

What Science Tells Us about Healthy Brains and Healthy Lifestyles – Overview and International Lifestyle Studies





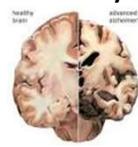
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Alzheimer's Statistics

- 6th leading cause of death
- 5.4 Million are living with Alzheimer's today
- **Prevalence of Alzheimer's disease doubles every 5 years after age 65**
- 13% over age 65 have Alzheimer's
- **Approximately 40% over age 85 have Alzheimer's or another dementia**
- It is a health & economic issue; costs \$200 billion+
- Only major chronic illness with no cure
- 2015 only \$600 million on research, \$300-400 mil added each year! FY2019 passed budget is \$2.3 bil.



Source: Alzheimer's Association

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Brain, Body & Nutrition Connection

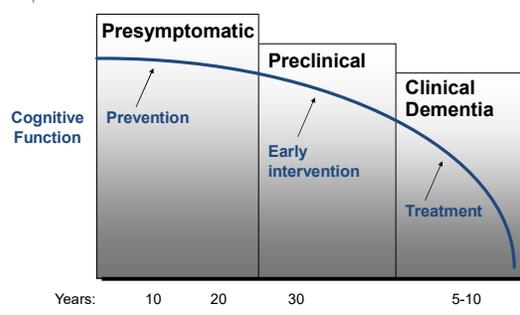
- Brain health is dramatically affected by health of the rest of the body
- Alzheimer's Disease, Parkinson's and most other degenerative neurologic diseases are chronic
- Alzheimer's Disease is complex, with many environmental and genetic risk factors
- AD a whole body disease: gut, liver, bile acids involved.
- Indications of auto-immune disease
 - Possible effect of long harbored viruses, and/or
 - bacteria in brain
- **Multiple pathways to same pathology?**



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Alzheimer's Disease Takes 2-3 Decades to Develop



Years: 10 20 30 5-10

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Chronic Conditions Influence Risk

- Cardiovascular Disease – aggressive management of BP to 120-130 reduces risk of MCI by nearly 20%
- Pre-Diabetes/Insulin Resistance and Diabetes
- Destructive Processes
 - ✓ Inflammation
 - ✓ Oxidative Stress




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How Do We Reverse Insulin Resistance & Block this Path to Dementia? At Least 5 Lifestyles Common To Help Blood Sugar & Brain:

- Exercise- we are made to move!
- Sleep
- Decrease stress
- Decrease inflammation – thru Exercise & Nutrition
- Appropriate nutrition e.g. MPN, MIND, Nordic or Mediterranean & less sugar!
- Interactive effect with hypertension

Source: Suzanne Craft 2007

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HOW DO WE PREVENT OR REVERSE A Shrinking Hippocampus?

- Nutrition of course, by reducing insulin resistance, oxidative stress, inflammation and more.
- But the story is even more exciting.

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Exercise HELPS US GROW NEW BRAIN CELLS.

- THE MORE WE EXERCISE, THE FASTER WE PRODUCE MORE BRAIN CELLS.
- WHICH AREA OF THE BRAIN IS AMONG MOST RESPONSIVE TO EXERCISE, GROWING MORE BRAIN CELLS?
- THE HIPPOCAMPUS!

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Brain and Body: We are One

- Whatever hurts heart and blood vessels harms the brain.
- Problems with glucose metabolism also threaten the brain. Diabetes, “pre-diabetes” and insulin resistance all increase risk.
- The organ & disease silos are disintegrating.
- Increasingly similar clinical recommendations.
- Healthy lifestyle, especially nutrition & exercise, helps prevent and treat most human chronic diseases.
- Thus **Healthy Lifestyles are helpful to both persons with dementia and to their carers who are at risk of depression and illness.**

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Possible Role for Microbes in Alzheimer's Risk and Progression

- Beta Amyloid or A-beta, is part of ancient immune system to protect the brain from microbial invaders (MGH)
- Production of beta-amyloid increases when foreign microbes are present and surround individual bacteria, viruses and perhaps other microbes, in order to neutralize their effects.
- This activity can lead to neuro-inflammation which may in turn get out of control, and lead to chronic problems, including excess A-beta, that help cause harm to the brain.
- Raises question of whether AD is an auto-immune disease. **Multiple pathways to AD?**

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Increased Brain Microbial Burden May Directly Exacerbate B-amyloid Deposition, Inflammation, & AD Progression

- Various microbes under study. <https://www.nature.com/articles/d41586-020-03084-9> Nov.4 & 10, 2020
- Some Herpes viruses dormant in brain for decades may for unknown reasons activate or aggravate the inflammation/A beta/Tau aspects of Alzheimer's disease (Dudley et al Mt. Sinai researchers found Herpes viruses 6 & 7 common in brains of people with AD—these are common viruses causing roseola in children under 3. June 21 2018 Neuron)
- Tanzi, MGH show mechanisms in lab and animals-virus seeds A B deposition-both HSV1 and Herpes 6a&b (Alzheimer's Disease-Associated β -Amyloid Is Rapidly Seeded by Herpesviridae to Protect against Brain Infection. Neuron Dec 2018 on-line July)
- Ruth Itzhaki in 1990s id'd “cold sore virus, i.e. herpes simplex virus 1 (HSV1), combined with certain genetic factor, account for 60 % AD cases” & recommended Anti-viral treatment. (J or Pathology, 2009) **Ignored and unfunded for decades.** “Most of us always acknowledged that amyloid was a very important feature of Alzheimer's — but it is just not the cause,” she says.

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Possible Role of Bacteria

- Other researchers are looking at resident bacteria dormant in the brain that under as yet unknown conditions can activate the same trio of AD components. (The antimicrobial protection hypothesis of Alzheimer's disease. Moir, Lathe & Tanzi)
- Nature 11/4/2020 reports 3 under study: *Chlamydia pneumoniae*, a cause of lung infections; *Borrelia burgdorferi*, the agent of Lyme disease; and, most recently, *Porphyromonas gingivalis*, which leads to gum disease
- Oral bacteria which cause gingivitis.
 - Commercially funded study found evidence of gingivitis bacteria in brains of people with Alzheimer's disease. (1.23.2019 in *Science Advances*, *Porphyromonas gingivalis* in Alzheimer's disease brains: S. Dominy (Cortexyme Inc)
 - An independent academic team found that repeatedly introducing gingivitis bacteria to wild-type lab mice resulted in oral infection that within a short time resulted in gingivitis bacteria in their brains, along with evidence of increase in beta amyloid, inflammation and neurodegeneration. (Ilievski V, et al. (2018) PLoS ONE 13(10)
 - MGH group doubts that gingivitis is the solo cause of sporadic Alzheimer's, but suggests it might contribute to the etiology or worsening of the condition in some people.

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Oral Health and Brain Health

- Epidemiological studies – cognitive impairment/decline and poor oral health e.g. tooth loss, are associated. But cause may be two-directional (Bei Wu et.al. Association Between Oral Health and Cognitive Status: A Systematic Review. *J Am Geriatr Soc.* 2016)
 - Poor oral hygiene and lack of dental care can result in gingivitis and infection close to the brain...may be found to be implicated in activation of beta amyloid (a current debate!)
 - People with cognitive impairment often have poor dental care practices...and resulting contribution to inflammation could accelerate cognitive decline.
 - People with low SES and who live in food deserts often suffer from poor dental care along with diabetes and heart disease; these neighborhoods typically lack dentists. A public health issue because in the US dental insurance including Medicare does not cover dental health.

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One Goal: Create Healthy, Robust, More Resilient Brain Tissue

- Healthy Brain tissue better withstands ravages of age, genetic vulnerabilities, environmental stresses, accidents, toxins (including certain anesthetics), and disease, including invasion of microbes.
- Nutrition, Exercise, Cognitive Training and Healthy Lifestyles help us enhance and strengthen brain neurons, synapses & dendrites and other body & brain cells relevant to brain health.
- Boost our immune system defenses?



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Maintaining Healthy Brain Tissue

- People with AD** have many remaining healthy brain cells and are creating new ones all the time.
- Proper nutrition, exercise and other healthy lifestyles, can help build new neurons, neurites & dendrites, keep brain cells healthy, to slow progression.
- Helps Caregivers and Family too!
- Improves mood and helps preserve cognition.

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Why Increased Interest in Public Health Lifestyle Approach for Brain Health?

- No drug on market other than blood pressure meds yet can slow risk, progression or prevent Alzheimer's disease nor other major dementias. (Some drugs look promising)
- Evidence is building that lifestyle can do all this, though maybe not as dramatically as a potential "blockbuster" drug.
- Many countries cannot afford expensive new drugs should they be found. Brain+ Lifestyles help Body too.
- With 20-30 years to "develop" AD pathology.....will drugs ever be the only answer? Combination tx likely.

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Remedy? Not a Pill or Surgery – Individual & Public Health Initiatives

- Restoration of good (& delicious) **nutrition** and **physical exercise** into our lives.
- Together with other healthy lifestyles to
 - decrease stress,
 - improve sleep,
 - balance energy,
 - boost immune system,
 - Decrease inflammation
 - increase social engagement,
 - Increase creative expression, &
 - improve community
 - While maintaining mental stimulation.

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Healthy Lifestyles- Many Facets



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Lifestyle Enhances Brain Health

- **EXERCISE***
- SLEEP
- **SOCIAL ENGAGEMENT***
- **COGNITIVE STIMULATION***
- CREATIVE-ART, MUSIC
- SPIRITUAL, PURPOSE
- CHI
- MANAGE STRESS & DEPRESSION
- LAUGHTER/HUMOR



NUTRITION* and Hydration (* all in FINGER trial in FINLAND & world wide FINGER)

see brainwellness.com for details

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What The Beagles Are Suggesting About Brain Health

- The beagle dog study suggests lifestyle affects brain health. (Milgram, Head, Cotman 2005)
- Two-year study – difficult learning task is outcome.
- 42 beagle laboratory dogs ages 7 to 11 years (average age when most dogs start to fail cognitively)
- Divided into 4 groups. (1) Usual Diet & Caged (2) Extra Nutrition (3) Play (4) Both Nutrition and Play



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Dog Study Shows Us the Way: Healthy Lifestyles Protect Brain Health

- RESULTS: % of dogs which perform learning tasks :
 - Only 25 % of beagles w/ standard care (living in cages) & usual canine diet;
 - 67% of beagles who got enriched diet with vegetables, citrus pulp, and vitamins E and C;
 - 80% who got physical exercise and social play (with other dogs, humans and toys) at least twice a week.
 - 100% of beagles who got both the enriched diet and exercise-play routine.



- THESE RESULTS SHOULD GIVE US HOPE WE CAN DO THE SAME FOR OURSELVES AS WE AGE.

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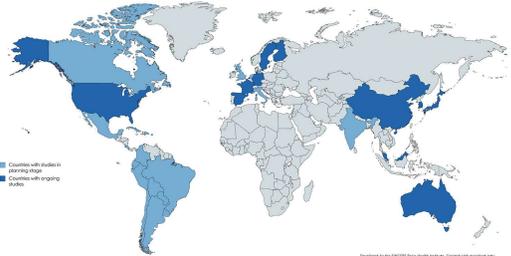
World wide FINGERS research on Lifestyle to Slow Cognitive Decline

- <https://www.alz.org/wwfingers/overview.asp>
- Dementia declared a public health priority by the World Health Organization (WHO), which has prioritized research into dementia prevention.
- The FINGER trial is first large, long-term RCT indicating a multi-domain intervention with exercise, diet, cognitive and social stimulation and management of vascular/metabolic risk factors may benefit cognition in subjects at risk of dementia.
- World Wide FINGERS facilitates use of data from several countries, including the Alzheimer's Association [U.S. POINTER study](http://alz.org/us-pointer/overview.asp).
- Opportunity for rapid knowledge dissemination and implementation.

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World Wide FINGERS (WW-FINGERS) 2018 Now 11+ funded studies, 13 more planned



Developed by the FINGERS Brain Health Institute. Created with mapbox.com

Slide courtesy of Alzheimer's Association: Note: Canada may join ww FINGER but will add a ketogenic supplement. Others have added SLEEP or GUT/Microbiome or other Lifestyle factors

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Lifestyle Clinical Trials during CoVid-19

- WWW FINGER Meetings have been held virtually via Zoom since Pandemic
- New focus on how to maintain studies during pandemic and keep all safe
- Virtual interventions and assessments; resumed in-person when safe
- Most studies have kept going despite pauses, and adding CoVid-19 sub-studies
- Australia was already conducted on-line and has had more success with participation than expected.



- Attendees AAIC 2019 Los Angeles

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US POINTER Clinical Trial Underway

- 5 study sites team up with existing healthcare systems, centered in Universities including 2 of PI of US POINTER
 - Sacramento, California (UC Davis)
 - Winston-Salem, North Carolina (Wake Forest Univ.)
 - Houston, Texas (Baylor College of Medicine)
 - Providence, Rhode Island (Butler Hospital)
 - Chicago, Illinois -2 sites (Rush University Medical Center and Advocate Health Care)
- 4-5 part intervention similar to FINGER using MIND diet
- Participant criteria: - 60 to 79;
 - Not a regular exerciser (generally less than 3 x per week) ;
 - No current memory or thinking problems
 - First degree family history of significant memory problems (mother, father, sibling)

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Protecting Brain Health through Lifestyle Intervention to Reduce

- **\$20 million+** investment see: <https://alz.org/us-pointer/overview.asp>
- 2-year intervention study to evaluate lifestyle “recipe”

			
Physical Exercise	Nutritional Counseling & Modification	Cognitive & Social Stimulation	Improved Self-Management of Health Status
<i>supervised aerobic exercise</i>	<i>dietary counseling on adherence to the MIND diet (Mediterranean-DASH Intervention for Neurodegenerative Delay)</i>	<i>computer-based cognitive training and group counseling to facilitate increased cognitive/social engagement</i>	<i>increased medical monitoring and self-management of cardiovascular / metabolic conditions</i>

alzheimer's association

Does this prevent or delay cognitive decline?

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Sleep Study added to US Pointer

- \$5.3 million grant from the U.S. National Institute on Aging (NIA) for the POINTER-zzz study to incorporate in-home sleep assessments in 700 participants enrolled in US POINTER study.
- Chronic sleep disturbances have been linked to an increased risk of cognitive decline and Alzheimer’s disease.
- Scientific evidence suggests that diet, exercise and cardiometabolic risk reduction can improve sleep, and that improved sleep may benefit cognitive function in older adults.
- The POINTER-zzz study will examine whether lifestyle changes might improve sleep quality.
- Uses a simple test completed at home. The test involves wearing a watch-like device for one or more days and nights to measure sleep apnea, restlessness and other sleep disruptions.
- The results may show us how to reduce or treat sleep disturbances, which could slow or prevent cognitive decline.

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Baker’s Exercise Protocols w/ AD & MCI

- Background: Other RCTs by Baker and others have shown that aerobic exercise improves cognitive function in adults at high risk for MCI and AD. ? How long, how intense, type, frequency. “3 mo not enough”
- Study reported at AAIC 2016 in *early stage AD patients*
- + Results: (1) *Lowered A-beta and Tau in CSF indicates slowed progression!* No drug on market can do this!
- (2) increased blood flow in key brain regions often compromised by aging & early AD pathology
- Intervention: **Moderate Intensity Aerobic Exercise** (control: stretching/ROM) **45 min- 1 hour long, 4 x week for 6 months.** Moderate: Over 70% of max heart rate
- “aerobic exercise ‘therapy’ for AD worth the sweat”

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Baker’s Recommendation:

- "I encourage people to find a class, a dance class, a swimming class," she says. "Find what you love, find a group, and make a commitment. But basically, sit less, walk more."
- Enough evidence to suggest exercise is helpful. 3 months not enough to see a difference. 6 months + needed. ? Intensity, duration, dose/frequency, type
- Purpose of EXERT Phase 3 study is to establish enough evidence that EXERCISE could be PRESCRIBED by physicians as **medical treatment** for memory loss. And thus paid for by Medicare

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Baker Summarizes Other Benefits of Aerobic Exercise

- Improves vascular function and benefits
- Improves lipid profiles,
- Protects against metabolic and cardiovascular disease,
- Promotes growth factor activity in the brain,
- Has favorable effects on inflammation (anti-inflammatory)
- Mitigates physiological & psychological stress responses,
- Improves mood.

– Quoted from Baker’s AAIC 2016 Abstract , Podium Presentations: Monday, July 25, 2016 P220

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