

# DIMENSIONS

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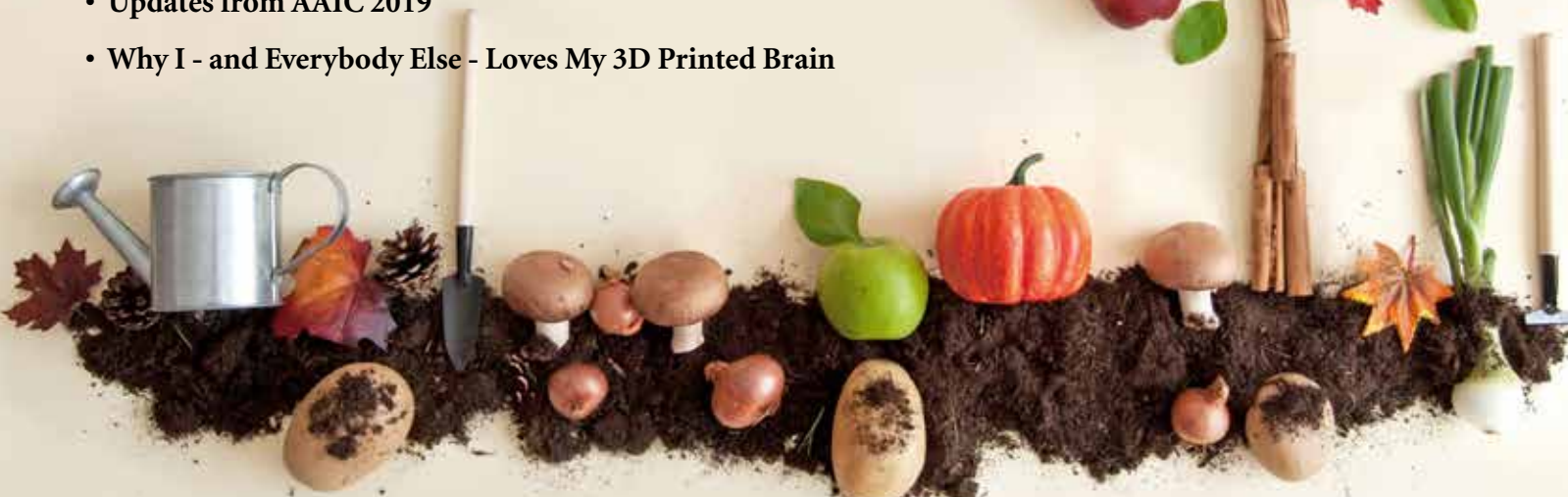
UW Memory and Brain Wellness Center

## FOOD FOR THOUGHT

Revitalizing Indigenous Knowledge about Healthy Eating

### In This Issue

- How TDP-43 is Changing Conversations about Alzheimer's
- The Cleansing Power of a Deep Night's Sleep
- S.O.A.R Program Takes People to New Heights
- New Models of Dementia Residences Around the World
- Updates from AAIC 2019
- Why I - and Everybody Else - Loves My 3D Printed Brain



## Hello Readers!

The UW ADRC and its associated clinical and educational programs at the UW Memory and Brain Wellness Center are pleased to bring you Dimensions for Fall 2019!

We hope this issue provides you with interesting reading material for the rainy days ahead. These pages feature new topics, including why researchers now consider improving sleep to be a mid-life intervention for dementia prevention, not-to-be-missed updates from the Alzheimer's Association International Conference 2019, and new faces at our Center. The interview with Valerie Segrest, a leader in the local tribal food sovereignty movement, is food for thought about healthy eating from a perspective you might not have heard before. For fun, read 'Why I - and Everybody Else - Loves My 3D Printed Brain', stories on outdoors programs at the MBWC, and poems from community members. As always, we hope you also hear an encouraging message about Alzheimer's disease and related conditions: persons living with memory loss and dementia have much to offer, strengths to work from, and wisdom to share.

We continue to be grateful for your interest and support of our work. The Ellison Foundation, the Richard M. and Maude Ferry Charitable Foundation, the Paul V. Martinis Estate, the Anderson Foundation, and the Sky Valley Whirlwinds, and other generous individuals and groups, make it possible for us to move faster in research and to reach out further into the community than ever before. We're all in with you. Happy reading!



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**DIMENSIONS** The University of Washington Alzheimer’s Disease Research Center (UW ADRC) is affiliated with the UW Medicine Memory and Brain Wellness Center (MBWC) and the Veterans Affairs Puget Sound Health Care System (VA). The UW ADRC has been funded by the National Institute on Aging since 1985 to facilitate cutting-edge research on Alzheimer’s disease and other neurodegenerative conditions that cause dementia. The UW ADRC focuses on Alzheimer’s disease biomarker research and advancing prevention methods and clinical treatment for dementia, particularly through precision medicine. The UW ADRC is also supported by the Friends of Alzheimer’s Research, the Ellison Foundation, and members of the public.

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# FEATURED PUBLICATIONS

## Neurology

**Individualized atrophy scores predict dementia onset in familial frontotemporal lobar degeneration. A. Staffaroni et al. *Alzheimer Disorders & Associated Disorders*, July 2019 // Kimiko Domoto-Reilly, Christina Caso, Walter Kukull**

Researchers recently made an important advance in characterizing a person's risk of familial dementia, a dementia syndrome directly linked to a specific marker in a person's genetic makeup, before symptoms arise. This research will help scientists identify those at risk early on, and help patients achieve the best possible outcomes by kickstarting interventions at the appropriate time point.

The study genetically tested 268 family members with a family history of frontotemporal lobar dementia (FTLD) and put subjects into categories based on whether or not they carried a pathogenic gene change. The researchers then used subjects' brain atrophy patterns and severity to develop a model that categorizes an individual into asymptomatic or demented cognitive status. The scientists found that their model was 90% accurate at categorizing mutation-carrying subjects, so they tested their model on a different group of subjects, to see if it could predict whether or not other mutation carriers without significant cognitive symptoms would later progress to dementia. Researchers created dementia risk scores based on degree of atrophy for the asymptomatic or questionably symptomatic participants, and they found that the score predicted the risk for whether or not the subject would go on to develop dementia over the next 5 years.

The UW ADRC has previously demonstrated that there is a wide range of timing of symptom onset within FTLD families. This research shows that individualized brain atrophy patterns may have strong potential for predicting timing of dementia onset, and that such techniques could be useful in guiding treatment for neurodegenerative disease.

## Precision Medicine Approaches

**Associations Between Depression, Traumatic Brain Injury, and Cognitively-Defined Late-Onset Alzheimer's Disease Subgroups. J. Bauman et al. *Molecular Psychiatry*, May 2019 // Shubhabrata Mukherjee, Emily Trittschuh, Mackenzie Moore, Susan McCurry, Wayne McCormick, Eric B. Larson, Paul K. Crane**

ADRC researchers have been working for years to study the nuance in clinical presentations of Alzheimer's disease-type dementia and define biological subtypes.

In previous work, ADRC researchers classified 4,050 Alzheimer's cases, from several major prospective cohort studies in the country, into specific groups based on their most prominent type of cognitive symptoms at the time of diagnosis (including memory, executive functioning, language, and visuospatial functioning). The study also found a particularly strong relationship between a particular variant of the APOE gene and risk for the memory loss subgroup. The APOE e4 allele is a strong risk factor for developing late-onset Alzheimer's for people with European ancestry.

For this study, the team investigated the occurrence of depressive symptoms and history of traumatic brain injury among these subtypes. They found that people with the memory subtype were less likely to report depression and restless sleep. The study found no differences in traumatic brain injury history across subtype groupings.

The discovery of these differences in risk for depression and restless sleep among these cognitive subtypes, along with their previous genetic findings, support the team's hypothesis that subgroups of clinical Alzheimer's disease have a biological basis. The group is now interested to further investigate the implications of restless sleep for dementia symptoms.

## Resilience and Risk

**Resistance and resilience to Alzheimer's disease pathology are associated with reduced cortical pTau and absence of limbic-predominant age-related TDP-43 encephalopathy in a community-based cohort.** C. Latimer et al. *Acta Neuropathologica Communications*, June 2019 // Caitlin S. Latimer, Nicole F. Liachko, Mitchell D. Kilgore, Laura E. Gibbons, Jonathan Henriksen, Martin Darvas, Kimiko Domoto-Reilly, Suman Jayadev, Thomas J. Grabowski, Paul K. Crane, Eric B. Larson, Brian Kraemer, Thomas Bird, C. Dirk Keene

'Resilience' is the term for a person who had a high level of Alzheimer's pathology in the brain, yet who stayed cognitively intact until death; while 'resistance' is a person who never develops any pathologic brain change. Previous UW ADRC research has shown that people were less likely to have been resilient during life if their brain tissue showed additional pathologies on top of the Alzheimer's disease hallmarks of amyloid and tau. These included vascular injury and Lewy bodies. This research study, which used autopsy brain tissue resources from the Adult Changes in Thought study, focused on a pathology that can appear in aging brains called TDP-43. They found that people who had been resilient or resistant to Alzheimer's disease pathology did not also show accumulations of TDP-43; yet almost all of the brains from age-matched people affected by symptoms of dementia during life did have TDP-43 pathology. This finding leads the team to suggest that TDP-43 undermines brain resilience and increases one's risk of developing dementia later in life, and it provides impetus to further development of biomarker tests for TDP-43 in living people, potentially as part of developing preventative treatments.

**For the full story, please flip to page 20 to read 'A Tipping Point: How TDP-43 is Changing Conversations about Alzheimer's Disease.'**

## Healthcare Economics

**Cost of Dementia in Medicare Managed Care: A Systematic Literature Review.** P. Fishman et al. *The American Journal of Managed Care* August 2019 // Paul Fishman, Lindsay White, Norma Coe, Paul K. Crane, Sungchul Park, Bailey Ingraham, Eric B. Larson

A recent systematic review that includes ADRC researchers found that most cost-analyses are backed by limited and dated evidence. Researchers identified and reviewed as many papers as possible from 1983 to 2018 that reported direct costs of older adults with Alzheimer's disease or related dementias in Medicare managed care plans.

While more and more people are enrolling in Medicare managed care, few papers report the care costs that individuals with Alzheimer's disease or related dementias can be expected to pay within these private health plans. Only a single study reports data less than 10 years old. These studies not only present out of date data, but also estimate annual costs for people with these forms of dementia with wide variability and use different study populations and methods. This makes comparisons between studies difficult, and relevance to policy less significant.

Medicare managed care enrollment is expected to continue to grow, and the cost of healthcare from individuals with Alzheimer's and related dementias is large and rising. This review suggests that research into the cost of these disorders within managed care needs to be more consistent, up to date, and detailed to provide more useful insights.

**\*Only UW-affiliated researchers and collaborators are listed**

## The Cleansing Power of a Deep Night's Sleep

How the Brain's Nightly Wash Cycle Protects Brain Health Over Decades

By Franklin X. Faust

Greek philosopher Aristotle once surmised that sleep helps the body filter its blood at the end of the day, sending dirty blood downwards and pure blood up to the brain. This idea echoes many early intuitions about the cleansing power of sleep. Two thousand years later, we know that getting good quality, consistent sleep makes for a clearer mind, while not getting enough puts you at a greater risk for many chronic medical conditions and age-related cognitive decline. It turns out the ancient minds had the right idea about sleep. Modern scientific approaches to understanding the brain's refreshing overnight processes could lead to a new preventative therapy for dementia.

The brain stays clean and operational thanks to the glymphatic system, the brain's biology of exchange. It jumps into action during sleep, acting like an all-in-one delivery and trash pick-up service for neurons. When you are deep asleep, cerebrospinal fluid in the glymphatic system rushes along right next to the brain's blood vessels, delivering key supplies while clearing away unwanted debris.

Some of this cellular trash is more or less benign, but some of these molecules are toxic and associated with neurodegenerative disease. Fortunately, the trash sitting outside of each cell is picked up by the same cerebrospinal fluid in charge of delivery. The glymphatic system then dumps the molecular trash back into the larger pools of fluid surrounding the brain, where it is cleared via waste disposal checkpoints. This elegant workflow of exchange helps keep the neurons of the brain supplied, clean, and functioning.

Back in 2012, Dr. Jeff Iliff, PhD led the team that initially defined the glymphatic system as the network of pathways that supports the clearance of waste from brain tissue during sleep. At the time, he was a postdoc at the Nedergaard lab at University of Rochester Medical Center. Now, as Professor in the UW Department of Psychiatry and Behavioral Sciences and Lead of the proposed UW ADRC Research Education Component, Iliff brings a greater focus on sleep's role in dementia risk to our Center. Since this study, we have learned much more about the glymphatic system's relevance to neurodegenerative disease and a good night's sleep.

Iliff's experiments on mice have found that the glymphatic system mediates the transport of Alzheimer's-associated proteins out of the brain, and that this process appears to slow as animals age and in the presence of vascular and traumatic brain injury. Research from several groups around the world has shown that this same kind of janitorial work is happening in the human brain as well.

"The advancements we've made in the past five years have given us some of the strongest evidence to date that what we see in animals may also be happening in humans," says Iliff. For example, researchers at the University of Oslo recently found that patients with dementia caused by normal-pressure hydrocephalus have been shown to have impairments in fluid movement through their brain tissue, suggesting that a weakened glymphatic system contributes to dementia in these patients. "When you're talking about a very fundamental biological process to brain function, its implications spread to many places and questions; it's just a matter of understanding the process well enough," says Iliff. He thinks that the glymphatic system will play an important role in future dementia research.

## **SLEEP, GLYMPHATIC CLEARANCE, AND DEMENTIA RISK**

One piece of the puzzle is how impaired glymphatic clearance can lead to dementia. “Proteins implicated in neurodegenerative diseases exist in healthy people, but they are naturally produced and removed at near-equal rates,” says Iliff. “When this balance is thrown off, these proteins can pile up, spread, and become a problem.” To study this balance, researchers at the Washington University in St. Louis have tagged the building blocks of these toxic proteins with safe radioactive labels, and infused them into human subjects. Scientists can then record how these building blocks appear and then disappear from the fluid surrounding the brain to measure how fast these toxic proteins are produced and cleared in aging and Alzheimer’s disease.

“These proteins might build up in two ways,” says Iliff. “They’re either produced too fast or removed too slowly.” Research shows that people with rare genetic mutations causing early-onset Alzheimer’s disease produce more disease-associated protein than the systems can clear. But the vast majority of Alzheimer’s cases are different. One study showed that in cases of the much more common sporadic late-onset version of Alzheimer’s disease, the rate of production doesn’t change, but the rate of clearance slows. Another study found this same pattern in older people without Alzheimer’s disease. These studies suggest that the slowed clearance of these proteins may be a root cause of diseases like Alzheimer’s.

New scientific clues suggest that issues with sleep may cause this slower clearance seen in aging and Alzheimer’s. Researchers found that losing just one night of sleep leads to an increase in amyloid beta, a protein in the brain associated with impaired neuron function and Alzheimer’s disease. An NIH study used positron emission tomography (PET) to scan the brains of 20 healthy participants after a full night’s rest and after 31 hours of sleep deprivation. The study found that the participant’s brains had about 5% more amyloid beta after that single night of sleeplessness. In light of two recent reports out of the Atherosclerosis Risk in Communities Study and the Framingham Heart Study, the connection between sleep and dementia is looking even more convincing. These studies have followed the health of young people for decades, and some of the participants who originally enrolled are now developing dementia. Researchers analyzed this gold-standard data and found that mid-life sleep disruption predicts cognitive decline later in life.

## **SLOW WAVE SLEEP AND THE AGING BRAIN**

Sleep is integrally tied to the brain’s essential biology of clearance and exchange. Recent findings in animals show that the bulk of glymphatic clearance occurs during deep sleep when slow wave activity is most abundant. “It’s well known that people sleep less and less, and more poorly as they get older,” says Iliff. “There is a particular depletion of slow wave activity as people age – so much so that many elderly don’t undergo much slow wave activity through the course of the night, even though they may be still sleeping six hours a night. In subjects with Alzheimer’s disease, sleep disruptions

are even more severe.” One of Iliff’s burning questions is why the slow wave activity of deep sleep would be the key to healthy glymphatic function.

His hypothesis has to do with what makes slow wave sleep so unique. During waking and during REM sleep, the brain’s activity is desynchronized as neurons connecting different parts of the brain fire in a cacophony of activity. But during slow wave sleep, the brain switches back and forth between brief periods of synchronous activity (called ‘up-states’) and synchronous inactivity (called ‘down-states’) about once every second. “We think that these oscillating periods of activity and inactivity may be helping to move water and salt through brain tissue, like waves over the surface of a lake,” says Iliff. If glymphatic “brain rinsing” is slowed or is given less time to run, as with the reduced amounts of sleep seen in people as they age, particularly slow wave sleep, this alteration might set the stage for the development of neurodegeneration. If people get less sleep as they age, and less slow wave sleep in particular, the brain’s glymphatic wash cycle is given less time to run. This slowed or decreased clearance might set the stage for the development of neurodegeneration.

This slowing of the brain’s custodial service may give toxic proteins a leg up, allowing them to spread through the brain unchecked and accelerate the worsening of cognitive symptoms. “Diseases like Alzheimer’s and Parkinson’s have a stereotyped progression. Protein aggregates accumulate in different parts of the brain as the disease progresses,” Iliff says. “An emerging idea in the field is these protein aggregates actually spread from cell to cell over time, moving through the space between the brain’s cells to affect other brain regions.” Iliff believes that the slowing of the glymphatic system’s cleaning process may influence how this spreading happens. Ensuring the glymphatic system works optimally could help slow neurodegeneration by flushing out proteins or chemicals in the spaces around the cells before they’re taken up into neighboring neurons.

## **EMERGING TREATMENTS FOCUS IN ON SLEEP**

Some scientists are working to develop new drugs to improve or restore glymphatic activity. Dr. Elaine Peskind, MD, Professor in the UW Department of Psychiatry and Behavioral Sciences and collaborator of UW ADRC, thinks that such a drug may already exist. She is studying prazosin, a drug used for treating PTSD, and its connection to sleep and glymphatic activity. “We think prazosin directly increases glymphatic function, and it may be independent of sleep,” says Peskind.

Prazosin blocks the signaling of the alpha-1 adrenergic receptor, which mitigates a type of brain activity called noradrenergic tone. This activity, produced by norepinephrine (the brain’s adrenaline), is high when you’re awake but more subdued while you’re asleep. Iliff’s research has shown that treating awake mice with prazosin and similar drugs that block the brain’s noradrenergic system causes an up-tick in deep sleep associated delta waves and an increase in glymphatic function, effectively turning the glymphatic system on even while the animal is still awake. >>

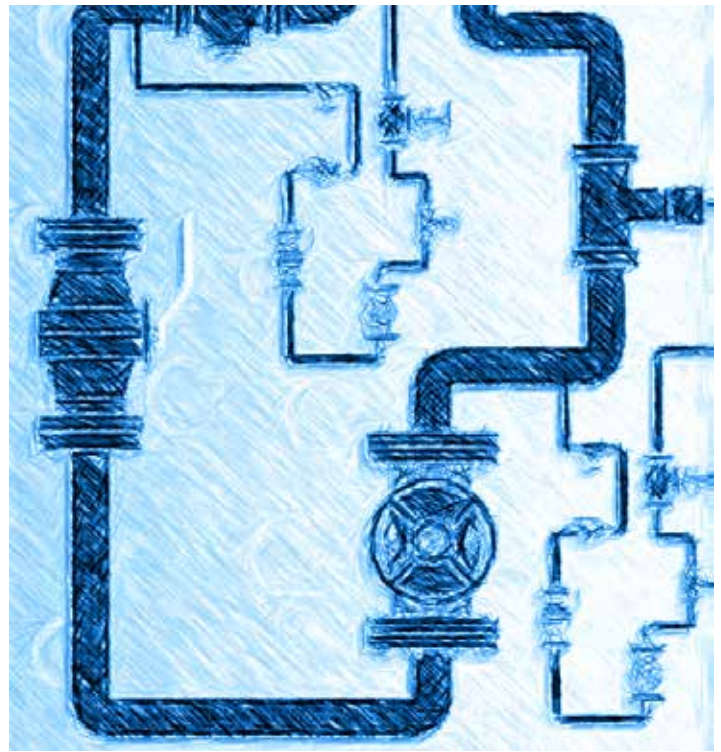
Peskind and her collaborators are pursuing this possibility in a new study. PoND, Prevention of Neurodegeneration, is a study that seeks to investigate if prazosin can reduce spinal fluid biomarkers for toxic proteins implicated in Alzheimer's, frontotemporal dementia, ALS, and Parkinson's, while also measuring glymphatic activity with a new MRI technique developed by UW Medicine researchers Dr. Swati Rane, PhD and Dr. Jalal Andre, MD. They will also find out if the medication really does improve sleep quality by measuring study volunteers' sleep and awake times over the course of a week, both before and after long-term prazosin treatment.

Prazosin is uniquely suited to the treatment of neurodegenerative disease because of its longstanding history and clinical safety. Prazosin was approved for hypertension in the early 1970s, and since then it has been tested in millions of people, primarily in men with hypertension and benign prostatic hyperplasia. Side effects are fairly trivial and are rarely reported.

But prazosin isn't just safe – it's practical for chronic, life-long use. "It's dirt cheap," says Peskind. "It's been off patent since the 80s, it is taken orally, and it causes very few side-effects. It could be taken for the rest of somebody's life as chronic management." By contrast, if recently developed antibody-based anti-amyloid drug therapies were shown to be effective, they would need to be administered intravenously and would cost somewhere between \$30,000 and \$50,000 annually. And while other trials have been focused exclusively on preventing cognitive impairment and dementia in people who already have accumulated amyloid, PoND is also focusing on preventing neurodegenerative disease before toxic proteins begin to accumulate.

This focus on glymphatic-based interventions for the prevention of dementia ushers in a welcome direction in a rapidly shifting field of medical research. The recent failure of aducanumab, an amyloid-clearing drug that made it to phase III clinical trials, has seeded the field with doubts over the hypothesis that removing amyloid will be enough to treat or prevent Alzheimer's disease symptoms. Many scientists wonder if the Alzheimer's research community needs to undergo a shift away from amyloid. "Up to this point, the field has been very amyloid focused, because that's where a lot of the early evidence in Alzheimer's disease pointed," says Iliff. "But people are starting to think much more broadly now." Prazosin's non-specific approach of enhancing glymphatic clearance hopes to cast a broader net in the prevention of neurodegenerative disease, potentially supporting the clearance of other toxic proteins, such as tau, alpha synuclein, and TDP-43.

While research at the UW may someday lead to new therapeutic approaches to preventing and treating diseases such as Alzheimer's disease, these newly emerging insights into the connection between sleep, aging, and neurodegenerative disease also provide an immediately relevant take-home message: How you are sleeping now matters to your brain health for decades to come. "If people know that how they sleep when they are in their 30s, 40s, and 50s is going to influence the way their brain functions in their 60s, 70s, and 80s, they might pay more attention to getting the recommended 7 - 9 hours per night,"



Iliff notes. "Many of us are starting to view sleep as a potentially modifiable risk factor, like high blood pressure or smoking, for the development of dementia later in life."

Tasked with keeping neurons freshly stocked and clean, the glymphatic system's biology has far reaching implications for a wide range of neurodegenerative disorders. Given the recent history and disappointments in Alzheimer's clinical trials, the study of something as broad-based as the glymphatic system carries hope for greater progress in how we treat cognitive impairment and dementia. No matter what advancements emerge in the next 2,000 years, a good night's sleep can only help. •




## TIPS FOR HEALTHY SLEEP

...from Dr. Michael Persenaire, M.D, Neurologist at the UW Memory and Brain Wellness Center.

- "Manage your circadian rhythms and keep your brain informed of where you are in the 24-hour cycle. Light exposure and having your body in an upright posture are both powerful signals to your brain that it's time to be awake, so limiting nighttime light exposure and exercising in the day can help you fall asleep at night."
- "Make sure that any environmental or medical conditions affecting sleep are being addressed. We like to remind patients that the consistent use of CPAP machines has been shown to make a significant difference in cognitive outcomes for people diagnosed with sleep apnea. Cognitive behavioral therapy has been shown to be particularly effective in treating insomnia."
- "Avoid or decrease substances that are clearly harmful for sleep, such as stimulants, caffeine, tobacco, and alcohol."





**CAN WE  
PREVENT  
ALZHEIMER'S  
DEMENTIA?**

**We are seeking healthy, medically stable volunteers over the age of 45 who do not have memory problems for a new approach to preventing Alzheimer's and other dementias.**

The study includes an assessment of your physical and mental health. You will also receive prazosin (a pill used for posttraumatic stress disorder and high blood pressure).

The study will take about 14 hours, spread over roughly 9 visits during a 3-month period. These visits will be at the Seattle VA. You will be compensated for each of your visits, with the total compensation for the study amounting to \$750 to \$825.

The PI of this study is Murray Raskind at S-116-MIRECC, 1660 S. Columbian Way, Seattle, WA 98108.

VA Puget Sound R&D Approved 04-18-2019

Please contact the research coordinator at **206.277.1491** or **1.800.329.8387 ext. 61491** for more information.

## WISDOM FROM OUR ELDERS

### The Storytelling of Jamestown S'Klallam Elder and Storyteller Elaine Grinnell

By Jackie Johnson, MC, (Makah Tribe) Partnerships for Native Health, Washington State University

On Thursday, August 8, 2019 Elaine Grinnell, Jamestown S'Klallam elder, shared her stories and knowledge on Indigenous Aging at University of Washington's Intellectual House. This storytelling event was hosted by Washington State University's Partnerships for Native Health, University of Washington Alzheimer's Disease Research Center, the Art of Alzheimer's, and Seattle's Department of Neighborhoods. Mrs. Grinnell told animated stories of growth, aging, and family roles, and she led a discussion about resiliency and destigmatizing aging.

Elaine began the event with a story about a grandfather teaching his young grandson lessons to transfer knowledge and to prepare the grandson for life after he passes on. The last lesson the grandfather taught the grandson is that small change can have large impacts. After, Mrs. Grinnell reflected about her grandfather, the source of her talent of storytelling, and the day she won a foot race between them. Today, being a grandmother of nine, she sees that her grandfather did this out of the love he had for her, and then to gauge his physical fitness. Competing in these races, he fought to stay active and prolonged the inevitable day that he wouldn't physically be able to race. Elaine related this memory to how she reminds and encourages herself to keep doing tasks, like walking unassisted, on her own for as long as she can, because it's easy to accept the offered assistance. But like her grandfather, she knows that maintaining strength and being active with family is healthier.

As with physical strength, mental and social strength is of high importance in aging. Mrs. Grinnell spoke about her uncle, who was diagnosed with Alzheimer's, the most common type of dementia. Her uncle was reluctant to acknowledge his initial memory loss until it became apparent to the family and the community when he drove around the small town of Sequim for eight hours. He was unable to remember his way home. After this, Elaine and her family created a caretaking plan for the uncle so that they could provide him with the best life moving forward. This entailed safety measures, such as taking away the car keys, and cultural measures, such as family prayers.

It is projected that 35% of the Native American population will develop dementia in the next 25 years. Fewer than 50% of cases of dementia are diagnosed in a clinical setting. There is no cure, but early diagnosis and interventions slow the symptoms and improve the quality of life. Family and community members are more likely to see the initial progress of the memory loss than elders themselves. With this knowledge, family and community members can encourage elders to have early screenings for mild cognitive impairment and dementia as well as advocate to community leadership that more screening tools are needed, such as training practitioners to conduct screenings. Having a well-rounded diet, exercising, learning a new skill, such as a language, and being social may reduce the risk of dementia and Alzheimer's disease.

The event concluded with a screening of the UW ADRC and Partnerships for Native Health's tribal outreach video on the prevalence of Alzheimer's among Native communities. Elaine spoke about the importance of individual resiliency – the refusal to be stagnant at any age. She closed with a message for families dealing with memory loss and dementia: "We shouldn't be ashamed. Our families should be there or someone who cares. Be brave. Don't give up, learn, and do something every day. Move forward not backward." •

>>Find the Indigenous Aging Resources page on the UW ADRC website: [uwadrc.org](http://uwadrc.org)

Photo credit: Chris Bennion

# New Faces at Our Center



**Charles Bernick, MD, MPH. Clinical Professor, UW Department of Neurology/  
Director, Clinical Trials, UW Memory and Brain Wellness Center**

Charles Bernick has researched Alzheimer's disease and treatments for 25 years and most recently served as Associate Director of the Cleveland Clinic Lou Ruvo Center for Brain Health. There, he guided the Professional Fighters Brain Health study, which is aimed at understanding the effects of cumulative head trauma on brain structure and function. He has been involved in various state initiatives to improve dementia care and research and studies of medications currently available for Alzheimer's disease. He has also served on the Alzheimer's Association's regional Medical and Scientific Committee. Dr. Bernick is now Clinical Professor in UW Department of Neurology/ Co-Investigator at the UW ADRC. As the new Director of UW MBWC Clinical Trials, he will help to bring new clinical studies to the Center.



**Jeffrey Iliff, PhD. Professor, UW Psychiatry and Behavioral Sciences, UW  
Department of Neurology/ Professor, Psychiatry, VA Puget Sound / Associate  
Director for Research, VA Northwest Network Mental Illness Research, Education,  
and Clinical Center**

Jeffrey Iliff focuses on neurodegeneration and traumatic brain injury research at the VA Puget Sound and at the UW Alzheimer's Disease Research Center. His work has probed the 'glymphatic' system, a brain-wide network of perivascular spaces that facilitates the clearance of waste products, including amyloid beta and tau, from the brain during sleep. Previously at Oregon Health & Sciences University, his group demonstrated that the glymphatic system become less efficient in the aging brain and in the young brain after traumatic brain injury. The studies suggest that impairment of glymphatic function may be one factor that renders the aging brain vulnerable to protein aggregation and neurodegeneration and may link brain trauma early in life with the development of dementia in later decades. His ongoing work aims to define the molecular and cellular underpinnings of impaired glymphatic function in the aging and post-traumatic brain, and to use novel MRI-based imaging approaches to extend these findings into clinical Alzheimer's disease and post-traumatic populations. Flip to page 6 for an article about his research, and visit the Iliff lab website: [www.ilifflab.com](http://www.ilifflab.com).



**Theresa Kehne, Research Coordinator, UW ADRC**

Theresa Kehne works as a Research Coordinator at the UW ADRC. She helps educate patients and families about the Clinical Core and upcoming clinical trials, and connects people to the research they would like to participate in. Theresa will also serve as a liaison between the MBWC clinic and the ADRC. In her previous position at Northwestern University, Bluhm Cardiovascular Institute, she primarily worked with hospital patients undergoing heart surgery, cardiovascular clinical trials, and other research projects led by heart surgeons. Before that, she worked with the State of Vermont, AmeriCorps\*VISTA, and community care teams, researching stable housing solutions and helping to provide wraparound medical and social services for neighbors experiencing homelessness in her home state of Vermont.



**s.weda'x**

huckleberry

(*Vaccinium membranaceum*)

# FOOD FOR THOUGHT

## Revitalizing Indigenous Knowledge about Healthy Eating

### An Interview with Valerie Segrest

By Meghan Jernigan (Choctaw Nation) and Genevieve Wanucha

**D**iverse, abundant, and nutrient-rich best characterize the traditional diets of the Coast Salish Tribes of the Pacific Northwest. Before contact with European populations in America, Native people in this region consumed almost 300 different species of plants, animals, fish and shellfish throughout the year. Harvesting in time with the seasons, people enjoyed and preserved nettle shoots, bracket fern root, bitterroot, cous root, soapberry, gooseberry, hazelnuts, acorns, dandelions, seaweeds, camas bulbs, many types of salmon, smelt, fowl, and game, along with a variety of other foods that are not easy to obtain today.

The movement of American settlers to the west rapidly altered ecosystems and restricted access to lands and waters, making it increasingly difficult for Coast Salish tribes to harvest and maintain traditional foods. From 1854 to 1856, seven treaties, including the Treaty of Point Elliott, established the reservation system for Washington tribes, limiting access to fishing and harvesting, and drastically altering the Coast Salish diet. By 1890, most tribes had been forced onto reservations, and government restrictions limited travel and food-centered cultural practices and celebrations. A diet largely comprised of milk, pork fat, sugar, beans, and wheat became the primary option.

This disruption of a nutrient-dense food system, and its effects compounded over generations, is reflected in the chronic health issues seen in American Indian communities today. Research has revealed high burdens of hypertension, type 2 diabetes, vascular brain injury, and stroke, all of which are risk factors for Alzheimer's and related disorders.

For Native people, revitalizing Indigenous food systems is a public health priority, our roadmap for disease prevention and overall wellness. [Food sovereignty](#) is the inherent right for people to define their own food and food waste systems and the economic, social, and cultural practices that relate to the production and consumption of food. "It is the right for people to eat what they want to eat, and that right shapes your diet and that shapes the food system that you live within," says Valerie Segrest, a member of the Muckleshoot Nation.

As the Director of Curriculum and Instruction for the Muckleshoot Tribe, Valerie Segrest is the leading voice in tribal food sovereignty. Her food systems work centers on traditional foods and plant medicines as critically woven into our overall health. She works as an educator and Native nutritionist, trained at Bastyr University. Through her tribal program and curriculum design, Valerie positions our link to the land with our legacy as tribal people.

On a busy Monday morning in a natural foods store in Federal Way, WA, Meghan Jernigan and Genevieve Wanucha of the UW ADRC outreach team met with Valerie Segrest to learn about her approach to traditional foods and how to harness the power of food to improve health, longevity, and spirit.

### **Talk to us about how you grew up eating, and how you came to be passionate about food and diet.**

I'm a military child. My father's retired Navy and my mom is a retired government worker. They took me all over the world as a child. So, I grew up immersed in other cultures and food systems. And then I'd come home to my grandmother, and my job was to always set the table. I think now that's what I do in life – try and figure out ways to set the table and make it beautiful. My mom also always made food really special, and I carry that on with my own children. Just yesterday, my 5-year old and I were walking through Pike's Place Market, and it's apple season. We were like, "The apples are ready, can you believe it?" It isn't always traditional food, but anything local, fresh, healthy, vibrant, beautiful, available, and seasonal. This approach to food has always made sense to me.

### **Can you tell us about your background and how you approach your work?**

My background is in traditional foods of the Pacific Northwest and food systems strategy, meaning how do we engage community in food and food systems work. And historically, our ancestors had strategies for how to manage a food system. It wasn't just that we were gathering and hunting and fishing to take food, but we were tending to the land at the same time. And that process involved a lot of thought and planning and knowing seasonal changes and the environment.

But as I engage with food, I take a step back and inspect the things that all of our food systems in this country have in common. What Native people are trying to do in [restoring their food systems](#), what the [Good Foods Movement](#) is trying to do, and even what the USDA nutrition standards are set for—they're all trying, in their own ways, to do the same thing: feed people really well. So, what are our commonalities? I like to live in that space.

### **How has the disruption in our foods systems impacted the health of Native people?**

We hear a lot, 'That happened 100 years ago. Get over it'. But what happened 100 years ago is our grandmothers gave birth to us. They had our mothers inside of them. One hundred years ago would have been close to Treaty times. The Civil War was just settling down. That's a lot of stuff going on in our country. And I don't think it's just our stuff. But for Native people, it was a change that happened really fast that we weren't asking for. And it was something imposed on us. Because of that, we have that genetic transmission of memory and knowledge through to several generations.

Ultimately, colonization disconnected us from a food system



Valerie Segrest

that was incredibly nutrient dense. Coast Salish ancestors would have had double what the USDA recommends for calcium per day. We're stuffed and starved because we're eating heavy foods that are empty of nutrients. There's extreme deficiency and then extreme excess of salt in one meal. We're missing out on all these opportunities to increase our nutrition, as our ancestors would have naturally been doing. It's just that we don't have the resources. We're seeing the lowest salmon runs ever. Herring and Ooligans don't come back here. That's our omega-3. That's our Vitamin D. That's our gut microbiome.

This historical disruption is the root cause of all of these severe health disparities that we're seeing related to inflammation, stress-related inflammation, and malnourishment: diabetes, cancer, and Alzheimer's disease.

### **Valerie, you have put forth traditional food principals of the native food sovereignty movement:**

- Food is at the Center of Culture
- Honor the Food Web
- Eat with the Seasons
- Eat a Variety of Foods
- Traditional Foods are Whole Foods
- Eat Local Foods
- Wild and Organic Foods are Better for Health
- Cook and Eat with Good Intention

**Among those principles, what are the key principles that you think have relevance for people who are trying to reconnect with their traditional food? What principles stand out as the most important? >>**

The traditional food principle that stands out as most important to me is: “Traditional Foods are Whole Foods.” For one example, you can have a cup of nettle tea and get your calcium supplement for the day. But, that’s not in the USDA food pyramid. Nettles also contain magnesium, phosphorus, and iron – all the things the body uses to manufacture blood. Your body doesn’t have to work hard to break the calcium apart because it is from a natural source, not chalk or animal product.

All of the key principles hinge on each other. What’s the most important is to use intention every step of the way. Whether you’re harvesting from the land or walking around a grocery store, ask: How am I showing up to this? One of my teachers would always say, as you’re harvesting the plants, you should be talking to yourself, or out loud, or to the plant, about how you’re going to take its life, how you’re going to transform it, and how it’s going to be medicine. How beautiful and vibrant do you want it to look on the table? You have to be intentional about approaching the food with good thoughts, and also while you’re eating it and thinking about how your body responds. Am I feeling good? Does this make me feel good? Do I like the flavor of it?

True, we have really busy lives and we have a lot going on. And we’re all suffering from chaos fatigue these days. We don’t need to also overburden ourselves with this pristine notion of a perfect diet. It’s too much. So, eat with good intentions and be grateful that you have it.

**Thinking within the context of food sovereignty, we are interested in local tribal community efforts to develop agricultural economies and tailored approaches to clinical care. The WSU Partnerships for Native Health team recently visited the Puyallup Tribe’s Qwibil Natural Healing and Research Center, focused on cannabis use research. In partnership with WSU’s Michael McDonell (Director of Behavioral Health Innovations), they will evaluate whether medicinal cannabis reduces opioid use and pain and improves the physical and mental health of clients. What do you think about medical cannabis use for Native elders?**

I think it’s a great place to move towards - acknowledging plant medicine as legitimate medicine. However, when you’re trying to diagnose something like gastritis, this roaming pain in the gut, it’s difficult to determine the cause. And taking a cannabis product or cannabidiol has the effect of blanketing the symptoms, and then we can’t sift through and locate problem. There are other plants that have cannabinoids them. It could also be a doorway into saying you could also use skullcap, or chamomile, or other plants that can do this particular thing very effectively, instead of this numbing for a condition where it’s hard to find the pain. But, I’ve seen it do miracles, and I’d rather people take that than opioids because I’ve seen a lot of elders lose their life in really terrible ways from opioids and I can’t imagine cannabis will have the same effect.

\*



Despite the disruption of traditional food, medicinal, and environmental systems, Native communities remain strong, innovative, and determined. The Coast Salish people ate a heart and brain-healthy diet hundreds of years before modern medicine, and current research draws firm links between nutrient-dense greens, fish, and berries, and their protection against oxidative and inflammatory mechanisms and vascular heart disease.

The most recommended foods for heart and brain health belong to certain classes of common foods, such leafy greens, berries, fish and seafood, olive oil, nuts and avocado. These foods form the basis of recommended approaches to healthy eating, such as the Mediterranean diet and DASH (Dietary Approaches to Stop Hypertension). In *Feeding the People, Feeding the Spirit: Revitalizing Northwest Indian Food Culture*, Valerie Segrest and Elise Krohn suggest ways to use easily found foods, which can offer the same texture and vitamins as the similar traditional food. For example, use blueberries for huckleberries, flax oil for Oolichan oil, green onion for wild onion, or grass-fed beef for venison.

Valerie has given permission to share a few heart and brain healthy recipes from the Muckleshoot Nation. We hope you prepare them with good intention and enjoy with loved ones. •

## Smoked Salmon, Cattail, Quinoa Salad

- 1 cup quinoa
- 2 cups water
- 2 Tablespoons olive oil
- 1 medium-sized onion
- 2 cloves garlic, minced
- 3 carrots, diced
- 1 cup chopped spring cattail shoots, peeled salmonberry sprouts, or leeks
- 2 Tablespoons chopped wild onion or ¼ cup chopped green onions
- 1 cup smoked salmon, cubed
- 1 Tablespoons lemon juice
- Salt and pepper to taste

Add quinoa to boiling water, then turn to simmer and cover until cooked, about 15 minutes. Add olive oil to a pan on medium heat. Add onions, garlic, carrots, and saute until onions are translucent. Add cattails and green onions and saute until tender. Toss in salmon and lemon juice. Add salt and pepper to taste. Serve hot or chilled.



## Vanessa's Wild Berry Pemmican (A concentrated mix of fat and protein, a so-called 'survival food')

- 1 cup dried venison, elk, or beef jerky
- 1 cup dried wild berries (*huckleberry or c. weda'x in Southern Puget Sound language*), *salal, blackcap raspberry, elderberry, salmonberry, service berry, soapberry, thimbleberry, wild blackberry, or wild strawberry*)
- 1 cup raw hazelnuts, walnuts, sunflower seeds, almonds
- 1/3 cup nut butter

With a knife, chop meat into very small pieces. Add dried berries, nuts, and nut butter. Blend well in a food processor. Store in a cool, dark place. This will keep for several months.

*Recipes as published in Feeding the People, Feeding the Spirit: Revitalizing Northwest Indian Culture by Valerie Segrest and Elise Krohn*





## Why I - And Everybody Else - Loves My 3D Printed Brain

By Genevieve Wanucha, MS

Have you ever wanted to hold your brain in your hands? Well, you can hold mine. It's a 3D model – at 100% scale and made of a super hard, glimmering grey resin. Its surface is a labyrinth of plump, curving folds. The 'gyri' (ridges) and the 'sulci' (crevices) rise and fall in convoluted patterns that are different across the two hemispheres, as if to mirror the extroverted introversion of its owner's personality. The asymmetry reminds me of how abstract, creative mental processes integrate with analytical, logical ones to produce our conscious perception and behavior.

I have wanted a 3D print of my brain ever since I realized it was possible, when research scientist Dan Peterson at the UW Integrated Brain Imaging Center (IBIC) provided several 3D printed brains of Alzheimer's patients as educational material for UW's annual Brain Awareness Day, offered to students in grades 2-12. But it wasn't until now that I had what the IBIC researchers needed to construct my brain model. This May, I got my hands on my magnetic resonance imaging (MRI) scan collected as part of a research study that I participate in each year – and in the specific file format to make it perfectly 3D printable.

Tim Wilbur, research scientist at IBIC, made my brain on his own 3D printer. The printer works by gradually layering segments of the object from the bottom up in thin threads of resin, based on the structural MRI data. The 100% scale brain print took the machine about 70 hours of continuous printing. Before now, our center was limited to brain models printed at just 50% and 75% scale.

"As an MRI technologist I get to see brains of many people, but only in the form of two-dimensional black-and-white pictures," says Wilbur. "Being able to hold a 3D print of a brain in my hands makes the brain real in a way that the pictures do not. The 3D print also makes it easier to appreciate not only the intricate shapes and contours of the brain structure but also simply the size of the thing, which somehow manages to seem both large – compared to the skull that holds it – and small – considering what it does and what it's capable of."

Printing 3D brains is a personal project for Wilbur, though it aligns well with his MRI duties at work. He keeps a few different models of his brain on display in the lab and they serve as talking points for curious research subjects and staff. He recently made a brain print for Dr. Todd Richards, PhD, Emeritus Professor of UW Radiology as a gift in honor of his retirement after 34 years of brain imaging research.

At first, I could not take my eyes off of this model, for I know with certainty that it offers a map, perhaps an unreadable one, of my unique traits, weaknesses, and artistic and creative strengths. Research in behavioral neurology, such as the work of Dr. Bruce Miller, MD, Professor of Neurology at University of California San Francisco, shows that the 'non-dominant' hemisphere (the right hemisphere is non-dominant for the majority of right-handed people) governs the production of visual art. I immediately leverage my position as the science writer for the ADRC, to embark on my most personal scientific journey to date: to decipher the map of my brain folds on that hemisphere. Can I find the basis, the origin of my identity as a creative artist?



A UW ADRC scientist who looked at my brain model pointed me towards a 2006 publication by neurologists at Beth Israel Deaconess Medical Center and Harvard Medical School, who studied the differences in brain structure in the motor cortex between 16 expert piano players, 16 expert string players, and 32 non-musicians (all right-handed). They found that they could detect anatomical differences by simple visual inspection of 3D renderings of MRI scans.

The researchers looked at the precentral gyrus, part of which controls hand and finger movement. The right side of it controls the left hand; the left side controls the right hand. This knob of brain tissue, in most people, folds into the characteristic inverted U-shape of an ‘Omega Sign’ on one or both sides of the brain. Studies have found that this brain area is longer and contains denser gray matter in expert musicians than in non-musicians.

When the researchers only looked at the “exceptionally prominent” Omega Signs, they found that the feature appeared more often on the right side in string players and on the left side in piano players. The hypothesis is that years and years of complex left-handed finger movements involved in playing a string instrument thickens up that bit of the right brain, and vice versa for piano playing. (Indeed, neuroanatomical studies of Albert Einstein’s preserved brain, which shows an Omega Sign, attribute this feature to the fact that he took violin lessons as a child.)

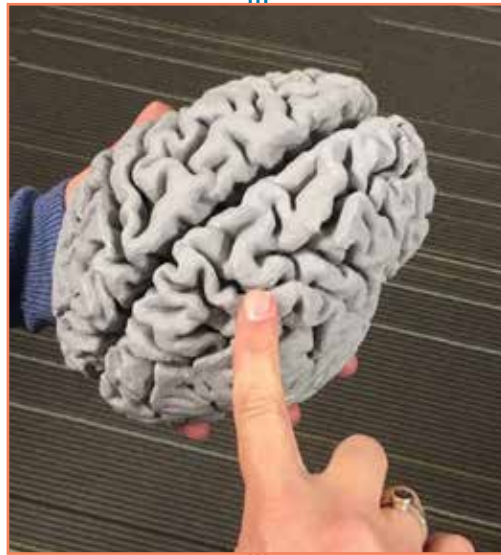
A thorough inspection of my 3D brain’s terrain shows I, too, have an Omega Sign in the right hemisphere (just like 34% of the non-musicians in the study, and 55% of the string players). In case you are wondering, I have never played a musical instrument. If only I had picked up a violin, would I have been a star orchestra player today? Or, more optimistically, perhaps the Omega Sign in my right hemisphere has something more fundamental to do with creative expressions, like my art and writing, which require well-controlled and finely detailed hand and finger movements.

Dr. C. Dirk Keene, Associate Professor of UW Pathology who leads the Neuropathology lab at the ADRC, quickly tamped down my self-involved wonderings when I brought the 3D print to his office. “You can think of the folding pattern of a brain like a fingerprint,” he says. “The 3D print is definitely showing you something real. This is not 21st century palm reading, but it’s not really possible to tell, just by looking at it, anything about what makes a person themselves.” (I still think that Omega brain fold is a conduit for my visual creativity.) He told me my brain looked normal.

I know that it is not the brain’s structure alone, but rather a person’s past experiences, and current social and environmental milieu, that influence and ultimately mediate their potential.

Still, the human brain creates that tangible sense of ‘me’ and my stable personality – one that may change and transform over time – and that’s incredible. While I reluctantly try to accept that my brain print will never serve as an accurate map of my talents and untapped potential, I am much more certain that the UW ADRC has a very interesting new, thought-provoking tool.

3D brain models, while not a scientific tool, are incredibly valuable in education and communication about neuroscience. “It’s kind of a solution in search of a problem,” says Dan Peterson of IBIC. “One potential idea would be to use the 3D prints as a communication tool during family conferences at the UW Memory and Brain Wellness Center clinic.



As part of my job at the UW ADRC, I help with community outreach activities and I’m always in need of tools to engage with the audience, often people who have different backgrounds and experiences than me. Even in the short time that I’ve had this model as a tool to bring to events, I’ve learned that the ability to show my own brain, instead of an anonymous person, has made all the difference in the potential to connect with a diverse array of people about brain science and medicine.

At a recent Alzheimer’s outreach event at the Kalispel Tribe’s Camas Clinic, clinicians and community members at our table took an interest in the brain model, as well as in the ADRC’s slides

of brain tissue. Their eyes widened upon realizing they were holding the brain of the person talking to them! At one point, the building security guard came over. I asked him if he wanted to hold the 3D printed brain. “Oh, no I don’t need to do that,” he said. “It’s my brain,” I responded. “....Well then,” he said, and took the brain into his hands. “Well, isn’t this something. How did you manage that?”

A 3D brain is a powerful conversation starter, one that lifts the fog of boredom and organically provokes emotional responses, surprise, wonder, and reflection, for everyone. I’m looking forward to the next UW Brain Awareness Day in March, where the children always ask us whose brain served as the model for the 3D print. It will be fun to tell them that the owner is standing right in front of them.

For me, this model is much more than an outreach tool, and I’m grateful for the personal journey into neuroanatomy that it sparked. It’s a powerful and comforting experience to hold this object that feels so solid and indestructible; I know how fragile the real thing actually is. As someone who lost loved ones too early to a neurodegenerative disease, holding this beautiful object in my hands creates motivation to use my brain for everything it’s worth, try and take care of it, and make sure I someday figure out where all those curvy paths lead. •

# NEW GRANTS AND FUNDING

Designed Vehicles for Blood Brain Barrier Traversal (NIH, R01)  
[David Baker, PhD](#)

Engaging older adults with cognitive impairment in planning for technology use in their care: the Identifying Needs for Optimal Remote Monitoring Tool (INFORM) (NIA K01) [Clara Berridge, PHD, MSW](#)

Characterizing how Herpes simplex virus-1 infection impacts known Alzheimer's disease pathways and neuropathological features. NIH grant (NIH, R01) [Martin Darvas, PhD](#)

ALLFTD: Advancing Research and Treatment for Frontotemporal Lobar Degeneration Consortium (ARTFL)/ Longitudinal Frontotemporal Lobar Degeneration Study (LEFFTDS) (NIH, U19). [Kimiko Domoto-Reilly, MD](#); [Thomas J. Grabowski, MD](#)

Understanding the functional impact of cumulative genetic risk in AD (NIH, R01) [Suman Jayadev, MD](#); [Gwenn Garden, MD, PhD](#); [Jessica Young, PhD](#); [C. Dirk Keene, MD, PhD](#), [Ben Logsdon, PhD](#)

Reversing tauopathy by inhibiting MSUT2 RNA-binding activity (NIA, R56) [Brian Kraemer, PhD](#)

Developing Neuroprotective strategies for Tau and TDP-43 Proteinopathy in FTLT (NINDS, R01) [Brian Kraemer, PhD](#)

Aging eyes and aging brains in studying Alzheimer's disease: Modern ophthalmic data collection in the adult changes in thought (ACT) study. (NIH, R01) [Cecilia S. Lee, MD, MS](#)

URBAN Native Elders: Risk and Protective Factors for Alzheimer's and Related Dementias (URBANE) (NIH). [Lonnie Nelson, PhD](#); [Clemma Muller, PhD, MS](#); [Dedra Buchwald, MD](#), [Thomas J. Grabowski, MD](#); [Meghan Jernigan, MPH](#); [Dean Shibata, MD](#); [James Gatenby, PhD](#).

Mass spectrometry of human tau to discover novel epilepsy biomarkers, American Epilepsy Society. [Nicholas Poolos, MD, PhD](#)

Global Alzheimer's Association Interactive Network Exploration to Evaluate Novel Alzheimer's Queries: Characterization of SNAP MCI using large harmonized datasets. Alzheimer's Association. [Swati Rane, PhD](#)

Non-invasive Quantification of Glymphatic Flow in Early Alzheimer's Disease. UW Royalty Research Fund. [Swati Rane, PhD](#)

Therapeutic Target Discovery in ADSP Data Via Comprehensive Whole-Genome Analysis Incorporating Ethnic Diversity and Systems Approaches (NIH, U01) [Ellen Wijsman, PhD \(UW Site PI\)](#) and Co-PIs from other institutions: [Anita DeStefano, PhD](#); [Eric Boerwinkle, PhD](#); [Philip De Jager, MD, PhD](#); [Myriam Fornage, PhD](#); [Sudha Seshadri, MD](#)

Role of HDAC2 as a modulator of aging and Alzheimer's disease phenotypes in stem-cell derived neurons. (NIH, K01) [Jessica Young, PhD](#)

Population Assessment of Alzheimer's and Related Dementias in Rural Northern Peru" (R21, NIH) [Joe Zunt, MD, MPH](#) (in collaboration with [Kimiko Domoto-Reilly, MD](#))

## AWARDS

2019 Junior Investigator Award from the American Epilepsy Society: Role of Alzheimer's disease-associated risk genes on seizure susceptibility. [Melissa Barker-Haliski, PhD](#) (Work is in collaboration with [Suman Jayadev, MD](#))

2019 Robert F. Schoeni Award for Research from the Ann Arbor Active Against ALS: A Novel Repeat Expansion that Bridges Genes Implicated in Amyotrophic Lateral Sclerosis. [Paul Valdmanis, PhD](#)

### NEW RESEARCH RESOURCES AND INFORMATION!

Check out the new page on the ADRC website titled Using ADRC and Related Resources.  
[www.depts.washington.edu/mbwc/adrc/page/research-resources](http://www.depts.washington.edu/mbwc/adrc/page/research-resources).

## ECHO Program funding to Disseminate Dementia Care Best Practices to Primary Care Practitioners in Washington State!



The University of Washington has received new funds, allocated in the state budget, to organize a cross-institutional collaboration to provide training on best practices, using the proven telehealth model of Project ECHO (Extension for Community Healthcare Outcomes). This project will provide a virtual connection for providers, available in our rural areas, and experts to offer education sessions and case conferences, with an emphasis on transforming practice and solving systemic issues that affect dementia care delivery. This resource will be coordinated by Dr. Kristoffer Rhoads, PhD, and Dr. Nancy Isenberg, MD, MPH, FAAN.

The UW Memory and Brain Wellness Center thanks Dr. Rhoads for stewarding this project on behalf of the WA State Dementia Action Collaborative.

**Come hear UW MBWC's Dr. Kristoffer Rhoads speak this fall about approaching Alzheimer's with health, hope, and help!**



### Spokane Alzheimer's & Dementia Conference

Wednesday, Oct. 30, 2019

The Centennial Hotel  
Spokane, WA

alzheimer's   
association

REGISTER: [www.tinyurl.com/yxqyct3u](http://www.tinyurl.com/yxqyct3u)



### Tri-Cities Alzheimer's & Dementia Conference

Wednesday, Nov. 6, 2019

Bethel Church  
Richland, WA

alzheimer's   
association

REGISTER: [www.tinyurl.com/yxcqswel](http://www.tinyurl.com/yxcqswel)

# A Tipping Point

## How TDP-43 is Changing Conversations about Alzheimer's Disease

By Genevieve Wanucha, MS

For 2 days in October 2018, in Atlanta, Georgia, a group of researchers gathered in a large conference room. There were 30 people – more if you counted those on speaker phone. The working group included international experts in brain imaging, clinical diagnosis, genetics, neuropathology, and neuropsychology, as well as the Director and other leaders of the National Institute on Aging's Alzheimer's Disease Research Centers Program. They were there to discuss a longstanding conundrum in Alzheimer's research. It was time to acknowledge that the field has crossed a tipping point, beyond which it is no longer possible to study brain health, Alzheimer's disease, or memory loss without paying attention to a protein called TDP-43.

TDP-43 protein (TAR DNA binding protein-43) is critically important for normal nervous system function, but it can undergo chemical changes and go rogue in the context of brain disease. It's bad news for brain cells. Abnormal clumps of TDP-43 are the hallmark pathology of amyotrophic lateral sclerosis (ALS) and half of frontotemporal lobar degeneration (FTLD) cases. It also can appear in other neurodegenerative diseases, including Lewy body dementia, Huntington's disease, and chronic traumatic encephalopathy.

Then there's the interesting and surprising occurrence of TDP-43 in the oldest old – the 80- and 90-year-olds who are diagnosed with Alzheimer's disease or memory loss and those who are not. Consider the emerging consensus from a large community-based autopsy study that TDP-43 pathology is found in 1 in 5 individuals over 80 years. About a fifth of the oldest old have severe TDP-43 associated with episodic memory loss, which mimics the symptom profile of classic Alzheimer's-type dementia.

Researchers at many centers, notably Rush University, Mayo Clinic in Jacksonville, Florida, the University of Kentucky, and the UW ADRC, have looked harder and in more brain areas for TDP-43 in their aging cohorts. They have found that, more often than not, TDP-43 is an additional microscopic finding in cases of classic Alzheimer's disease (defined as the presence of amyloid beta plaques and tau tangles) in older age groups. Most strikingly, TDP-43 pathology appears to hasten the cognitive decline in patients with co-existing Alzheimer's pathology.

"So, we got together in Atlanta because we really felt strongly that researchers and clinicians should know that we are finding something else in the brain that seems to be very important," said Dr. Julie Schneider, MD, MS, Professor of Pathology at Rush University and a leader of TDP-43 research, who spoke at the ADRC's 2019 MODEL-AD Conference. "As our population ages, the landscape of what we are trying to treat is also going to change. The field needs to recognize that memory loss or dementia in older people may very well not be Alzheimer's

disease, as traditionally defined."

This issue is significant news in medicine and public health, but it's actually not a new discovery in the neuropathology field or a newly anointed human disease. "TDP-43 in older brains is something that neuropathologists have known about since 1993," says Dr. C. Dirk Keene, MD, PhD, Associate Professor in UW Pathology and member of the consensus working group meeting. "But the condition hasn't had a name and we've never had a way to talk about it. The idea of the meeting was that if we could come up with a common language around TDP-43, then at least we could communicate to each other and the public and have a common protocol for research around the country."

Some Alzheimer's researchers say it's too early to issue guidelines and definitions around TDP-43 in older brains, before the field truly understands the details such as how TDP-43 in older brains is different than the TDP-43 in FTLD (typically a younger onset dementia). Yet, the working group in Atlanta decided that it's past time to issue some definitive statement on the issue. At the meeting, they agreed that until specific biomarkers for TDP-43 exist, clinical trials will need to be designed to account for TDP-43 proteinopathy. For example, if drugs to treat Alzheimer's pathology are tested in patients who also have TDP-43 in their brains, then the treatment effect might be diluted, so a larger number of participants should be enrolled.

### A NEW UNDERSTANDING OF BRAIN RESILIENCE

The UW ADRC has been studying TDP-43 at an accelerating pace in all autopsied brains over the past few years. Led by Dr. Caitlin Latimer, MD, PhD, Assistant Professor in UW Pathology, the ADRC has added nuance to the understanding of what TDP-43 actually means for the brain health of older adults. In a study published in *Acta Neuropathologica Communications* this year, Latimer found a strong correlation between the presence of TDP-43 pathology in the brain and those diagnosed with dementia in life.

Her study, which used autopsy brain tissue resources from the Adult Changes in Thought study, puts a special twist on the concept of resilience. 'Resilience' is the term for a person who had a high level of pathology in the brain, yet who stayed cognitively intact until death; while 'resistance' is a person who never develops brain pathology at all. In Latimer's study, she showed that the brains of older people who had been resilient or resistant to Alzheimer's disease pathology did not show TDP-43 pathology; yet almost all of the brains from age-matched people affected by symptoms of dementia during life did have TDP-43 pathology. Her findings give independent support to earlier work out of the Mayo Clinic showing that resistance to TDP-43 may be a big part of resilience to Alzheimer's pathology.



Latimer goes as far as to suggest that retaining cognitive health late into life may very well depend on simply being resistant to developing TDP-43 pathology.

“When I finished this study, I had so many questions,” says Latimer. “Do TDP-43 and tau interact to cause disease? Is there a relationship in space and time between TDP-43 and Alzheimer’s disease pathology in the brain? What genetic factors confer resilience or resistance to these different pathologies?” These are questions that require supplementing the study of postmortem brain tissue with innovative techniques in molecular biology, such as modeling the toxic protein pathways in worms, mice, and human induced pluripotent stem cells models.

#### INSIGHTS FROM TDP-43 EXPERTS

Dr. Nicole Liachko, PhD, Research Assistant Professor in UW Division of Gerontology & Geriatric Medicine, entered the field as a scientist studying neurodegeneration around the same time that TDP-43’s toxic effects were becoming known in ALS and FTLN in 2006. “I haven’t been surprised to see researchers finding TDP-43 in multiple neurodegenerative diseases including Alzheimer’s,” she says. “I’ve been following that aspect of the field since the beginning. I’ve been excited about it for 10 years, and finally everyone else is excited too.”

The Liachko Lab uses *C.elegans* worm models of human ALS, FTLN, and Alzheimer’s to study important aspects of the diseases. Worms are valuable tools in Alzheimer’s research because they have transparent bodies and simple nervous systems, which allow researchers to observe physiology in living detail. In recent worm model work, Drs. Liachko, Latimer, and Brian Kraemer, PhD, Research Associate Professor in UW Division of Gerontology & Geriatric Medicine, observed that tau and TDP-43 together make disease symptoms and progression much worse in the worms, even worse than would be expected if effects of tau and effects of TDP-43 were just

added together. This finding may help explain why humans with both pathologies experience accelerated.

However, worm models are an artificial system; Liachko notes that the findings are only a jumping off point to study human biology. “In humans with Alzheimer’s disease, in neurons that show pathology, some will have tau aggregates, and others

will have TDP-43. So, the question is, how are the neurons with TDP-43 making the tau pathology worse? Is it via synaptic connections, or through support cells in glia? It’s a fascinating question.”

Liachko’s team uses a technique that interferes with gene expression called RNAi. With this method, researchers can reduce the expression of individual genes in a worm’s genome and watch what happens as consequence. They search for ‘enhancers,’ or genes for which if you reduce their expression, it worsens symptoms, as well as ‘suppressors,’ or genes for which if you reduce expression, it improves things.

“What we have learned is that there are a number of cellular pathways that influence TDP-43 for better or worse, suggesting that there may be more than one way to intervene and improve TDP-43 toxicity,” says Liachko. “If we can figure out which is easiest to target and has the least side effects in cells, then we can hopefully pursue a treatment.”

But how does healthy TDP-43 become toxic in the first place?

Dr. Paul Valdmanis, PhD, Assistant Professor in UW Medical Genetics and ADRC collaborator, has an interest in TDP-43 from his background in the genetics of familial ALS and FTLN and helped to identify pathological variants in TDP-43 and TDP-43-related mechanisms as a major component of the diseases. He has insights into how healthy TDP-43 transforms into a problem for brain cells in ALS and FTLN, and perhaps different neurodegenerative conditions. >>

“**As our population ages, the landscape of what we are trying to treat is also going to change. The field needs to recognize that memory loss in older people may very well not be Alzheimer’s disease, as traditionally defined.**”

Healthy TDP-43 is what is called an ‘RNA-binding protein,’ which means that it helps strands of RNA in the cell get translated into useful proteins. To fulfill this purpose, TDP-43 searches for particular sequences of RNA or other proteins floating around the brain cell, and it has affinity for certain ones.

“TDP-43 pathology appears across many diseases most likely because it is associating with other toxic proteins or substances aggregating at the same time,” he says. Valdmanis thinks that, in the brain cells of a person already developing toxic aggregations, TDP-43 still tries to do its normal job – but it runs into big trouble. “Maybe there is something within the pre-existing toxic inclusions that is sending out a signal for TDP-43 to associate,” he says. When TDP-43 reaches the destination, it finds a hornet’s nest and transforms into a problem itself.

The science of TDP-43 and neurodegenerative disease is still young and full of unanswered questions. Valdmanis wants to know the critical RNA or protein targets that TDP-43 naturally associates with, and how that interaction leads to aggregations in the setting of disease. “If we could figure out what that intermediary signal is, between TDP-43 and its biological targets, we could work to try to prevent that association and break down the propensity of some of these proteins to aggregate,” says Valdmanis. “We could precisely target the aberrant process central to a disease, without hindering all of the other targets that TDP-43 is supposed to interact with normally.”

In the field of medical genetics and behavioral neurology, TDP-43 has united ALS researchers and FTLD researchers, particularly since the 2011 discovery of a genetic expansion that causes both diseases. Now, new genetic treatments in development for ALS patients could also help prevent or delay forms of familial FTLD. “Perhaps advances in TDP-43 science in FTLD-ALS fields can benefit progress in Alzheimer’s disease, and vice versa,” says Valdmanis.

### IT’S NEVER TOO LATE

The implications of the field’s evolving conversation are enormous and there are wide gaps in knowledge and diagnosis, but the tectonic plates of Alzheimer’s disease research have already shifted. At a public forum in January 2019 offered by the UW Institute for Stem Cell & Regenerative Medicine, a panel of ADRC researchers fielded questions from a curious audience after learning about multiple pathologies of dementia. “Is studying amyloid worth it anymore? Is the era of pursuing treatments for amyloid over?” they asked. Keene disagreed. “It’s not that we are abandoning amyloid, which is definitely a key player in Alzheimer’s disease; rather, TDP-43 gives us another target.” He pointed out the possibility that if a therapeutic could get rid of amyloid in the brain, then perhaps TDP-43 would never develop, so the field needs to understand the relationship between amyloid, tau, and TDP-43.

The results of the Atlanta working group were published in the journal *Brain* in 2019. Because TDP-43 pathology can occur on its own, independent of Alzheimer’s pathology, and because it looks to have a specific pattern of deposition and spread in the brain, researchers determined that TDP-43 in older brains is a distinct disease entity, named LATE (limbic-predominant age-related TDP-43 encephalopathy). The term LATE is primarily for use in the research world, to give guidance on how to characterize TDP-43 in research studies. Keene emphasizes that the new guidelines are only a basic minimum for ADRCs, and that individual centers can go further with innovative methods of TDP-43 research.

So what does this mean for patients? Currently, there is no way to detect TDP-43 in the brain during life, so no one can get a clinical diagnosis of LATE until biomarker tests are available. For now, neurologists are left with a process of elimination. “Doctors should suspect LATE if a patient screens negative on an amyloid or tau PET scan,” says Dr. Nina Silverberg, PhD, of the National Institute on Aging’s Alzheimer’s Disease Research Centers Program. Yet, few patients can obtain these specialty scans. Some worry that people diagnosed with Alzheimer’s will be confused as to whether they have the correct diagnosis, while doctors don’t have the tools to help clarify.

But Keene and researchers at the UW ADRC think that the effort to put a name and definition to LATE will benefit the public in the long run, especially when biomarker tests for amyloid, tau, and TDP-43 reach clinical usage. “The fact is that age-related cognitive decline can be caused by many things. At least we are forming a way to talk about this reality with our doctors and in the media,” he says. “I want a future where I can go to the doctor, and for them to say, ‘You have a build-up of amyloid and some tau, but no TDP-43 or vascular damage. And here’s a new treatment that may work for you.’ That’s the bottom line here.”

In light of this formal definition of LATE and the coming changes in the landscape of dementia prevention and treatment, the language we use to talk about dementia is requiring more and more nuance. “It’s important to distinguish between the pathology of Alzheimer’s disease – which is the presence of amyloid and tau in the brain – and the clinical syndrome,” says Dr. Thomas Grabowski, MD, Professor in UW Neurology and Radiology. “The term ‘Alzheimer’s-type dementia’ can serve as a placeholder term to describe a syndrome of memory loss that can have many underlying disease causes, including LATE.” In the robust conversation to continue, we should all remember that it’s never too late to ask questions and learn more about this rapidly changing field of science. •

*Genevieve Wanucha, MS, is a science writer and leader of the communications team of the UW Memory and Brain Wellness Center/ Alzheimer’s Disease Research Center. Contact: gwanucha@uw.edu*

# Our Garden Program in the News!

The September 15th, 2019 issue of the *Seattle Time's Pacific Northwest Magazine* contains a story on our Garden Discovery Walks! Writer Colin McCrate explores how this collaborative program harnesses the healing power of the environment to help people with memory loss.

The story 'Our Better Nature' is available online at [www.tinyurl.com/yxahq3tg](http://www.tinyurl.com/yxahq3tg)



ROW by Colin McCrate

The collaborative, innovative Garden Discovery Walks program harnesses the healing power of the environment to help people with memory loss.

## Our Better Nature

**S**PENDING TIME in the garden is a great way to relax and focus your mind. Whether you seek to relieve chronic stress, solve an elusive puzzle or just stop thinking about work, a walk through the garden is often the best mind-altering experience you can get.

Many famous thinkers throughout history have used the garden as a tool to help figure out complex problems. As a young biology student, I remember reading about Charles Darwin's habit of daily garden walks on his dedicated "Thinking Path." My personal love of walking was at least partially inspired by this. I figured, "If garden walks helped Darwin conceive the theory of evolution by natural selection, what can they do for me?"

While no one quite knows how nature affects the brain, there is little doubt that it does. As the renowned neurologist Oliver Sacks commented, "In 40 years of medical practice, I have found only two types of nonpharmaceutical therapy to be vitally important for patients with chronic neurological diseases: music and gardens."

Given the potential for gardens to positively affect the brain, perhaps it should be no surprise that garden walks can be effective therapeutic tools for people with memory loss.

Enter the Memory and Brain Wellness Center at UW Medicine and Seattle Parks and Recreation. These honorable institutions have partnered to create a unique and progressive treatment for memory loss called Garden Discovery Walks. In fact, this program is so progressive that Seattle Parks is the only park department in the country that offers dementia-friendly recreation programming.

For the past three years, a noble band



**RIGHT:** Horticultural therapist Laura Rumpf works with a Garden Discovery Walks participant at Seward Park Audubon Center. Therapists, doctors and volunteers have partnered to organize monthly garden walks, followed by nature-based art crafting, for people with memory loss.



**LEFT AND ABOVE:** A group with Garden Discovery Walks gazes at plantings at Bradner Gardens Park.



Participants stroll along a shady trail at Durr Gardens.

pace, with options to sit and rest along the way. The program visits a new garden each month, with notable sites including Kibota Garden, Seward Park, Dunn Gardens, Bradner Gardens Park and Bellevue Botanic Gardens. The two-hour program includes a guided tour followed by nature-based art crafting with licensed horticultural therapist Laura Rumpf.

The concept of the program is simple: Spend time in nature. While nature brings cognitive stimulation for everybody, it can be especially helpful for people with dementia. By creating a safe environment, garden walks can reduce anxiety and make it easier for those with memory loss to interact with people around them. The art-crafting part of the experience allows participants to engage their motor skills and access their inner creativity.

The experience is so powerful that new spaces in the program rarely open up. Because participants see the greatest benefits from repeated exposure, registered walkers are given priority in monthly sign-ups. Over the past three years, friendships, community and a waiting list have been built.

Colin McCrate (left photo). Find him at [colinmccrate.com](http://colinmccrate.com) and on Instagram @colinmccratephoto.

The program is offered by the UW Memory and Brain Wellness Center and Seattle Parks and Recreation, with sponsorship from Family Home Care Resources. If you would like more information about this program, please contact Cayce Chairs at [cayce.chairs@seattle.gov](mailto:cayce.chairs@seattle.gov), 206-615-0100.

The 3rd Annual **UW Nature & Health Symposium** is an all-day conference that brings together professionals and community leaders in the fields of health, conservation, design and planning, and education to learn from each other and explore common goals and collective strategies related to the human health benefits of being in nature, from gardens to wildlands.

One of the presentations will focus on horticultural therapy and garden programs for people living with dementia. Come see Laura Rumpf, Registered Horticultural Therapist and co-coordinator of the Garden Discovery Walks program, share her insights from years of experience.

Learn More and Register: [www.tinyurl.com/y55qdqdd](http://www.tinyurl.com/y55qdqdd)

October 30, 2019, 9:30 a.m. to 5:30 p.m. Intellectual House, 4249 Whitman Court, UW, Seattle.



**Coming to Life**

It is not only the trees  
that come to life in the  
Sweetness and Joy of Spring  
We all know that, don't we?  
Gaiety insists on taking over  
Our hearts  
For no other reason  
And we give in with joy that  
We did not know was there.  
If you listen closely,  
The rain will cheer you  
And the flowers will notice  
With approval  
And you are home.

*Barbara Ring*

**A Mix of Sun and Clouds; The Kindness of Reality**

Living comes and goes.  
In the midst of it,  
We are invited to grow  
No matter what is emerging  
As if each life of each person  
Represents endless possibilities  
For joy and hilarity.

It's the same wisdom  
That fills the full moon  
Just in time for love.

*Barbara Ring*

**About the Author**

Barbara Ring lives in upstate New York. She spent her professional life as an educator. She embraced writing poetry in her retirement and continued to write as long as she was able after a diagnosis of Alzheimer's disease. She passed down her love of writing to both of her adult children.

**The Interview**

Publisher, editor, agent  
Which of these will I see?  
With my novice writer's back-  
ground  
What will he ask of me?

Confident, prepared and stoic  
He sits upon his throne.  
Four other writers in the room  
Yet I feel alone.

He rises slowly...calls my name.  
I am on the bubble.  
I'm chosen first and am petrified.  
That, for me, spells trouble.

I pitch my piece, the silence  
screams.  
I'm trembling in fear.  
How long can I take this torture?  
Seconds seem like a year.

"Fantastic! Genius! I love it!"  
Oh, joy! He's quite impressed.  
My shaking knees and boggled  
mind  
Can safely take a rest.

He shakes my sweaty hand and  
smiles.  
My face begins to beam.  
Then, suddenly, to my dismay,  
I awaken from my dream.

*Sherry Schievelbein*

**About the Author**

Sherry Schievelbein was born and raised in Appleton, Wisconsin. Prior to her high school years, she and four other girl scouts toured Europe for nearly the entire summer. A few years later, she married her partner. Their careers took them all over the country. Upon retirement, the two settled in Washington to be near their children and grandchildren. Through all of this adventure, Sherry has enjoyed writing poetry and prose, drawing on her many life experiences.

**I Like Ike**

Buttons galore of red, white and  
blue.  
I wear them with pride  
In devotion to you.  
I gather free buttons and  
No one's complaining...  
They hope we will use them  
To help with campaigning.

Medals and ribbons,  
You're the man of the year.  
Our town is so honored  
That you're coming here.  
A grand holiday!  
A trip to the station  
To hear the man speak  
Who will soon lead our nation.

But the train rushed right by  
As though lightning had flashed.  
We cheered and we shouted.  
The last car went past.  
There, on its platform  
You stood oh, so grand!  
You smiled, looked right at me.  
Gave a wave of your hand.

The train was gone.  
One small moment was mine.  
Love at first sight  
For a kid who's just nine.

*Sherry Schievelbein*





## The S.O.A.R. Program takes people to new heights!

By Marigrace Becker, MSW

This summer, the UW Memory & Brain Wellness Center added a new outdoor opportunity to its menu of education, support and social programs. S.O.A.R., which stands for Shared Outdoor Adventures for Resilience, brought together 23 people with younger onset Alzheimer's and family members to complete a low ropes course in a supportive team environment. Activities blended physical challenge, mutual reliance and creative solution-seeking – such as walking along a cable suspended 3 feet off the ground while leaning on a friend's shoulder, or balancing a large-scale teeter totter as a group.

“It was incredible to see both the individual and team strengths during the activities. Everyone had something to contribute in each challenge,” says Dr. Carolyn Parsey, PhD, a neuropsychologist at the UW Memory & Brain Wellness Center, who helped design the program.

Through this tangible experience of overcoming challenge, group members reinforced their strengths and built confidence that could transfer back to their daily life. Meanwhile, they nurtured their relationship with their family by relying on each other in new, outside-the-box situations.

“We really liked it,” said one care partner Andy. “It was super fun to work with other people to solve problems. And it was wonderful to have lots of different experiences.”

“Oh yeah – it's all of it!” his wife Anne agreed.

S.O.A.R. was developed by Dr. Carolyn Parsey and program manager for community education and impact Marigrace Becker, led by professional facilitators from Northwest Teambuilding, and received financial support from Jefferson House and The Inn at Belle Harbour.

The ropes course facilitators repeatedly applauded the keen ability of team members to leave ego behind and help each other out – an ability that may have emerged during the memory loss journey.

“We have a word for a team that is this in tune with each other – we call them ‘high functioning,’” one facilitator noted.

At the core of S.O.A.R. is the idea that many strengths remain in the midst of memory loss – including social connectedness, appreciation for the natural world, and physical ability. With the initial pilot program off the ground – literally – the next step will be evaluating the program's impact and considering possible expansion to new activities, venues, and audiences. •

> Would you like to stay in the loop about what's next for the S.O.A.R. program? Contact [mbecker1@uw.edu](mailto:mbecker1@uw.edu).

## Dispatches from the 2019 Alzheimer's Association International Conference and More!

By Angela Hanson, MD., Geriatrician, UW Memory and Brain Wellness Center

This year, I had the opportunity to travel to two fun cities to learn about updates in Alzheimer's disease and Geriatric Medicine. I was pleased to hear at these two conferences that a lot of researchers are working on studying brain health: whether it's how to keep our brains healthy through the stress of surgery, or figuring out the specific health recommendations that will help reduce our risk of developing dementia.

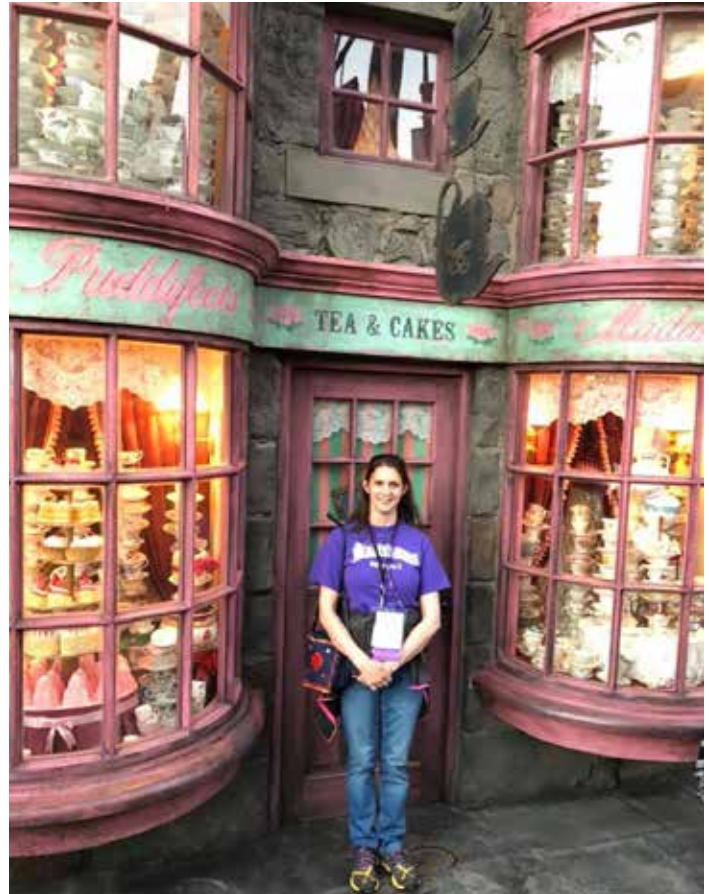
### Staying Strong after Surgery

The American Geriatric Society annual meeting was in Portland, Oregon in May. I attended a talk by Dr. Tom Robinson from Denver who studies how to keep older patients safe when they undergo surgery. I found out about a resource called "Strong for Surgery" which focuses on several key areas to prevent surgical complications in older adults. Some of those areas include optimizing nutrition before and after surgery, smoking cessation, reviewing all medications before surgery, and preventing delirium while in the hospital.

One worrisome surgical complication that is more common in older adults is delirium. Delirium is a state of confusion that comes on very suddenly and lasts hours to days. Lots of factors can contribute to it, and it can last for days to weeks after it develops. The ideal situation is to prevent delirium. Although there is no sure way to prevent delirium, I found out about this resource which can help older adults and their families if they find themselves needing surgery:

#### Six Tips to Reduce Confusion in Older Patients After Surgery

- Ask your physician to conduct a pre-surgery cognitive test — an assessment of your mental function. The physician can use the results as a baseline for comparison after surgery.
- Be sure your caregiver, a family member or friend visits or stays with you as you recover, and carefully observes your physical and mental activity after surgery so that they can report anything troubling to your physician.
- Check with your physician before taking medications prescribed after surgery that can affect your nervous system, such as those for anxiety, seizures, muscle spasms or sleep aids.
- If you wear hearing aids or glasses, ask that they be made available as soon as possible after the procedure, so that you can hear and see clearly.
- Request a hospital room for recovery with a window if possible, so you can tell whether it's day or night.
- If you will be staying overnight in the hospital, pack a clock and a calendar, and other familiar objects from home such as a family photo, to help you readjust.
- Find online at: [www.asahq.org/brainhealthinitiative/toolsforpatients/sixtips](http://www.asahq.org/brainhealthinitiative/toolsforpatients/sixtips)



The AAIC Sunday party was at Universal studios and our Memory Team loved the sweet Harry Potter ride!

### Help from Hearing Aids

Epidemiologists are researchers who study risk factors for diseases, and a few studies have shown that hearing loss is a risk factor for Alzheimer's disease. Does this finding mean that if we treat hearing loss early, that we might be able to prevent or slow the progression of Alzheimer's?

One study that I learned about in Portland seems to support this idea. This study comes from the United Kingdom (Maharani et al. *Journal of the American Geriatrics Society*, 2018). This group looked at 2,040 adults aged 50 and older in the 'Health and Retirement Study' who were using hearing aids for the first time. In this study, the participants had their memory tested every 2 years. There was an average level of memory loss for the group, but after they started wearing hearing aids, the memory decline slowed down somewhat. Although the hearing aids didn't completely stop memory loss, these results are encouraging and support the idea that we should screen for hearing loss and treat it as early as possible. The researchers theorized that hearing aids might delay cognitive decline by preventing the social isolation of hearing loss, as well as improve mood and promote self-efficacy.

## Reversible risk factors for Alzheimer's

Hearing loss is not the only reversible risk factor for cognitive decline. Epidemiologists have been describing a lot of other risk factors, but it isn't always easy to intervene. How do we get this information to the public and translate the studies into practical things to do? There were several talks at the Alzheimer's Association International Conference that I went to in Los Angeles in July about this issue.

Research at University of Exeter Medical School showed that people who scored higher on a 'healthy lifestyle index' had a lower risk of developing dementia. A healthy lifestyle includes not smoking tobacco, getting regular physical activity, eating a healthy diet, and avoiding excess alcohol intake. They also looked at the impact of Alzheimer risk genes. Conclusion: "Genetic and lifestyle factors are strongly and independently associated with risk of all-cause dementia. Our findings suggest that adherence to a healthy lifestyle can offset genetic risk and support engaging in healthy lifestyle interventions to prevent or delay dementia. The risk of all-cause dementia was more than halved among participants with a high genetic risk following a favorable lifestyle compared with an unfavorable lifestyle." In other words: even if you have a family history of dementia, it is not a guarantee that you will get it and there are many things you can do to reduce your risk.

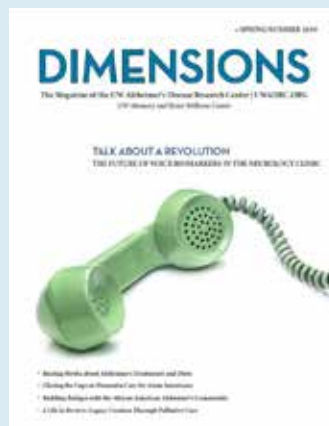
A study from the United States showed similar findings. A group from Rush University in Chicago looked at 5 lifestyle factors and found that the greater number of healthy lifestyle factors someone adhered to, the lower their Alzheimer's risk was. Even just following one of the recommendations was better than none. Impressively, the risk of Alzheimer's was 59% lower in those who followed 4 or 5 of the recommendations. Here are the 5 factors: Not smoking cigarettes, participating in moderate or vigorous physical activity at least 150 minutes a week, light to moderate alcohol consumption, following the MIND diet (similar to a Mediterranean diet), and engaging in cognitive activities later in life.

Finally, I was excited to hear about a group of researchers studying how to bring all this information together into a busy clinical setting. They have set up two research clinics (one in New York City and one in Puerto Rico) and their goal is to tailor Alzheimer's prevention therapy to each person depending on their individual risk factors: in other words, personalized medicine. Their methods are available in the publication (Isaacson RS et al. *Alzheimer's and Dementia*, 2018) and they focus on three key areas: anthropometrics (including weight and body fat distribution), blood biomarkers including testing for high cholesterol and diabetes, and cognitive testing. Many of the recommendations are focused on cardiovascular health as well as making sure patients are treating any conditions that are affecting their cognition such as poor sleep or depression. •

Learn more on the UW ADRC website page **Evidence-Based Prevention:** [www.depts.washington.edu/mbwc/adrc/page/prevention](http://www.depts.washington.edu/mbwc/adrc/page/prevention)

## Support the Alzheimer's Disease Research Fund

Donations help support patient- and family-centered care, research breakthroughs in Alzheimer's disease and related disorders, and the training of tomorrow's physicians. And by giving — perhaps in gratitude for care, or in memory of a loved one — you can help improve the lives of your friends, your family, and others in your region. If you would like to be our partner in enhancing health and changing lives, please contact the UW Medicine Advancement Office at 206.543.5686. To donate online, please visit [www.supportuwmedicine.org/adrc](http://www.supportuwmedicine.org/adrc).



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# Villages, Town Square Day Care, and Smart Homes: New Models of Dementia Residences Around the World

By Deepa Subramaniyan

*Deepa Subramaniyan is a clinical research professional working in Switzerland and is a former member of the ADRC Clinical Study team*

Families caring for persons with dementia need all the support they can get, but their options are often limited to conventional care homes or even locked facilities. For the person with dementia, this arrangement restricts their ability to engage with the community. The idea of being truly independent and living with dignity after diagnosis is quickly gaining attention, with innovations emerging around the world.

One such novel concept – “the dementia village” – began operating in the Netherlands in 2009. De Hogeweyk was a first of its kind independent housing village for people living with dementia, in a safe town-like environment complete with shops, cafes and hair salons. Its success has led to other such communities and care centers based on the concept of independent/codependent living.

The dementia village serves as a community for people, rather than a facility for patients. In order to get a clearer picture of how this influential model works in practice, I spoke to Donna Phillips, a graduate of University of Southern California Aging Services Management, who is interested in dementia-friendly communities and visited De Hogeweyk several times between 2015 and 2017. She explained that about 150 residents in De Hogeweyk are grouped in households of six people, with two assistants who do not live there. These households function like a family home. All members of the house sit together to plan the budget and meals. Residents can visit the various parts of the village independently – whether shopping at the grocery store or getting a haircut.

The design of the dementia village includes streets, gardens, shops, cafes, and residences with elements of different cultures, lifestyles, and social classes to help residents feel connected to the space and also reminisce about their past. The outside grounds are built with courtyards that are strikingly different from one another. Some feature a chess pattern, fountains, or other contrasting architectural elements that serve as visual cues to aid the residents’ sense of location. The villagers can wander the grounds and courtyards unaccompanied. According to the De Hogeweyk designers, the intention is to enhance wellbeing and allow residents to remain active in everyday life, in ways that mirror their lifelong hobbies and preferences.

In such a system, one might think staffing could be a challenge, but Phillips tells me the staffing is lean. There is a clerk working in the grocery store, maintenance and gardening personnel, a cashier for the cafe, reception desk staff, assistants for the houses, and volunteers. A medical office and nurses are available for medical emergencies. At nights, residents sleep in their house on their own. There are no cameras anywhere because of stringent European privacy laws. The reception desk staff stay at the village through the night and are alerted by a sound system to any anxiety and movement. This level of staffing has worked well. Residents are occupied through the day with various activities and vigorous walking to encourage better sleep. Their overall physical fitness is many times better than in conventional settings. The residents are also taken outside the village, to visit markets or enjoy other activities such as horse riding. These scenes are almost unimaginable in traditional care centers.

In order to become a resident at De Hogeweyk, a person must require round the clock care. Priority is given to people who have struggled to find housing in other facilities due to frequent wandering or high agitation. The cost of care is about \$6,000 a month.

I wondered how an unlocked facility worked effectively in managing care of people with severe symptoms. Phillips reiterated that the approach to care here is allowing people to act by instinct. Residents can explore the area as much as they would like, which reduces agitation and avoids confrontational situations. If a dangerous situation ever evolves, the staff are trained to exude warmth and calm



**A scene from De Hogeweyk, courtesy Hans Erkelens**

rather than concern or shock. Psychotropic drugs are not used for treatment.

Some of the other dementia villages designed on the principles of De Hogeweyk are Bangalore, India's NKISA and Rome, Italy's Villaggio Emanuele. "The Village" in Langley, British Columbia recently opened its doors in Summer 2019 and a village being constructed in Bern, Switzerland may open later this year.

While dementia villages are a welcome effort to minimize the care family's load and provide a level of freedom and independence to the person with dementia, they are not without downsides. States Phillips, "the dementia village is an example of the most important ways to provide care: maximize autonomy and minimize negative behavior. However, creating a segregated community for dementia affected can feel like a separation from community. We need an inclusive approach."

For De Hogeweyk to work, some medical and legal rules and regulations had to be adjusted. This makes it a lot harder to replicate in other locations. Phillips thinks that a more inclusive village with space for family, students, and others would create a peaceful, welcoming environment and enforce the idea that people with dementia should belong and thrive in the community at large, rather than being kept separate.

Other communities and day care centers have taken inspiration from De Hogeweyk but follow different care strategies. Glenner Town Square in California, which opened its doors in 2018, is a day care center for people living with dementia which recreates the surroundings to reflect common scenarios of the 1950s and 60s. Started by Dr. George Glenner, a physician and researcher at UCSD, Glenner Town Square is designed to be adaptive and set to update every ten years.

The concept of reminiscence therapy is used to stimulate the memories of people with dementia, with events from their teens to 30s. Long term memories which are more preserved might be rekindled by a sight, sense, or smell from the past. The stores, libraries, diners, salons, and even music played inside the facility are designed to resemble the period. The familiarity of surroundings seems to calm people and offers symptomatic benefits such as decreased agitation and confusion. Glenner has structured activities throughout the day, but people can choose whether to participate. The cost of care here is about \$500 a week for 8 hours of care per day. Family and caregivers report it is worth the cost, given that their loved ones come back home in a happier mood and calmer state.

Another such care center in Haarlem, North East Netherlands offers simulation as a way of reminiscence therapy. There are simulated bus rides, beach outings, and relaxation rooms that residents can use independently in the center. The settings are made to resemble natural scenarios with water wave sounds, ice cream vendors, heating fans, and sand in the beach rooms, and relaxation rooms with realistic wall paintings of scenic pictures. This setup is akin to a children's museum where there is pretend play with different themes.

In my search for newer avenues of care for the elderly, I spoke to Kavan Peterson, Chief Operating Officer for Minka homes and communities, a key player in the Momentia Seattle movement and supporter of UW Memory and Brain Wellness

Center's efforts to empower people with memory loss and their families. He is also Co-Founder and Director of Dr. Bill Thomas's ChangingAging blog and tour. Peterson and Thomas aim to change the way we perceive aging and challenge negative stereotypes. As for dementia villages, Peterson believes they only perpetuate segregation of persons with dementia. He states, "People living with dementia deserve to live in their communities, and we can make that happen." Minka homes were designed with this in mind.

Minka homes are relatively affordable homes with adaptable design based on Edo Period Japanese joinery techniques, which allow for easy modification to accommodate unique disabilities. The Minka concept and ChangingAging principles are being applied as the team converts a vacant school in Pennsylvania into a community of Minka homes where people of all ages and abilities are invited to live. This idea is called MAGIC, a dementia-friendly Multi Ability multi-Generational Inclusive Community that features smart homes built with Minka designs and universal adaptability to individual needs.



**A Minka home, via ChangingAging.org**

Peterson highlights the feasibility of Minka homes – they are prefabricated in a robotic factory by 3D printing and delivered as cargo. The cost of a studio layout is about \$100,000, plus the shipping, finalization, and finishing costs after set up at the location. The company states that the scaled down residences can offer the opportunity to remain in a familiar home and embrace aging with a focus on changing abilities rather than disabilities.

From dementia villages to new smart home design, these diverse approaches all seek to maximize independence and recognize inherent human dignity amid changing abilities. These efforts drive home the idea that guides Seattle's dementia-friendly movement and is influencing cities around the country: aging should be thought of as a period of continued growth, new connections, and renewed hope rather than a period of decline. •

## Living – and Contributing – with Memory Loss: The Role of Peer Mentors at the UW Memory and Brain Wellness Center

By Marigrace Becker, MSW

People with memory loss and their families play a key role in the UW Memory & Brain Wellness Center’s mission to promote well-being. Whether participating in advisory groups, helping develop programs and resources, or supporting others as peer mentors, volunteers who live with memory loss are making a vital contribution.

Philip Culbertson, who lives with Alzheimer’s, has served at the MBWC since October 2015. A committed member of our Community Education and Impact advisory group, Philip has provided feedback on a variety of our education and support programs. A skilled and prolific writer, he and his daughter both contributed content to our [“Living with Memory Loss”](#) handbook, sharing insights gleaned through their firsthand experience. Meanwhile, he helped design our introductory class for people recently diagnosed, [Memory Loss: A Guide to Next Steps](#).

“I really like helping out in these ways,” he states. “It makes me feel good about myself too.”

One of his favorite volunteer roles is acting as a peer mentor in the monthly class he helped design. As a peer mentor, Philip serves alongside other volunteers on a Q&A panel, fielding common questions about living with memory loss – How do you tell others about your diagnosis? What do you do for brain health? What community resources have been helpful to you?

Attendees often arrive feeling a bit hesitant, unsure what to expect and still adjusting to their diagnosis. Philip’s warm sense of humor, and his openness about his own Alzheimer’s diagnosis, quickly helps relax the group. Along with information and resources, they leave with uplifted spirits and the realization that they’re not alone.

“I like helping people to have a happier life. That’s the most important thing,” he states.

Sarah Parkhurst, who lives with mild cognitive impairment and volunteers each month with Philip as a peer mentor, also has had a long history of service at the MBWC. Sarah began volunteering in October 2014 as a member of the advisory group for the study of HABIT, a brain and body wellness program developed by the Mayo Clinic. From there, she was one of a small cadre of people with memory loss who helped develop the content and format of our “Living with Memory Loss” handbook, including co-authoring an article for people who have retired from driving and want transportation alternatives.

“I feel proud that I was able to be a part of putting these resources together,” says Sarah. “People often wonder, ‘where do we go from here?’ Having something concrete like a Handbook really helps.”

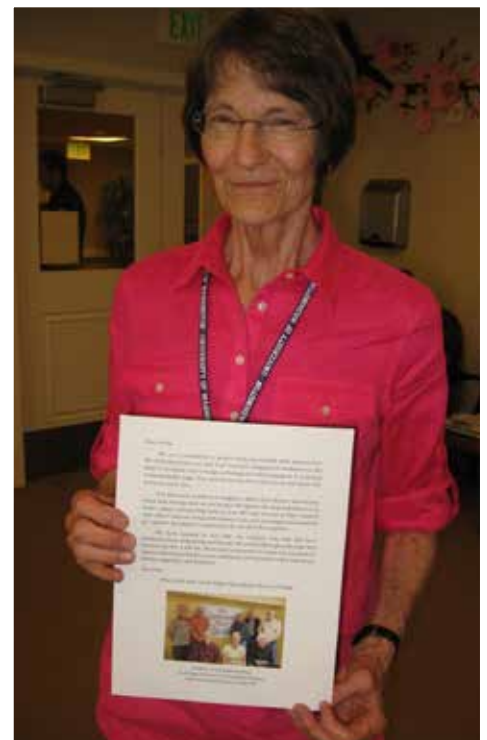
In her ongoing role as peer mentor, Sarah shares strategies that have worked for her – for example, always putting her keys and wallet in the same spot in her home. She also tells people about useful community resources, such as the monthly early stage memory loss support group she attends at the Greenwood Senior Center.

“I always wish I would have had a class like this when I was diagnosed,” says Sarah. “Getting that news can be so overwhelming. But coming to this class and seeing so many people who look like you and are going through the same thing – there’s a sense of camaraderie, and it helps you see that life continues beyond diagnosis.”

Reflecting on the class experience, participants regularly note the invaluable opportunity to hear from role models who are finding ways to adapt to their memory loss. “It gives you hope,” noted one attendee. >>



**Volunteer Philip Culbertson and his daughter Katie, who both contributed content for our Living with Memory Loss handbook.**



**Volunteer Sarah Parkhurst holds up an encouraging letter written by people with memory loss, that gets read in the monthly memory loss class she helped design. Read this letter, on the page to your right.**

Dr. Pamela Dean, a VA Medical Center neuropsychologist and Assistant Professor at UW who serves on the panel alongside Philip and Sarah, acknowledges the important contribution of the peer mentors.

“The peer mentors share their journey with humility, openness and humor, and give families a personal perspective of what it’s like to live with memory loss,” states Dean. “This helps break down stigma and provides encouragement in the midst of uncertainty.”

The UW Memory & Brain Wellness Center includes a diverse team of memory experts, including neurologists, geriatricians, neurologists, psychiatrists, and neuropsychologists. Yet we’re especially grateful for team members with the expertise of lived experience – people with memory loss themselves – who offer crucial perspectives and contributions. UW Memory & Brain Wellness Center Director Dr. Thomas Grabowski, MD agrees:

“We so appreciate the peer mentors and other volunteers who share their stories and contribute from their strengths to the people with memory loss that we serve. They inspire hope in the newly diagnosed, and they are key to modeling a community of support.” •

> If you have been diagnosed with memory loss and want to meet a peer mentor like Philip or Sarah at our introductory class – or if you’d like to explore volunteer opportunities yourself - contact us at [mbecker1@uw.edu](mailto:mbecker1@uw.edu), 206-744-2017.

Dear friend,

We are a community of people living successfully with memory loss. We understand that you also have received a diagnosis of memory loss. We want to recognize your courage in finding out what is going on. It is normal to feel disbelief, anger, fear, and denial, but know that you are not alone. Our hearts go out to you.

You may want to hide your diagnosis. Many of us did too, but we have found that sharing what we are living with lightens the load and allows us to lessen stigma surrounding memory loss. We urge you not to hide. Connect with others who are living with memory loss, and encourage your family to get support. Acceptance is important. We are all in this together.

We have learned to live with our memory loss and still have productive lives with family and friends. We would like to give you hope that you too can live a full life. There will be obstacles to come, but you have an opportunity to give back to your community and yourself, and to experience beauty, happiness, and kindness.

Sincerely,

Walt, Mark, Bob, Sarah, Roger, Ron, Helene, Rick, and Midge



Members of The Gathering Place  
Early Stage Memory Loss Enrichment Program  
Greenwood Senior Center, Seattle, WA



*Thank you for reading!*

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