



**HealthPartners®**  
*Center for Memory & Aging*

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# **New Approaches to Treating and Preventing Alzheimer's and other Brain Disorders**

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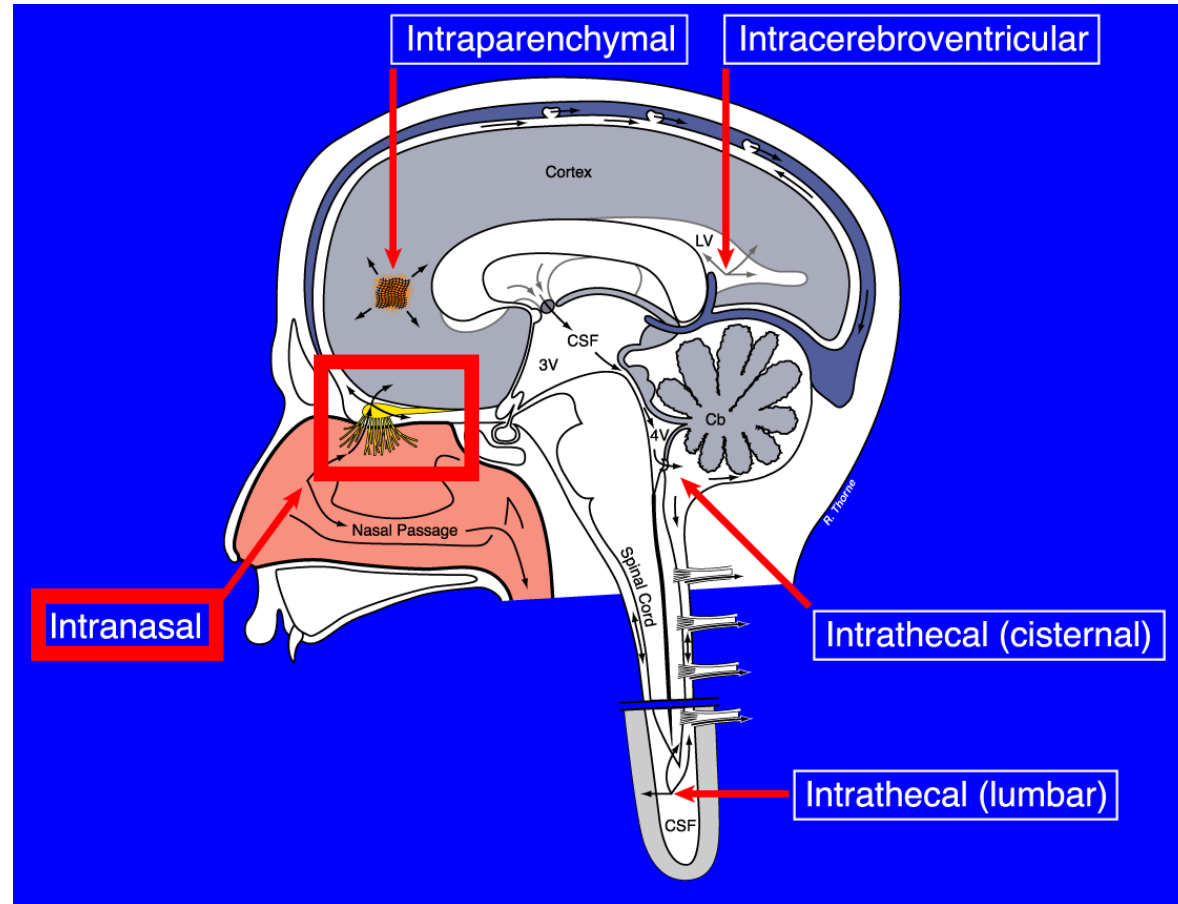
Ramsey County Library--Roseville

September 12, 2019

# Why Has It Taken so Long to Develop a Treatment for Alzheimer's Disease?

- The blood-brain barrier which protects the brain, our most important organ, severely limits the kind of therapeutics that can be delivered to the brain.
- Also, administering drugs as a pill or a shot leads to numerous side effects in other organs.
- HealthPartners Neuroscience has solved the blood-brain barrier problem for scientists around the world, and **an unusual dream gave us the first clue.**

# Bypassing the Blood-brain Barrier



Thorne and Frey Clinical Pharmacokinetics 40: 907-946 (2001)

# Intranasal Delivery to the Brain

- Is non-invasive.
- Bypasses the blood-brain barrier.
- Results in rapid delivery to the brain along the nerves involved in smell.
- Reduces systemic exposure and unwanted side effects.

# Alzheimer's Disease is the Most Common Type of Dementia.

- Dementia is a general term describing degenerative brain disorders characterized by loss of short term memory, confusion and disorientation.
- Alzheimer's disease accounts for 65% of dementia cases with the rest being due to Lewy Body Dementia, vascular dementia, Frontotemporal dementia and other diseases.
- While others have reduced amyloid in the brain to treat AD without success, we have taken a very different approach.
- Insulin signaling and brain cell energy decrease in AD, while iron and inflammation increase in the brain. Our intranasal treatments target these serious problems.

# Iron Accumulates Abnormally in the Brain in Alzheimer's and other Brain Disorders.

- Iron accumulates abnormally in the brain in Alzheimer's, Parkinson's, Stroke, Traumatic Brain Injury (TBI) and other brain disorders.
- Iron promotes oxidative damage which inactivates the human brain receptor required for memory and other key brain components required for normal brain function.

# Deferoxamine Treats Alzheimer's

- Deferoxamine (DFO) is a generic drug that binds iron and has been used to treat iron overload in the blood in humans for decades.
- In a two year clinical trial in patients with Alzheimer's disease, intramuscular DFO was shown to reduce decline by 50% but had significant side effects and does not cross the blood-brain barrier well.
- Consequently, we have developed and patented intranasal DFO to treat Alzheimer's and other brain disorders.

# Intranasal DFO Protects Brain Cells and Improves Memory & Movement.

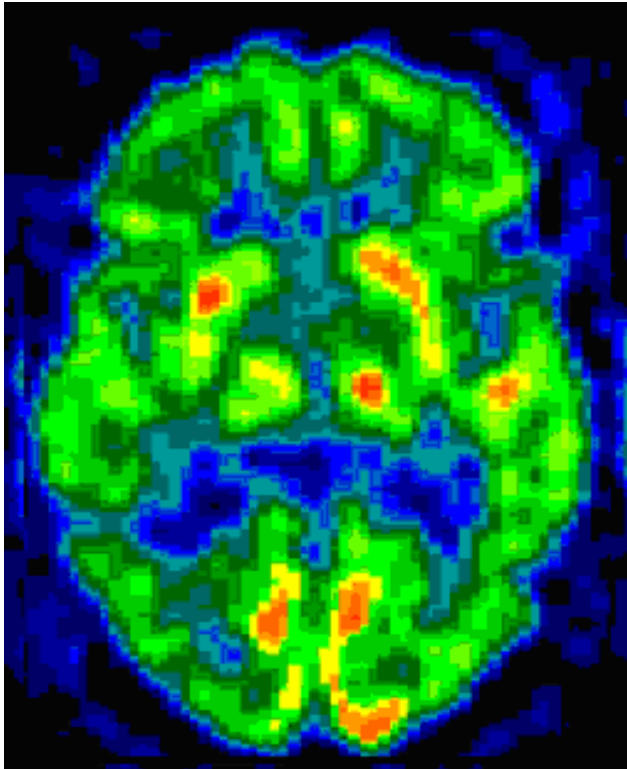
- Intranasal DFO reduces memory loss in a mouse model of Alzheimer's disease and improves memory in normal mice.
- Intranasal DFO treats Parkinson's disease in animal models.
- Just a few nose drops of DFO given before or after a Stroke, reduces brain damage in rats by 55%.
- As funding becomes available, we will conduct clinical trials of this treatment in people with Alzheimer's Parkinson's, Stroke and other brain disorders.



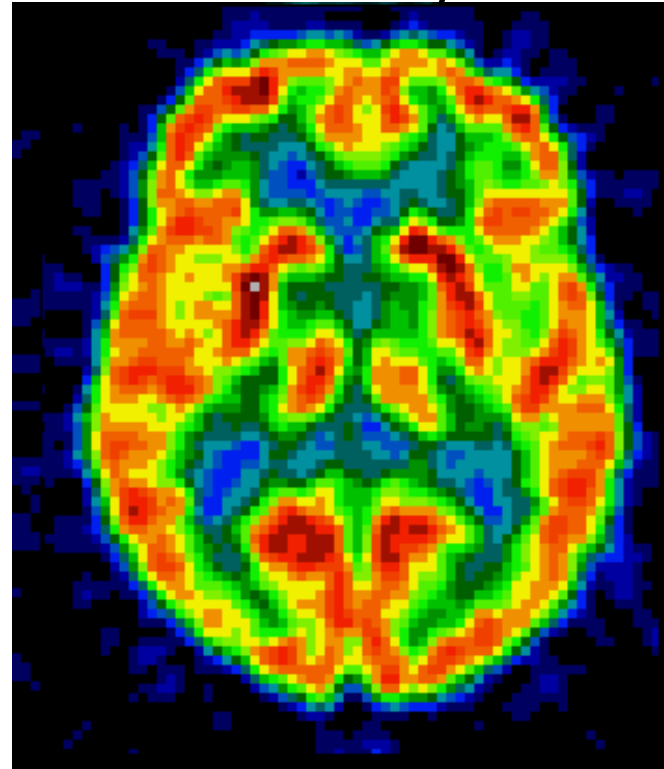
# Alzheimer's Patients' Brains Do Not Take Up Glucose Properly.

## Glucose Uptake & Utilization (FDG-PET)

Alzheimer's Patient



Normal Elderly Adult



Li...de Leon et al. (2008) Eur. J. Nucl. Med. Mol. Imaging

# Intranasal Insulin Improves Memory in Patients with Alzheimer's Disease.

- Insulin signaling is reduced in the brains of Alzheimer's patients causing "**diabetes of the brain**" which leaves brain cells starved for energy and unable to function normally.
- **We discovered and patented the intranasal insulin treatment for Alzheimer's disease and Parkinson's disease.**
- **Six trials in Alzheimer's patients and five trials in normal human adults demonstrated improved memory following intranasal insulin treatment with no change in the blood levels of insulin or glucose.**

# Intranasal Insulin Clinical Trials are Being Conducted at HealthPartners.

- The NIH and Obama administration cited intranasal insulin as the most promising treatment in development for AD in 2012. Additional trials are still needed to obtain FDA approval for intranasal insulin as a treatment for Alzheimer's and other memory disorders.
- We have been conducting clinical trials of intranasal insulin, funded by our donors, at the Center for Memory & Aging in the HealthPartners Neuroscience Center in St. Paul. We are currently testing intranasal insulin as a potential treatment for Frontotemporal Dementia (FTD).

# Michael Rosenbloom M.D.



Principal Investigator: Intranasal Insulin Clinical Trials

Director, Center for Memory & Aging



# Diabetes Doubles the Risk for Alzheimer's.

- Diabetes doubles the risk for getting Alzheimer's disease which is not surprising since diabetics have a deficiency of insulin signaling.
- Human studies are needed to determine if intranasal insulin can reduce the risk of Alzheimer's disease in the millions of people with diabetes.
- Intranasal insulin improves cognition in individuals with Type 2 diabetes and may benefit those with Type 1 diabetes by helping the brain respond to hypoglycemia (low blood sugar). This is important since hypoglycemia in those with Type 1 can sometimes be fatal.



# Intranasal Insulin Treatment of Parkinson's Disease

- In a small clinical trial at Harvard and the University of Massachusetts, the intranasal insulin treated patients had a better total score compared to the placebo group which suggested preservation of verbal fluency and memory.
- The intranasal insulin treated patients also had less disability and improved movement when compared to baseline.
- The placebo group had no change.

# Intranasal Insulin May Also Treat Other Brain Disorders

- Because **Epilepsy** involves decreased glucose uptake and metabolism, and decreased glucose metabolism can cause seizures, we plan to conduct a clinical trial of intranasal insulin in individuals with **Seizures**.
- Our first clinical trial of intranasal insulin treatment of **PTSD** should begin in 2019 with Yale University.
- **Intranasal insulin treatment improves recovery after Traumatic Brain Injury in rats.** We need funding to test this in humans with **Concussion and Traumatic Brain Injury**.

# Intranasal Adult Stem Cells Treat Alzheimer's, Parkinson's and Other Brain Disorders in Animals.

- We discovered that adult stem cells, obtained from our bone marrow, bypass the blood-brain barrier when administered as nose drops and specifically target the damaged areas of the brain in animals to treat Alzheimer's, Parkinson's and other brain disorders.
- Intranasal stem cells are anti-inflammatory and can supply what the brain needs to regenerate and to treat Alzheimer's, Parkinson's, MS, stroke, brain tumors and neonatal brain damage including perhaps cerebral palsy.



# Intranasal Therapeutic Cells Treat Neurological Diseases in Animals.

Parkinson's Disease (6-OH-DA)	I.N. MSCs Rats	Improved motor function and reduced pro-inflammatory cytokines to normal levels.	Danielyan et al. (2011)
<b>Alzheimer's Disease</b> (3xTg-AD)	I.N. MSCs Mice	<b>Improved memory and decreased soluble amyloid.</b>	Danielyan et al. (2017)
Neonatal Ischemia  Neonatal Brain Damage Perinatal Brain Damage	I.N. MSCs Mice  I.N. MSCs Mice I.N. Umbilical Cord Cells	Improved sensory motor function. Reduced loss of white and gray matter. Cognitive/Sensorimotor improved. Preserves myelination.	Van Velthoven et al. (2010)  Donega et al (2013) Opplinger et al (2016)
Stroke (MCAO)	I.N. MSCs Rats	Reduced neuronal cell death.	Wei et al. (2012)
Multiple Sclerosis (EAE)	I.N. T Reg Cells Mice I.N. aNSCs	Reduced inflammation and disease symptoms. Function recovery/remyelination.	Fransson et al. (2012) Wu et al. (2013)
Brain Tumors	IN NSPCs Mice IN MSC-TRAIL	Targeted brain tumors and improved survival.	Reitz et al. (2012) Balyasnikova (2014)
Spinal Cord Injury	IN MSCs	Improved motor function and reduced lesion size.	Ninomiya et al. (2015)

# Our Discoveries Are Revolutionary

- Our intranasal treatments represent a dramatic departure from the last 40 years which have focused entirely on efforts to treat Alzheimer's by reducing the accumulation of beta amyloid.
- This amyloid strategy has resulted in decades of failed human clinical trials as witnessed by the latest 18 billion dollar loss by Biogen. Similar losses occurred in the failed efforts of Eisai, Roche, Lily, Pfizer, J&J and Merck, who also developed drugs to reduce amyloid to treat Alzheimer's disease. While some of these drugs did reduce amyloid, none improved memory in people with Alzheimer's disease.

# Preventing Memory Loss and Reducing the Risk for Alzheimer's Disease.

- Protecting the brain from injury
- Exercise (3 times per week, 45 minutes each time)
- Diet (The Mind Diet), Turmeric/Curcumin, Green Tea
- Keeping mentally and socially active
- Maintaining high normal blood levels of vitamin D
- Maintaining normal blood levels of vitamin B12
- Maintaining normal blood levels of thyroid hormone.

# Plants and Humans Evolved Together.

- Plants are not only the major source of food and nutrients in our diet required for health but also are the source of many of our medicines.
- Plants are the original source for perhaps 40% of the pharmaceuticals in use in the United States today.
- Foods derived from plants can have both nutrient and pharmacologic effects on our brains.

# The MIND Diet Is Associated with Reduced Incidence of Alzheimer's Disease.

These authors investigated the diet-Alzheimer's disease relationship in a prospective study of 923 participants, ages 58 to 98 years, followed on average 4.5 years.

MIND diet associated with reduced incidence of Alzheimer's disease, Bennett and Aggarwal from Rush University and Harvard School of Public Health, *Alzheimer's & Dementia* 2015;11(9):1007-14.

# Greater Adherence to the MIND Diet May Protect Against Alzheimer's Disease.

- This prospective study of the MIND diet provides evidence that greater adherence to the overall dietary pattern may be protective against the development of Alzheimer's disease.
- The estimated effect was a 53% reduction in the rate of Alzheimer's disease for persons in the highest tertile of MIND scores and a 35% reduction for the middle tertile of scores compared with the lowest tertile.

# Details of the MIND Diet.

## **These 10 food groups are included:**

- Green leafy vegetables (spinach, kale, chard, collard greens and salad greens): At least six servings a week
- Other vegetables: At least one a day
- Nuts: Five servings a week (walnuts, pistachios, sunflower nuts)
- Berries: (blueberries, strawberries) Two or more servings a week
- Beans: At least three servings a week
- Whole grains: Three or more servings a day
- Fish: Once a week (salmon, tuna, herring, sardines, black cod)
- Poultry (chicken or turkey): Two times a week
- Olive oil: Use it as your main cooking oil.
- Wine: One glass a day

# Details of the MIND Diet.

## **Eat Less of these foods:**

- Red meat: Less than four servings a week
- Butter and margarine: Less than a tablespoon daily
- Cheese: Less than one serving a week
- Pastries and sweets: Less than five servings a week
- Fried or fast food: Less than one serving a week



# Treating & Preventing Alzheimer's Disease

- Studies suggest that the MIND diet reduces the risk of developing Alzheimer's disease.
- Turmeric and green tea are also likely helpful.
- Consider not only Big Pharma but also Little Farmer!
- Diet, exercise and remaining socially and mentally active are important for maintaining brain health and reducing the risk of Alzheimer's and other brain disorders.
- **Discovering INTRANASAL insulin, deferoxamine and stem cells moves us toward FDA approval to treat and prevent Alzheimer's and other brain disorders.**

# Following the MIND Diet: It's tough, but someone has to do it.



# Key Take Home Messages

- We discovered that therapeutics for treating Alzheimer's and other brain disorders can be intranasally delivered to the brain, solving the problem created by the blood-brain barrier. This intranasal method of treatment is now being used by scientists and clinicians around the world.
- The intranasal insulin treatment we discovered safely improves memory in people with Alzheimer's disease.
- Intranasal deferoxamine and adult stem cells treat Alzheimer's in animals. As funding becomes available, we will also test these in humans.

# Contact Us



To support our work, find us online at  
[www.Alzheimersinfo.org](http://www.Alzheimersinfo.org)



For more information email us at  
[MemoryLoss@HealthPartners.com](mailto:MemoryLoss@HealthPartners.com)



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[www.Facebook.com/FightMemoryLoss](http://www.Facebook.com/FightMemoryLoss)



Call us at 651-495-6565 for more information.  
Call us at 651-495-6306 to schedule a visit with  
the Center for Memory & Aging.



# Applying our Treatments to Children and Newborns

- Preemies: Neurological disorders of low birth weight infants
- Cerebral Palsy (improper cell migration or myelination...)
- Neonatal Hypoxic-Ischemia (HIE)
- Autism and Social Communication Disorder (gestational diabetes)
- Shaken Baby Syndrome / Concussion and Traumatic Brain Injury
- Posttraumatic Stress Disorder (PTSD)

# Applying our Treatments to Children and Newborns

- Down Syndrome (including AD after age 35)
- Type 1 Diabetes (Hypoglycemia Unawareness)
- Stroke
- NBIA, PKAN, Hallervorden–Spatz syndrome
- Lysosomal Storage Disorders
- Seizures and Seizure Disorders such as Epilepsy or West Syndrome
- Headache (chronic migraine and cluster headache)
- Attention Deficit Disorder