Alzheimer's RESEARCH CENTER

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Progress Towards the Treatment and Prevention of Alzheimer's

Directors of the Alzheimer's Research Center

William H. Frey II, Ph.D.

Leah R. Hanson, Ph.D.

In this Issue:

Intranasal Insulin Improves Memory

Decreased insulin signaling in the brain contributes to both memory loss and brain degeneration in individuals with Alzheimer's disease. However, it is difficult to treat patients with insulin without causing side effects. At the Alzheimer's Research Center, we developed an intranasal insulin delivery method that targets insulin to the brain without causing unwanted side effects. When sprayed high into the nasal cavity, insulin travels rapidly into the brain along the nerves involved in smell. Our intranasal insulin treatment has been shown by researchers in Germany to improve both memory and mood in normal adults. Along with our collaborators at the University of Washington we showed that intranasal insulin improves memory, attention and functioning in patients in the early stages of Alzheimer's disease and in patients with mild cognitive impairment. Research is now in progress to determine how long the benefit of intranasal insulin can be maintained with prolonged treatment. Our current intranasal insulin clinical trial assess the safety and benefits of this treatment over a six month period using the most advanced nasal spray device for delivering insulin to the brain.

Who We Are

The Alzheimer's Research Center relies on charitable donations, bequests and grants to conduct internationally recognized research for Alzheimer's disease, Parkinson's disease, stroke and other nervous system disorders. The research center has been located in St. Paul, MN for over 35 years.

How to Donate

Donations can be made either by mail or phone. To mail in a donation, checks can be sent to Alzheimer's Research Center, 640 Jackson Street, Mail Stop 11202C, St. Paul, MN 55101. To make a credit card donation please call us at 1-800-229-2872. Make checks payable to "RHF-Alzheimer's Research". If you would like your donation to be in memory of someone include their name and the family's name and address so we can forward an acknowledgement to them. Gifts made to the Center are processed through Regions Hospital Foundation, a charitable organization that as part of its mission raises funds on behalf of the Alzheimer's Research Center and other programs in patient care, medical research and education. Should you wish to discuss making a planned gift or special bequest to Alzheimer's research call 1-800-229-2872.

What is Alzheimer's Disease?

Alzheimer's disease is characterized by loss of recent memory, confusion, disorientation and sometimes a change in personality. Patients suffer from progressive degeneration and loss of brain cells and acetylcholine, the chemical messenger needed for memory.

Other causes of memory loss include deficiencies of thyroid hormone or vitamin B12; also small strokes can affect memory and cognition. These causes of memory loss can be detected with blood tests or a brain scan such as a CT or MRI.

Individuals with significant memory loss should get a thorough neurological exam to rule out other potential causes of dementia. While research is being conducted, there is currently no definitive test for Alzheimer's disease short of an autopsy, following the death of the patient.

Patients with memory loss or confusion should be evaluated by a neurologist or by a physician familiar with dementing illnesses. If no other cause for dementia can be determined, the physician may give a diagnosis of probable Alzheimer's disease.

Vitamin D deficiency increases the risk for Alzheimer's Disease

Vitamin D deficiency markedly increases the risk of dementia and Alzheimer's disease. It is extremely prevalent among the elderly and is not uncommon in younger adults as well. In addition, vitamin D deficiency is associated with an increased risk of stroke. Therefore, low blood vitamin D concentrations increase the risk of dementia and Alzheimer's disease through both neurodegenerative and vascular mechanisms. Consequently, anyone interested in reducing their risk for Alzheimer's disease should have a blood test to determine their level of vitamin D. If their vitamin D level is low, they should speak with their physician about correcting this deficiency.

Additional Risk Factors for Developing Alzheimer's Disease

Aging is a major risk factor for Alzheimer's disease. The incidence and the prevalence rate for Alzheimer's disease doubles every 5 years after the age of 65. However, some individuals develop Alzheimer's disease in their 50's or rarely even earlier.

Family history of Alzheimer's disease increases the risk for developing Alzheimer's disease. Having the APOE4 genotype significantly increases the risk for late onset Alzheimer's disease.

Diabetes is associated with an increased risk for developing Alzheimer's and decline in cognitive function.

Obesity, or having a large amount of abdominal fat, increases the risk for Alzheimer's disease.

Poor Diet that contains a high intake of total fat, saturated fat, and total cholesterol increases the risk of dementia. Reduced consumption of fish containing omega-3 fatty acids also increases the risk for age-related cognitive decline and Alzheimer's disease.

Smoking increases the risk for Alzheimer's disease.

Lack of mental activity and exercise in mid-life may be a risk factor for developing Alzheimer's.

Head trauma with loss of consciousness may be a risk factor for Alzheimer's disease.

Planning for a gift to the Alzheimers Research Center from your estate

If you would like to discuss providing for the future of the Alzheimer's Research Center through an estate gift to ensure their continued progress toward developing and testing new treatments for Alzheimer's disease, please call us at 1-800-229-2872.

Intranasal deferoxamine binds iron that accumulates abnormally in the brain in Alzheimer's, Parkinson's and other brain disorders

Free iron accumulates abnormally in the brains of individuals with Alzheimer's disease, Parkinson's disease, stroke, traumatic brain injury and other brain disorders where the free iron causes oxidative stress and brain damage. Treatment with deferoxamine, an approved generic drug that binds iron, has been found in animals to treat a variety of brain disorders of this type as described below. This is an example of repurposing an existing drug to treat Alzheimer's disease, Parkinson's disease, stroke and other brain disorders by using noninvasive intranasal delivery to bypass the blood-brain barrier and target the drug to the brain.

Along with our collaborators at the San Francisco VA Medical Center, we have discovered that intranasal deferoxamine bypasses the blood-brain barrier to treat and prevent brain damage in animal models of Parkinson's, Alzheimer's, stroke and certain other major neurological disorders. In addition to treating and reducing brain damage from stroke, intranasal deferoxamine significantly improves memory in normal mice and reduces memory loss in mouse models of Alzheimer's disease. It also protects the brain against degeneration and improves movement function in animal models of Parkinson's disease. We are now seeking to test this non-invasive, inexpensive and practical method of treatment and prevention in patients with Alzheimer's disease, Parkinson's disease, stroke, concussion, hemorrhage, traumatic brain injury and other brain disorders.

The National Institute of Aging has funded some of the safety studies necessary to enter human clinical trials with intranasal deferoxamine, and the results to date are promising. While a two year clinical trial of intramuscular deferoxamine was shown to reduce cognitive decline in Alzheimer's patients by 50%, there were some side effects. One intranasal deferoxamine safety clinical trial was conducted in humans, and it showed no significant side effects. Intranasal deferoxamine may also be extremely useful to protect military personnel from brain damage associated with closed head injury and for rapid treatment in the field to treat those who have experienced a closed head injury. Similarly, it may be useful to treat auto accident victims who have had a head injury.

Symptoms of Dementia

Memory loss – Forgetting conversations and events that happened recently.

Disorientation – Not knowing where you are and how you got there, getting lost close to home, not knowing what year or month it is.

Language problems – Difficulty putting thoughts into words, difficulty finding simple words, forgetting what you are trying to say, sometimes even before you have completed saying it.

Problems performing usual tasks – Planning and making a meal, balancing a checkbook, following a recipe, etc.

Misplacing things – Losing things or putting them in odd places.

Problems with concentrating, abstract thinking and judgment – Wearing inappropriate clothing, giving money or private financial information to telemarketers, having difficulty understanding and using numbers, etc.

Loss of interest and initiative – Discontinuing pursuit of their usual activities and interests, watching TV for extended periods of time and sleeping a great deal.

Changes in mood, behavior and personality – Mood swings, irritability, aggressiveness, depression, anxiety, suspiciousness, loss of inhibitions and wandering.

Changes in visual and spatial perception – Difficulty understanding and interpreting what is seen.

Our Mission Statement

Our mission is to improve the treatment and prevention of Alzheimer's disease and other neurologic disorders by advancing scientific knowledge through creative and collaborative research. We strive to educate the community and serve as a resource, bringing together patients, families, research centers, universities, and pharmaceutical companies with the common goal of curing Alzheimer's disease.

Developing Treatments for Alzheimer's, Parkinson's, stroke, multiple sclerosis, brain tumors and other disorders using intranasal adult therapeutic cells • • • • • • • • • • •

Together with collaborators in Germany, especially Lusine Danielyan M.D., Dr. William H. Frey II of the Alzheimer's Research Center discovered that therapeutic cells, including adult stem cells, immune cells and genetically-engineered cells, can be delivered to the brain using the intranasal delivery method. This method was shown to successfully treat Parkinson's disease in an animal model with intranasal adult bone marrow derived mesenchymal stem cells. Intranasal stem cells bypass the blood-brain barrier to target the brain by traveling along the olfactory neural pathway. Once in the brain, adult stem cells were shown to target the damaged areas of the brain specifically to treat the underlying disease.

Researchers at University Medical Center Utrecht in the Netherlands have demonstrated the effectiveness of intranasal stem cell treatment in an animal models of neonatal cerebral ischemia, neonatal brain damage and subarachnoid hemorrhage. Researchers at Emory University in Atlanta have used our intranasal stem cell treatment successfully in an animal model of stroke, and researchers at Uppsala University in Sweden have demonstrated that intranasal immune cell therapy reduced symptoms and inflammation in multiple sclerosis. Intranasal adult neural stem cells have also been shown to improve an animal model of multiple sclerosis as have intranasal mesenchymal stromal cells. Still other researchers have reported that intranasal stem cells target and treat brain tumors.

Along with collaborators, Dr. Frey has also reported that intranasal adult stem cells and other therapeutic cells target the areas of the brain damaged by Alzheimer's disease in mice. This delivery and treatment method can facilitate the development of adult stem cell, immune cell and genetically-engineered cell therapies for Alzheimer's, Parkinson's, stroke, multiple sclerosis, ALS, PSP, Huntington's, neonatal ischemia, brain tumors, traumatic brain injury and spinal cord injury.

In humans, our own nerve cells are known to reach the brain by using this same olfactory neural pathway during development. In addition, pathologic cells, such as the amoeba Naegleria fowleri found in polluted water, are known to enter the brains of humans by this same pathway and cause amoebic infection of the brain. Fortunately, we have now discovered how to use this pathway to deliver therapeutic cells to the brain to treat brain disorders.

Medications for the Treatment of Mild to Moderate Alzheimer's Disease • • •

Aricept ***®*** *(Pfizer, Inc.) – FDA approved 1996* has been shown to improve the cognitive abilities of some patients and may slow the progression of Alzheimer's disease. It has become the drug of choice for treatment of Alzheimer's disease. However, patients treated with Aricept may decline abruptly if the medication is ever discontinued.

Razadyne ***®*** ***(****Janssen, Inc.) – FDA approved 2000,* is also for patients with mild to moderate Alzheimer's disease. It improves activities of daily living such as dressing, eating, using the bathroom, preparing meals, and using a phone; all which are things that demand much of a caregiver's time.

Exelon® *(Novartis, Inc.) – FDA approved 2000,* is available for the treatment of mild to moderate Alzheimer's disease. It has been proven to have a positive effect on the three main areas of overall functioning, including behavior, cognition, and activities of daily living. A skin patch form of Exelon has recently been approved, which may lessen side effects such as nausea and vomiting.

Namenda® (*Forrest Pharmaceuticals*) – *FDA approved 2003*, for treatment of moderate to severe Alzheimer's disease. It has been shown to improve ability to think, activities of daily living, and behavior. It has also been shown to provide additional benefit when taken in combination with Aricept.

A Note to Caregivers

If you are a caregiver, be sure to care for your own health too by eating a balanced diet, exercising, and implementing a stress management regimen. A study at Stanford University found that older women, who averaged 72 hours a week caring for a demented family member, benefited significantly from moderate exercise such as brisk walking for half an hour, four times a week. It can also help to take a break by using a respite care service or asking other family members or friends to help out. For assistance with finding and using a respite care service, contact The National Council on Aging at 1-800-222-2225.

Tips for Brain-Healthy Living

Our brain interprets the world around us, gives us the capacity for rational thought, is responsible for our personalities, holds our memories, and controls our bodies. Yet, despite it's importance, brain health is often overlooked. Improve your cognitive health with these 5 keys to brain-healthy living.

Social Engagement

Being socially active is a great way to challenge your brain, and also helps maintain support networks. Studies show that people who isolate themselves have a greater risk for developing dementia than people who remain socially engaged.

Ideas to increase social engagement:

- **Keep in touch** with family and friends. Be the one to initiate phone calls or get-togethers. If it seems hard to find the time, schedule time to connect.
- **Join a club or activity.** Find something that interests you by looking at community newsletters, bulletin boards, or online.
- **Make an effort** to attend often overlooked social events like class reunions, workplace gatherings, or community meetings. Volunteer for a cause or campaign that you've always wanted to support.
- **Take advantage of casual encounters.** Chat with someone in line at the grocery store, or get to know your neighbors.

Mental Stimulation

Keeping mentally active is an important part of brain health. Challenging yourself to think actively and try new things builds connections between brain cells, like exercising your body builds up muscle cells.

Exercise your brain with these activities:

- **Play strategy games**, or try games specifically designed to exercise your brain.
- **Read and write daily.**
- **Seek new activities** and unfamiliar settings, like traveling or a new hobby.
- **Continue your education** by taking a class or learning a new language.
- **Try doing things with your non-dominant hand.** If you're right-handed, use your left hand to brush your teeth & open doors, or take the first stair with your left leg.
- **Take up new hobbies.** Hobbies involving hand-eye coordination and mental calculation (like sewing, woodworking) are great ways to involve different parts of the brain. Either playing or listening to music can have a positive effect on the brain.

Cardiovascular Health

Heart health is closely linked to brain health. Cardiovascular problems like high blood pressure, heart disease, stroke, diabetes, and high cholesterol increase the risk of developing dementias like Alzheimer's disease and vascular dementia. Help your brain by following these heart-healthy guidelines:

- **Don't smoke**, and avoid second hand smoke. There is a strong link between heavy smoking and certain brain diseases.
- **Maintain a healthy weight.** Being overweight or obese increases the risk for type 2 diabetes, which is also strongly linked to decreased brain function.
- **Manage your blood pressure & cholesterol.**
- **Moderate sugar, salt, and alcohol consumption.**

Looking for other ways to boost your memory? Get plenty of sleep and avoid excess stress.

Learn how to live well with Alzheimer's: The Living Well Book

Here is a link for tips on how to live well with a dementia diagnosis. It is a guide for persons with mild cognitive impairment (MCI) & Early dementia.

https://www.healthpartners.com/ucm/groups/public/@hp/@public/documents/documents/cntrb_028820.pdf

More Tips for Brain-Healthy Living

Physical Activity

Physical activity is one of the best ways to improve or maintain brain health. The brain receives energy and nutrients from the blood, so getting your heart rate up while exercising helps the brain get the fuel it needs. And it needs a lot of fuel – although the brain only makes up about 2% of the body by weight, it uses more than 20% of daily energy intake.

How much exercise should you get to boost your brain-power? One study showed that older people who exercised for 30 minutes at least 3 times a week had nearly 40% lower risk of dementia. If spending 30+ minutes at the gym seems daunting, here are some alternate ways to get active.

Incorporate exercise into family activities. Take a walk after dinner, play croquet in the yard, stroll through an apple orchard or pumpkin patch, head to the park, take a bike ride, fly a kite, enjoy a museum, go shopping, do some cleaning or yard work, wash the car by hand, toss a Frisbee, or play with the dog.

Work in short bouts of activity throughout the day. Take 10 minutes and jump rope, do some squats, lunges and jumping-jacks, do yoga poses and stretch, climb the stairs, or simply get up and walk around.

Take up an active hobby like gardening, dancing, horseback riding, coaching youth sports, sailing, or golf. Exercise doesn't have to feel like work.

If you're limited by physical restrictions, look for alternate ways to exercise. Many exercises can be done while seated (try a recumbent bike or seated weight exercises). Swimming or water aerobics are great alternatives to weight-bearing exercise. Yoga and tai chi are also good low-stress exercise options.

Nutrition

A healthy diet both improves everyday mental function and reduces the risk for chronic age-related brain diseases. Adopt a healthy diet by eating fresh vegetables, fruits, and lean meats. Dark-skinned vegetables and fruits tend to have more brain benefits. Cut back on foods high in unhealthy fats and cholesterol. Instead, use mono- and polyunsaturated fats (like olive oil) and choose grilled or baked foods over fried foods. The following foods are particularly good for brain health.

Blueberries and other berries help protect the brain from oxidative stress and may slow age-related cognitive decline.

Fish like mackerel, trout, tuna, and salmon are rich in omega-3 fatty acids, which are essential to proper brain function and have anti-inflammatory properties. Fish are also a healthier substitute for red meats high in saturated fat.

Nuts and seeds are good sources of vitamin E, which has been associated with decreasing cognitive decline caused by aging. But watch the serving size and avoid salted or coated nuts.

Avocados contain healthy fats and vitamins and may promote both cardiovascular and brain health. Try spreading mashed avocado on bread rather than using mayonnaise or butter. Like nuts, avocados are high in calories, so limit a serving to ¼ or ½ an avocado.

Whole grains have a number of health benefits, and may play a role in decreasing risk for brain diseases. Good options include oatmeal, brown rice, barley, rye, millet, quinoa, or whole grain breads, pastas, and flour. But be sure to look for the word "whole" before the grain – terms like "multigrain," "100% wheat," or "stone-ground" don't necessarily mean the product is whole grain.

The Alzheimer's Research Center is a legal assumed name of the HealthPartners Research Foundation, a Minnesota nonprofit corporation, and is located on the campus of Regions Hospital at 640 Jackson Street, Saint Paul, Minnesota 55101.