTIVE TREATMENT FOR REDUCING RECURRENT UTIS WOULD CERTAINLY BE A WELCOME RELIEF TO MANY WOMEN WHO SUFFER IN SILENCE.

The science of preventing, diagnosing, and treating UTIs continues to evolve. In the meantime, be aware of how they can affect your physical and mental health. If you or a loved one experiences sudden unexplained confusion, like Dinerman's grandmother, seek medical attention right away. You should also consult your healthcare provider if you or a loved one have UTI symptoms to discuss the pros and cons of the best treatment options with a view to minimizing the inappropriate use of antibiotics.

s a reader of Mind Over Matter[®], you are likely aware of mild cognitive impairment (MCI), an early stage of memory loss and thinking problems associated with a greater risk of developing Alzheimer's disease (AD) and other forms of dementia. But have you heard about mild behavioural impairment (MBI)?

MBI is a neurological syndrome that describes the emergence of new and persistent mood, behaviour, or personality disturbances after age 50. Individuals with MBI have a higher risk of developing AD and dementia.

"Traditionally, we treat individuals experiencing neuropsychiatric symptoms like anxiety and depression with psychiatric medications. However, if their symptoms meet the criteria for MBI, we should also be evaluating these people for underlying, emergent dementias," said Dr. Zahinoor Ismail, clinician scientist and Professor of Psychiatry, Neurology, Epidemiology, and Pathology at the Hotchkiss Brain Institute and O'Brien Institute for Public Health at the University of Calgary, Alberta.

RECOGNIZING MBI AS A RISK SYNDROME FOR DEMENTIA WILL ALLOW MORE PEOPLE TO ACCESS NEW TREATMENT OPTIONS FOR PREVENTING OR DELAYING DEMENTIA AND MAKE EARLIER CARE PLANS WITH PHYSICIANS AND FAMILY MEMBERS AS SOON AS POSSIBLE.

Dr. Ismail's work has focused on MBI for more than a decade. He led the international panel that created and validated the accepted criteria for diagnosing MBI, and a measurement tool called the MBI Checklist, which is now used in clinical trials of new drugs for preventing AD. \Rightarrow

Mild Behavioural Impairment

WHAT YOU NEED TO KNOW ABOUT

NON-COGNITIVE MARKERS OF DEMENTIA

You, a care partner, or your physician can download a copy of the MBI Checklist, which has been validated for completion in person, online, or by telephone. Canadian adults can also access it by participating in the CAN-PROTECT study, an online longitudinal study of brain aging detailed later in this story.

This article summarizes what you need to know about MBI from our interview with Dr. Ismail.

NEUROPSYCHIATRIC SYMPTOMS OF DEMENTIA

Neuropsychiatric symptoms of dementia (NPS) are sometimes referred to as non-cognitive dementia symptoms. Common NPS include anxiety, depression, irritability, agitation, apathy or indifference, delusions, and hallucinations.

NPS in AD have been known for more than 100 years. Dr. Alois Alzheimer's first case, Auguste Deter, presented with emotional distress and delusions of infidelity *before* she experienced memory loss and vision and language problems. After she passed away, autopsy results of her brain revealed plaques, tangles, and neuronal loss, later known as classic manifestations of AD.

NPS are associated with faster cognitive decline and an accelerated timeline to severe dementia and death from dementia. They are also associated with higher institutionalization rates, greater functional impairment, worse quality of life, a higher burden of other markers of dementia, and an increased burden of care partner stress.

WHAT'S SURPRISING, THOUGH, IS THAT NPS OCCUR BEFORE DEMENTIA IN *MORE THAN HALF* OF THE PEOPLE WHO DEVELOP AD, FRONTOTEMPORAL DEMENTIA, AND OTHER DEMENTIAS.

According to a large study by researchers at Johns Hopkins University, NPS were present before dementia for about two-thirds of cognitively normal individuals who later developed dementia without MCI, and for 55% of people who had MCI and went on to develop dementia. The study findings were published in *Alzheimer's & Dementia (Amsterdam)* in 2019.

"We tend to be 'cogno-centric' – thinking only cognitive assessments can provide early warning signs of impending dementia," said Dr. Ismail. "But the brain does lots of other work, controlling moods, behaviours, and personality. Disruptions in these areas can also indicate individuals might be on their way to developing dementia."

"Identifying NPS in cognitively normal individuals represents an important window of opportunity for preventing, delaying

SEX DIFFERENCES IN NPS LINKED TO AD

Recently, researchers at Johns Hopkins University and the University of Thessaly in Greece found that the associations between NPS and the incidence of AD were different for women and men. Their paper was published in the Journal of Neurology in 2023. Highlights of the findings were as follows:

For individuals who were cognitively unimpaired at the beginning of the study:

- moderate to severe apathy was a strong predictor of future AD in men but significantly less predictive in women;
- mild depression and agitation were predictors of AD in women but less so in men; and
- moderate to severe depression was linked to a higher risk of AD for both sexes, but the risk was significantly higher for men than women.

or reducing the severity and impact of dementia in individuals at risk."

MBI CRITERIA

To define and capture the broad range of NPS associated with dementia risk, an international team of researchers developed and published the diagnostic criteria for MBI in 2016. Dr. Ismail was Academic Co-Chair of the research team, the U.S. Alzheimer's Association-International Society to Advance Alzheimer's Research and Treatment (ISTAART) Neuropsychiatric Syndromes Professional Interest Area, and led the development of the MBI concept.

An MBI diagnosis requires evidence that a change has occurred in symptoms falling under one of these five neuropsychiatric domains:

- 1. decreased motivation: decreased motivation or drive, loss of interest
- emotional dysregulation: mood (depression) or anxiety symptoms, dysphoria (dissatisfaction with life), euphoria (intense elation)
- impulse dyscontrol: agitation, irritability, poor frustration tolerance, impulsivity

- 4. social inappropriateness: lack of empathy, loss of insight, loss of social graces or tact
- 5. abnormal perception or thoughts: delusions or hallucinations

IF NPS IN THESE DOMAINS APPEAR FOR THE FIRST TIME AFTER THE AGE OF 50, PERSIST FOR AT LEAST SIX MONTHS, AND REPRESENT CHANGES IN AN INDIVIDUAL'S USUAL PERSONALITY OR BEHAVIOUR, AND ARE NOT EXPLAINED BY ANOTHER DISORDER OR A PRE-EXISTING DEMENTIA DIAGNOSIS, THEY MEET THE CRITERIA FOR MBI.

THE MBI CHECKLIST

To make the MBI Criteria actionable, Dr. Ismail and colleagues created an instrument called the MBI Checklist. Their paper describing the handy tool was published in *Journal of Alzheimer's Disease* in 2017.

Today, the MBI Checklist is available in 30 languages and used worldwide in dementia research, including by the U.S.

National Alzheimer's Coordinating Center, the central hub for coordinating the National Institute of Aging's Alzheimer's Disease and Research Centers Program. Dr. Ismail was lead author of the national guidelines published in *Alzheimer's & Dementia* following the 5th Canadian Consensus Conference on the Diagnosis and Treatment of Dementia.

The MBI Checklist is an easy-to-use, two-page questionnaire that covers 34 items across the five MBI domains. Since even subtle changes in NPS in advance of cognitive impairment can predict dementia, there are checkboxes for indicating whether the symptoms are mild, moderate, or severe in intensity.

Dr. Ismail pointed out that researchers interpret MBI Checklist results carefully and in context. "The cut-off score for identifying MBI depends on an individual's baseline cognitive status," he said. "For example, eight points or more would be concerning for a cognitively normal individual, indicating they should see a clinician for a neurological evaluation. For someone with a pre-existing MCI diagnosis, a score of six or more would raise concern."

DIFFERENT TYPES OF BRAIN IMPAIRMENT

MILD COGNITIVE IMPAIRMENT (MCI)

MCl is an early stage of memory loss and thinking problems that do not affect a person's ability to carry out usual daily activities but are serious enough to be noticed by others.

The incidence of MCI increases with aging, but it is not part of the typical aging process, the Alzheimer's Association says.

Studies estimate that 10 to 15% of individuals with MCI go on to develop dementia each year, and about one-third of people with MCI develop Alzheimer's disease (AD) within five years. Also, some people diagnosed with MCI do not experience further cognitive decline, and some revert to normal cognition, according to the Alzheimer's Association.

Neuropsychiatric symptoms (NPS) are common in MCI and are consistently associated with a higher risk of dementia and poorer cognitive and psychosocial function, according to several population and clinic-based studies. The estimated annual rate of progression to dementia for individuals with MCI and NPS is 25%. For MCI without NPS, the annual rate of progression to dementia is estimated at 10 to 15%. MILD BEHAVIOURAL IMPAIRMENT (MBI) MBI is a neurological syndrome defined by mood, behaviour, or personality disturbances occurring for the first time after the age of 50 and persisting for six months or longer.

The NPS of MBI are sometimes called non-cognitive dementia symptoms. They stand out as distinct changes from an individual's usual mental, behavioural, and emotional health and are noticeable by the individual or their care partner, friend, or physician.

There is growing evidence that shows that MBI symptoms in cognitively normal individuals and those with MCI are linked with known AD markers. These markers include amyloid, tau, neurodegeneration, and AD risk genes.

MBI can emerge at any point on the dementia development continuum, from normal cognition to subjective cognitive decline to MCI, and signifies greater risk in all three groups compared to those without MBI. I MUST ALSO EMPHASIZE THAT ONLY NEWLY EMERGENT SYMPTOMS SHOULD BE SCORED - NOT MOOD, BEHAVIOUR, OR PERSONALITY SYMPTOMS THAT HAVE EXISTED OVER A LIFETIME. SYMPTOMS MUST ALSO BE PRESENT FOR SIX MONTHS OR MORE. FOR EXAMPLE, SHORT-TERM ANXIETY AFTER A BIG DISAGREEMENT WITH YOUR SPOUSE IS NOT LIKELY TO BE RELATED TO AN UNDERLYING DEMENTIA.

Individuals with symptoms that meet the MBI Criteria should also have a complete medical check-up to rule out other conditions that may be causing NPS, such as untreated hypothyroidism, Dr. Ismail said.

The MBI Checklist has been validated for completion by individuals, care partners, or physicians. However, it's essential for a physician or clinician to interpret the results in context with an individual's overall medical and psychiatric history. You can download a free copy by visiting mbitest.org after agreeing to some conditions and terms of use.

RESEARCH IN PROGRESS TODAY

Researchers are currently using the MBI Checklist in clinical trials of new drugs for preventing AD in cognitively normal individuals with amyloid beta deposits, which indicate a higher risk of developing AD. For example, investigators are using the tool in the Phase 3 TRAILBLAZER-ALZ 3 study to see if the medication donanemab reduces the likelihood of developing dementia.

Dr. Ismail has seen that effect in one of his patients who participated in one of the original clinical trials for aducanumab (Aduhelm®), the anti-amyloid antibody approved by the U.S. Food and Drug Administration in June 2021 but not yet approved in Canada. The patient had been taking the drug over the past seven years. When the study ended, and he had to stop taking the drug, his cognition declined. However, after going back on the drug in an extension of the trial, his cognition improved with every dose.

HIS WIFE SAID HE WAS NOT JUST COGNITIVELY BETTER, HE WAS NO LONGER IRRITABLE, ILLUSTRATING THERE IS A NEUROBIOLOGY TO BEHAVIOUR DISRUPTION RELATED TO ALZHEIMER'S THAT IS DISTINCT FROM WHAT WE USUALLY THINK ABOUT PSYCHIATRIC CONDITIONS.

The CAN-PROTECT Study (www.CAN-PROTECT.ca), a nationwide study for evaluating risk factors and resilience in brain health as Canadian adults age, includes the MBI Checklist. Dr. Ismail is leading the study in partnership with colleagues at the University of Exeter in the United Kingdom.

Individuals 18 and older located anywhere in Canada with access to a computer or touchscreen device can participate. Once yearly, they complete a set of brain health assessments, including cognitive function tests, brain training games, daily function assessments, questionnaires about diet, activity, lifestyle, medical history, and a mental health assessment.

Each assessment takes about an hour, so the annual commitment to participate is about three to seven hours at the participant's leisure, depending on how many assessments individuals choose and those required. The researchers hope to recruit 10,000 participants and plan to collect data for 20 years.

"We are tracking changes over time," Dr. Ismail said. "Participants can opt in to be notified if their cognitive test scores drop over time and receive a suggestion to get checked out by their healthcare provider."

"We are also enrolling caregivers of people living with dementia for caregiver-specific assessments. Informal caregivers, including partners, friends, family members, and formal caregivers, such as long-term care nurses, personal care aides, occupational and recreation therapists, and physicians, are eligible to take part in the study," said Dr. Ismail. "Our goal is to learn more about the burden of dementia caregiving so that we may develop better supports."

At the time of our interview, the CAN-PROTECT study had enrolled more than 2,000 participants. While the original cut-off age was 40, Dr. Ismail said they dropped it recently to 18.

BRAIN AGING AND RESILIENCE DON'T MAGICALLY START AT 40," DR. ISMAIL SAID. "BY OPENING UP THE STUDY TO CANADIANS 18 AND UP, WE CAN TRACK MORE PEOPLE OVER TIME AND ASSESS RISK AND RESILIENCE ACROSS THE LIFESPAN. WE HOPE OUR FINDINGS WILL OFFER A ROBUST LOOK AT BRAIN HEALTH AS PEOPLE AGE.

Being aware that NPS of dementia are core to the dementia process and recognizing MBI as a neurological syndrome that predicts future dementia is essential, especially given the rapid anticipated growth in the number of individuals living with AD and other dementias. The MBI Checklist will make it easier for individuals, care partners, and physicians to spot MBI, helping more individuals at risk access new treatment options for preventing or slowing AD and dementia.

You've Got to Have Baith

THE MIND & BODY BENEFITS OF SPIRITUALITY

or more than a decade, Women's Brain Health Initiative (WBHI) has been sharing evidence-based information about brain health in easy-to-understand and engaging formats, including in Mind Over Matter[®]. In 2022, WBHI launched the BrainFit - Habit Tracker app to support individuals in establishing and maintaining brainhealthy habits. The app allows users to choose from more than 100 habits but also features the opportunity for users to create their own unique habits to track.

A few months after the app's launch, an analysis of useradded custom habits revealed that spiritual practices, such as praying or attending religious services, were significant. Delving into the research literature, WBHI discovered that spirituality and religion have been studied scientifically and are indeed relevant to brain health.

PRAYER CAN CALM THE NERVOUS SYSTEM, HELP REDUCE ANXIETY SYMPTOMS, ANGER, AND REACTIVITY TO NEGATIVE EMOTIONS, AND POSITIVELY IMPACT EPISODIC MEMORY IN OLDER ADULTS.

Backed by the evidence, Engage in Spiritual Practice was added as a habit that others could also track without needing to add it manually.

Research on spirituality and prayer is complex. While related, religion and spirituality are different, involving many facets that can be "measured" differently.

This article focuses on academic reviews and meta-analyses, which combine findings across multiple studies to reach broad conclusions.

Combined, consistent evidence supports a positive connection between religion/spirituality and various aspects of health, i.e., physical, cognitive, and mental ones. However, the strength of these connections is typically modest, and some studies have found negative associations.

PHYSICAL HEALTH BENEFITS

In the 2018 book, *Why Religion and Spirituality Matter for Public Health: Evidence, Implications, and Resources*, Dr. Doug Oman and colleagues examined more than 100 peer-reviewed meta-analyses and systematic reviews of religion/spirituality and health.

The authors concluded that, collectively, the evidence indicates religious/spiritual involvement is associated with better health in most cases.

ALTHOUGH MUCH OF THE RESEARCH IS CORRELATIONAL, RESEARCHERS NOTED THAT A COMPELLING CASE CAN BE MADE THAT THE ASSOCIATION IS CAUSAL, I.E., RELIGION/ SPIRITUALITY DIRECTLY INFLUENCES HEALTH.

"Dozens of studies have found religion/spirituality to be generally protective against all-cause mortality, with \bigcirc

some evidence suggesting lower rates of cardiovascular, gastrointestinal, and respiratory mortality, in particular," said Dr. Oman, a professor at University of California, Berkeley.

"Much research also indicates that religious/spiritual involvement is associated with other physical health benefits, including lower rates of cardiovascular diseases, cancer, and disability, as well as lower levels of pain."

COGNITIVE BENEFITS

In a 2017 systematic review of 17 studies published in *The Gerontologist*, Dr. Mark Oremus and colleagues investigated the effect of religion and spirituality on cognitive function. The studies used varying definitions of religious and spiritual involvement.

For example, some looked at private religious practices such as prayer, reading religious books, watching/listening to religious programs on TV or the radio, fasting, or donating to the poor, while others examined the effects of formal/organizational religious practices such as going to a place of worship for services or meetings.

Some used self-rated measures, while others used observerrated measures. And some did not measure externally visible actions at all and instead considered religious affiliation, religious beliefs, or religious self-identity.

THE RESEARCHERS FOUND THAT MOST (82%) OF THE INCLUDED STUDIES REPORTED POSITIVE ASSOCIATIONS BETWEEN RELIGION/SPIRITUALITY AND COGNITIVE FUNCTION.

Specifically, the evidence reviewed suggests that religious or spiritual involvement may help protect against cognitive decline in seniors from a Christian background. More research is needed to look at the potential impact of religion/ spirituality on the cognitive function of adults of other ages and religious denominations.

Another review - by Dr. Océane Agli and colleagues, published in 2014 in *International Psychogeriatrics* - suggests that spirituality/ religion can even benefit older adults who already have dementia.

Three of the 11 articles included in this review showed that individuals who were more deeply involved in their spirituality/religion tended to experience a reduction or stabilization of their cognitive disorders. The other eight articles showed that using spirituality/faith in daily life helped individuals with dementia improve their quality of life through coping strategies, maintaining hope, and providing meaning in their lives. **RELIGION VS. SPIRITUALITY** Although related and overlapping concepts, religion and spirituality are not the same.

Religion involves adhering to beliefs, values, rituals, and practices proposed by an organized institution devoted to the divine or transcendent.

Spirituality is a broader concept, involving a subjective experience where individuals strive to connect with the sacred and discover answers to questions about the meaning of life. This might involve regular spiritually-inspired individual practices such as meditation or journaling, or be spontaneously experienced as feelings of awe, perhaps while in nature.

People can be either religious or spiritual, a combination of both, or neither.

MENTAL HEALTH BENEFITS

Much research, including a meta-analysis by Dr. Bert Garssen and colleagues, has shown a consistent but modest association between religiousness/spirituality and various measures of mental health.

In that meta-analysis of 48 studies - published in 2021 in *The International Journal for the Psychology of Religion* - the researchers concluded that there is evidence for a positive but small effect of religiousness/spirituality on mental health overall. When they looked at specific types of spirituality/ religiousness, though, they found that only two types were significantly related to mental health: participation in public religious activities and the importance of religion.

Just what types of mental health benefits might spirituality/ religion provide? A 2021 review by Dr. Giancarlo Lucchetti and colleagues - published in *World Journal of Clinical Cases* - found a large amount of evidence related to numerous psychiatric disorders.

"Our review revealed solid evidence linking spirituality and religiousness to reduced rates of depression, suicidality, and substance use. We also found promising results for other diagnoses, including post-traumatic stress disorders, psychosis, and anxiety," said Dr. Lucchetti, an associate professor in the medical school at Federal University of Juiz de Fora in Brazil. IT'S PRETTY CLEAR THAT SPIRITUALITY/ RELIGIOUSNESS IS ASSOCIATED WITH MENTAL HEALTH, AND WE SUSPECT THE EFFECTS ARE LIKELY BIDIRECTIONAL. THAT MEANS THAT SPIRITUALITY/RELIGIOUSNESS CAN AFFECT MENTAL HEALTH, BUT MENTAL HEALTH CAN ALSO AFFECT SPIRITUALITY/RELIGIOUSNESS.

WHY ARE RELIGION/SPIRITUALITY & HEALTH LINKED?

What is it about religious or spiritual beliefs and practices that could be influencing health? There is no single mechanism to explain the relationship. Rather, researchers believe that many potential underlying mechanisms may be involved.

What's interesting is that several of these potential mechanisms are among the Six Pillars of Brain Health: stress management, mental stimulation, and social activity. (The Six Pillars of Brain Health are key modifiable evidence-informed lifestyle factors that help reduce dementia risk. And, because the body is complex with all its parts and systems interrelated in many ways, what's good for the brain is good for the healthy functioning of the entire body.)

Some of the potential explanations for the association between religion/spirituality and health include:

- the activities involved in religious services such as singing, praying, and listening to sermons - can provide mental stimulation;
- religious activities often include social elements that can provide mental stimulation in addition to social engagement. The social network created through religious involvement can increase social activity outside of direct religious activities, e.g., friendships develop, and volunteering may happen, resulting in a more socially engaged lifestyle overall;
- most religious teachings encourage supporting and caring for others, so people who are members of a religious community often have access to greater amounts of social support. The resulting help in times of need can help reduce stress and boost health and well-being;
- religious/spiritual individuals may feel emotionally supported by their experiences of a divine presence who listens to their prayers and provides comfort;
- religious/spiritual involvement may provide mental stimulation as participants ponder "deep" thoughts about the meaning of life;

- people with strong religious or spiritual faith tend to have a greater sense of meaning and life purpose, which helps reduce the impact of life's stressful events and protect against anxiety and depression;
- religious involvement tends to encourage healthy behaviours and discourage risky behaviours, e.g., more frequent religious attendance is strongly linked with lower alcohol consumption, never smoking, and more exercise;
- spirituality/religion are associated with positive human virtues, such as gratitude, forgiveness, compassion, and altruism, which may play a role in improving various aspects of health, especially mental health; and
- some religious behaviours, such as contemplative prayer, can reduce self-focus, worry, and rumination, thereby reducing stress and positively contributing to mental health.

Although most studies have found spirituality/religion to be associated with better health outcomes, some have found negative associations. One explanation for the inconsistent findings is that different facets or measures of religion/ spirituality may be associated with different aspects of health.

For example, research has found that positive religious/spiritual coping (e.g., feeling like the Divine is supportive and forgiving) is associated with positive mental health, while negative coping (e.g., feeling unheard, abandoned, or punished by the Divine) is associated with various negative mental health outcomes, including anxiety, depression, and addiction.

More research is needed to flesh out with more certainty which facets of religion or spirituality are responsible for the associations with health benefits, positive and negative.

HELP SENIORS CONTINUE RELIGIOUS PARTICIPATION

As people get older, they may need support to be able to continue participating in religious activities. Given the many benefits of religion/spirituality for multiple aspects of health and well-being, it is important that older adults be supported in continuing to participate.

So, if you know of an isolated elder who would enjoy attending religious gatherings – perhaps a parent, grandparent, aunt/uncle, or neighbour – consider offering them a lift, or connecting them with community services that offer these types of rides.

Into the Blue

BLUE ZONES - LIVING LONGER & BETTER

oida Medina's life in her 80s has been both active and
 healthy. She practiced medicine until the age of 83 and
 loved her job. Now at 85, she has scarcely slowed down at all and, in fact, finds she is busier than ever with volunteer work, community activities, and physical exercise. When Medina visits family in Loma Linda, California, she enjoys going to the Drayson Center a couple of times a day to play pickleball, often in the company of people in their 90s.

The term "blue zones" is a colloquial expression coined by author Dan Buettner to describe geographical regions inhabited by some of the planet's most elderly individuals. Mr. Buettner introduced this term while researching regions where people enjoy remarkably long lifespans.

Ikaria (Greece): Ikaria is an island in Greece where people eat a Mediterranean diet rich in olive oil, red wine, and homegrown vegetables.

Sardinia (Italy): Sardinia is home to some of the oldest men in the world. They live in mountainous regions where they typically work on farms and drink lots of red wine.

Okinawa (Japan): Okinawa is home to the world's oldest women, who eat a lot of soy-based foods and practice tai chi, a meditative form of exercise.

Nicoya (Costa Rica): The Nicoyan diet is based around beans and corn tortillas. The people of this area regularly perform physical jobs into old age and have a sense of life purpose known as "plan de vida."

The Seventh-day Adventists in Loma Linda, California (USA): The Seventh-day Adventists are a very religious group of people. They're strict vegetarians, or eat very little meat, and live in tight-knit communities.

"I was told I was the baby!" she said with a laugh in an interview with Mind Over Matter[®].

Medina is a member of the Seventh-day Adventist Church, which owns and operates Loma Linda University and the Drayson Center on the campus. Loma Linda's Seventh-day Adventist Church community is identified as one of five blue zones, places, or groups of people, in far-flung parts of the world where residents tend to live longer, healthier lives.

Medina credits her good health to various factors common in blue zones. Along with regular exercise, she eats fresh, unprocessed food in moderate amounts, with no meat and only the occasional fish. She also points to her volunteer work, a strong sense of community within the church, and a general feeling of purpose. "I chose to do this so I can have a good quality of life and be useful, even to the end."

Journalist Dan Buettner popularized the blue zones concept after he wrote a 2005 article in National Geographic magazine entitled "The Secrets of Long Life." Among those diverse communities, he identified nine common principles, which he described to Mind Over Matter®:

- Move Naturally. People living in the blue zones tend to be active, not necessarily in the sense of going to the gym, but of walking and doing physical tasks like gardening.
- Purpose. Much as Loida Medina described, it translates into "why I wake up in the morning." Mr. Buettner said: "Knowing your sense of purpose is worth up to seven years of extra life expectancy."
- 3. Down Shift. People in blue zones have methods of reducing stresses. For Seventh-day Adventists, it's daily prayer; Ikarians like to nap, and Sardinians do their own happy hour where they gather for a glass of wine.
- 80% Rule. Okinawans have a tradition that advises them to stop eating when their stomachs are 80% full.
- **5. Plant Slant.** Their diets are dominated by vegetables, with small amounts of meat or none at all.
- **6. Wine @ 5.** People in all blue zones (except the Adventists) drink alcohol moderately and regularly, limiting it to one or two glasses of wine per day.
- **7. Belong.** All but five of the 263 centenarians Mr. Buettner interviewed belonged to a faithbased community.
- 8. Loved Ones First. Residents of blue zones place a high value on family, keeping aging parents or grandparents close by or in the home.
- Right Tribe. The world's longest-lived people chose

 or were born into social circles that supported healthy behaviours.

The blue zones concept has grown into an industry led by Mr. Buettner, spawning a Netflix series, eight books, and what he calls the Blue Zones Project.

"Yes, I am very inspired; it has been my work for the past 20+ years," he said. \bigcirc

The Blue Zones Project is a nationwide well-being improvement initiative that helps communities shape their environments to make healthy choices easier.

> Airdrie, Alberta, took it seriously enough in 2018 to commit \$1.5 million over three years to promote the blue zones philosophy, with the goal of making the city "Canada's healthiest community." They proposed promoting more nutritious foods in grocery stores, to decrease smoking rates, and improve the walkability of neighbourhoods.

The initiative had to be abandoned because of pandemic disruptions, so the Airdrie case study is incomplete, although the town has expressed interest in reviving some elements.

The blue zones concept has critics, including some who question the demographic record keeping in some rural communities, suggesting that some people might not be as old as they claim.

However, Dr. Michael Kobor of the University of British Columbia believes it is worthy of study.

"There is some real science to it. It's pretty clear that folks there don't just live long lives but healthy lives," he told Mind Over Matter®.

Dr. Kobor is a professor in the university's Department of Medical Genetics and was recently appointed to the newly created Edwin S.H. Leong UBC Chair in Healthy Aging - A UBC President's Excellence Chair.

He specializes in epigenetics, a field that studies how social and environmental factors become biologically embedded in our genes to influence human health and well-being. He notes that many of the healthy living ideas in blue zones are already well-established.

"It's really an intuitive concept, but now it's become a bit of a marketing gimmick, with blue zones diets, a cookbook, and now the Netflix show," said Dr. Kobor.

It does, however, have enough merit to warrant serious research. He and his team are working with colleagues from Stanford University to examine biospecimens from Costa Rica, Greece, and Italy, making comparisons at the molecular level with specimens from non-blue zones residents to try to discover any differences. WHAT WE'RE TRYING TO UNDERSTAND IS HOW ENVIRONMENTS AND EXPERIENCES GET UNDER THE SKIN TO AFFECT BIOLOGY, AND WHAT WE CAN LEARN ABOUT POSSIBLE PREVENTIONS OR INTERVENTIONS TO HELP US HAVE A LONGER HEALTH SPAN.

As part of his research, he studies differences between the sexes. He says that while women almost universally tend to be healthier than men as they age and have longer lifespans, in blue zones, the differences are smaller.

Dr. Kobor is also keen to discover if there are any of what he calls "mini blue zones" in Canada. He has heard anecdotally of places where people live longer and healthier but needs further investigation.

A better understanding of blue zones can help inform public policy choices to promote exercise, social interaction, and healthy diets, with the goal of lives that are not only longer but healthier.

Since Mr. Buettner's article launched the blue zones movement, there have been positive and negative changes. He says enlightened public policy choices in Singapore have now made that city-state a new blue zone. At the same time, the encroachment of North American diets onto Okinawa has cut into lifespans.

"Okinawa is fading and should no longer be considered a blue zones location," said Buettner. "The outlook for all of the blue zones around the world is not promising, as they are all eroding. They will likely be gone in a generation. As soon as the standard American diet comes in the front door, longevity leaves out the back door," he explained.

Kim Knowlton, the Director of the Drayson Center at Loma Linda University, is Loida Medina's daughter. Every morning, starting at 7 a.m., Knowlton sees "some pretty healthy seniors," many in their 80s and 90s, coming in for interval training and water aerobics classes.

"That's one reason they like to come, but there's also the social component. It's the purpose and the community, and that's what we also promote," said Knowlton, who takes her mother's lead in following a principally plant-based diet, with occasional fish.

"It's not just the blue zones that can do this; anywhere in the world can do it. I'm glad this is getting out," she added.

Her mother concurs: "I like this concept because it is not only the individual that's affected, it's the whole community. It's good to live well - maybe not long, but well." @

Decision Fatigue

WHAT ARE THE SIGNS & WHAT TO DO ABOUT IT

our alarm goes off in the morning, and your decision-making begins. Some of the decisions you might be making within the first hour of getting up include:

- Will you hit snooze on your alarm or get up? (And you might make this decision multiple times.)
- Will you look at anything on your phone before getting up? If so, you may make many decisions about what you see, responding to emails, or clicking on some ads in your social media feed.
- Will you exercise this morning? If so, what exactly will you do? Go for a run? Lift some weights? Do some yoga or something else? How long will you exercise?
- Will you meditate this morning? Or journal? Or do some reading or contemplative prayer?
- > What music will you listen to while you shower?
- What coat will you wear? Which shoes? Will you take an umbrella?

- What will you have for breakfast? Will you pack a lunch, and if so, what will you put in it?
- Will you wash your hair today?
- What clothes will you wear? What accessories?

As your day continues, you'll make thousands more decisions, some small and some big, some that you are conscious of and some that you are not.

Everyone's life and commitments are different, so the types of decisions each person will make each day will be unique.

However, it's universal that everyone makes thousands of decisions each day. Research by Dr. Brian Wansink and colleagues found that study participants made almost 220 daily decisions about food and drink alone! (Those findings were published in 2007 in *Environment and Behavior*.)

All of this endless decision-making can be exhausting and overwhelming in some cases, leading to a phenomenon referred to as decision fatigue. (ح)

SIGNS OF DECISION FATIGUE

When people experience decision fatigue, they commonly respond in one of four ways to conserve mental energy:

- 1. Procrastination. They put off making the decision until later;
- Impulsivity. They make rash decisions, neglecting to think through potential consequences, e.g., overspending while online shopping or grabbing junk food in the checkout line at the grocery store;
- Avoidance. They avoid deciding at all and do nothing; or
- Indecision. They take a long time to decide, reviewing and re-reviewing available options for much longer than necessary.

Other potential signs of decision fatigue include feeling regret or dissatisfaction about decisions made; feeling exhausted, irritable, or overwhelmed; having trouble sleeping; and experiencing brain fog, headaches, or digestive upset.

WHAT IS DECISION FATIGUE?

The term "decision fatigue" describes how one's ability to make decisions is increasingly impaired after repeated acts of decisionmaking. It is a mental and sometimes emotional exhaustion that makes it increasingly hard to make subsequent decisions.

WHAT CAUSES DECISION FATIGUE?

It's important to note that not all decision-making leads to decision fatigue, and not everyone will experience the phenomenon.

SEVERAL VARIABLES CAN CONTRIBUTE TO DECISION FATIGUE, INCLUDING A PERSON'S STRESS LEVEL IN GENERAL, THE NUMBER OF DECISIONS THAT MUST BE MADE IN A SHORT PERIOD OF TIME, AND THE COMPLEXITY AND IMPORTANCE OF THE DECISIONS BEING MADE.

"High levels of stress and having to make lots of complex decisions with important implications will tend to deplete mental and emotional energy faster, making decision fatigue more likely," said Dr. Cheryl Hurst, a U.K.-based behavioural scientist. "Another variable that can contribute to decision fatigue is choice overload." "Choice overload" is a term researchers use to describe having too many options. It is becoming increasingly common in all aspects of life. For example, U.S. grocery stores used to offer 7,000 to 8,000 items from the 1970s to the 1990s but now carry 40,000 to 50,000 items, including about 275 types of cereal alone!

Economics and psychology researchers have argued that more choices are often desirable and can lead to better outcomes. Generally, people are drawn to larger choice sets; they instinctively feel like having more options will give them more decision freedom and that, ultimately, they'll be able to find the best item/outcome for their needs.

HAVING TOO MUCH CHOICE, HOWEVER, CAN MAKE DECISION-MAKING DIFFICULT, TIME-CONSUMING, STRESSFUL, AND UNSATISFYING.

Brain scan research has shown that making choices from large sets of options is associated with a greater cognitive load. Your brain must work harder to decide when there are more options to wade through.

In a book chapter in *Routledge Handbook of Bounded Rationality* (2020) titled "Cognitive and affective consequences of information and choice overload," Dr. Elena Reutskaja and colleagues explained that having an abundance of choice can be beneficial, but only up to a point, after which the availability of additional options becomes detrimental and choice overload sets in.

Research suggests that selecting from a larger choice set is associated with several negative impacts, including greater perceived decision difficulty, lower motivation to make a decision, decreased confidence in one's choice, more confusion, and poorer quality of decisions.

"When it comes to optimal decision-making, it appears that a moderate number of choices is best," said Dr. Hurst. "Ideally, you don't want too many or too few options."

WHAT INCREASES THE LIKELIHOOD OF DECISION FATIGUE?

Anyone can experience decision fatigue when faced with the need to make a lot of weighty decisions repeatedly over a short period of time. However, there are certain situations where decision fatigue may be more likely to occur, including:

- during difficult or stressful times, e.g., when planning a funeral or even a wedding;
- when the person making the decision has perfectionist tendencies, making them more prone to overthinking every decision to get everything "right"; and

when the person making the decision lives with anxiety, depression, or post-traumatic stress disorder, all of which can sometimes make it more difficult to make even simple decisions.

TIPS FOR AVOIDING & ADDRESSING DECISION FATIGUE

Below are some steps you can take to help reduce the likelihood of experiencing decision fatigue and/or address it when it does occur.

Reduce the number of decisions you need to make. You can do this by:

Streamlining your choices, e.g., reduce the number of TV channels and podcasts you subscribe to; have a minimalist wardrobe with limited items that all coordinate.

"The fewer options you have to choose from, the easier decision-making will be," explained Dr. Hurst.

Following set routines and habits, e.g., always have tacos on Tuesday or always do an aerobics class at the gym on Mondays, Wednesdays, and Fridays at 7 a.m.

"When you commit to a routine or habit, you only have to make the decision once upfront, thereby relieving yourself from giving mental bandwidth to the subject again and again," said Dr. Hurst.

"Remember, our decision-making abilities tend to worsen over the course of a day, meaning there's a finite number of good decisions we can make each day. So, you don't want to waste any of those good decisions on things like what to wear or eat. Instead, put those types of low-importance, repetitive tasks on autopilot, and reserve your prime mental resources for decisions that really matter, like big work-related choices."

Reducing the amount of information you take in, e.g., unsubscribe to non-essential emails, especially ones that are always selling you something.

"If you don't even see the latest deals being offered by your favourite retailers, you won't have to spend any time and energy thinking about whether to buy something or not," said Dr. Hurst. "And you'll decrease the likelihood of making impulse purchases of things you don't need."

If possible, delegate decision-making to others. Ask yourself, is this something I need to decide, or can I let someone else do it?

"Can your co-worker decide what to include in the meeting minutes? Can your spouse choose the paint colour? Can your friend choose the restaurant for lunch?" asked Dr. Hurst. "Let others make some of the decisions, and then make sure you don't second-guess or micromanage the decisions they made. Of course, they may choose differently than you would have, and they may sometimes make mistakes, but remember, you make mistakes, too!"

Make big decisions when you're rested and not hungry.

"Get enough good-quality sleep, take breaks as needed throughout the day, and fuel your body and brain with nutritious food at regular intervals to support good decision-making and help avoid decision fatigue," advised Dr. Hurst.

"Related to this, it can also be helpful to make your most important decisions in the morning."

Don't second-guess decisions already made. Perfectionism may be to blame if you tend to do this a lot.

"Stop seeking the perfect outcome for every decision and instead let 'good enough' be your standard for all but the most important decisions," advised Dr. Hurst.

"Then, once a decision is made, don't waste any additional time or energy worrying about whether it was the right decision or not, as that will only increase the odds of experiencing decision fatigue."

WHEN TO SEEK PROFESSIONAL HELP

Decision fatigue is an acute experience, not a chronic one – meaning it should be a temporary, short-lived phenomenon, not something that a person lives with long term. Most people will occasionally experience decision fatigue, which typically resolves itself within a few hours or days.

If someone struggles with decision-making daily, something else might be happening.

If you're experiencing symptoms of decision fatigue that don't get better fairly quickly, perhaps after a bit of deep rest and exercise, you might want to consult your doctor or a therapist. They can help advise about actions to address what you are experiencing and perhaps identify and help with underlying things that are going on.

"It's important to watch for signs of decision fatigue and take proactive steps to prevent it or bounce back from it quickly, because, when left unaddressed, decision fatigue doesn't just feel unpleasant, it can lead to poor decisions, burnout, and more."

On the Cover

WITH LORI HICKEY & CHERYL HICKEY

sk Cheryl Hickey and her mother, Lori, what they learned from each other about maintaining a healthy lifestyle, and you hear some gentle kidding.

"Absolutely nothing!" said Cheryl, amid laughs as she and Lori spoke to Mind Over Matter® on the phone.

She was not serious. The fact is that amongst all the ups and downs in a TV career of more than two decades, including 18 years as co-host of ET Canada, Cheryl has been sustained by lessons from her parents.

I CAN REMEMBER WHEN WE WERE REALLY LITTLE, WE'D TALK ABOUT WHAT WENT RIGHT IN THE DAY. MOM ALWAYS TAUGHT ME THAT WHEN BAD THINGS HAPPEN, AS THEY DO, YOU ALSO HAVE TO GIVE THE SAME ATTENTION TO THINGS THAT WERE GOOD. IT'S ABOUT WHERE YOUR ATTENTION GOES, WHERE YOUR ENERGY GOES. THAT'S SOMETHING THAT'S BECOME EVEN MORE IMPORTANT AS WE GROW OLDER.

It was an attitude that grew out of Lori's own life experience. Born in England, her parents immigrated to Canada when she was four years old. Lori describes them as hard-working, good people, but reticent about showing affection. "I learned that when I had children, there would always be all kinds of hugs. And there were," said Lori.

She and her late husband, John, a teacher, raised three children in Owen Sound, Ontario. Cheryl is the youngest. While they may not have deliberately given close attention to a healthy diet, they did stress the value of eating fresh vegetables. The Hickeys maintained a large garden in the backyard, and the children devoured the produce.

"I'd take the kids down to pick the peas and beans, and the bowl would be empty by the time we returned to the house," she said. "I used to freeze broccoli, beans, and corn and do a lot of pickling and preserve making. Quite frankly, it was out of necessity to be able to feed your family."

Cheryl has vivid memories of all the fresh foods on the Hickey table, with salads often becoming a full meal. The habit stuck with her, and as an adult, she pays attention to her diet, which incorporates healthy servings of vegetables, eating sufficient protein, and minimizing sugar intake.

Her daily schedule includes getting up at 6 a.m. and carving out time for meditation and journaling.

"For me, mindfulness is a big part of my day. I meditate using an app called Mindvalley. It was a game-changer," she said.

Sometimes, if I'm struggling, I might meditate two or three times a day. It's good to have time to just be quiet and think.

Lori has also adopted mindfulness. She once went on a four-day meditation retreat. "It was one of the best things I've done. I'm not as good as Cheryl at daily meditation, but I do it when things get rough for me mentally."

Later in life, Lori also embraced daily exercise: "I know that it's essential for good health and for coping with anxiety. It's been a part of my life for a long time."

All of her self-care regimes were challenged when her husband, John, developed a rare brain disease, progressive supranuclear palsy (PSP), which eventually left him paralyzed from the neck down. She was his principal caregiver for the first three years until it became too difficult. John spent the final five years of his life in a care facility, Baycrest, until he died in January 2023.

While Lori speaks highly of Baycrest, the experience has left her and her daughter angry that there are not more supports available for home care.

IN OUR SOCIETY, IT'S SO UNFORTUNATE THAT COUPLES WHO SPENT 40, 50, 60 YEARS TOGETHER HAVE TO END UP BEING SEPARATED IN THE FINAL STAGES OF LIFE DUE TO ILLNESS. IF WE COULD BE SUPPORTED IN OUR HOMES WITH EXTRA CARE AND NURSING INSTEAD OF HAVING TO GO TO A NURSING HOME, IT WOULD BE SO MUCH BETTER.

"This makes me so fiery," added Cheryl. "Unless you're a multimillionaire, you have no choice but to move into a facility. Why can't we make home care affordable? Why can't we change this? That infuriates me. The other thing is that there's a silver tsunami with so many more seniors. We have no idea how much worse things are going to be."

Her aunt, who has dementia, has been in hospital for months, awaiting a space in a long-term care home, with a likely further wait of up to six months.

"I'm so angry about what we have done. And how we've dropped the ball with seniors," said Cheryl.

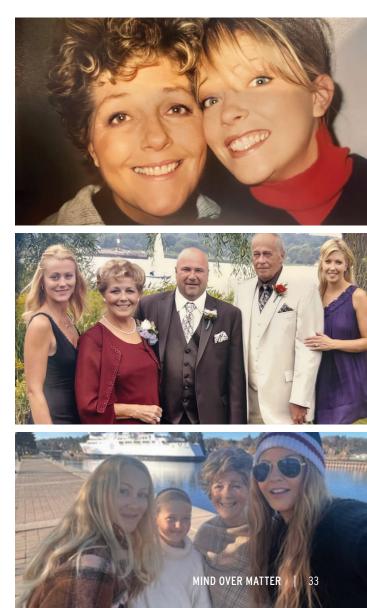
Both she and her mother welcomed the opportunity to help support the mission of Women's Brain Health Initiative (WBHI) in

promoting brain health. "It's so important to look after yourself, from a nutritional point of view, and to handle stress," said Lori.

UNDERSTANDING BRAIN HEALTH IS JUST SO INCREDIBLY IMPORTANT," ADDED CHERYL. "I'VE COME TO LEARN THE DETRIMENTAL ROLE STRESS PLAYS ON THE BRAIN, AND THAT'S WHY I WORK HARD TO MANAGE MY STRESS. THE WORK THAT WBHI DOES IS REALLY KEY BECAUSE WE NEED FUNDING FOR RESEARCH INTO WOMEN'S BRAINS.

For mother and daughter, doing the photo shoot for the cover of Mind Over Matter[®] was a rare treat and a first for Lori: "That's Cheryl's thing. But it was lovely. I loved spending the day with her. And it's an important cause."

"It was very special," said Cheryl. "A nice snapshot; a moment in time that we'll always have. We shared a lot of laughs. And it was in honour of Dad. We felt like he was there." 🛞





DRINK WATER

Insufficient hydration can impair short- and longterm memory function and contribute to brain fog, headaches, sleep issues, stress, anger, and depression.



WALK Walking at a moderate to vigorous intensity level is a form of aerobic exercise that provides cardiovascular conditioning; heart health is connected to brain health.



DEEP BREATHIN Engaging in slow, deep bre blood pressure, increase r alertness, and reduce anx anger, and confusion.

ging doesn't necessarily mean slowing down. New research and mounting evidence have uncovered advancements in lowering our risk of developing cognitive impairment and dementia through our lifestyle choices and reinforcing the Six Pillars of Brain Health: nutrition, exercise, mental stimulation, stress management, sleep, and social activity.

Taking up habits to improve your Six Pillars gives you the best chance to stave off dementia, even if you are genetically predisposed to Alzheimer's. The superstar habits shared here will help safeguard your brain health, so give them a try!

Unlocking

EVIDENCE-INFORMED HABITS F



POWER DOWN

Exposure to screens (e.g., TV or smartphone) disrupts sleep because of the light these devices emit, which affects melatonin levels and interferes with sleep's circadian rhythms.



LIMIT ALCOHOL

Drinking alcohol is associated with many health problems, including an increased risk of high blood pressure, heart disease, and diabetes (all risk factors for dementia).



READ Reading stimulates your b neural connectivity, conce and memory, reduces stre relaxation, and improves s



G eathing can lower elaxation and iety, depression,



EAT THE RAINBOW Colourful foods contain distinct phytonutrients with various health benefits, including neuroprotection, and anti-inflammatory, antioxidant, and antimicrobial properties.



STRENGTH TRAIN

Strength or resistance training enhances cognitive performance and protects the hippocampus, a complex part of the brain with a major role in learning and memory.



OR DEMENTIA RISK REDUCTION

Dementia does not necessarily have to be our fate as we age. Prevention may be the answer for many of us to avoid this insidious disease. If we can't avoid it, let's do what we can to delay it as long as possible. We have more control over our cognitive fate than we may have realized.



LOOKING FOR AN EFFECTIVE WAY TO BUILD AND MAINTAIN BRAIN-HEALTHY HABITS? Then download the BrainFit -Habit Tracker app for free today!



rain, enhances ntration, ss, promotes leep.



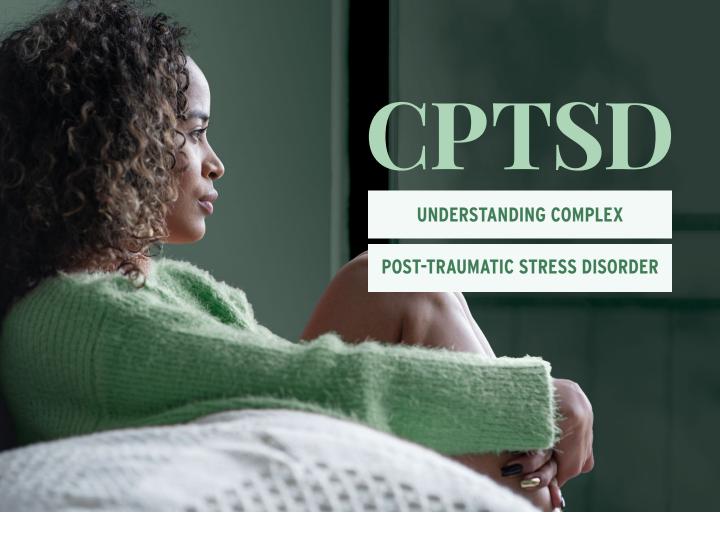
VOLUNTEER

Volunteer activities, especially in late life, provide social interaction and cognitive stimulation, and are associated with better executive function and episodic memory.



SIT LESS

Sitting for long periods slows blood flow to the brain and can temporarily cloud thinking and memory. Long-term, sedentary behaviour can thin the region of the brain involved in memory formation.



hen a new client came into the office of B.C. psychotherapist Carolynn Turner, she was in obvious distress. The woman was self-harming and had frequent thoughts of suicide. Although she was an esteemed professional in her field, she frequently dissociated at work, losing track of what she was doing for hours at a time.

The woman had been diagnosed with major depressive disorder decades earlier and been told "this was just how her brain worked," recalled Ms. Turner, the Clinical Director and Founder of Lavender Counselling.

But after spending some time working alongside the woman and learning about her history of severe childhood neglect and physical abuse, together they reached a different conclusion: the woman was actually suffering from complex PTSD.

WHAT IS COMPLEX PTSD?

Complex post-traumatic stress disorder, or CPTSD, is a mental health condition caused by chronic trauma or trauma that occurs over a long period of time. Symptoms often include anxiety, flashbacks, dissociation, poor emotional regulation, and difficulty with relationships.

A KEY DIFFERENCE BETWEEN COMPLEX AND TYPICAL PTSD IS THE UNDERLYING CAUSE.

While PTSD stems from a single traumatic event, like a car crash, complex PTSD is caused by trauma that happens continuously or repeatedly over time, like childhood abuse, sexual abuse, or domestic violence.

Studies have found that women are more likely than men to experience complex PTSD and report more severe symptoms.

This may be because more women and girls experience chronic traumas like sexual abuse and domestic violence.

A BROKEN ALARM SYSTEM

Trouble with emotional regulation is a hallmark of complex PTSD, said Dr. Maria Espinola, a licensed clinical psychologist and CEO of the Cincinnati-based Institute for Health Equity and Innovation. That means people may overreact to seemingly small problems or become numb and not respond at all.

Living with long-term fear and distress can disable the body's natural alarm system, she said. Normally, when someone is faced with a life-threatening emergency, an internal alarm goes off. Their breathing and heart rate speed up, priming them to react quickly to jump out of the way of a speeding car or fend off an attacking dog. When the emergency passes, things calm down again.

"It's not supposed to go on for years and years, but that's what happens with complex PTSD," Dr. Espinola explained. "Your alarm system gets broken."

FOR SOME PEOPLE, THAT MEANS GETTING STUCK IN A CONSTANT STATE OF ALERT, UNABLE TO TELL THE DIFFERENCE BETWEEN REAL AND PERCEIVED THREATS. OTHERS SIMPLY SHUT DOWN.

"That's where you hear survivors say things like, 'Everyone was telling me he wasn't a good person, but I couldn't see it,'" she said. "That's very typical, and it's because their alarm system has not been working properly."

WHEN RELATIONSHIPS FEEL UNSAFE

Because abuse typically occurs at the hands of someone the person trusts who is in a position of power over them, like a parent or an intimate partner, people with CPTSD often have trouble forming or maintaining relationships, Dr. Espinola said.

"If you couldn't trust those who were supposed to care for

AN ESCAPE INTO THE MIND

"Dissociation" is the experience of feeling disconnected from yourself or the world around you. It's a common symptom of complex PTSD (CPTSD).

That's because CPTSD typically stems from situations where the person could not escape their abuse, such as a child being neglected or sexually assaulted by a caregiver, said Dr. Espinola.

"If we cannot leave a situation physically, we find a way to escape mentally," she explained. "That's what dissociation does."

While this "escape" may have helped the person survive their abuse, when it continues for years afterwards, it can be distressing for the survivor and interfere with their daily life.

In addition to therapy, mindfulness practices can be helpful for people who experience dissociation, Dr. Espinola said, because it helps them feel safe in the present moment. you, how could you trust new people in your life?" she asked. "It makes sense."

Again, people respond in different ways. Some put up emotional walls and don't let anyone close, while others become overly trusting, seemingly losing their ability to recognize red flags and warning signs.

Issues with physical intimacy are a common symptom when the trauma involves sexual abuse, Dr. Espinola said. Survivors may avoid sex altogether, or they may become hyper-sexual. Some go back and forth between the two extremes.

ONE OF THE MAIN FEATURES OF CPTSD IS LACK OF BALANCE.

HOW CPTSD AFFECTS THE BRAIN

Complex PTSD is a relatively new diagnosis. The World Health Organization officially recognized it in 2018, when it was added to the International Classification of Diseases, and it has not yet been added to the Diagnostic and Statistical Manual of Mental Health Disorders, the main reference used by North American mental health professionals, as a separate condition.

Because it's so new, research on CPTSD is still limited, Ms. Turner said. However, related studies indicate how the disorder can affect the brain.

AFFECTS MEMORY AND COGNITION.

Research has found that chronic stress can cause long-term changes to the hippocampus, a part of the brain that manages learning and memory. Repeated exposure to stress also impacts the amygdala - the brain's fear centre.

"It begins to leave us in a state where we are biologically and psychologically primed to be seeking safety, and to see the world as unsafe," Ms. Turner explained.

But while scientists are still piecing together clues about how CPTSD affects the brain, they will likely soon know much more. "We've seen an explosion in research around complex PTSD," she said.

GETTING HELP

Fortunately, there is hope for people living with CPTSD.

"I tell people, 'you don't have to live like this,'" said Dr. Espinola, who uses a treatment called Dialectical Behavioural Therapy, or DBT. "Treatment can change people's lives." Э The first stage of therapy typically starts with stabilization and safety - an especially important step for people who are suicidal or self-harming. Treatment then moves on to addressing the specific issues the patient is experiencing and working on skills to manage them.

A COMMON MISCONCEPTION IS THAT ALL TREATMENTS FOR CPTSD WILL FOCUS ON DISCUSSING THE PERSON'S TRAUMATIC EXPERIENCE.

In reality, Dr. Espinola explained, there are treatments that place more emphasis on building strategies and resilience to address the person's current problems. That could mean practicing techniques to reduce dissociation or learning to set healthy boundaries in relationships.

In some cases, exposure therapy, or trauma processing, can be helpful in relieving symptoms like flashbacks, she added.

For effective treatment, it's important to find the right therapist, Ms. Turner noted. Look for someone who is trained in CPTSD, and make sure you feel safe and comfortable with your therapist.

Ms. Turner said she's seen some patients benefit from medication, especially in cases where the person needs additional help becoming stable or managing suicidal thoughts.

IS IT ANXIETY OR CPTSD?

Complex PTSD (CPTSD) is often confused with other mental health disorders, including depression, anxiety, borderline personality disorder (BPD), and ADHD. These conditions can sometimes be the primary diagnosis without recognizing the underlying CPTSD.

"We see misdiagnoses across the spectrum," Ms. Turner said. Unfortunately, some of these labels can come with a sense of shame, reinforcing the person's belief that they are "broken," "flawed," or somehow to blame, and compounding their CPTSD.

Adding to the challenge of diagnosis, CPTSD can also occur in tandem with other conditions like major depressive disorder, generalized anxiety disorder, and BPD.

Working with a trained mental health professional can help identify the heart of the difficulty so you can create a plan for treatment. "It can often be a really helpful part of therapy, as long as it's not pushed on the client," she said.

SUPPORT HEALING WITH SELF-CARE

Self-care is key when recovering from CPTSD, Dr. Espinola noted. Start with the simple things, like ensuring you get enough sleep and eating regular, healthy meals. "Finding balance is one of the main goals," she said.

Moving your body, and balancing activity with rest is another important step, she added.

Dr. Espinola shares solutions for insomnia and other self-care tips on her YouTube channel.

MINDFULNESS AND GROUNDING TECHNIQUES CAN BE ESPECIALLY HELPFUL FOR PEOPLE SUFFERING FROM CPTSD.

Jon Kabat-Zinn, who developed mindfulness-based stress reduction, defines mindfulness as "awareness that arises through paying attention, on purpose, in the present moment, non-judgmentally."

"Mindfulness can be a way of living," Dr. Espinola said. "Grounding skills, on the other hand, are techniques that can help you cope with specific symptoms of trauma, such as flashbacks and intrusive memories. Grounding skills help people bring their attention into the here and now and away from the past."

One simple and popular technique she teaches involves asking someone to place a frozen orange on the palm of their hand while engaging their senses. The practice helps calm her most-distressed clients, she said.

"It's a physical reaction that happens because the frozen orange requires your entire attention," she explained. "You have to focus on the present moment, and that's when you have the opportunity to realize that you're safe."

A PATH FORWARD

Healing from CPTSD has been a gradual process for Ms. Turner's client. With several years of therapy, the woman worked through layers of shame and mistrust to form new, healthy coping techniques, and eventually learned how to accept herself and give herself grace.

Over time, she felt better and experienced significant relief. "It's like this heavy weight had been lifted," Ms. Turner said. "This person is feeling like a proud mom again, proud of their contribution to society, and most importantly, feeling like they know and like themselves."

Rewiring the Brain

WILL TRANSCRANIAL MAGNETIC STIMULATION

WORK FOR ALZHEIMER'S DISEASE?

Best-selling author Jenny Lawson, also known as "The Bloggess" to her online followers, struggled with a year-long episode of deep depression that medication couldn't budge. She decided to try transcranial magnetic stimulation and had 40-minute treatments on weekdays for seven weeks.

By day seven, she thought they might be working, and after day 20, she was sure they were making a difference. After day 36, Lawson told her husband and daughter she wanted to go on a family vacation.

Transcranial magnetic stimulation (TMS) is a non-invasive treatment that applies pulses of magnetic energy to the brain.

It is an approved and proven effective therapy in Canada and the United States for treating major depressive disorder that does not respond to medications.

For more than a decade, scientists have been exploring the potential of TMS for treating Alzheimer's disease (AD). Research findings to date are encouraging, but more work lies ahead to answer outstanding questions before determining if TMS could be an effective treatment for warding off AD or slowing its progression.

This article provides an overview of how TMS works for depression and the rationale, emerging clinical trial \bigcirc

evidence, and outstanding questions under investigation for its use as a potential treatment for AD.

HOW TMS WORKS FOR DEPRESSION

TMS passes repetitive, focused magnetic pulses through the skull to stimulate electrical activity in targeted brain regions.

CONDITIONS APPROVED FOR TMS VARY BY COUNTRY

HEALTH CANADA APPROVAL:

2002 - major depressive disorder that does not respond to medication

U.S. FDA CLEARANCES:

- 2008 major depressive disorder that does not respond to medication
- 2013 migraine with aura
- 2017 obsessive compulsive disorder
- 2020 smoking cessation
- 2021 anxiety together with major depressive disorder

Since the original approvals of TMS for major depressive disorder, manufacturers have created a variety of different TMS devices.

EUROPEAN APPROVALS:

The BrainsWay Deep TMS[™] device is approved for use in Europe to treat AD, Parkinson's disease, post-stroke rehabilitation, post-traumatic stress disorder, and symptoms of schizophrenia. The device uses an H-coil, which delivers a deeper and broader stimulation pattern compared to the standard figure-8 coil.

ALZHEIMER'S DISEASE APPROVAL HISTORY:

- 2012 approved in the European Union and Israel for mild to moderate AD
- 2017 approved in Australia for mild to moderate AD
- 2019 The U.S. FDA turned down the first request for a TMS application for AD*

* The U.S. FDA denied clearance for the neuroAD[™] Therapy System made by Neuronix, stating that while the device met safety standards, clinical trial results did not demonstrate effectiveness. The device, intended for treating individuals with mild to moderate AD, consists of a chair fitted with a TMS coil and a computer screen to present cognitive training exercises during neurostimulation treatments. The neuroAD[™] Therapy System has been approved and in clinical use in the European Union, Australia, and Israel since 2017. A hand-held device or helmet containing a magnetic coil is placed on the scalp and delivers the pulses.

A typical treatment course of repetitive TMS (rTMS) involves 20 to 30 sessions delivered once daily on weekdays over four to six weeks at a clinic.

High-frequency pulses of 5 to 20 Hz are directed to the dorsolateral prefrontal cortex (DLPFC), an area of the brain located at the top front of your head, where you might wear a hair band. The DLPFC plays a role in working memory, task planning and switching, goal-driven attention, problemsolving, and novelty seeking.

A single TMS pulse is strong enough to stimulate cells in the target area. Repeated pulses cause changes in connections between neurons - a concept called neuroplasticity.

Lawson told People Magazine the pulses felt like an invisible chisel drilling holes into her head while having an ice cream headache. While sensory experiences are personal, most people describe the treatment as feeling like a woodpecker tapping or someone poking their head with a finger. "I've never had a patient living with depression who couldn't tolerate it," said Dr. Mark George, the psychiatrist and neurologist who pioneered rTMS. "They all say it's not pleasant, but they're willing to undergo it to treat their depression."

About 50 to 60% of people with medication-resistant depression experience a clinically meaningful benefit from TMS, and symptoms disappear entirely for about one-third of those individuals, according to a 2020 Harvard Health Blog post authored by Dr. Adam Stern, director of psychiatry at Beth Israel Deaconess Medical Center's Berenson-Allen Center for Noninvasive Brain Stimulation.

"One out of 10 American psychiatrists uses TMS to treat individuals with treatment-resistant depression," said Dr. George, distinguished university professor of psychiatry, radiology, and neuroscience, and Layton McCurdy Endowed Chair in Pyschiatry and director of the Brain Stimulation Laboratory at the Medical University of South Carolina.

IT WORKS FOR A MAJORITY OF PEOPLE WITH DEPRESSION, NO MATTER THE CAUSE OR WHETHER IT'S A FIRST INSTANCE OR RESULTS FROM OTHER CONDITIONS, SUCH AS A STROKE. I LIKE TO SAY WE'VE GOT A NAIL CALLED DEPRESSION AND A HAMMER CALLED TMS. THE TYPE OF NAIL DOESN'T MATTER - TMS WORKS.

THE RATIONALE FOR USING TMS FOR ALZHEIMER'S

"Progress in treating Alzheimer's with rTMS has not been the same home run we have seen in depression," said Dr. George. "Alzheimer's is a neurodegenerative disease that involves damage to neurons that, at a certain point, can't be restored. With depression, the neurons are not damaged and only need retraining."

Dr. George recalled treating a colleague's wife who struggled throughout her life with recurrent depression and later developed AD. The colleague noticed she was depressed and not looking after herself as well as she had been doing, so he asked Dr. George to treat her with rTMS.

The treatment did not change her underlying AD. However, it lifted her depression enough that she returned to mostly taking care of herself, allowing her to live at home longer until she needed the next level of care.

Up to 40% of individuals living with AD suffer from significant depression, according to the Alzheimer's Association.

"In each square millimetre of the brain, there are millions of neurons, and each neuron is hypothetically connected to others by synapses. Given that the brain has about 80 to 100 billion neurons in total, theoretically there are at least two to the power of 80 to 100 billion synapses, an astronomically high number," explained Dr. Zahra Moussavi, professor in the Department of Electrical and Computer Engineering and Biomedical Engineering Program at the University of Manitoba, and Canada Research Chair in Biomedical Engineering, Tier 1.

"The hope with rTMS as a treatment for Alzheimer's is that it will encourage the generation of new synapses as workarounds for those that are no longer functioning properly."

LATEST EVIDENCE FOR TREATING ALZHEIMER'S

An 82-year-old woman named Brigit was the first participant in a groundbreaking clinical trial of rTMS as a treatment for individuals living with AD. Led by Dr. Moussavi at the University of Manitoba, the trial was the first study of rTMS as a potential treatment for AD in Canada.

Brigit would usually say she was in her 20s and had no children. After seven days of rTMS, she was frustrated with the treatments and said they were uncomfortable. Her husband reminded her she'd agreed to participate in the study because she wanted to remember her three children. She then named two of her children and one grandchild. Even if it was not entirely correct, Brigit's recaptured memory was a breakthrough. The next day, she returned to saying she was in her 20s and had no children. Still, Dr. Moussavi was encouraged to continue her work in collaboration with colleagues at McGill University, in Montreal, and Monash University, in Australia.

Throughout the five-year trial, more than 150 patients with mild to moderate AD randomly received either rTMS or a sham treatment to the DLPFC. The study results were remarkable and, at the same time, raised additional questions: 68% of participants showed a significant improvement in cognition that lasted more than two months post-treatment - including those who received the sham treatment. These results were published online in the journal *Neurotherapeutics* in February 2024.

On further investigation, Dr. Moussavi and colleagues discovered that while the sham coil they used produced sensations and sounds identical to the actual coil, it still induced a low current in the brain.

"Another group confirmed this brand of sham coil produced up to 25% of the magnetic field intensity of a real coil," said Dr. Moussavi. "While we can't say rTMS made a difference compared to the sham treatment in our study, our results still demonstrated rTMS is worth investigating further as a potential treatment for Alzheimer's."

One of the outstanding questions about applying rTMS to AD has been determining the best area of the brain to target.

Researchers in Italy recently reported the first results for applying rTMS to the precuneus, an area at the top back part of the brain.

The precuneus is a vital node of the default mode network, an essential network that plays a role in the brain's resting state and abstract thoughts, such as reminiscing and future planning. It is also the earliest brain region affected by amyloid deposition, gray matter loss, and disconnection between essential regions and brain networks in AD development.

The study included 50 study participants, with an average age of 74, and 52% were women. They randomly received rTMS or a sham treatment to the precuneus for five days per week for two weeks, followed by 22 weeks of once-weekly maintenance treatments.

At the end of the study, the rTMS group showed stable cognitive and functional performance according to various standard assessments, but those in the sham group continued to decline. Patients in the rTMS group also showed increased activity in gamma brain waves, which play a role in working memory, whereas the sham group did not. The study results were published in *Brain* in November 2022 and presented at the Clinical Trials on Alzheimer's Disease (CTAD) conference in Boston in October 2023.

"Stabilizing cognitive decline is a promising finding from this study, one of the largest to date in patients with Alzheimer's," said Dr. Moussavi.

MORE RESEARCH, HOWEVER, IS NEEDED TO DETERMINE WHETHER THIS TREATMENT APPROACH IS THE BEST STRATEGY FOR AD.

In another study presented at the CTAD 2023 conference, researchers from Korea reported results from their trial where they applied rTMS to the parietal lobe in a small number of individuals with early AD and evidence of amyloid deposits.

THE PARIETAL LOBE SITS ABOVE THE HIPPOCAMPUS, WHICH PLAYS A MAJOR ROLE IN LEARNING AND MEMORY AND IS ANOTHER AREA AFFECTED IN EARLY AD DEVELOPMENT.

After 20 sessions over eight weeks, the rTMS group of 18 patients showed higher cognitive and functional performance scores than the sham group of 12 patients. Brain imaging revealed increased working connections between the hippocampus and precuneus in the actual treatment group, which aligned with improved cognitive scores.

WHAT'S NEXT

Dr. Moussavi and Dr. George both agree many questions remain for applying rTMS as a treatment for AD, including the optimal brain area to target, the frequency and the total number of pulses used, the duration of treatment and whether maintenance sessions are required, and if it will be most helpful in people with mild cognitive impairment (MCI) or those who have been diagnosed with mild to moderate AD.

At the same time, manufacturers continue to develop newer types of TMS.

AT THE MEDICAL UNIVERSITY OF SOUTH CAROLINA, DR. GEORGE AND COLLEAGUES ARE NOW CONDUCTING A CLINICAL TRIAL TO DETERMINE THE OPTIMAL DOSE OF AN ACCELERATED FORM OF TMS, CALLED INTERMITTENT THETA BURST TMS, FOR PATIENTS WITH MCI.

Individuals with MCI are more likely to develop AD or other forms of dementia than people without MCI. Depression is also common

among people living with MCI. The FDA recently approved intermittent theta burst TMS as a once-daily treatment for depression, so the effects of treatment are known.

In this innovative study, participants with MCI choose six treatment days within a two-week period. On each treatment day, they receive multiple treatments in sessions lasting about 2 1/2 hours. Pulses are administered in three-minute periods. Study participants randomly receive active or no stimulation in each session.

THETA BURST STIMULATION IS MORE EFFICIENT AND MORE SIMILAR TO HOW THE BRAIN TALKS TO ITSELF, SO WE CAN USE FEWER, QUICKER PULSES THAN STANDARD RTMS.

"A shorter course of therapy would certainly be more convenient for patients." If this study can answer essential questions about the optimal dose for theta burst TMS in individuals with MCI, Dr. George and colleagues plan to conduct a larger, multisite trial to confirm their findings.

Dr. Moussavi is also designing more studies to find answers to outstanding questions about whether rTMS might help people with AD. For example, she has been investigating using a new diagnostic and monitoring technology called electrovestibulography (EVestG) to predict which patients will most likely respond to treatment.

EVestG measures electrical signal activity in the external ear canal. Clinicians are already using it to measure the severity of persistent post-concussion syndrome and major depressive disorder.

So far, the preliminary results have been encouraging: EVestG predicted which patients responded positively to rTMS with a high degree of accuracy. "I'm keen to add EVestG to future studies to ensure we are treating the patients most likely to benefit," Dr. Moussavi said.

Dr. Moussavi's mother's experience with AD continues to inspire her research. After establishing her lab in 2009 and securing research funding in 2013, Dr. Moussavi visited her mother in Iran. "I told her, 'Mom, I did it all for you.' She was not verbal at the time," Dr. Moussavi said. "She kissed me and smiled, and one week later, she passed away. Now, I hope that my work will be able to help others."

Are you interested in learning about clinical studies of TMS for AD? Search clinicaltrials.gov for studies in your area and discuss with your healthcare provider.

Secondary Traumatic Stress

THE COST OF CARING

hen Françoise Mathieu was a civilian therapist working with the military, one of her clients was a nurse case manager who had never seen combat but was experiencing symptoms identical to those of post-traumatic stress disorder.

"It wasn't until the mid-1990s that we started studying secondary traumatic stress," said Ms. Mathieu, who is a registered psychotherapist in Kingston, Ontario, and Executive Director of TEND. This organization offers training and education on secondary traumatic stress (STS) to help professionals, such as healthcare providers and first responders.

Since then, when research mostly focused on fields like pediatric oncology nursing, it has become apparent STS can affect people in a much broader range of occupations, as well as individuals in many other groups, from family members caring for loved ones with life-threatening illnesses, to foster parents, teachers, and even children.

That means understanding STS could be an important way to guard our own well-being and that of our communities. Read on to learn more about STS, including what it is, how it affects people, who's impacted by it, and how to treat it.

WHAT IS STS?

STS (ALSO KNOWN AS INSIDIOUS TRAUMA) IS ONE OF SEVERAL RELATED TERMS THAT DESCRIBE THE PSYCHOLOGICAL TOLL THAT CAN BE WROUGHT BY INDIRECT OR SECOND-HAND EXPOSURE TO OTHERS' TRAUMA.

Direct trauma, in contrast, refers to a traumatic event that occurs directly to us. Another similar term to STS is vicarious traumatization (VT), which describes what can happen when someone like a therapist is repeatedly exposed to detailed, traumatic stories. "These stories hitch a ride with you," Ms. Mathieu explained.

VT tends to be cumulative, and its signature quality is a negative shift in worldview. It is sometimes referred to as compassion fatigue or empathy fatigue. While sharing similarities to indirect trauma, STS can occur suddenly after a single event. However, even in scientific literature, VT and STS are sometimes used interchangeably.

And indeed, some mental health professionals believe the \ominus

distinction is not important. According to the TEND website, "whether you call it STS or VT, what we are referring to is the impact of indirect exposure to difficult, disturbing and/or traumatic images and stories of the suffering of others ... and the way it might impact us as individuals and professionals. Over time, repeated exposure to difficult content can have a negative impact on our functioning and overall mental health."

THE IMPACT OF SECONDARY TRAUMA

While neither VT nor STS are official diagnoses, the diagnostic criteria for post-traumatic stress syndrome (PTSD) have been expanded to include witnessing trauma to others and repeated or extreme exposure to details of a traumatic event as qualifying stressors.

"When we call something secondary, it's almost diminutive, but the experience of secondary traumatic stress can be exactly as if you'd experienced it primarily," said Dr. Nathalie Reid, Director of the Child Trauma Research Centre at the University of Regina.

It seems as if the brain doesn't distinguish between the two it shifts into survival mode in both situations.

"When we perceive a threat, we're flooded with hormones that prepare us to fight, flee, or freeze," explained Diana Tikasz, a registered social worker and trauma and organizational health specialist in private practice in Hamilton, who is affiliated with TEND. This response "is very normal, and can even be good for our growth, noted Dr. Lise Milne, an associate professor in the University of Regina's Faculty of Social Work who is also affiliated with the Child Trauma Research Centre, "but when it happens in excess, we can start to experience troubling symptoms."

PTSD and STS are thought to be due to prolonged "amygdala hijack," meaning the fear centre of the brain does not shut off appropriately.

Consequently, you may constantly feel as if you're in danger. As the word "hijack" implies, normal function can be inhibited in other brain areas responsible for memory (the hippocampus), decision-making, and emotional control (the pre-frontal cortex).

And indeed, the symptoms of PTSD and STS, "are the same,"

Ms. Tikasz said. For example, symptoms characteristic of PTSD include "flashbacks, nightmares, and intrusive thoughts," she noted. "These can happen in secondary trauma, but it's not about your own material."

STS can cause a range of other physical, cognitive, and behavioural symptoms. These include "memory problems, hopelessness, anger, cynicism, poor sleep, and minimizing of adversity around us," Dr. Milne added. Also on the list of possible symptoms are hypervigilance (feeling jumpy or on edge), avoiding specific people or places, and difficulty concentrating or making decisions.

OVER TIME, STS CAN LEAD TO STRAINED RELATIONSHIPS, PROFESSIONAL BURNOUT, AND SUICIDAL THOUGHTS.

In the longer term, like other forms of toxic stress, it can cause a type of "wear and tear on the body and the brain," known as allostatic overload, Dr. Milne said. "With prolonged exposure, that's where we can see physical and physiological outcomes that can last across a lifespan if it isn't addressed as early as possible."

While there is scant research specifically in STS, according to *Epigenetics of Stress and Stress Disorders*, published in 2022, "a large body of research has linked PTSD to a variety of physical health outcomes, including the leading causes of death and disability: heart disease, stroke, diabetes and dementia."

"Both mental and physical health are very much affected by trauma," said Dr. Ruth Lanius, a professor of psychiatry and Director of the Post-Traumatic Stress research unit at Western University's Schulich School of Medicine and Dentistry in London, Ontario.

IS STS WIDESPREAD?

It's hard to pinpoint how common STS might be overall. "We don't have incidence rates outside of certain specialized populations," Ms. Mathieu explained. Those "that were first studied were folks who work in child protection, people who work with survivors of sexual violence, veterinarians, and animal care technicians."

RESEARCH SUGGESTS THAT THE RATE AMONG THERAPISTS AND COUNSELLORS WHO CARE FOR THOSE IN HIGH-TRAUMA OCCUPATIONS IS RELATIVELY HIGH.

For instance, in a study of 224 mental health professionals working with U.S. military patients, published in *The Journal of Nervous and Mental Disease* in 2013, STS prevalence was nearly one in five – 19.2%.

Arguably, research on STS has never been more relevant since, according to "Stress in America 2023," a report from the American Psychological Association, there is mounting evidence our society is experiencing the psychological impacts of collective trauma related to COVID-19, global conflicts, inflation, climate-related disasters, and racism and racial injustice.

However, based on other research, STS may be at least as widespread in therapists and counsellors with a broader client base. One study of 256 social workers in Montana, for example, found that nearly 41% met the criteria for PTSD. This research was published in *Traumatology* in 2017.

Recently, STS has been recognized as affecting teachers and other school personnel. "Educational assistants, school support specialists, and counsellors in schools experience secondary traumatic stress," said Dr. Reid, who was just four days into her teaching career when the 9/11 terrorist attacks took place.

Shortly after the Child Trauma Research Centre opened four years ago, she said, "we quickly realized we couldn't even think about engaging with child trauma if we weren't engaging with the experiences of the practitioners entrusted with their care."

STS is not always vocation-related, however. Studies have found it affects groups such as family care partners of cancer patients and partners of people with PTSD, suggesting trauma can ripple outwards within families.

Children can also be susceptible to STS.

For instance, according to research conducted among junior and senior high school students 18 months after the massive wildfire in Fort McMurray, Alberta, not only did 37% meet conditions for a probable diagnosis of PTSD, but kids who had moved to the community after the cataclysmic event also showed higher rates of PTSD symptoms. The study appeared in the journals *BMC Psychiatry* and *Frontiers in Psychiatry* in 2019.

Research suggests that certain life circumstances increase the likelihood of developing STS. Growing up with a parent living with mental illness is one example of a list of predisposing factors for STS.

PEOPLE WITH A HISTORY OF ADVERSE CHILDHOOD EXPERIENCES HAVE A HIGHER RISK OF DEVELOPING PTSD IF THEY'RE EXPOSED TO SUBSEQUENT TRAUMA.

Adverse Childhood Experiences (ACEs) is a broad category that goes beyond physical and emotional abuse and neglect. For example, "You may have been loved and felt safe, but did your parents go through a divorce, or was one of them abusing substances?" Ms. Mathieu noted.

She explained that a free online questionnaire called the Adverse Childhood Experiences self-test asks you if before age 18 you have had any of these difficult things happen. "If you score higher on ACEs, you are more vulnerable to secondary traumatic stress."

Women may be disproportionately affected by STS, as well.

Female-identifying individuals are far more likely to be family caregivers. They also outnumber men in many helping professions, such as nursing and social work. Whatever the reasons, women may be more prone to STS than their male peers.

According to a systematic review of gender findings in research looking at secondary traumatic stress in health professionals, published in *Trauma, Violence & Abuse* in May 2015, "almost all the studies based on PTSD symptomatology show greater female susceptibility."

BURNOUT VS. STS/VT

Burnout is different from vicarious traumatization and secondary traumatic stress. A state of physical and emotional exhaustion, usually related to work, burnout doesn't necessarily involve loss of compassion for the recipients of one's care or a damaged view of the world (for instance, coming to the belief that most people are inherently bad).

One major distinction is that burnout can occur for various reasons, including a lack of control over how a job is carried out and an overload of responsibilities.

STS TREATMENT

"There are some effective treatment modalities" for STS, says Françoise Mathieu, a Kingston, Ontario-based registered psychotherapist, speaker, and founding member of the Secondary Traumatic Stress Consortium.

Trauma-focused cognitive behavioural therapy (TF-CBT) and eye movement desensitization and reprocessing (EMDR) therapy can be helpful. TF-CBT is a form of counselling aimed at building skills to manage difficult emotions in a healthier way, while EMDR treatment is intended to change the way traumatic memories are stored, thereby reducing the associated emotional intensity and sense of immediacy.

While it is too early to say whether treatment could potentially moderate the risk of later dementia, some evidence, albeit indirect, hints that it may. A 2022 study, which analyzed data from 13 studies involving more than 1.6 million people, found that the dementia risk associated with a history of PTSD was lower in veterans than in the general population.

The authors of the paper, which appeared in *The British Journal of Psychiatry*, noted that since veterans had been more likely to access treatment, "this may indicate that PTSD-related dementia could be modified by intervention."

THE SIGNS OF STS

Ms. Mathieu encourages people to be alert for clues that they might be on the path toward developing STS. "It's a continuum from healthy functioning at one end to being really functionally impaired at the other end," she said, with many people occupying a yellow zone just bordering full-blown STS.

EACH OF US HAS AN INDIVIDUAL SET OF EARLY WARNING SIGNS THAT SIGNAL ESCALATING STRESS LEVELS.

These can range from physical symptoms (like headaches or lack of appetite) to emotional (irritability, for example) and behavioural hints (such as doom-scrolling or compulsive shopping).

For those working in helping professions, "there are some informal checklists you can use to pick up on STS symptoms," Dr. Milne said. "Are they exhausted all the time? Are they feeling dissociated from work? Are they afraid to come to work? Those types of things are quite common" in STS.

HOW TO MITIGATE STS

IF SOMEONE NOTICES SUCH CHANGES OR BEGINS EXPERIENCING A SURVIVAL RESPONSE FOLLOWING AN INTENSELY DISTRESSING EVENT, SEVERAL STRATEGIES MAY HELP AVERT A DOWNWARD SLIDE.

In the case of an immediate stress spike, "we know that nervous systems resonate with other nervous systems, so if the person is with someone they feel safe and secure with, their nervous system can start to regulate a bit more," Ms. Tikasz said.

However, for those with a history of childhood trauma, a human presence may have the opposite effect. "Individuals who have been hurt by their caregivers often tend to feel more safe with animals," Dr. Lanius explained.

Certain techniques that take only seconds can act as a reset button for the parasympathetic nervous system, which governs the fight-or-flight response. "That can be use of breath, such as longer exhales than inhales, or soothing touch, like cold water splashed on our hands or faces," Ms. Tikasz said.

These measures can help pave the way to using talk to diffuse stress further. "When a stress response is extreme, we don't have access to language very easily," Ms. Tikasz said. "Once our language centres come onboard a little bit, then it's important we do some talking to build a narrative around what we're experiencing that isn't going to keep us stuck."

Daily habits can also affect our susceptibility to toxic stress.

"I invite people to think about what you are putting into your sweet, beautiful nervous system," said Ms.Mathieu. Caffeine, task-switching, social media use, and media consumption can all have a negative impact, while adequate sleep, time spent with loved ones (including pets), and exercise have the opposite effect. "For me, it's really about how we address our nervous system dysregulation on a day-to-day basis," she said.

However, this type of self-care is only a fraction of the equation. "This notion of 'just do yoga, and you'll be fine' puts the responsibility on individual people who already feel like they don't have time to do anything more than they're doing," said Dr. Reid.

"With some secondary trauma responses, self-care isn't going to touch it - it needs different strategies," stressed Ms. Tikasz. "If we don't understand that, there can be lots of shaming and blaming." Workplace leadership, support, and culture play a critical role in helping workers reduce potential exposure to traumatic events, said Dr. Milne.

I CAN SAY FROM MY RESEARCH THAT LEADERSHIP NEEDS TO PAY ATTENTION TO WORK HOURS, WORKLOAD, SICK TIME, PERSONAL DAYS, AND ACCESS TO COUNSELLING SUPPORTS.

"They also need to provide opportunities for their employees to connect with peers and colleagues so people don't feel alone in their experiences," she added.

As well, more work needs to be done to squash the stigma that is associated with admitting one is experiencing secondary trauma, both within helping professions and society as a whole.

For example, Dr. Milne recalled earlier in her career, "I refused to go on sick leave because I thought it would make me look weak," she said. "Looking back, I suffered as a result of not having a workplace that meaningfully supported prevention or response to secondary traumatic stress, but also because I had guilt about 'who am I to be feeling like this?' - I'm not the person that experienced the trauma."

Dr. Reid added that professionals need to challenge the dominant narratives in caring professions "that a good teacher or a good

RESOURCES

Real Self Care: A Transformative Program for Redefining Wellness (Crystals, Cleanses, and Bubble Baths Not Included), by Pooja Lakshmin, MD. Penguin Life, 2023

Child Trauma Research Centre childtraumaresearch.ca

Secondary Traumatic Stress Consortium stsconsortium.com

TEND tendacademy.ca

ACES test acestoohigh.com/got-your-ace-score/

caseworker can hear traumatic stories all day and go back the next day with a smile on their face. Preventatively, the most important thing we can do is to spread knowledge (about STS) so people can have the tools to check in with themselves and say: 'wait a minute, I'm not sleeping well, I don't want to hang out with my friends like I used to - there's something going on.'''



Anxiety Disorders

EXPLORING HOW THEY RELATE TO

THE MECHANICS OF THE BRAIN

nxiety disorders are the most prevalent mental illnesses in the world. According to data from the "Global Burden of Disease Study 2019" published by Dr. Yang and colleagues in Epidemiology and Psychiatric Sciences in 2021, there was an estimated 45.82 million cases of anxiety disorders in 2019, which constituted a 50% increase in cases over 30 years.

There are disparities based on sex, with women suffering from anxiety disorders 1.6 times as often as men. While it is well established that the prevalence of anxiety disorders is higher for women than for men, there is limited research on sex-related differences and a poor understanding of the mechanisms that underscore experiences of anxiety.

Because of this, identifying appropriate therapies for anxiety disorders continues to be challenging for health professionals, and there are only a few therapeutic targets for pharmaceuticals in treating anxiety.

WITH THE DEVELOPMENT OF SOPHISTICATED TOOLS OVER THE LAST TWO DECADES, NEUROSCIENTISTS HAVE DISCOVERED THAT THE NEURAL CIRCUITS THAT ACCOMPANY ANXIETY ARE INCREDIBLY COMPLEX AND INTERCONNECTED.

Optogenetics is a modern technique that uses light to stimulate the activity of neural pathways and can provide insights into individual neural pathways within complex circuit systems.

As more mechanistic data is gathered, we may be able to modify the activity of specific pathways, and this could be beneficial for developing new therapeutic approaches.

Dr. Bénédicte Amilhon is an assistant professor at Université de Montréal, and Principal Investigator for a project that examines sex differences in specific neural circuits - serotonergic circuits - that regulate anxiety. This project is supported by Brain Canada Foundation, the Azrieli Foundation, and Health Canada through the Future Leaders in Canadian Brain Research grant.

Mind Over Matter[®] (MOM) interviewed Dr. Amilhon to learn more about her project and its contributions to our knowledge of anxiety disorders.

MOM: Can you tell us more about what you are studying and the methods that you are using?

Dr. Amilhon: Generally speaking, compared to other research domains like physics and mathematics, neuroscience is quite young. One of the reasons is because in the past, we had not developed the powerful tools to be able to study the brain in a high level of detail, and precisely probe the roles of the identified circuits.

To understand intricate circuits in animal models and the differences between sexes or between individuals in relation to specific behaviours is an important first step, or preclinical step.

Our project is trying to understand the mechanics of the brain, but not the brain as a whole, a very specific population of neurons - serotonergic neurons - and their connections in the brain. We are really trying to pinpoint a subpopulation of neurons that release serotonin in a particular region of the brain, the ventral hippocampus, that we know is important for anxiety.

WE ARE USING OPTOGENETICS, BEHAVIOURAL STUDIES, AND OTHER METHODS TO STUDY HOW A SMALL GROUP OF NEURONS INFLUENCE ANXIETY LEVELS DIFFERENTLY IN MALES AND FEMALES. (=)

WHAT IS THE DIFFERENCE BETWEEN FEELING ANXIOUS & AN ANXIETY DISORDER?

Anxiety is a state of arousal in response to a perceived threat that has emotional (e.g., apprehension), physiological (e.g., sweating, racing heartbeat, muscle tightness), and cognitive components (e.g., worrying). Feeling anxious is considered part of normal, healthy functioning and is linked to the "fight-or-flight" stress response.

Mild levels of anxiety can be helpful and protective, by alerting us to danger and motivating us to pay attention. For instance, if you feel anxious before a test or presentation, you may work harder to be prepared. If you feel anxious when coming down a steep hill, you may pay closer attention to each step so that you do not slip and fall.

When anxiety is persistent or interferes with normal functioning, it becomes pathological.

An anxiety disorder is when your arousal response is disproportionate to the threat or situation and disruptive to daily function: all stimuli become arousing and overwhelming.

Essentially, anxiety becomes an anxiety disorder when too many things are perceived as very important and draw your attention when they should not, or too many things are perceived as threatening when they should not be threatening.

There are several types of anxiety disorders like social anxiety disorder and separation anxiety disorder, each with specific clinical characteristics and triggers. Symptoms common to a range of anxiety disorders include insomnia, excessive fear, and panic attacks. Serotonergic neurons are nerve cells that use the hormone serotonin as a neurotransmitter. Serotonin plays a large role in mood in general, and anxiety states in particular. As such, many anti-anxiety and anti-depressive medications act on the serotonergic system.

Because mice and humans respond similarly and show a reduction in anxious behaviours when certain medications like anxiolytics, benzodiazepines, or SSRIs are administered, mice provide a good model for studying anxiety.

As you can't give animals questionnaires about how anxious they feel, we get behavioural readouts of what we interpret as different anxiety levels in relation to environments that are potentially threatening.

MOM: How do you study the behaviour of mice and explore sex differences in anxiety levels?

Dr. Amilhon: Mice have a natural tendency to explore new environments. When you observe mice moving around, you'll notice that they tend to stay in more secure areas like dark corners and will rarely wander into the open areas.

We exploit this natural tendency to explore in a lab setting where some parts of the environment are more potentially threatening than others. Darker, more confined areas are perceived as less threatening, and brighter, more exposed areas are more threatening.

One way that we assess levels of anxiety is to observe how many times during a fixed period, like ten minutes, a mouse will enter a potentially threatening area and how long it will stay there. We use this information to estimate overall levels of anxiety and use the same test for male mice and female mice.

As part of our research, we used optogenetics to manipulate the activity of a specific subpopulation of serotonergic neurons for male and female mice and observed different behaviours.

Female mice seemed to show more risk assessment and enter less into the open areas. But male mice did not change the number of times they were out in the open areas.

MOM: How can mechanistic research translate into therapeutic targets?

Dr. Amilhon: The number of drugs that we have for anxiety disorders and their efficiency is not optimal. Relative to medications for other types of disorders, development of medications for mood disorders has been very slow despite their prevalence.

What is motivating this research is that we need to understand the system and how it works precisely. We are gathering fundamental information about the mechanics of the brain.

At some point in the future, we might be able to say, "Now that we know that this brain pathway plays this role in modulating anxiety, let's go look at patient data. Let's go investigate specific types of receptors or markers that we could change to modulate this specific brain pathway."

You need to start with the mechanics of the brain to then think of new therapeutical targets and new ways of approaching and pursuing treatment for anxiety disorders.

MOM: Could learning about specific brain pathways involved in anxiety disorders be helpful for other brain conditions where there are known sex differences?

Dr. Amilhon: You must be open-minded in science and neuroscience because you can find useful information in research domains that are quite different from yours. I hope that whatever we're doing in the lab in terms of neural circuits and anxiety might spark new ideas or catch the attention of someone that is working in another field of research so that they take a new perspective on their own research.

Any information is valuable and informative outside its own field of research. Many brain diseases show sex differences in prevalence. I hope that what we're finding in relation to anxiety might be helpful and informative for other types of neurological diseases.

Women's health and the mechanics of the female brain have really been overlooked in the past, but women's health is important because 50% of the world's population is female. Society is changing, and this parallels changes in our research culture and the way we think about scientific problems.

MOM: What final thoughts would you like to share with our readers?

Dr. Amilhon: We need to remember that research takes a long time. Great discoveries do not come exactly when or where you think they will come from. Science is curiosity driven and something beautiful that can have impacts on fields that you did not think of initially.

wave of recent scientific discoveries is changing our understanding of Alzheimer's disease (AD) and other dementias and pointing the way toward earlier, more precise diagnosis and treatment.

Up to 30% of people who have been labelled as having Alzheimer's disease are misdiagnosed. ⊙

Telltale Sign

ADVANCES IN DIAGNOSING ALZHEIMER'S DISEASE

This startling statistic is according to the "World Alzheimer Report 2021" from Alzheimer's Disease International. But what does it mean?

That estimate is based on research that compares health records of individuals who were diagnosed with AD while living and the results of post-mortem brain autopsies. In one study, for example, Canadian researchers examined more than 1,000 people in the (U.S.) National Alzheimer's Coordinating Center database, whom teams of specialists had followed for many years before death.

The research, which was published in *Alzheimer's & Dementia* in July 2016, found "the error rate is approximately 22%," said Dr. David Munoz, a neuropathologist at St Michael's Hospital in Toronto, and one of the study co-authors. "That was divided into almost equal categories of 11% false positive and 11% false negative."

In other words, in half of these cases, the individuals' brain tissue lacked the deposits of two abnormal proteins – amyloid and tau – that are hallmarks of AD. Instead, their brains showed evidence of other types of dementia.

The others had been diagnosed with other forms of dementia, but samples of their brains did contain the amyloid plaques and tau tangles considered characteristic of AD.

It's also worth noting that if the brain of a person diagnosed with AD showed evidence of both it and another form of dementia - vascular dementia, for instance - "that was considered a correct diagnosis," Dr. Munoz explained, since this type of "mixed pathologies" is common.

This discrepancy is largely due to the way that AD has traditionally been diagnosed.

"The diagnosis was what we call clinical," said Dr. Howard Chertkow, a cognitive neurologist, Chair in Cognitive Neurology and Innovation, and Director of the Kimel Family Centre for Brain Health and Wellness at Baycrest in Toronto.

This usually involved a history, physical exam, and tests to evaluate thinking, learning, and memory, "supported by blood tests to look for reversible cases, like low thyroid, and supported by brain imaging, so you didn't miss a brain tumour," Dr. Chertkow explained.

"The diagnosis of Alzheimer's was made when there was a

progressive dementia, with no other clear explanation, like a problem in the blood, or an infection."

Dr. Michael Borrie, a geriatrician and Medical Director of the Aging Brain and Memory Clinic at St. Joseph's Health Care London: Parkwood Institute, and an investigator with the Lawson Health Research Institute's Cognitive Clinical Trials Group, compares the process to trying to detect specific problems in a used car by driving it and listening for certain noises.

A CLEARER PICTURE

OVER THE LAST DECADE, HOWEVER, SCIENTISTS HAVE DEVISED METHODS OF DETECTING THE PRESENCE OF AMYLOID AND TAU ABNORMALITIES IN LIVING PEOPLE.

"Probably the most important two developments have been (testing of) cerebral spinal fluid, and the possibility of detecting amyloid with a PET scan," of the brain, said Dr. Munoz.

Testing of a sample of the cerebral spinal fluid (CSF, which is obtained via spinal tap) can detect changes in the levels of so-called biomarkers for AD – specific forms of amyloid and tau.

According to a 2022 report by the Canadian Agency for Drugs and Technologies in Health (CADTH) on emerging technologies for early diagnosis of AD, "in the CSF, amyloid-beta1-42 decreases throughout the course of the disease, and T-tau and P-tau181 increase." (T refers to "total" and P to "phosphorylated.")

CSF testing can help rule out AD in people with results in the normal range. It can be useful in some other circumstances, such as identifying AD in people with atypical presentations or symptoms.

PET imaging can be done to look for accumulation of either amyloid or tau in the brain. Before the scan, an individual is injected with a dye that will bond to the protein in question.

Areas where the protein has accumulated in the brain will "light up" on the image. "We know now that if the (amyloid) PET scan is negative, the patient cannot have Alzheimer's," said Dr. Munoz.

However, if the scan is positive, it does not mean the patient does have the disease, he added. That's because "someone could have a significant buildup of the amyloid protein, but not have dementia," said Dr. Sarah Main, research scientist for the Alzheimer Society of Canada and a research associate at the Brain and Body Lab at the University of Waterloo.

BASED ON THE RESULTS OF AUTOPSY STUDIES, IT'S ESTIMATED THAT MORE THAN 25% OF COGNITIVELY NORMAL OLDER PEOPLE HAVE SUCH AMYLOID DEPOSITS - THEIR BRAINS ARE SOMEHOW ABLE TO CONTINUE FUNCTIONING WELL DESPITE DAMAGE WROUGHT BY THE PROTEIN.

Consequently, PET scanning is not suitable for people who don't have dementia symptoms. Expert guidelines from the 5th Canadian Consensus Conference on the Diagnosis and Treatment of Dementia do not recommend routine screening in asymptomatic individuals – even those with risk factors – with either PET or cognitive testing.

As well, the consensus report discourages, "the use of amyloid and tau imaging without memory decline, outside of the research setting."

Currently, in Canada, CSF testing and amyloid PET scans are mostly limited to use in research, and specialized memory clinics. (CSF testing is only done by one Canadian lab and is not covered by all provincial health plans; and the majority of Canada's 57 PET-CT scanners, which are concentrated in urban centres, are primarily used for oncology. "In some places in Canada, it's impossible to get a scan," noted Dr. Chertkow.)

IS IT AD?

These tests are just two of the numerous advances that are revealing a much more nuanced picture of AD and other dementias. But they are invasive or hard to get.

"If you ask do all the people with what we've been calling Alzheimer's disease in the clinic over the past 30 years have amyloid in the brain, we can now answer that question much more precisely," Dr. Chertkow said, thanks to research involving PET scanning.

There was a big study called IDEAS in the U.S., which found that about one-third of patients labelled as having Alzheimer's did not have any amyloid.

These early findings from the Original IDEAS (Imaging Dementia-Evidence for Amyloid Scanning) study were published in *Alzheimer's & Dementia* in July 2017.

With this, and other technological developments, "we're beginning to understand there's a bunch of other conditions that produce the signs and symptoms of Alzheimer's disease,

CONDITIONS THAT CAN MIMIC DEMENTIA

"There are several conditions that can present like Alzheimer's that are perfectly treatable," said Dr. David Munoz, a neuropathologist at St. Michael's Hospital in Toronto. The following are among the most common.

Medication side-effects or interactions. A wide range of medications can impair thinking and memory, including older-generation antihistamines, sleep aids, opioid painkillers, tricyclic antidepressants, corticosteroids, and drugs used to treat urinary incontinence.

Mood disorders. Both anxiety and depression can cause cognitive symptoms, such as problems with attention and working memory, and difficulty making decisions.

Obstructive sleep apnea (OSA). This type of interrupted breathing during sleep can cause deficits in executive functions, attention, and memory. The good news? In a study involving 167 people with OSA, published in *Sleep* in January 2022, "cognitive function across all cognitive domains improved after six months of CPAP," (using a continuous positive airway pressure machine during sleep).

Thyroid dysfunction. A shortage or overabundance of thyroid hormone caused by an under- or over-active thyroid gland can cause problems with memory and concentration.

Vitamin B12 deficiency. Too-low levels of this vitamin (which is primarily found in animal foods) can cause difficulty in thinking and reasoning as well as memory loss, according to the Harvard Medical School blog. Since 10 to 30% of older people lose the ability to properly absorb the nutrient from sources like meat, Health Canada advises adults over age 50 to consume foods fortified with B12, or take a supplement to meet their needs. The recommended daily allowance is 2.4 micrograms.

but chemically they're different when we look at the brain," Dr. Chertkow explained.

COVID-19 & COGNITIVE DECLINE

A large-scale study from the U.K. highlights the detrimental effects certain lifestyle factors can have on brain function in older adults. Researchers analyzed results of tests taken by 3,142 participants in the long-term PROTECT study, comparing results collected prior to COVID (March 2019 to February 2020), to those collected one and two years later.

Strikingly, cognitive function and working memory in older adults declined faster in the first year of the pandemic (when lockdowns took place), regardless of whether they had been infected with the virus. The paper was published in *The Lancet Healthy Longevity* in November 2023.

In a comment on that study, in the same journal issue, Dr. Dorina Cadar, Director of the Cognitive Epidemiology, Dementia and Ageing Research lab at the University of Sussex in the U.K., wrote that, "the study also highlights reduced exercise, alcohol use, depression and loneliness as key risk factors that affected the rates of cognitive decline in the older population during the COVID-19 pandemic."

WITH GREATER CHEMICAL PRECISION, WE'RE REALIZING WE WERE LUMPING TOGETHER PEOPLE WHO HAD DIFFERENT PROTEINS IN THEIR BRAIN CAUSING THEIR COGNITIVE IMPAIRMENT.

Until very recently, however, this knowledge, "wouldn't have made a difference to your treatment," Chertkow noted. (Arguably, however, early diagnosis could nonetheless offer valuable time to find support, and plan for future care.)

GOING BEYOND SYMPTOMS

The landscape is changing, however, with the arrival of the first "disease-modifying" drugs for AD. Unlike older AD drugs, which can only manage symptoms, the newer generation drugs use specific antibodies that can remove amyloid from the brain.

By January 2023, the U.S. FDA had approved two anti-amyloid drugs specifically for patients with mild or early dementia; however, they're not yet available in Canada.

But there has been an update on this front. Biogen, the

co-developer of both of these drugs, announced in late January 2024 that they were halting the development and commercialization of one of them: Aduhelm (aducanumab).

The company said in a press release that they made this decision to free up more resources for the other medication, Legembi (lecanemab), and to develop different AD treatments, not because of safety or efficacy concerns with Aduhelm.

Despite the fact these anti-amyloid medications only modestly slow memory and thinking decline in people with early AD, they represent a significant turning point, because it is now possible to narrow down who they could potentially help.

"If the patient does not have Alzheimer's disease, these drugs pose a risk of complications without any benefit," Dr. Munoz said. "On the other hand, if you fail to make the diagnosis, then the individual misses the opportunity," to benefit from treatment.

Given their limited benefit and significant cost – approximately US\$26,000 to US\$28,000 – these anti-amyloid drugs may not have an enormous impact in themselves.

What's most promising about them is that with tests like CSF, it's now possible to objectively measure their effects, which could prove particularly valuable in clinical trials in the future, not just of candidate drugs but non-drug therapies, too.

"These things are going to help us find out which interventions, or combinations of interventions, are helpful and start to align these lifestyle interventions with (how they are) modifying the underlying biochemistry," said Dr. Borrie.

Similar advances may be on the horizon for other forms of dementia. For example, "we are starting to see publications of new biomarkers for Lewy body disease," Dr. Borrie said. While there are no treatments for LATE as yet, "they're just figuring out a blood test for that," noted Dr. Chertkow.

"For people with just a tauopathy, there are experimental treatments against tau," he said. "We're transitioning into a time over the next ten to 15 years where we'll have potentially disease-modifying drugs targeting these different proteins. Then it will make a big difference, with people being diagnosed at this level of precision."

THE REAL GAME-CHANGER WILL BE BLOOD TESTS, WHICH HAVE NOT ARRIVED IN CANADA OUTSIDE OF RESEARCH.

Dr. Chertkow continued, "It's predicted that within two to three years, blood tests will be available in Canada" for AD. Even now, "blood biomarkers in research are redefining the diagnosis of underlying Alzheimer's disease in people with mild symptoms, or even those with no symptoms but a strong family history who are at risk of dementia in the future," Dr. Borrie said. "The blood biomarkers will also be important for following treatment."

HOW MACHINE LEARNING & LIFESTYLE CHANGES CAN HELP

According to Dr. Borrie, another area of research that holds promise for early detection of mild cognitive impairment and dementia is machine learning. A project at Baycrest that offers a free, evidence-based brain health assessment called Cogniciti "has about 130,000 people who have taken the test," he said.

"If you get repeated measures over time, you can analyze many data points and possibly see subtle changes and patterns of different trajectories." In the meantime, other research findings point to immediate steps people can take to improve their brain function and stave off or at least slow cognitive decline.

For example, "a study came out from Finland in 2015 that had people with two or more risk factors for cognitive impairment and randomized them to the treatment arm - which was exercise, mental stimulation, control of vascular risk factors, and dietary education - versus just giving people advice," said Dr. Borrie.

"Both groups improved, but the people who got the more intensive program did better." For instance, compared to the control group, participants in the intervention arm saw a 40% greater improvement on complex memory tasks and 83% greater improvement on tests of executive function (complex planning and thinking skills).

The results of this trial, dubbed FINGER (Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability), were first published in *The Lancet* in March 2015.

There's even evidence that this kind of intervention can bolster brain function. "Dr. Montero-Odasso, a geriatrician in our division who runs the Gait and Brain Lab, recently published results from the SYNERGIC Study, where they've shown people with mild cognitive impairment can improve their cognitive performance using exercise and mental stimulation." Dr. Borrie said. (The study appeared in the July 2023 issue of *JAMA Network Open*.) "That's really powerful - as powerful as any drug option."

•••• People can be doing things that might alter the trajectory of decline.

The measures may seem familiar - the same factors are linked with a reduced risk of developing dementia. Regular exercise appears to be the most powerful, said Dr. Munoz, "probably because it maintains the health of blood vessels." Poor blood vessel health can lead to damage that can cause vascular dementia, which commonly overlaps with and can accelerate the progress of AD.

Other non-drug strategies Dr. Borrie recommends include eating a Mediterranean-style diet, staying socially active, engaging in mentally stimulating activities, restorative sleep, "and alcohol reduction or cessation," he said. "Anything above two standard drinks per week increases the risk of all kinds of different conditions."

Maximizing managing other vascular risk factors is also crucial, he added. This includes smoking cessation as well as recognizing and treating medical conditions, such as "hypertension, hyperlipidemia, diabetes, and atrial fibrillation," Dr. Borrie said.

Detecting such treatable risk factors is one reason to see your doctor if you notice changes in your memory that affect your daily functioning, such as impaired work performance, "forgetting meetings, forgetting codes, or not being able to remember seven digits at a time," Dr. Borrie said.

A CHECK-IN WITH YOUR DOCTOR ALSO PRESENTS THE OPPORTUNITY TO PICK UP AND ADDRESS OTHER POTENTIALLY REVERSIBLE CONDITIONS THAT CAN CAUSE DEMENTIA-LIKE SYMPTOMS.

"Some people dismiss memory impairment because they think it's part of normal aging," said Dr. Borrie. (And indeed, according to the "World Alzheimer Report 2021," in highincome countries like Canada, an estimated 60% of people with dementia are undiagnosed.) He urges people to take potential warning signs seriously. "Try to get a diagnosis earlier, and address those risk factors that need attention."



DIGITAL TECHNOLOGY DESIGNED

WITH & FOR OLDER ADULTS

There was a time not so long ago when Paul Lea could not step outside his door without being overcome with fear. In 2008, he suffered a massive stroke, which was followed by a diagnosis of vascular dementia two years later. It left him confused and unable to leave his apartment unaccompanied because he feared getting lost.

"I'd panic when I'd go outside and go right back in."

"For six years, life was hell. My daughter had to take time from her life to basically teach me how to live. I didn't go out," Lea told Mind Over Matter[®].

Then he met Ron Beleno. Beleno spent years as the principal care partner for his father, and, in the process, learned all about how technology could assist both care partners and people with dementia.

"He was my mentor. ... He introduced me to the tech that could help me," said Lea.

Through Beleno, Lea became involved with AGE-WELL, a Canadian research network that supports developing and deploying technologies that support people as they age. Lea learned how technology could help overcome his challenges. It changed his life. Now, he no longer fears going outside, confident that technology loaded on his phone will ensure that his door locks behind him, that he won't get lost, and that he can easily connect with his daughter to assure her he is OK.

(Technology) gives me freedom and peace of mind.

He also uses an app called MAXminder, which reminds him when to take the seven to eight daily medications he is prescribed, a common concern among people dealing with cognitive decline.

"(Without it), I think I would get confused about my medications and when I'm supposed to take them."

MAXminder is one of dozens of innovations developed with the help of an AGE-WELL grant.

It came to be thanks to Drs. Jeffrey Jutai and Virginie Cobigo of the University of Ottawa, who brought in tech developer Dinis Cabral to design a reminder app, hoping to improve the products already on the market.

"Most of them were not designed for people with cognitive

impairment who might struggle with technology," Mr. Cabral, the CEO of JLG Health Solutions, told Mind Over Matter®.

WE NEEDED SOMETHING STRAIGHTFORWARD, SUPER SIMPLE. THERE COULDN'T BE A LOT OF BUTTONS ON A SINGLE SCREEN, JUST ONE OR TWO, WITH LARGE ICONS AND FONTS FOR PEOPLE WITH WEAKER VISION.

Crucially, early versions of MAXminder were tested with people with cognitive issues, like Lea, who provided valuable feedback on how to make it work for those who would actually be using it. It also has a care partner component, which helps them ensure that their loved one is keeping up with their meds.

Mr. Cabral says that once people start using the app, they like it and are prepared to set aside their pill boxes and calendars. But the tricky part is getting them to try.

"Technology is going to be important for helping people as they grow older, and there's a lot of technology out there. One of the big challenges for doing this is how do we get the technology into the hands of older adults, how do you get them to start using it, so they can really see the value of what it can do?" he said.

That is part of the mission of Dr. Alex Mihailidis, AGE-WELL's Scientific Director.

"There are significant opportunities here," he said in an interview with Mind Over Matter[®].

AGETECH IS NOT A REPLACEMENT FOR PEOPLE, BUT IT'S AN IMPORTANT TOOL IN THE TOOLBOX TO SUPPORT HEALTHY AGING. IT CAN HAVE A SIGNIFICANT IMPACT ON THE LIVES OF OLDER ADULTS AND THEIR CAREGIVERS.

Dr. Mihailidis, an engineer, first became interested in this kind of technology when he was in grad school at the University of Toronto. A colleague told him about the challenges of caring for a spouse with early-onset dementia.

"He said, 'Wouldn't it be great if tech could help?"

That was the start for him, and many others have jumped aboard. In less than a decade, the AgeTech sector has grown dramatically in Canada, with AGE-WELL supporting about 65 startups.

"We've come a long way. We started from being a country with

basically no AgeTech industry whatsoever. Our startups were leaving to go to the U.S. Now we have a small but growing sector," said Dr. Mihailidis.

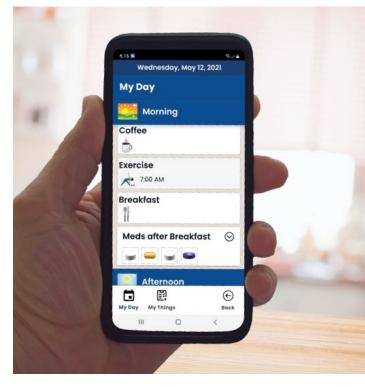
He is involved on many levels, including co-leading the development of new standards for long-term care (LTC) homes by the CSA Group, a reaction to the heartbreaking loss of life during the COVID-19 pandemic.

The new standards include recommendations to expand the use of technologies in the LTC sector, with such innovations as a device that allows a single staff person to safely transfer a resident to a stretcher from a bed or systems that can more effectively monitor the vital signs of people with severe dementia. Innovations that can ease the burden of overworked staff.

Along with reminders and tech support in the home, Dr. Mihailidis says that artificial intelligence may soon be able to predict when someone is experiencing cognitive decline by analyzing changes in how they move around their home.

While they represent important advances, developing sophisticated monitoring systems raises privacy issues. Part of AGE-WELL's work is to examine the policy implications.

"This type of tech may not be for everyone," said Dr. Mihailidis. "Some people don't want to use it, while others will be willing to accept it because the alternative may be needing to leave their homes." →



AGETECH'S BENEFITS ARE NOT ONLY FOR THOSE DEALING WITH COGNITIVE DECLINE BUT CAN ALSO MAKE A BIG DIFFERENCE IN THE LIVES OF PEOPLE WITH PHYSICAL CHALLENGES.

Betty Faulkner has coped with essential tremors for most of her life. They started in her mid-20s and grew progressively worse as she aged. Now, at 78, she shakes all over. People often mistake it for Parkinson's. Essential tremors are not lifethreatening, but they are life changing.

"You can't carry a glass of water, you cut yourself, and I can't tell you how often I've stabbed myself in the eye while putting on makeup," Faulkner told Mind Over Matter[®] from her home in St. Albert, Alberta.

She had a severe reaction to medications, so they were not an option. Instead, she did her own research online about assistive devices, which brought her to an AGE-WELLsupported startup called Steadiwear, which was developing a glove that stabilizes hand tremors.



In 2020, she got on the line with the creators in Toronto, who told her the Steadiglove was still in the early stages of design, but they agreed to send it to her to try. She found it "big and clunky" but also effective.

"It made such a difference," said Faulkner. "It doesn't stop (the tremors) completely, but it was enough to get back to normal life. It gave me back some sense of normality."

Faulkner advised the developers to work toward a smaller, more streamlined version, which they did with the next iteration. Now, she is excited to soon receive the latest generation of Steadiglove, which incorporates her feedback.

"Tech is really helping people get back to living a normal life."

The future of homes for older people is being previewed at a replica "smart apartment" at Ottawa's Bruyère Research Institute. A team co-led by Dr. Frank Knoefel, a physician in the Bruyère Memory Program, is testing various sensor-based smart technologies that can help older adults live independently and safely.

The team, funded partly by AGE-WELL, uses the acronym SAM3 (Sensors and Analytics for Monitoring Mobility and Memory). They seek to go beyond the smart home applications that are already widely available (think Alexa).

THE CONVENIENT AND FUNKY TECHNOLOGY IS BEING DEVELOPED AND BEING SOLD. WE'RE TRYING TO MAKE IT SOCIALLY RESPONSIBLE AND MAKE A DIFFERENCE IN PEOPLE'S LIVES.

The researchers have developed systems that can remind people that it is time to eat or advise someone with dementia who had gotten up in the night that they should go back to bed or sound an alarm to wake a care partner if they are about to wander outside. Where the innovations need to improve is in guiding someone with cognitive decline in more complicated tasks, such as making a meal.

"There are technological issues that are far from solved. Human behaviour is extremely complex," said Dr. Knoefel. "Even the Amazons and Googles, with very significant financial resources, have challenges."

But AgeTech is already transforming lives like Lea's. From the man fearful of leaving his apartment, he is not only living independently but has become an advocate for people living with dementia and a tester of new technologies.

For him, "the potential is unlimited." 🌑

How Old Are You Now?

BIOLOGICAL AGE VS. CHRONOLOGICAL AGE

our chronological age increases at a steady pace for every trip around the sun. However, your "biological age" may speed up or slow down depending on how you live your life.

BIOLOGICAL AGE REFERS TO AN ESTIMATE OF HOW OLD YOU ARE ON A CELLULAR LEVEL AND DEPENDS ON COMBINATIONS OF GENETICS, LIFESTYLE, AND THE ENVIRONMENT THAT YOU LIVE IN.

As you move through adolescence into young adulthood, the pace of aging changes and your chronological age and biological age diverge.

Everyone knows that you cannot choose your parents and control the genes that you inherit. But scientists have learned that there are behavioural and environmental factors under your control that can play a fundamental role in how your genes work (gene expression) and subsequently, your biological age.

Lifestyle and the environment alter gene expression over time through cellular processes known as epigenetics, and "epigenetic clocks" are modern tools that allow us to study those changes to tell us about biological age.

From countless studies on lifestyle factors, we know that the most protection from healthy habits occurs when they're

adopted and sustained from a young age. But which habits will play the biggest role in keeping your cells young, and what's the optimal "dose" for each lifestyle change? In the future, epigenetic clocks may help to answer these questions.

EPIGENETIC CLOCKS

To learn more about epigenetic clocks, Mind Over Matter® interviewed Dr. Calen P. Ryan, a research scientist at the Robert N. Butler Columbia Aging Center at Columbia University Mailman School of Public Health.

"The processes of life result in damage to the molecules inside our cells. Over time we believe that this damage accumulates, first affecting the cells, then the tissues that are made up of those cells, and eventually our organs, leading to the many diseases and declines that we associate with aging," said Dr. Ryan.

Epigenetic clocks are based on a process called DNA methylation (DNAm) and allow researchers to predict and study the course of aging and aging end-points while an individual is still alive.

One approach to developing an epigenetic clock, called supervised machine learning, involves creating a statistical model from predictable epigenetic variation in tissue samples and then testing the model. \bigcirc In 2013, Dr. Steve Horvath developed an epigenetic clock to predict chronological age using samples from 51 different tissues and cells and documented his findings in *Genome Biology*. Over the last decade, this clock has been used to examine many different outcomes and remains one of the most well-studied to this day.

Once a clock is trained and tested, it can then help to study specific age-related outcomes. Some of the earliest clocks were devised to predict age itself, but over time, have evolved to quantify the pace of biological aging and mortality and the onset of disease.

HOW CAN WE USE EPIGENETIC CLOCKS?

Epigenetic clocks have proven to be powerful tools that can provide insights into age-related phenomena that arise in concert with predictable changes at the cellular level. For example, it turned out that epigenetic clocks trained to predict chronological age were useful for studying biological age.

WHEN A PERSON'S CHRONOLOGICAL AGE DID NOT CORRESPOND WITH THEIR PREDICTED BIOLOGICAL AGE, IT SUGGESTED THAT THEY WERE AGING FASTER THAN EXPECTED AND MIGHT BE AT HIGHER RISK FOR SOME DISEASES OF AGING.

Soon, researchers realized that predicting chronological age wasn't the right goal and started using the same molecular markers and statistical tools to predict morbidity and mortality, even before clinical outcomes manifested. This allowed researchers to predict people's biological age and potential health outcomes without extensive follow-up of participants.

In a review of epigenetic clocks published in *American Journal* of *Human Biology* in 2020, Dr. Ryan described nearly a dozen well-researched epigenetic clocks that can predict a wide range of diseases and risk factors at the population level, like cardiovascular disease, Type 2 diabetes, and chronic obstructive pulmonary disease (COPD) with a high level of accuracy.

Newer epigenetic clocks are looking at capturing variations in susceptibility to the effects of lifestyle factors to show, for instance, whether being sedentary will take a larger toll on predicted age for some groups versus others.

"One of the most surprising things about these clocks is that blood-based measures can tell us about biological aging in

organs all over the body," explained Dr. Ryan. To reflect aging in different organ systems more effectively from blood, a new Systems Age clock has been developed at Yale University.

DNAm can be analyzed from previously stored samples (e.g., dried blood spots), which allows scientists to re-examine previous studies, collect and bank samples for future use, and even pool data with new information to advance our understanding of aging.

For example, a recent study published in *JAMA Network Open* in 2024 examined DNAm from blood samples collected from cohorts of participants as part of the Framingham Heart Study. The Framingham Heart Study is an ongoing cohort study that has followed generations of participants, with enrollment of the first group beginning in 1948.

Dr. Ryan was part of this research team interested in looking at educational mobility between generations - the educational attainment of parents versus their offspring. Results showed that participants who were more educated than their parents tended to have a slower pace of aging as measured by the DunedinPACE epigenetic clock and lower mortality risk.

Epigenetic clocks can also be used as surrogate predictors to answer new questions as our knowledge advances.

We now have a tool that can go back through older data sets and be used to predict new measures.

> "If there was a study carried out five years ago when we didn't have a particular clock, or we did not measure something we're interested in, we might be able to use these methods to go back and estimate that clock or a surrogate measure without collecting new data. That vastly increases our ability to do science and answer cutting-edge questions," Dr. Ryan added.

STUDYING SEX DIFFERENCES USING EPIGENETIC CLOCKS

Epigenetic clocks provide insights into sex differences in lifespan. Between childhood and adolescence, male tissues begin to age at a different rate and show significantly advanced epigenetic age versus female tissues by early adulthood. This is consistent with males typically having a shorter lifespan versus females. In an innovative study that included pairs of male-female fraternal twins, researchers from the Gerontology Research Center at the University of Jyväskylä in Finland found that male twins had faster epigenetic aging when compared to female twins, and differences were larger in an older group of twins compared to a younger group of twins.

Published in *The Journals of Gerontology* in 2022, Kankaanpää and colleagues found that sex differences were partially explained by larger body mass index and higher rates of smoking among males.

Authors suggested that differences in sex hormones (i.e., estrogen and testosterone) and their action on tissues may also contribute to differences in epigenetic age. Further research is needed to better understand the roles and mechanisms of sex hormones on epigenetic aging.

LIMITATIONS FOR EPIGENETIC CLOCKS IN PREVENTIVE HEALTH CARE

If epigenetic clocks have such wide-ranging predictive capabilities, why aren't they used more often as a proxy measure for age and health risk, or used as a tool for preventive health care to motivate healthy habits?

First, epigenetic analyses are currently too expensive for many research studies and cost-prohibitive in public healthcare settings. Specialized instruments are required to examine genomes, quantify DNAm, and estimate epigenetic age.

These instruments are costly and technically challenging to use, which limits the number of research labs worldwide that do these types of analyses. Available approaches to derive and study DNAm, and methods to measure DNAm also require considerable staff time.

Dr. Ryan shared that his lab typically budgets US\$250 - US\$350 to analyze each sample. This means epigenetic testing for a typical study with 1,500 participants could cost around US\$500,000!

Though there are efforts to develop clocks that run at a fraction of the price, we don't yet know how such data could inform care in hospital and clinical settings or motivate individuals to adopt healthier habits.

Data from epigenetic clocks is most informative for population-level data and generally aligns with what is already known about lifestyle and environmental risk factors, particularly among middle-aged and older people. "We don't yet know how far back we can go and still get accurate estimates of how epigenetic age predicts health outcomes and mortality later in life," said Dr. Ryan. Another consideration is that the socio-demographic diversity of samples used to develop epigenetic clocks is presently limited. Dr. Ryan explained, "Broadly speaking, we have the most data on middle-aged and older people, particularly white Americans and Europeans, and this population is where we're best at predicting a range of outcomes."

We don't yet know whether existing algorithms used to predict aging outcomes equally applies for other age groups, like young adults, or for people living in other places and circumstances. In an article published in *Environmental Epigenetics* in 2023, Watkins and colleagues explained that because epigenetic clocks currently available have been derived from data with poor reporting of sociodemographic characteristics, this may introduce bias into the aging estimates and limit generalizability to diverse populations.

To illustrate, we have learned that sociodemographic factors like education and neighbourhood characteristics can affect DNAm via exposure to pollution or poor access to nutritious foods. It follows that epigenetic clocks calibrated to account for these characteristics may have better predictive capabilities.

THE BUSINESS OF EPIGENETIC TESTING

Epigenetic age testing entered the direct-to-consumer market only a few years ago, and today, more than a dozen companies offer these services. This process involves collecting your own samples (e.g., cheek swab, dried blood spot from a finger prick, or urine), sending it to a lab, and receiving tailored wellness reports with suggestions on what may help to slow down the aging process. The price of one-time testing ranges from about US\$250 - US\$500, and some companies even offer a monthly subscription so that you can have your estimated biological age tracked over time.

BEFORE YOU RUSH TO SIGN UP FOR EPIGENETIC TESTING, IT IS IMPORTANT TO CONSIDER THAT OUR KNOWLEDGE OF EPIGENETIC TESTING IS STILL RELATIVELY NEW, AND IT IS PRESENTLY BEST SUITED FOR STUDYING INFORMATION AT A POPULATION LEVEL.

You'll also need to consider whether having a report recommending healthy habits and avoiding unhealthy habits will motivate you to improve your lifestyle and sustain it over time. As a final thought, Dr. Ryan shared, "Epigenetic clocks are powerful tools that are changing how we study biological aging. But epigenetic age is just one piece of information in a constellation of other things and should be interpreted in the broader context of health measures."

All By yself

THE COGNITIVE HEALTH IMPACT OF CHRONIC SOCIAL ISOLATION

mong the many hard lessons learned during the pandemic was the impact of social isolation. It showed up most vividly in the heartbreaking stories of elderly people living in long-term care facilities who were cut off from their families. But it is a phenomenon that hurts people of all ages and in many ways.

Researchers have long believed that isolation early in life can have damaging long-term consequences, including an elevated risk of social anxiety disorder, which the U.S. National Institute of Mental Health defines as "an intense, persistent fear of being watched and judged by others. This fear can affect work, school, and other daily activities. It can even make it hard to make and keep friends."

Finding new ways of treating social anxiety disorder is a focus of Dr. Derya Sargin's work. The University of Calgary researcher is studying how social isolation among young people affects the brain at the cellular level.

"The brain is so central to our being and our functioning. My main goal is to understand how the brain functions so we can develop effective treatments. That's the main thing that draws me to this research," Dr. Sargin told Mind Over Matter[®].

Supported by a 2020 Future Leaders in Canadian Brain Research grant from Brain Canada, the assistant professor in the Faculty of Arts' Department of Psychology is conducting her research by undertaking detailed studies of the brain cells, or neurons, of mice.

Through this work, Dr. Sargin and her colleagues deprive rodents of regular social contact during adolescence and then observe them as they develop behaviours that roughly mimic social anxiety in humans. Already, her team has made an important and exciting discovery.

WE FOUND A GROUP OF CELLS THAT ARE CRITICAL FOR SOCIAL INTERACTION, AND WE ALSO FOUND THAT THE ACTIVITY OF THESE CELLS IS COMPROMISED WHEN ANIMALS ARE ISOLATED.

The next step for her and her team is to explore the possibilities of interventions. "We're studying how can we specifically target those circuits and improve social behaviour."

This project is one of three Brain Canada-funded studies exploring aspects of brain cell function in which Dr. Sargin leads or participates as a team member.

The second, co-funded by the Alzheimer's Association International Research Grant Program, focuses on serotonin, Alzheimer's disease (AD), and sex differences. Serotonin is a chemical released by neurons that is central to social, cognitive, and mood regulation. A severe loss of serotonin neurons has been seen in the early stages of AD, often before the disease is diagnosed.

THIS EARLY DISRUPTION IN THE BRAIN'S SEROTONIN SYSTEM HAS BEEN ASSOCIATED WITH SYMPTOMS LIKE MOOD CHANGES AND SOCIAL IMPAIRMENTS, WHICH CAN BE SEEN MUCH EARLIER THAN THE MEMORY DIFFICULTIES ASSOCIATED WITH AD.

While the contribution of the serotonin system seems to be critical in AD progression, scientists do not yet know why this disruption happens or how it may contribute to the progression of dementia.

She and her colleagues are using mouse models to study how serotonin neuron dysfunction affects the progression of the disease and whether stimulating serotonin circuits can improve behaviour. Exploring sex differences is a central part of the research.

"For example, we found that if you inhibit one neural pathway you can disrupt social behaviour with one sex but not the other. So that's why we're trying to delve into these specific circuits to characterize which is more relevant for which sex. Of course, it's very important in terms of coming up with treatment approaches for all genders," said Dr. Sargin.

Sex differences have historically been understudied, and she points out that studies that do consider them are more expensive because researchers need more lab animals.

"That's why organizations like Brain Canada, especially with their grants for early career researchers, have been critical for establishing our labs, for getting published and for doing the kind of research I want to do. I'm very grateful," she said.

Dr. Sargin is a team member of a third Brain Canada-funded study, which is also supported by Women's Brain Health Initiative (WBHI). It is led by Dr. Jonathan Epp, an associate professor in the Department of Cell Biology and Anatomy at the University of Calgary (who also happens to be her life partner).

We know that females with AD tend to exhibit faster cognitive decline than males. To better understand this trend, the study by Drs. Epp and Sargin aims to pinpoint potential mechanisms that may be involved.

Using a specialized imaging technique, they can observe the activity of a specific group of neurons in the brains of

female and male mice as the animals undergo a series of memory tests.

Through this testing, the researchers have observed that the activity of those neurons in females is impaired much earlier in the progression of AD than it is in males.

By stimulating or blocking this group of neurons with light, the researchers can increase or decrease their activity and observe its effect on the animal's behaviour. The effect is telling.

"Using light to stimulate these neurons allows us to enhance learning and memory function in the females and, likewise, if we go into the males and inhibit those neurons, we can impair memory to the same sort of extent that we see in the female mice," said Dr. Epp. "We think these neurons play an important role in the early cognitive impairments that are occurring in females."

Dr. Sargin says the implications are important: "If we can understand the underlying mechanisms, we can develop therapeutic interventions."

Dr. Epp echoed Dr. Sargin's gratitude for the funding support. "Looking back on the first six years of my career, I'm not sure how I would have done it without these grants from Brain Canada. They had such a phenomenal impact on getting this research done. I don't think we could have done it otherwise," said Dr. Epp.

"We are proud to support groundbreaking research projects like this one, which sheds light on critical sex differences in brain function. This work has the potential to significantly impact our understanding of diseases like Alzheimer's and pave the way for targeted therapeutic interventions," said Dr. Viviane Poupon, President and CEO of Brain Canada.

WBHI Founder and President Lynn Posluns added, "Their research into sex differences in the brain is exactly the kind of project WBHI was founded to support. They ask essential questions that have been neglected for far too long."

To learn more about Brain Canada and the research it funds, visit braincanada.ca.

Two superfood-packed salads to try this spring that will satiate the palate and protect your brain.

Brussels Sprout and Barley Salad with Lemon-Honey Vinaigrette

III SERVES 2 AS A SIDE OR STARTER ⊕ 30 MINUTES

INGREDIENTS

SALAD

- + 1 tablespoon grapeseed oil
- 1/2 cup roughly diced savoy cabbage
- + 1/4 cup cooked barley (Spelt, quinoa, or brown rice would make excellent substitutes)
- 2 Brussels sprouts trimmed and finely sliced with a mandolin or knife
- + 2 tablespoons roughly chopped dill
- 2 tablespoons lightly crushed toasted walnuts

- + 1 tablespoon of raisins
- + 1 teaspoon of capers, roughly chopped
- 1 tablespoon of crème fraiche or sour cream

DRESSING

- + 2 tablespoons of lemon juice
- + 2 teaspoons of Dijon mustard
- + 2 teaspoons of honey
- 2 tablespoons +
- 1 teaspoon of olive oil Salt and pepper to taste

Superfood Fact: High in fibre, vitamins K, C, and A, folic acid, but low in calories, Brussels sprouts are delicious, nutritious, and versatile.

INSTRUCTIONS

1. Heat a pan over medium high heat. Add the oil. When you can see thin wisps of smoke coming from the pan, add the cabbage. Spread out on the pan. Do not stir or toss. Allow the cabbage to caramelize deeply. It should look almost burned. Take off heat, cool on a tray and set aside.

2. Mix the cabbage with the rest of the salad ingredients together in a bowl except for the crème fraiche.

3. Make the dressing. In a bowl put the lemon juice, Dijon, and honey. Whisk together. Slowly drizzle in the olive oil, whisking all the while, until you have an emulsified vinaigrette. If it splits and you can see blotches of oil, this means you added the oil too fast. Don't worry, it will still taste good, it just will have slightly less desirable mouth feel.

4. Dress the salad with the vinaigrette and season with salt and pepper. It should be sour, sweet, and a little piquant from the mustard.

5. On a serving plate, place a dollop of crème fraiche. Spoon the salad over the crème fraiche and serve.



SERVES 2 AS A STARTER 30 MINUTES

INGREDIENTS

- + 2 tablespoons of skinned hazelnuts
- + 2 tablespoons of sunflower oil
- 4 3/4" slices of butternut squash, cut into rounds and peeled and seeded if needed
- + 2 tablespoons of butter
- + 2 3/4" slices of Granny Smith apple
- + 1 teaspoon of apple cider vinegar
- + salt
- + 1/2 a green onion, finely sliced
- + 10 large picked mint leaves

Superfood Fact: Butternut squash is rich in vitamins A, C, and B, folate, potassium, and fibre, contributing to optimal brain health.

INSTRUCTIONS

1. Heat a toaster oven or oven to 325°F and place the hazelnuts on a tray and roast in the oven for 10-15 minutes until just lightly browned. Let cool, place on a cutting board and crush with the bottom of small pot until broken into large chunks but not powdery. Set aside.

2. Put a large non-stick pan over medium heat. Add the sunflower oil. Place the squash rounds in the pan and let them cook for 4-5 minutes. You want them heavily caramelized, almost burned. Flip the squash over and repeat the cooking process on the other side. Once cooked, remove from pan, cut in half and keep somewhere warm. If your pan is not big enough to cook all the pieces of squash at once, do this in batches.

3. Heat a small pan over medium high and add the butter. Once the butter starts frothing, keep a close eye on it and remove once the milk solids floating in the butter are a dark nutty brown. Remove immediately from the heat and place in a bowl.







Scan for more salads & brain-healthy recipes created by Haan **4.** Slice apple pieces into finger-width batons.

5. Assemble the salad: place the apple and the squash in a medium-sized mixing bowl. Coat with the butter and vinegar and season with salt. Taste for seasoning and add more vinegar or salt if necessary. Gently combine the remaining ingredients in the same bowl. Check for seasoning once more. Slide onto a plate and serve immediately.

MEMORY**MORSELS**

This edition's recipes are courtesy of Haan Palcu-Chang, a Taiwanese-Romanian, global, and award-winning chef.

For more recipes and the latest from our Featured Foodie, Haan Palcu-Chang, visit: memorymorsels.org

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66



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