Avoid Alzheimer's and Build a Better Brain

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Co-directors, Alzheimer's Prevention Program
Loma Linda University Health

The Incredible Brain

87 billion cells

1x10^{50} power

Consumes 25% body's energy

1 quadrillion connections

Jane Goodall

Ellsworth Wareham

Dementia

The most devastating disease of the 21st century

The Tsunami

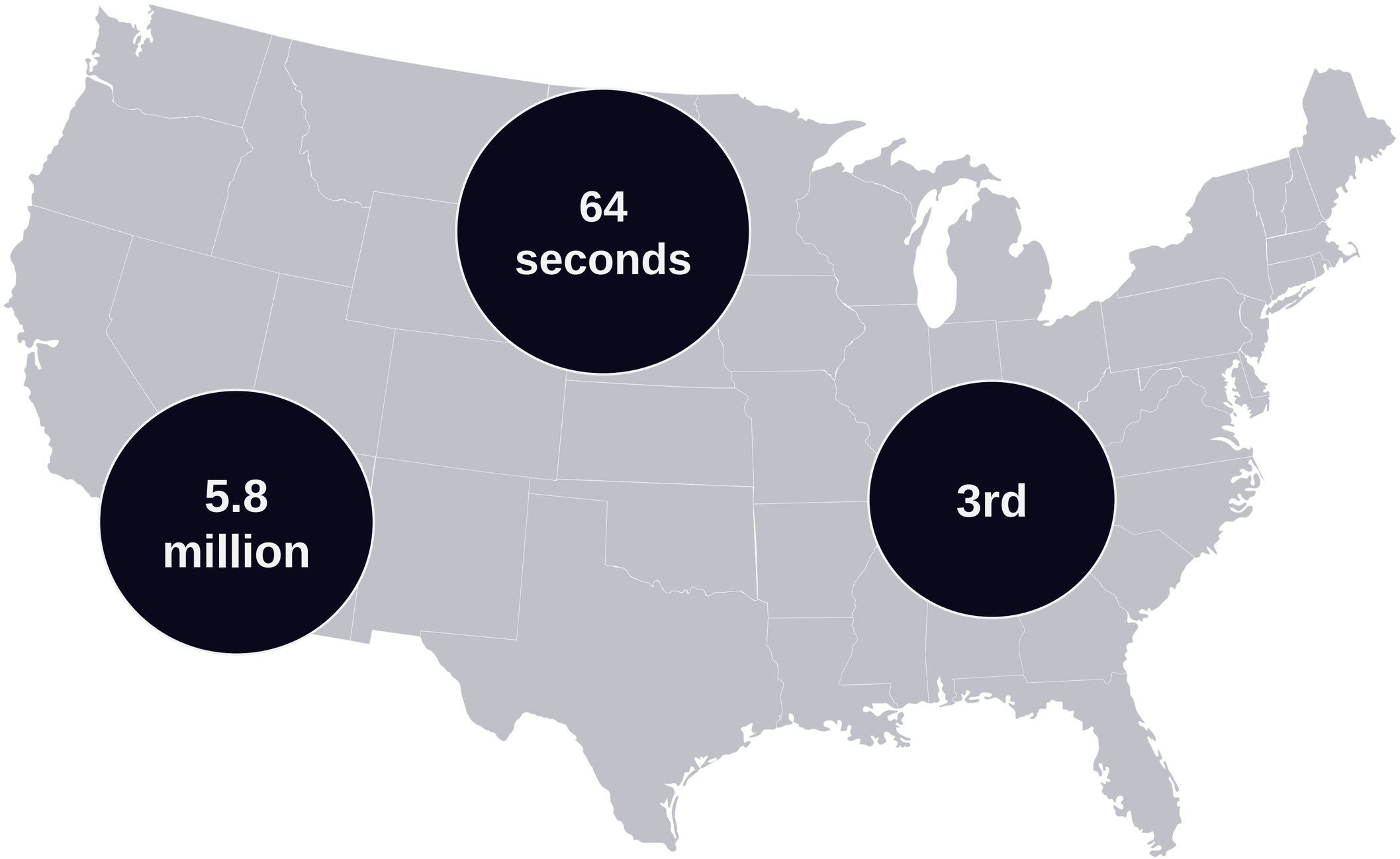
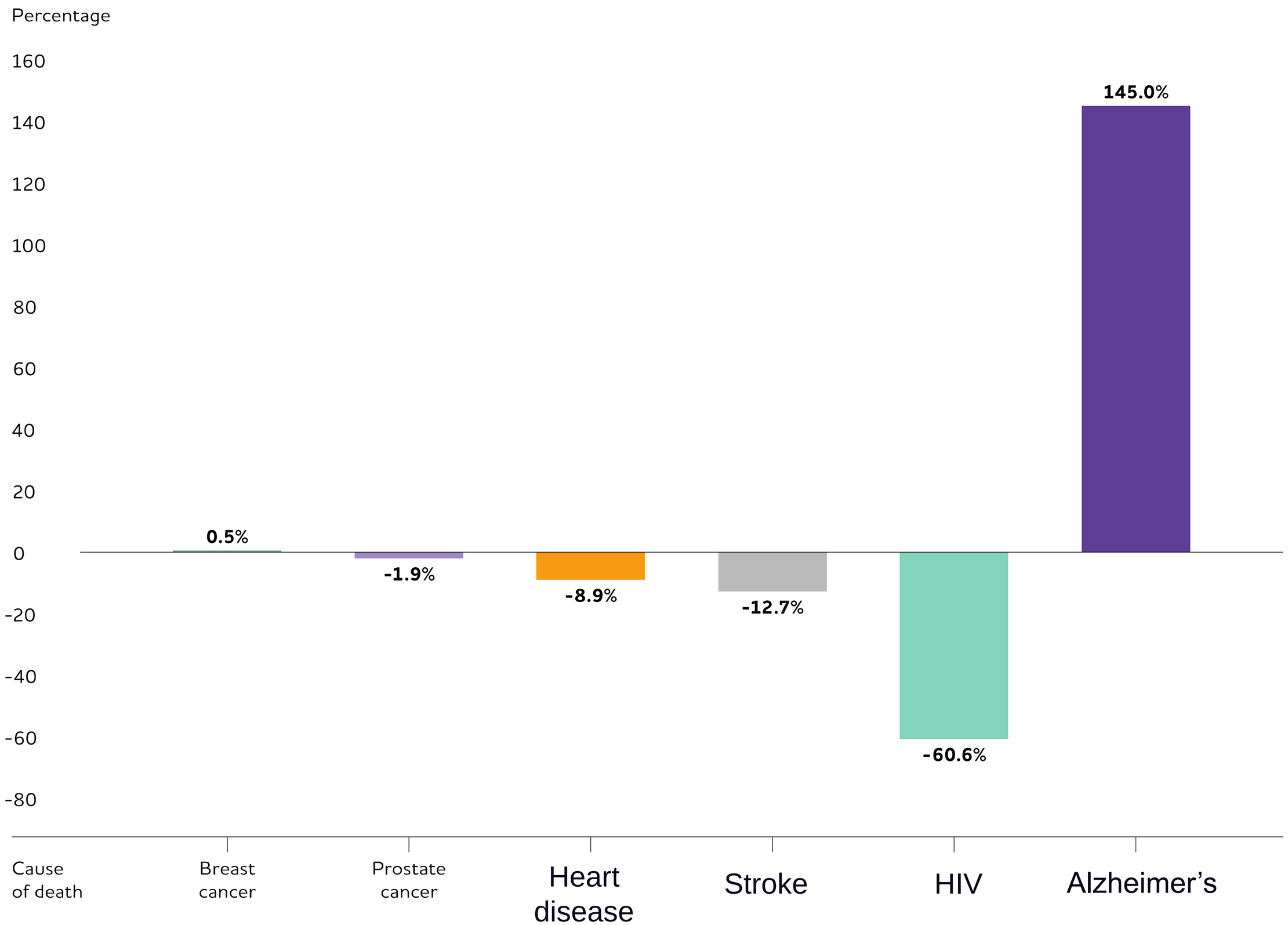


FIGURE 5

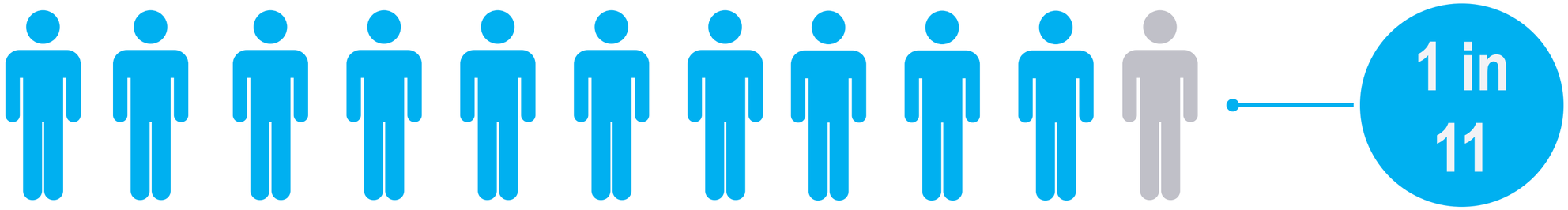
Percentage Changes in Selected Causes of Death (All Ages) Between 2000 and 2017

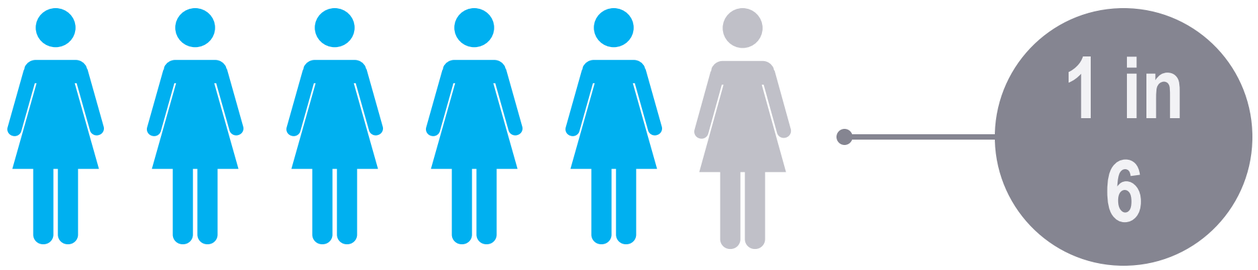


Created from data from the National Center for Health Statistics.[248,259]

1 in 10 | **people age 65 and older has Alzheimer’s disease**

Alzheimer’s
gender differences





20

years or more before symptoms appear, the brain changes of Alzheimer’s may begin

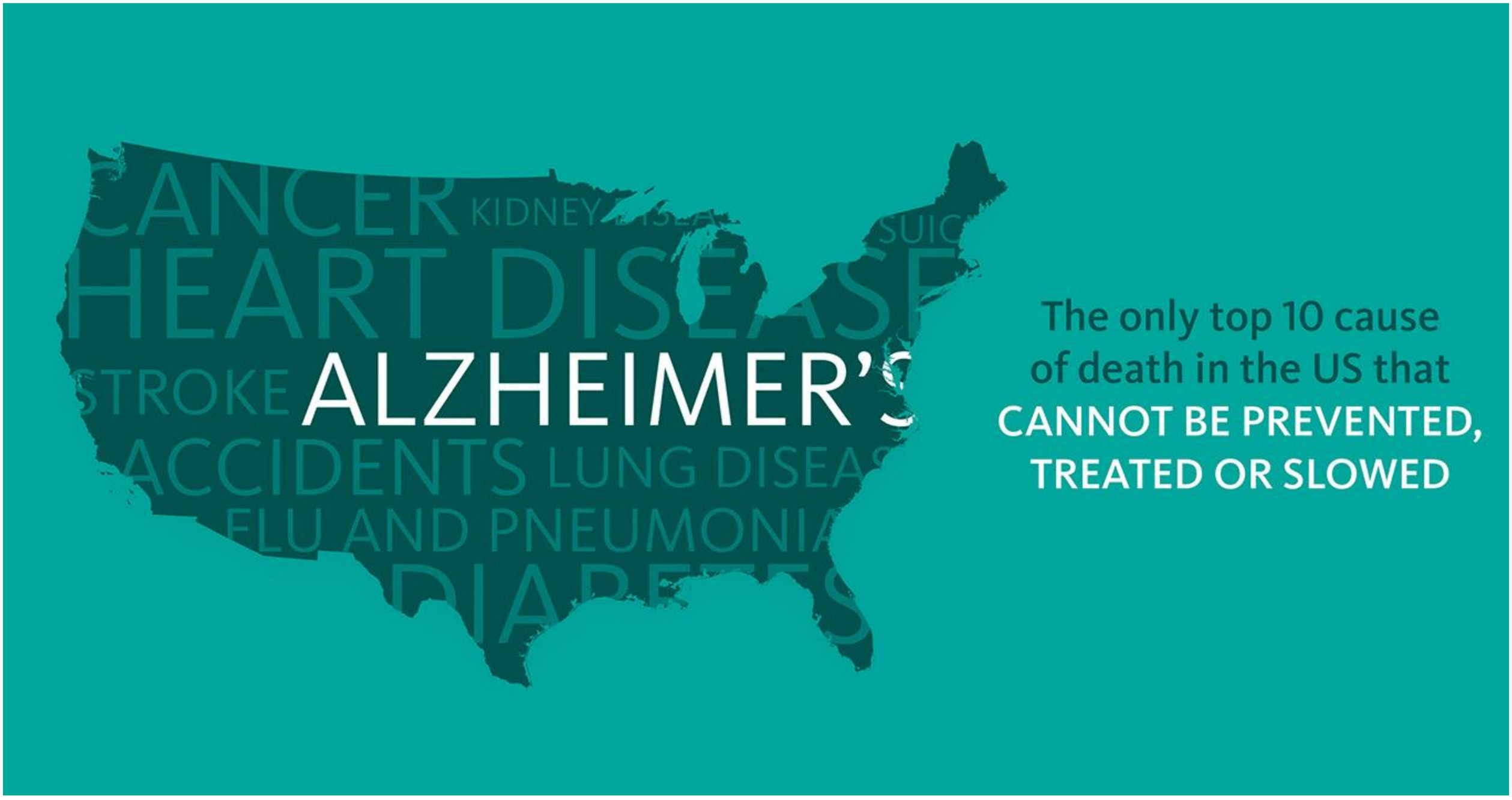
$290 billion

total annual cost for caring for individuals living with Alzheimer's or dementia in 2019

16 million | **Americans with Alzheimer's by 2050**

$3 trillion | **cost of Alzheimer's by 2050**

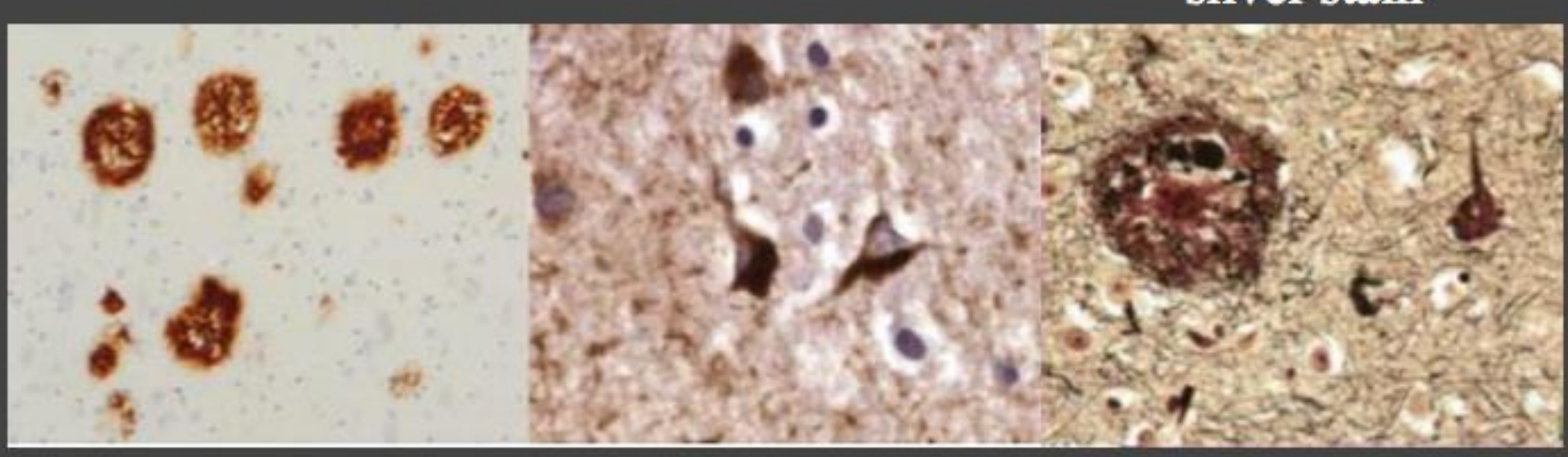
The Big Myth


CANCER
KIDNEY
HEART DISEASE
STROKE
ALZHEIMER'S
ACCIDENTS
LUNG DISEASE
FLU AND PNEUMONIA
DIABETES
The only top 10 cause
of death in the US that
CANNOT BE PREVENTED,
TREATED OR SLOWED

Alzheimer's diagnosis

- Definitive diagnosis is only made at autopsy, with classic findings of amyloid plaques and tau tangles

Aβ plaques | Tau tangles | Both pathologies on silver stain



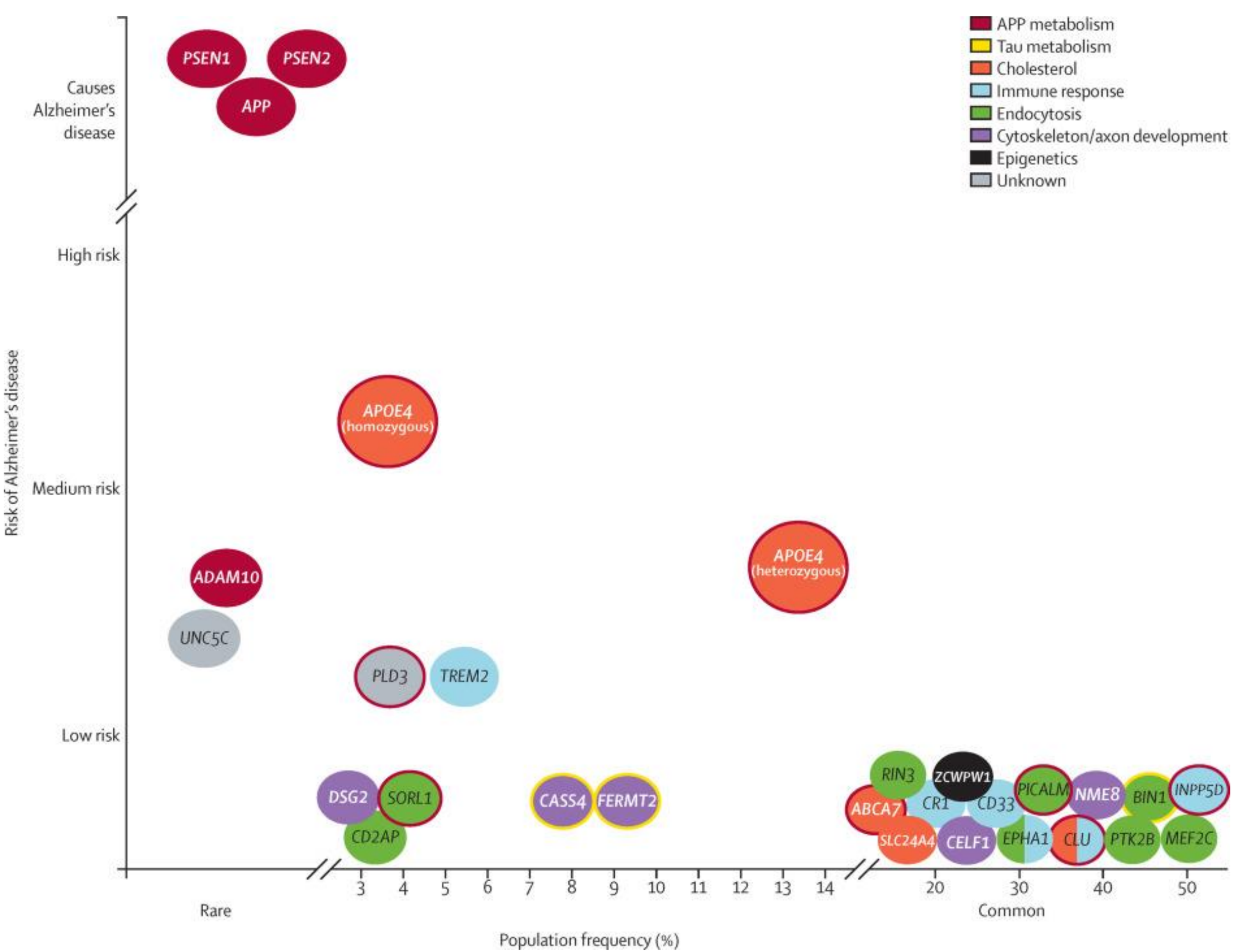
Serrano-Pozo et al., 2011

100%

Alzheimer’s drugs **failed** in more than 400 clinical trials

Genes do not determine destiny

They give us a range of when disease manifests


APP metabolism
Tau metabolism
Cholesterol
Immune response
Endocytosis
Cytoskeleton/axon development
Epigenetics
Unknown
Causes Alzheimer's disease
High risk
Medium risk
Low risk
Risk of Alzheimer's disease
PSEN1
PSEN2
APP
APOE4 (homozygous)
APOE4 (heterozygous)
ADAM10
UNC5C
PLD3
TREM2
DSG2
SORL1
CD2AP
CASS4
FERMT2
RIN3
ZCWPW1
ABCA7
CR1
CD33
PICALM
NME8
BIN1
INPP5D
SLC24A4
CELF1
EPHA1
CLU
PTK2B
MEF2C
3 4 5 6 7 8 9 10 11 12 13 14
20 30 40 50
Rare
Common
Population frequency (%)

Genetic Risk, Lifestyle and Dementia

Abstract ID: 31424

Abstract:

Elzbieta Kuzma, PhD[1,2]; Ilianna Lourida, PhD[2,3]; Eilis Hannon, PhD[2]; Thomas J Littlejohns, PhD[4]; Kenneth M Langa, MD, PhD[5]; Elina Hyppönen, PhD[6,7] and David J Llewellyn, PhD[2,8], (1)University Medical Center Hamburg-Eppendorf, Hamburg, Germany, (2)University of Exeter Medical School, Exeter, United Kingdom, (3)PenCLAHRC, Medical School, College of Medicine and Health, University of Exeter, Exeter, United Kingdom, (4)University of Oxford, Oxford, United Kingdom, (5)University of Michigan, Ann Arbor, MI, USA, (6)University of South Australia, Adelaide, Australia, (7)University College London, London, United Kingdom, (8)Alan Turing Institute, London, United Kingdom

Can dementia risk due to genes be counteracted by adherence to a healthy lifestyle?

Genetic Risk, Lifestyle and Dementia

- 157,369 UK Biobank participants of European ancestry aged 60 years or older
- Dementia Risk Index: High, medium or low
- Healthy Lifestyle Index: Favorable, intermediate and unfavorable

Genetic Risk, Lifestyle and Dementia

- 668 dementia cases

- The **risk** of incident dementia **was ~ 50% higher among participants with a high genetic risk** in comparison with those with a low genetic risk

- Participants with a **high genetic risk and an unfavorable lifestyle** were **more than three times more likely to develop dementia** compared with those with a low genetic risk and favorable lifestyle

Genetic Risk, Lifestyle and 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

- **Adherence to a healthy lifestyle can offset genetic risk**

Impact of Healthy Lifestyle Factors on the Risk of Alzheimer's Dementia; Findings from Two Prospective Cohort Studies

Abstract ID: 31381

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Klodian Dhana, MD, PhD[1]; Denis A Evans, MD[1]; Kumar B Rajan, PhD[2]; David A Bennett, MD[3] and Martha Clare Morris, ScD[1], (1)Rush University Medical Center, Chicago, IL, USA, (2)University of California Davis, Davis, CA, USA, (3)Rush Alzheimer's Disease Center, Chicago, IL, USA

To what extent does the combination of lifestyle factors reduces the risk of Alzheimer’s disease?

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To what extent does the combination of lifestyle factors reduces the risk of Alzheimer’s disease?

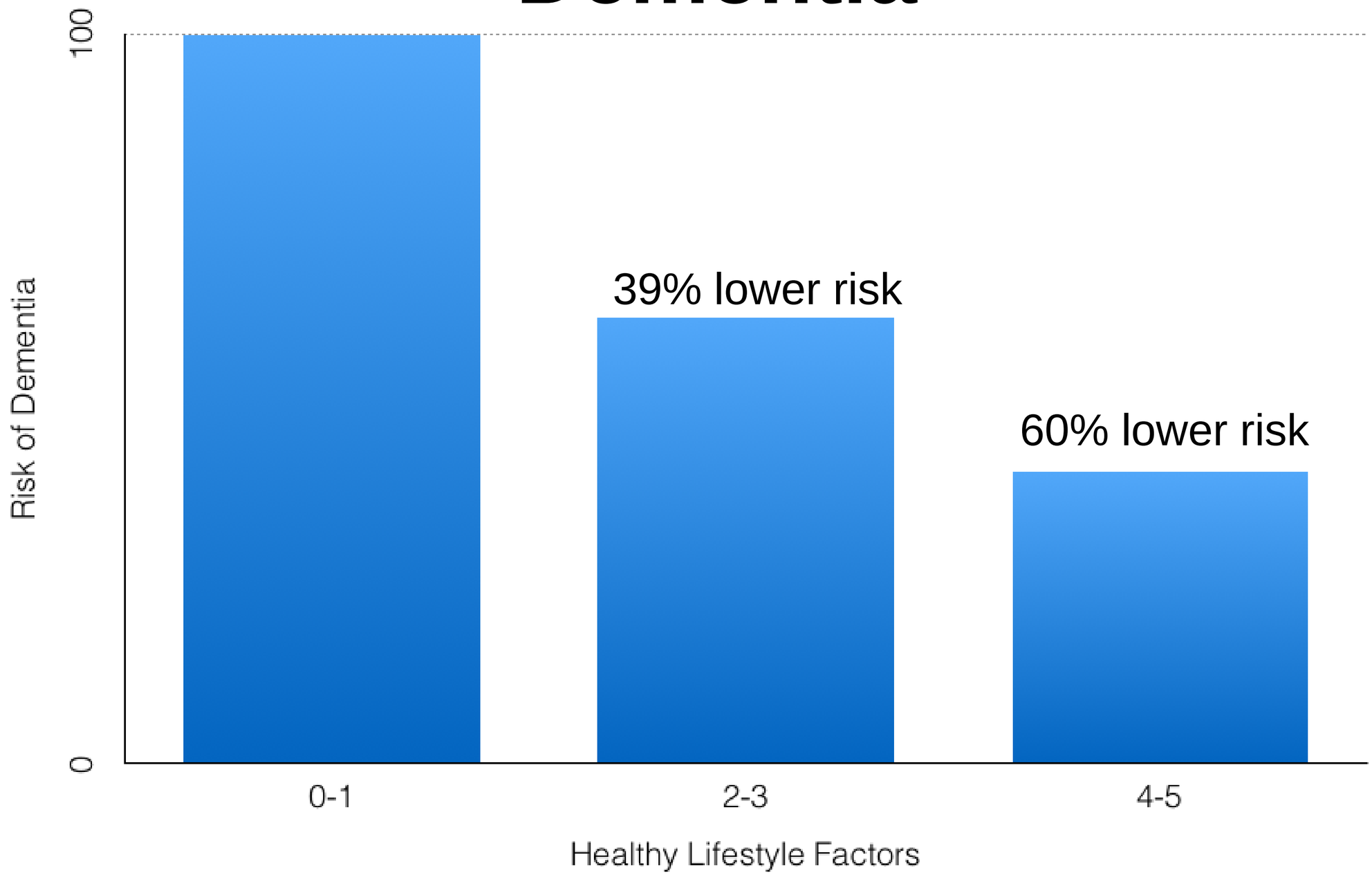
Impact of Healthy Lifestyle Factors on the Risk of Alzheimer's Dementia

- Chicago Health and Aging Project (n=1431) and Rush Memory and Aging Project (n=920) followed for 9.1 years (median)

- Healthy lifestyle score: no smoking, more than 150 minutes of moderate/vigorous physical activity, light alcohol consumption, high quality MIND diet, and engagement in cognitive activity

- 0 to 5 score

Impact of Healthy Lifestyle Factors on the Risk of Alzheimer's Dementia

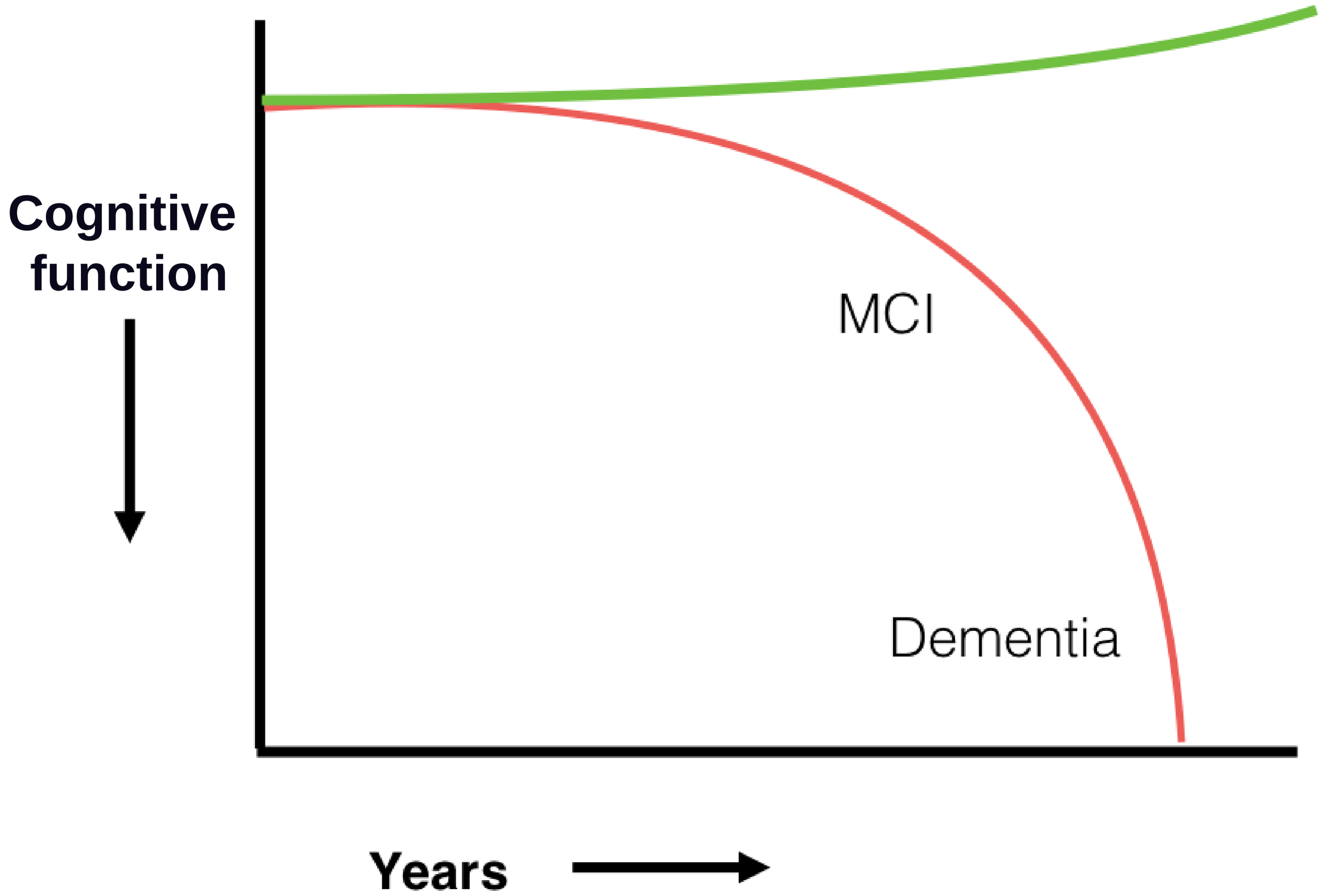


NEUROLOGICAL HEALTH

Alzheimer's Meeting: Lifestyle Factors Are the Best—and Only—Bet Now for Reducing Dementia Risk

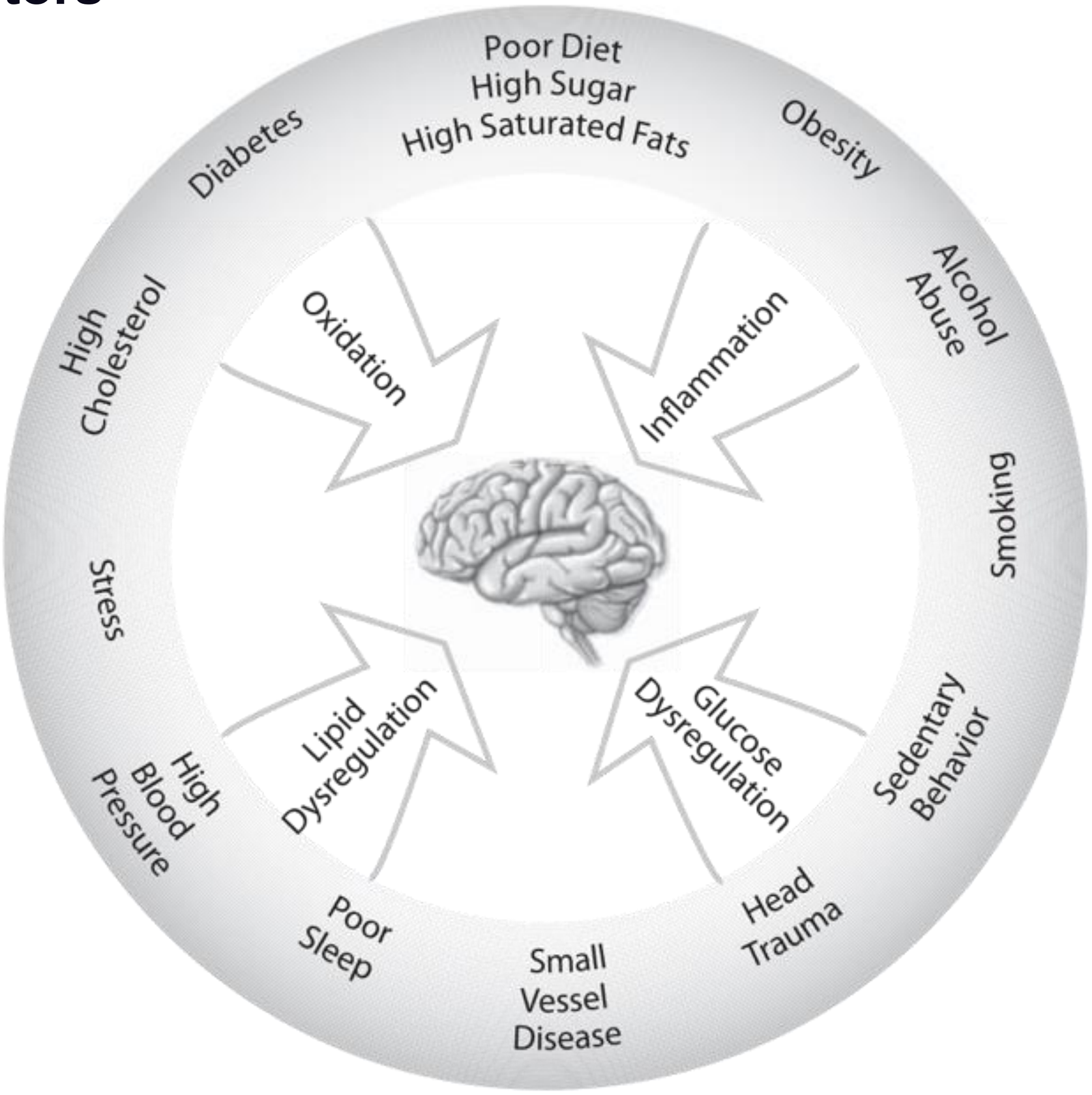
Researchers are still optimistic about finding disease-altering medicines—just not anytime soon

By Karen Weintraub on July 18, 2019

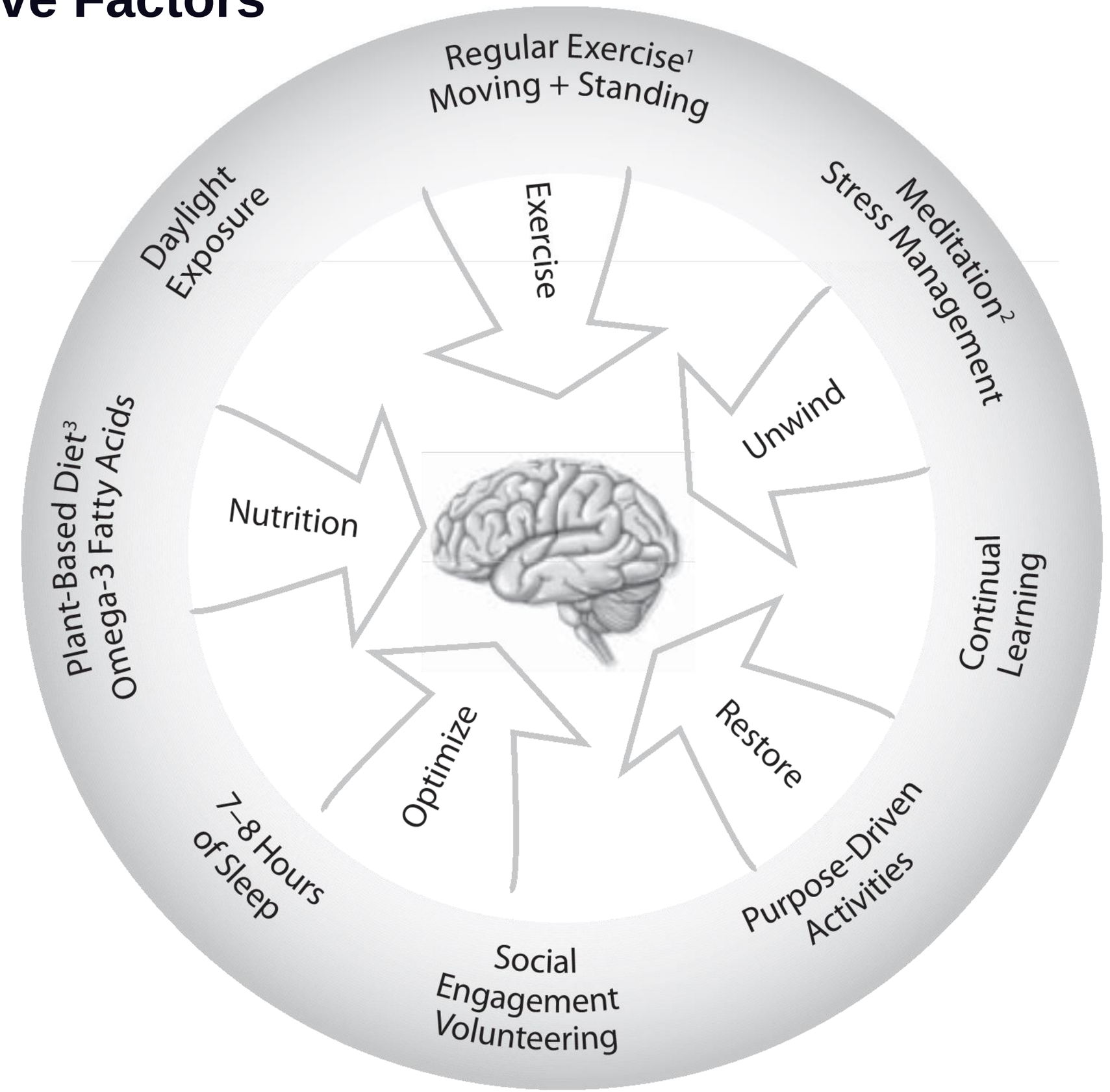

Cognitive function
MCI
Dementia
Years

Prevention is the new treatment.

Risk Factors



Protective Factors



The NEURO Plan

N	E	U	R	O
Nutrition	Exercise	Unwind	Restorative Sleep	Optimize cognitive activity

Nutrition

Alzheimer's Genes, Cholesterol and Blood Pressure

- 1449 participants, ages 65-79 years
- **Apo E4 allele** increased odds by **2 folds**
- **Elevated midlife total cholesterol** level increased the odds up to **3 times** and **systolic blood pressure** increased odds up to **2.5 times** even after adjustment for Apo E genotype and other confounding factors

Kivipelto, et al. Ann Intern Med. 2002;137:149-155

Dietary Fats and the Risk of Incident Alzheimer’s Disease

The Chicago Health and Aging Project

Longitudinal study, 2500 older adults, those who consumed **higher amounts of saturated and trans fatty acids** over a six-year period had a **higher risk of developing Alzheimer’s**, while those eating **fats derived from plants had a lower risk.**

Morris, et al. (2003). Archives of Neurology, 60(2), 194– .200

“The Incidence of Dementia and Intake of Animal Products: Preliminary Findings from the Adventist Health Study ”

Adventist Health Study

A 1993 study titled “The Incidence of Dementia and Intake of Animal Products,” found that in a group of over 3,000 individuals, **those who ate meat—including those who ate only poultry and fish—had twice the risk of developing dementia compared to vegetarians**.

Giem, et al. (1993). Neuroepidemiology, 12(1), 28– .36

“Midlife Serum Cholesterol and Increased Risk of Alzheimer’s and Vascular Dementia Three Decades Later”

Kaiser Permanente Northern California Group

9,900patients, individuals with **high cholesterol** during midlife had a **57% higher risk of developing Alzheimer’s disease** later on. Even **borderline high cholesterol** increased the risk of Alzheimer’s by **.23%**

Solomon, et al. (2009). Dementia and Geriatric Cognitive Disorders, 28(1), 75– .80

“Dietary Fat Types and 4-year Cognitive Change in Community-Dwelling Older Women”

Women’s Health Study

- Nearly 6,000 women followed over a 4-years

- **Higher saturated fat intake** was associated with a poor trajectory of cognition—specifically a **faster decline in memory by 70%**

- Women with the **lowest saturated fat intake** had the **brain function of women six years younger**

Okereke, et al. (2012). *Annals of Neurology, 72*(1), 124– .134

“Diet Cluster in Relation to Cognitive Performance and Decline in the Northern Manhattan Study”

Researchers at Columbia University found that **participants who ate a plant-based diet** had a **lower risk of cognitive decline over a span of six years** compared to those who ate a standard American diet.

Gardener, et al. (2017) *Neurology, 88*(16), S15–003.

“Mind Diet Associated With Reduced Incidence of Alzheimer’s Disease”

Rush University Memory and Aging Project:

- 1000 patients, ages 58-98
- Strict adherence to the MIND diet (promotes plant-based diet, limits meat and dairy) resulted in a **53% reduction in risk for Alzheimer’s**.
- Even **moderate adherence** to the diet was associated with a **35% risk reduction**.
- Participants who showed high adherence to the diet had **cognitive functioning equivalent to a person who was seven and a half years younger**.

Morris, et al. (2015). Alzheimer’s & Dementia, 11(9), 1007–1014.

CALIFORNIA TEACHERS STUDY

- In 1995, 133,479 female public school teachers and administrators were enrolled in the study
- Geographically and socioeconomically diverse
- Mail paper questionnaires every 4-5 years
- Linked with California Cancer Registry

NATIONAL CANCER INSTITUTE · CCR · oshpd · UNIVERSITY of CALIFORNIA IRVINE · CANCER PREVENTION INSTITUTE OF CALIFORNIA · USC University of Southern California

Mediterranean Diet Score Construct

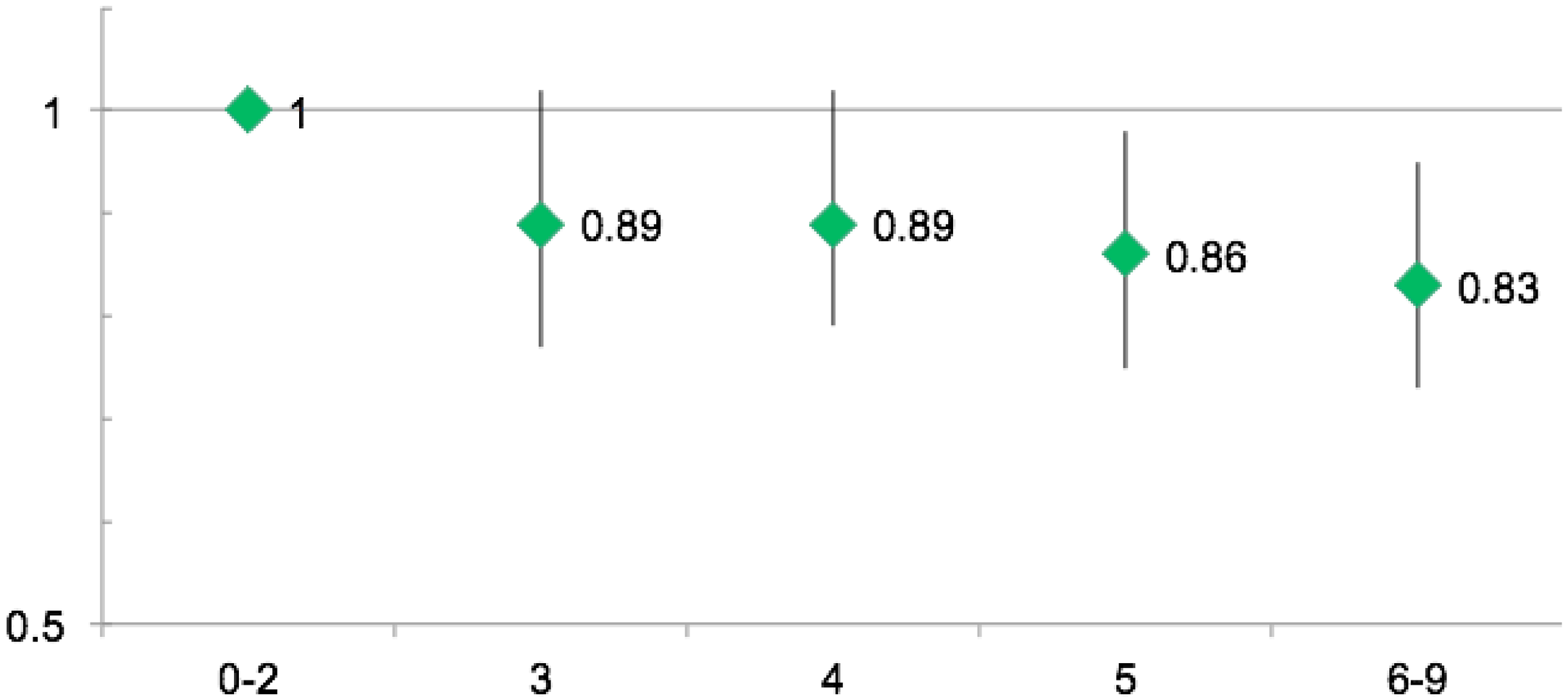
High Score

- Vegetables
- Fruits
- Whole grains
- Nuts and seeds
- Legumes
- Fish - as a source of omega fats

Low Score

- Meat, poultry, and dairy

Mediterranean Diet and all stroke incidence



Adjusted* Hazard Ratio Mediterranean Diet Score groups
)p trend (0.009

*Age, race, SES, moderate plus strenuous physical activity, kilocalories, BMI, smoking, hypertension, diabetes, atrial fibrillation, hypercholesterolemia, history of cardiac disease and menopausal status and hormone therapy.

Submitted for publication to *Stroke*.

Supplements

- Most randomized controlled trials on nutritional supplements for the prevention of AD have remained inconclusive so far

- Low DHA (omega 3 fatty acids) levels have been associated with lower cognitive status

- Low vitamin B12 levels are associated with cognitive impairment

Artide

The Association Between Diabetes and Dementia Among Elderly Individuals: A Nationwide Inpatient Sample Analysis

Journal of Geriatric Psychiatry and Neurology
2016, Vol. 29(3) 120-125

DOI: 10.1177/0891988715627016
jgpn.sagepub.com
SAGE

Dean Sherzai, MD, MAS, PhD(c)[1], Ayesha Sherzai, MD[2], Keith Lui, MD[2], Deyu Pan, MS[3], Daniel Chiou, MD[2], Mohsen Bazargan, PhD[3], and Magda Shaheen, PhD, MPH[4]

Abstract

Background/Aim: To date, few studies have cross-examined the relationship between diabetes mellitus (DM) and dementia nationally. There is also a lack of evidence regarding dementia subtypes and how this relationship changes among older individuals. The objective was to better delineate this relationship and influence of multiple comorbidities using a nationwide sample. Methods: Data were obtained from the Nationwide Inpatient Sample 1998 to 2011 using appropriate International Classification of Diseases, Ninth Version codes. Descriptive and bivariate analysis was performed. Multivariate nominal logistic regression models adjusted for age, sex, race, and comorbidities explored the independent relationship between Alzheimer dementia (AD), non-Alzheimer dementia (VaD), and diabetes. Results: 21% of the participants were diabetic patients, 3.7% had AD, and 2.2% had VaD. Diabetes prevalence in AD, VaD, and no dementia groups were 20.6%, 24.3%, and 26.2%, respectively. In the unadjusted model, those with DM had lower odds of AD (odds ratio [OR] 0.73; 95% confidence interval [CI] 0.72-0.74) and VaD (OR 0.91, 95% CI 0.89-0.92). Adjusting for age, sex, race, and comorbidities, diabetic patients had significantly higher odds of VaD (OR ¼ 1.10, 95% CI 1.08-1.11) and lower odds of AD (OR 0.87, 95% CI 0.86-0.88). Inclusion of interaction terms (age, race/ethnicity, depression, stroke, and hypertension) made the relationship between diabetes and VaD not significant (OR 1.002, 95% CI 0.97-1.03), but the relationship of DM with AD remained significant (OR 0.57, 95% CI 0.56-0.58; $P < .05$). Conclusion: Patients with a diagnosis of diabetes mellitus had lower odds of having AD. Age, race/ethnicity, depression, stroke, and hypertension modified the relationship between DM and both VaD and AD. Further exploration of the relationship between DM and AD is warranted.

Keywords

dementia, vascular dementia, Alzheimer disease

Journal of the Neurological Sciences 388 (2018) 97–102

Contents lists available at ScienceDirect

Journal of the Neurological Sciences

journal homepage: www.elsevier.com/locate/jns

Insulin resistance and cognitive test performance in elderly adults: National health and nutrition examination survey (NHANES)

Ayesha Z. Sherzai[a,*], Magda Shaheen[b], Jeffrey J. Yu[c], Konrad Talbot[d], Dean Sherzai[a]

[a] Loma Linda University Health, Department of Neurology, CA, United States
[b] College of Medicine, Charles R. Drew University of Medicine and Science, University of California Los Angeles, Los Angeles, CA, United States
[c] School of Medicine, University of California, Irvine, CA, United States
[d] Department of Neurosurgery, Cedars-Sinai Medical Center, Los Angeles, CA, United States

ARTICLE INFO

Keywords:
Cognitive test performance
Diabetes
Insulin resistance
Elderly

ABSTRACT

Objectives: To examine the relationship between homeostatic model of insulin resistance (HOMA-IR) and cognitive test performance among population ≥ 60 years in a national database.

Hypothesis: Higher insulin resistance is associated with lower cognitive test performance score in the population ≥ 60 years.

Participants: We analyzed data from the National Health and Nutrition Examination Survey (NHANES) 1999–2000 and 2001–2002.

Measurements: Cognitive test performance was measured by the Digit Symbol Substitution (DSS) exercise score. The main independent variable was the homeostasis model assessment of insulin resistance (HOMA-IR). We used bivariate analysis and generalized linear model adjusting for age, gender, race, education, body mass index, and systolic and diastolic blood pressures; total cholesterol, low density lipoprotein (LDL), high density lipoprotein (HDL) and triglyceride levels; and physical activity, diabetes mellitus, stroke, and congestive heart failure. STATA 14 was used to analyze the data taking into consideration the design, strata and weight.

Results: Of the 1028 participants, 44% were male and 85% were white. The mean age was 70.0 ± 0.28 (SE) years. Their average HOMA-IR was 3.6 ± 0.14 and they had a mean of 49.2 ± 0.8 correct DSS score in the cognitive test. Adjusting for the confounding variables, HOMA-IR was associated with decline in DSS score (B = −0.30, 95% confidence interval = −0.54 and −0.05, p = 0.01). The model explained 44% of the variability of the DSS score (R^2 = 0.44). Significant predictors of decline in DSS score were age, gender, race, and education (p = 0.01).

Conclusion: Insulin resistance as measured by HOMA-IR was independently associated with lower cognitive test performance score among elderly participants aged ≥ 60 years. Longitudinal studies are needed to test the mechanism and the causal relationship.

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Ideal Diet for the Brain

- Emphasizes whole food, plant-based diet
- Eliminates meat, poultry and dairy
- Specifies consumption of berries, green leafy vegetables and beans

Work Towards Eliminating

- Sugar
- Meats
- Pastries and sweets
- Cheese and dairy
- Extracted Plant Oil, especially tropical (coconut oil)

Nutrition

Whole food plant-based diet prevents neurodegenerative and neurovascular diseases

Saturated fats are associated with insulin resistance and inflammation

Vitamin and nutrients are best derived from food, not supplements

Exercise

“Physical activity and the risk of dementia: The Framingham Study”

Framingham Longitudinal Study

- Daily brisk walks resulted in a **40 percent lower risk** of developing Alzheimer’s later in life.

Tan, et al (2010). *Alzheimer’s & Dementia, 6*(4), S68.

“Physical activity and risk of cognitive decline: A meta-analysis of prospective studies”

- A 2010 meta-analysis of fifteen studies and nearly 34,000 people found that a **high level of physical activity** could lower the risk of **cognitive decline by 38 percent.**

- Those participants who engaged in a **less intensive, more moderate form of exercise still had a 35 percent lower risk** of cognitive impairment.

Sofi, et al. (2011). *Journal of Internal Medicine, 269*(1), 107–117.

“Mediation of Cognitive Function Improvements by Strength Gains After Resistance Training in Older Adults with Mild Cognitive Impairment”

- Effects of a **resistance-training** program (2-3 times a week for 6 months) on a group of older **adults with MCI** were measured

- Nearly **47 percent of the participants achieved normal cognitive scores after the intervention**, and that these results were maintained over a period of eighteen months

- **Greater leg strength was extremely effective at improving cognitive performance**

Mavros, et al. (2016). Journal of the American Geriatrics Society, 65(3), 550–559.

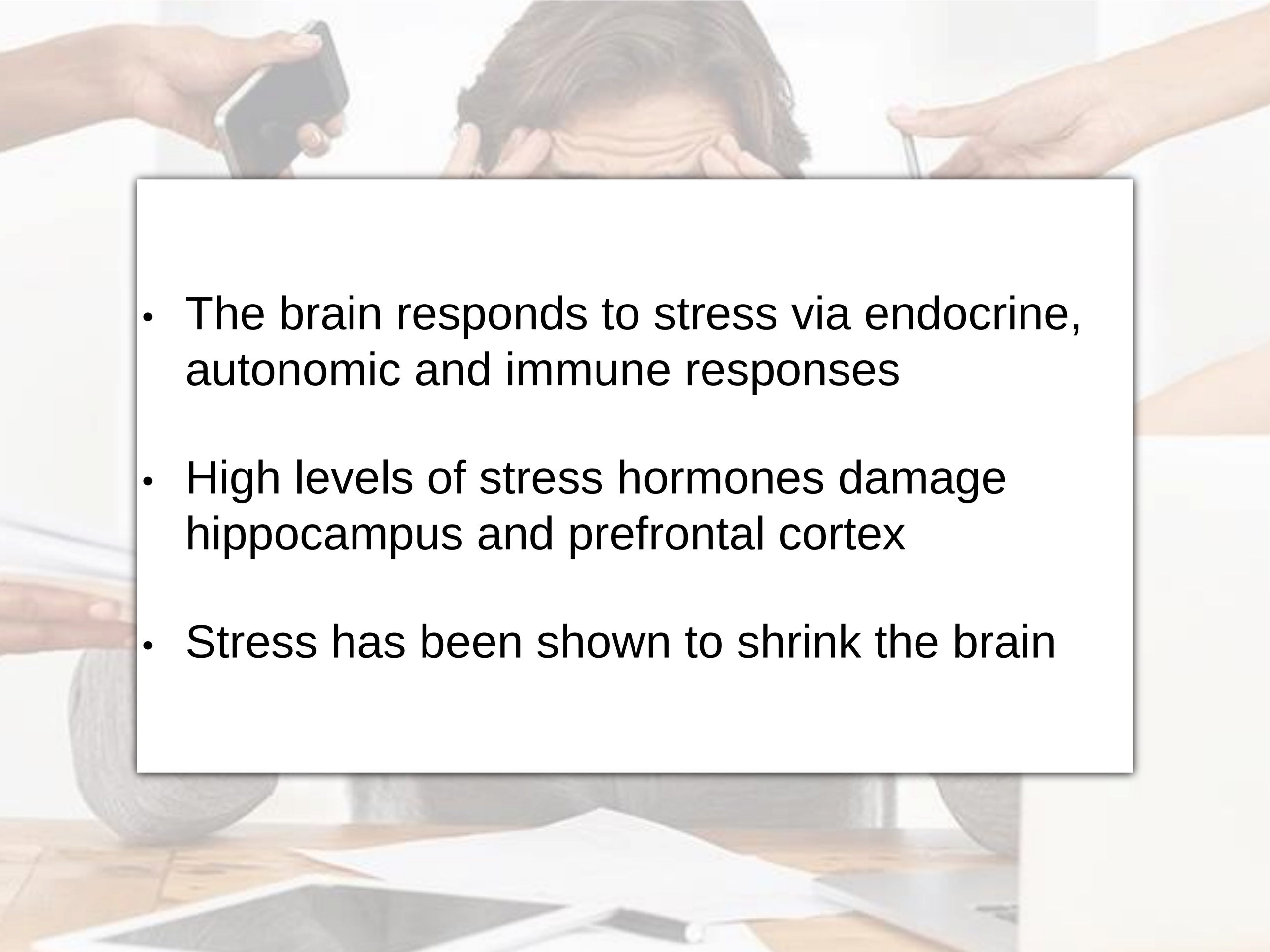
Exercise

Regular moderate to strenuous activity grows the brain

Sedentary behavior nullifies the benefit of strenuous exercise

Leg strength is associated with a bigger brain

Stress



- The brain responds to stress via endocrine, autonomic and immune responses

- High levels of stress hormones damage hippocampus and prefrontal cortex

- Stress has been shown to shrink the brain

“The effects of chronic stress on hippocampal morphology and function: an evaluation of chronic restraint paradigms”

- Elderly subjects with increased cortisol levels had on average a **14 percent reduction in hippocampal volume and impaired hippocampus-dependent memory.**

- When the hippocampus is damaged by cortisol, it struggles to regulate the body’s stress system and results in the secretion of even more cortisol, a vicious cycle that in turn damages more cells.

McLaughlin, et al. (2007). *Brain Research, 1161,* 56–64.

“Reduced age-related degeneration of the hippocampal subiculum in long-term meditators”

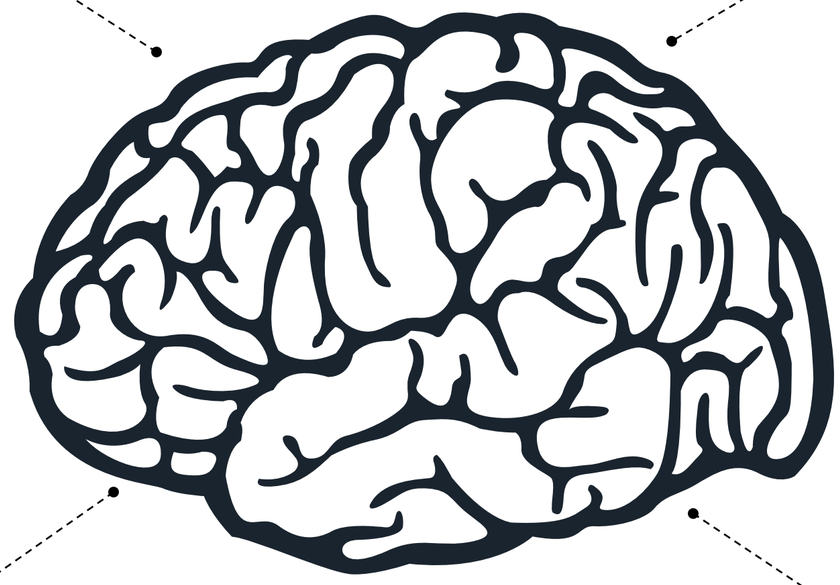
- In a study conducted at UCLA, **meditation increased hippocampal volume in a sample of elderly individuals**.

Kurth, et al. (2015). *Psychiatry Research: Neuroimaging, 232*(3), 214 -218.

Good Stress

Boosts new cell connection

Sharpens memory



Speeds learning

Creates brain resilience

Stress Perception

Perception of stress is a critical factor: it must be under your control

Bad Stress

Damages hippocampal cells

Impairs motivation and energy

Impairs learning

Damages brain blood vessels

Identify your stresses

Activities that are not under your control can easily become a stressful situation. Sometimes, elements that may have been a challenge have now become a stress – revisit each challenge.

01

Be mindful of each task

Multitasking is a misnomer.
We don’t use 10% of our brain.
We use 100% of our brain, but very inefficiently.
Learn to **focus 100% of your attention** one task at a time.
Learn to be a **minimalist**

02

03

First thing first.

Plan, delegate, postpone, or cancel the rest.

Prioritize

04

Shown to reduce stress hormones in the brain

Starters: 5-10 of mindful breathing

Basic: Daily Mindful Meditation

Advanced Transcendental Meditation

Meditate

Sleep

Sleep Deprivation Shrinks the Brain

- **Sleep deprivation can cause microglia** (the brain's specialized waste clearance cells) **to destroy healthy neurons and their connections**

- The damage is **cumulative over the long term**, and may explain the **brain shrinkage found in individuals who consistently fail to get enough sleep**

Durmer, et al. (2005). *Seminars in Neurology*, *25* (1), 117–129.

“Obstructive sleep apnea and Alzheimer’s disease: A systematic review and meta-analytic approach”

- In a review and meta-analysis of seven studies, which included more than 13,000 participants, scientists at the University of South Florida reported that sleep apnea **increased the risk of Alzheimer’s** disease by **70 percent.**

Bubu, et al. (2015). *Alzheimer’s & Dementia, 11*(7), P452.

Restorative Sleep

Sleep apnea can increase the risk of Alzheimer’s by 70%

Sleep cleanses the brain of bad proteins and other waste

Memories are consolidated during different sleep stages

Optimize

Cognitive Reserve Mitigates the Impact of Hypertension on Cognitive Trajectories

Abstract ID: 30301

Abstract:

Anja Soldan, PhD[1]; Corinne Pettigrew, PhD[1]; Yuxin Zhu, PhD[2]; Mei-Cheng Wang, PhD[2]; Rebecca F Gottesman, MD, PhD[1] and Marilyn S. Albert, PhD[1], (1)Johns Hopkins University School of Medicine, Baltimore, MD, USA, (2)Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA

The negative impact of hypertension on cognitive trajectory was reduced among those with a higher cognitive reserve.

The London Taxi and Bus Driver Study

- **Taxi drivers consistently had a larger hippocampus due to the complexity** of daily activity

- **More complex navigation led to more complex spatial knowledge, which in turn led to a bigger, more resilient brain**

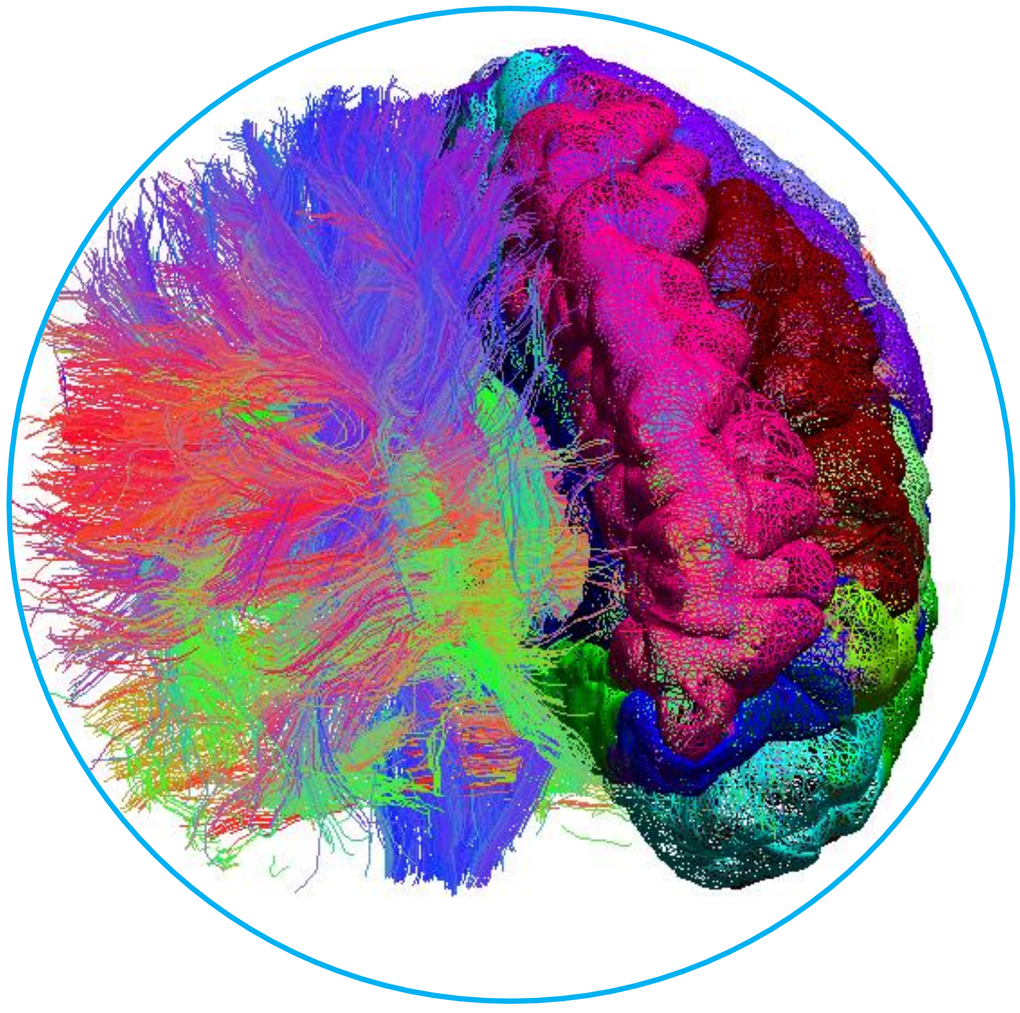
The Nun Study

- Autobiographies 60 years after they were written
- Brain autopsy results
- Nuns with high linguistic abilities earlier in life did not show evidence of Alzheimer’s despite having abundant the lesion of Alzheimer’s in their brain

“The Efficacy of Cognitive Intervention in Mild Cognitive Impairment (MCI): a Meta-Analysis of Outcomes on Neuropsychological Measures”

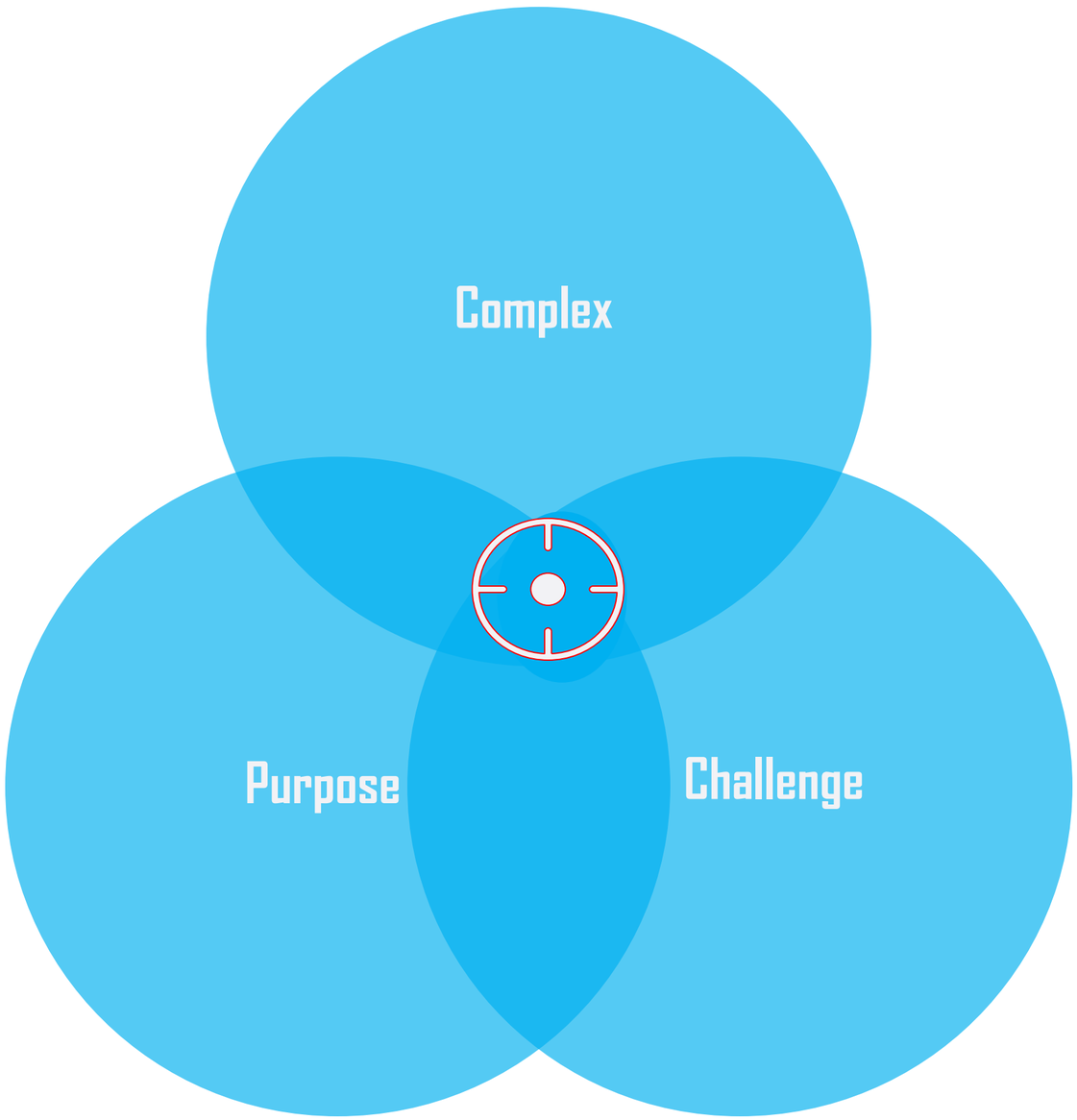
- Individuals with Mild Cognitive Impairment (or pre-dementia state) who received **cognitive training, involving multiple modalities**, were likely to display **improvement on outcome measures of cognition after the intervention**.

Sherman & Sherzai, et al. (2017). *Neuropsychology review*, 1-45.



- **Synaptic connections** are your protection
- **Cognitive reserve** is the most important protection
- **Complex activities ('idea density' and job complexity)** associated with increased brain capacity and size

Achieve Optimal
Brain Capacity



Complex Activities

Real life activities

- Learning a new language
- Group activities
- Reading - retrieve, review, recall
- Playing a musical instrument
- Learning to dance
- Project management

01

Challenging Activities

02

Forces neuronal connectivity

- Learning a new language
- Writing an article, story, report
- Learning a new skill at a work
- Memorizing longer lists

03

Around your Purpose / Fun

- Managing a higher level project
- Working towards a promotion
- Volunteer

Purpose

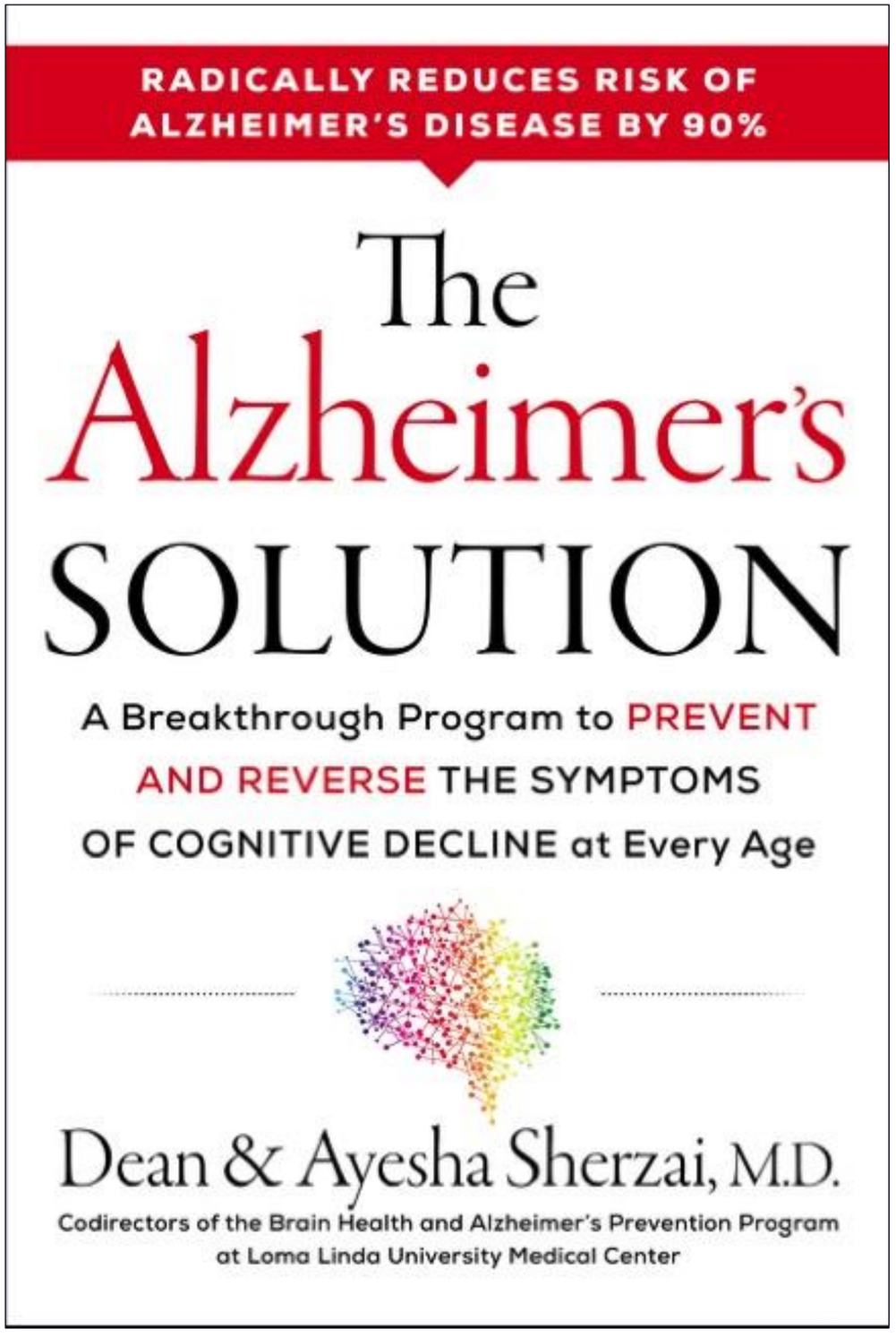
Brain health starts at home and at work

Every single decision with regards to lifestyle has a profound impact on the ultimate brain capacity

Healthy Minds Initiative

- Community based study of lifestyle and cognitive health in 1700 participants in collaboration with Beach Cities Health District
- 3 years
- Cognitive test, brain MRI, blood biomarkers, lifestyle questionnaires
- NEURO Plan

Healthymindsinitiative.org



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