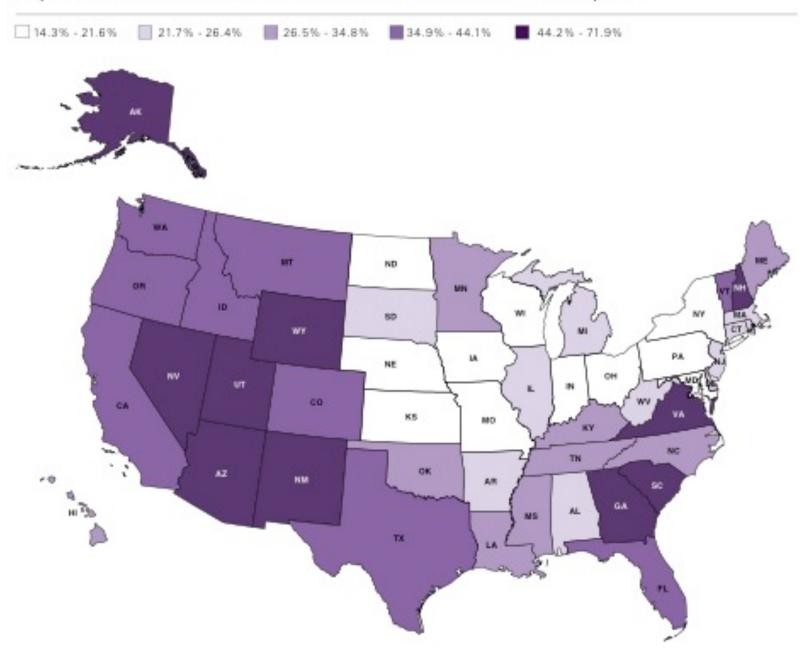
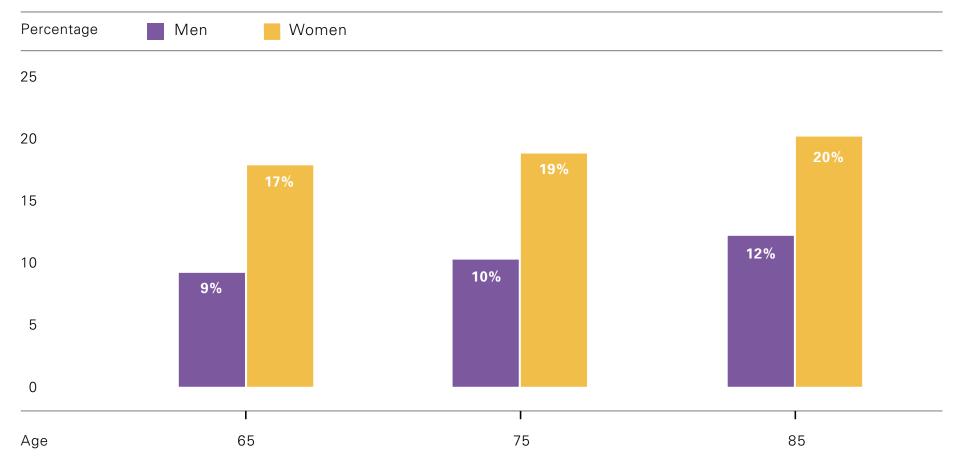
HOPE BRUNCH 2015

Research Update

Neil Kowall MD

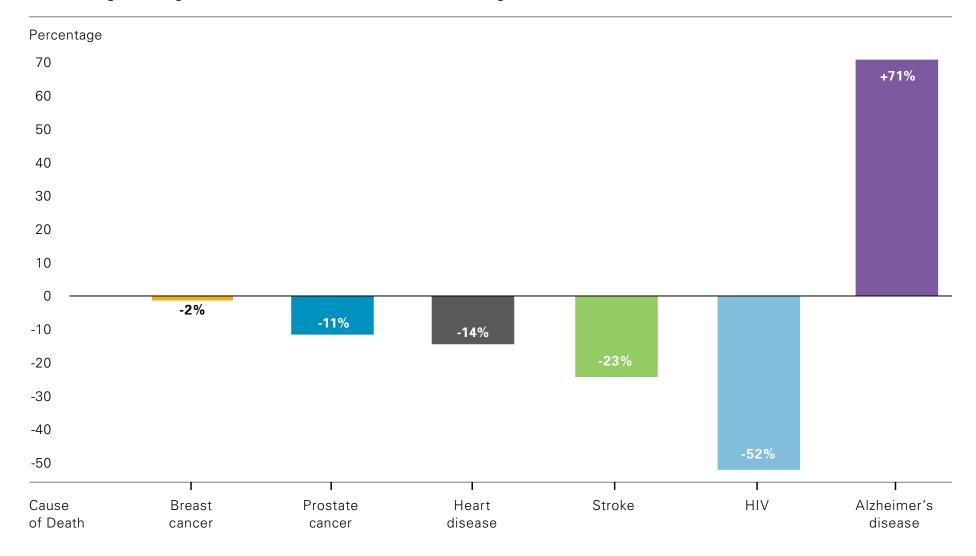


Projected Increases Between 2015 and 2025 in Alzheimer's Disease Prevalence by State



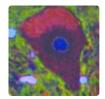
Estimated Lifetime Risk for Alzheimer's, by Age and Sex, from the Framingham Study

Created from data from Seshadri et al.¹⁵⁶



Percentage Changes in Selected Causes of Death (All Ages) Between 2000 and 2013





Research News

Can Exercise Slow the Progression of Alzheimer's Pathology?

ADD TO MY ALZFORUM

13 Aug 2015

Researchers report multiple benefits of aerobic exercise on brain function, including some hints it could slow tau pathology.

Exercise Boosts Cognition In Symptomatic Disease



ADD TO MY ALZFORUM

13 Aug 2015

At the right intensity and treatment duration, aerobic exercise can sharpen thinking skills and improve brain function even in cognitively impaired people, say researchers.

Aducanumab, Solanezumab, Gantenerumab Data Lift Crenezumab, As Well

ADD TO MY ALZFORUM

10 Aug 2015

At AAIC, new data on three anti-A β antibodies reinforced a sense of hope that A β immunotherapy may yet work out. Challenges with each antibody notwithstanding, all four leading candidates, including crenezumab, are now in Phase 3.

Too much TV could raise the risk of Alzheimer's, study suggests

By Fredrick Kunkle July 20

It turns out that too much TV might damage your brain and also raise the risk of developing Alzheimer's disease — and that the effects could show up much sooner than previously believed, a new study suggests.

Researchers at the Northern California Institute for Research and Education in San Francisco who investigated the association between sedentary lifestyles, cognitive performance and the risk of developing dementia found that people who watched a lot of television — namely, four hours or more per day — scored significantly lower on measures of cognitive performance in middle age.

The study, which tracked people for 25 years beginning in young adulthood, found that people who also reported low levels of physical activity performed worse on cognitive tests.

AP / July 20, 2015, 7:33 PM

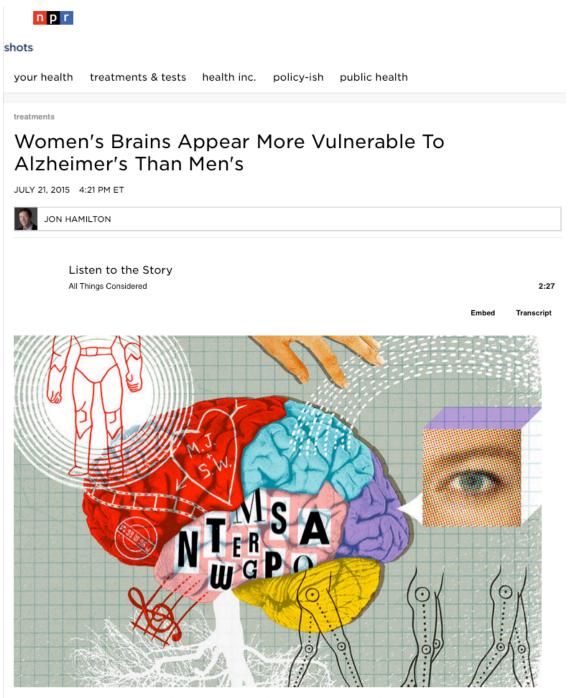
Growing evidence links sleep problems, Alzheimer's

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To sleep, perchance to... ward off Alzheimer's? New research suggests poor sleep may increase people's risk of Alzheimer's disease, by spurring a brain-clogging gunk that in turn further interrupts shut-eye.

Disrupted sleep may be one of the missing pieces in explaining how a hallmark of Alzheimer's, a sticky protein called beta-amyloid, starts its damage long before people have trouble with memory, researchers reported Monday at the Alzheimer's Association International Conference.



Women with mild cognitive impairment, which can be a precursor to Alzheimer's, tend to decline faster than men. Lizzie Roberts/Getty Images/Ikon Images

1. Learn a second (or third, or fourth) language.

Aside from raising cultural awareness and expanding cultural horizons, adding another language to your vocabulary may delay the onset of Alzheimer's by 4 years.

2. Drink raw fruit and vegetable juices.

A 2006 study from Vanderbilt University found that drinking fruit and vegetable juices more than three times a week could cut the risk of developing Alzheimer's by 76%.

3. Add a vitamin K supplement to your diet.

Known as "the forgotten vitamin," vitamin K plays a crucial role in anti-aging and may prevent Alzheimer's. Because vitamin K is not found in most multivitamins many people consume it through green leafy vegetables or a vitamin K supplement.

4. Reduce stress.

Many studies have linked anxiety with the development of Alzheimer's, especially in people who are already at risk for the disease. A recent study showed that people who had mild cognitive impairment and reported high levels of anxiety were 135% more likely to develop Alzheimer's.

5. Commit to regular exercise.

Regular exercise may preserve hippocampal volume which is the first part of the brain attacked by Alzheimer's. Good exercise choices including walking briskly, dancing, swimming, cycling and even gardening.

6. Laugh more.

Researchers have found that laughter is more than good for the soul. Playing, laughing, and being active helps to engage the brain, grow new brain cells, and ultimately prevent Alzheimer's.

7. Run 15 miles per week.

Logging at least 15 miles per week may reduce your risk of Alzheimer's by 40% according to a new study.

8. Consume more fruits.

A study completed early in 2014 showed that fruits containing a compound called fisetin has Alzheimer's fighting properties. Commonly found in strawberries and mangos, fisetin has antiinflammatory properties that effectively combated the onset of Alzheimer's in mice.

9. Make time for meditation.

Quieting your mind may be more important than you might think in Alzheimer's prevention. A study from 2013 showed that people who performed meditation and yoga had less brain atrophy than those who did not. Meditation can increase protective tissue in the brain, can help seniors feel less stressed and reduces the hormone cortisol, which has been known to increase the risk of developing dementia.

10. Eat more fish.

Fish is high in omega-3 fatty acids which can control blood clotting, build cell membranes in the brain, protect against heart disease, protect against brain atrophy and slow Alzheimer's and dementia.

11. Quit smoking.

A report from October 2014 from the World Health Organization found that smokers have a 45% higher risk of developing dementia than non-smokers and also claimed that 14% of all dementia cases could possibly be attributed to smoking.

12. Adopt a Mediterranean diet.

Following a Mediterranean diet high in fish, chicken, olive oil and other foods high in omega-3s, may improve cognition and lower the risk of cognitive decline.

13. Learn early Alzheimer's symptoms.

Early detection is the key to slowing the progression of Alzheimer's. Learning and recognizing symptoms as they first appear means that more treatment options are available. Early signs and symptoms of Alzheimer's can include losing track of dates, vision problems and trouble completing familiar tasks.

14. Sleep better.

Lack of sleep has been linked to a myriad of health problems

including stress and increased cortisol, both of which are risk factors for Alzheimer's. In addition, a waste-draining system that clears the brain of beta-amyloid is more active while we sleep.

15. Limit sugar intake.

Diabetes has been closely linked to Alzheimer's with some researchers even calling the disease a third type of diabetes. Manage sugar intake and blood sugar levels to keep your brain healthy.

Study Shows Promise in Detecting an Individual's Likelihood of Developing Alzheimer's

Method relies on an algorithm of six memory, brain-imaging and biological measures

Some 80% of the sample predicted by the biomarker combination to go on to develop abnormal memory problems truly went on to develop them, while 20% would have been classified as a false negative. The algorithm, 75% of the time, correctly predicted who wouldn't go on to develop memory problems.

The six measures in the algorithm included a genetic assessment of whether an individual had a variant of the ApoE4 gene, two memory tests, the level of a protein called tau found in the cerebrospinal fluid and MRI measurements of two brain regions.

New saliva test may catch Alzheimer's disease early

By Liza Lucas, Special to CNN Updated 8:19 PM ET, Mon July 20, 2015

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(CNN) – A test detecting Alzheimer's disease early may become easily available thanks to one plentiful bodily substance: saliva, a recently released study shows.

The saliva test was presented at the 2015 Alzheimer's Association International Conference in Washington this week. Though research is still in its infancy, the saliva test represents the exciting future of diagnostic tools in development for the detection of the neurodegenerative disease.

Early signs that drug 'may delay Alzheimer's decline'

By James Gallagher Health editor, BBC News website

22 July 2015 Health

A reanalysis of the cognition scores of the patients with mild Alzheimer's suggested taking the drug had cut the rate of the disease's progression by about 34%.

The implication is that the amount of cognitive decline normally seen in 18 months would take 24 months with the drug.

In the extension of the original trial, all of the 1,000-plus mild Alzheimer's patients participating were given solanezumab.

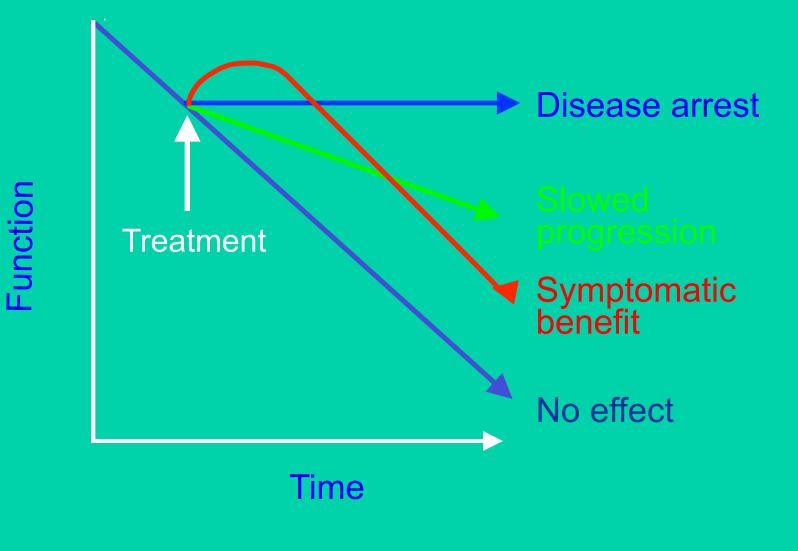
So, at the end of the extension, half of them had been taking the drug for three and a half years while the other half had been taking it for two years.

The latest data shows those taking solanezumab for the longest time still had better scores of cognitive function.

This suggests the course of the disease was being slowed.

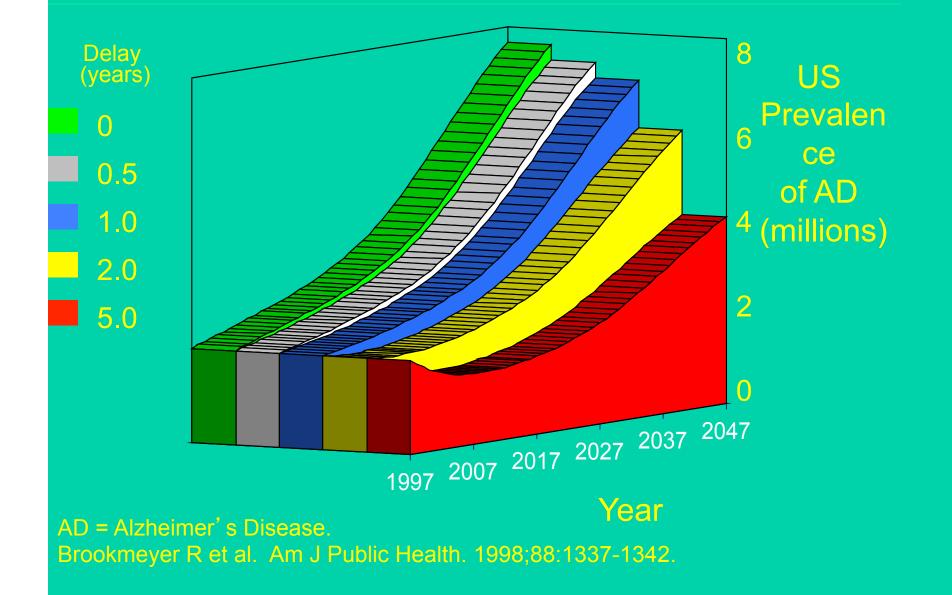
If the patients' brains had continued to decline at the normal pace and the drug had been merely helping with symptoms, then all of the patients participating in the extension of the original trial - whether they had been taking solanezumab for three and a half or two years - would have had similar scores of cognitive function.

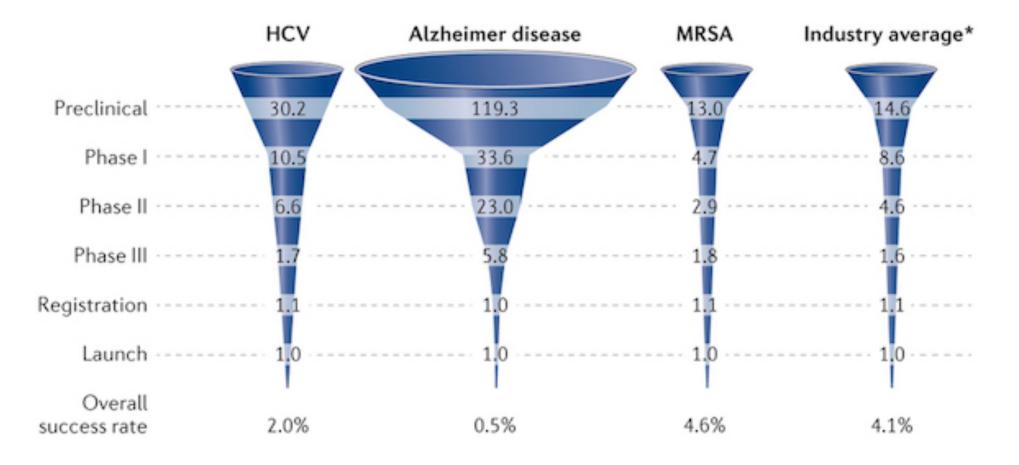
Treatment Outcomes



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Potential Impact of Interventions to Delay Onset of Alzheimer's Disease





Nature Reviews | Drug Discovery

Clinical Trials in Predementia Stages of Alzheimer Disease

Jagan A. Pillai, мввз, PhD^{a,*}, Jeffrey L. Cummings, MD, scD^b

Box 1 Categories of medications to be considered for treatment of predementia population
Neurotransmitter therapies
Cholinergic
Nicotinergic
Serotonergic
Cannabinoid
Histaminergic
Phosphodiesterase inhibition
Protein-related therapies
Antiamyloid
• Tau related
• TDP-43 related
Cellular processes
Anti-inflammatory
Antioxidant
Mitochondrial
Peroxisome proliferator-activated receptor (PPAR) agonists
Synaptic maintenance
Myelin maintenance
Restoration
Growth factors
Stem cells
Synaptic enhancement

Actively Recruiting Studies

AD = Alzheimer's Disease; MCI = Mild Cognitive Impairment

STUDY TITLE	CURRENTLY RECRUITING	STUDY DESCRIPTION
Health Outreach Program for the Elderly (HOPE)	Healthy adults, MCI, AD	HOPE is the main registry of participants. People who join HOPE attend a yearly visit in which their memory and thinking abilities are evaluated. They also participate in other BU ADC-affiliated studies. Interested volunteers may join this important registry if they can attend a yearly visit with a study partner and are 65 or older with or without memory concerns or 50 or older with memory concerns.
Anti-Amyloid in Asymp- tomatic Alzheimer's Disease Study (A4)	Healthy Adults	This clinical trial is examining the effects of Solanezumab in patients who have not been diagnosed with AD, but have concerns about their memory. Patients are asked to come to the BU ADC once a month for 3 years. Interested volunteers may be eligible if they are between 65-85 years old and are able to attend monthly visits with a study partner.
BAN2401 Clinical Trial for MCI and early AD	MCI	This clinical trial is examining the effects of BAN2401 in patients with MCI. Patients are asked to come once every 2 weeks for 18 months. Interested volunteers age 50-80 with a diagnosis of MCI, and who can attend bi-monthly visits with a study partner, may be eligible.
NOBLE Study	Mild to Mod. AD	This clinical trial aims to evaluate the safety and efficacy of an oral medication (T817MA) compared to placebo in subjects with mild to moderate AD. Subjects between 55 and 85 years old who are currently receiving treatment with Aricept (donepezil) or the Exelon patch may be eligible.
Amylin, Amyloid-beta Peptide, and Alzheimer's Disease	Healthy adults, MCI, AD	This study aims to develop a blood test for Alzheimer's disease by repurposing an FDA-approved diabetes medication called Pramlintide, which also has the potential to diagnose and treat AD. Participation involves one visit, which will include one injection of the medication, followed by several blood draws. Volunteers age 50-90 may be eligible if they do not have diabetes.
Challenge Diagnostic Test for Alzheimer's Disease	Healthy adults, AD	This proof-of-concept trial is a follow-up study of the Amylin, Amyloid-beta Peptide, and Alzheimer's Disease study. It aims to further develop a blood test for Alzheimer's disease by evaluating different dose levels of a repurposed FDA-approved diabetes medication called Pramlintide. This study takes place over three visits. Volunteers age 50-90 may be eligible if they do not have diabetes.
Emotional Perception, Neuropsychiatric Symptoms and Caregiver Experience in AD	Healthy adults, AD	Researchers are examining how changes in emotional perception in people with dementia due to Alzheimer's disease impact the experience of their caregivers. The goal is for the results of this study to be used to improve services for people with Alzheimer's disease and their caregivers. The researchers are looking both for couples affected by Alzheimer's disease and couples in which both spouses are not experiencing memory loss.
Alzheimer's Association Dementia Care Coordination Project	All forms of dementia, MCI	This study's goal is to evaluate approaches to care coordination and patient/caregiver education for those with AD or other dementias. Caregivers are recruited to complete questionnaires both pre- and post-testing, after which they will be assigned to one of two groups. The treatment group will receive dementia care coordination from the Alzheimer's Association immediately. The control group will be referred to the Alzheimer's Association after a 2-year delay. Volunteer participants may be eligible if they are age 50-110 and are caring for someone with AD or another kind of dementia.
AMARANTH Study	MCI, Mild AD	The purpose of this study is to assess the efficacy and safety of AZD3293 compared with placebo in subjects with MCI due to AD and early stage (mild) dementia of the Alzheimer's type. Subjects between 55 and 85 years old may be eligible to participate.

FORUM Study	Mild to Mod. AD	This clinical trial aims to evaluate the safety and efficacy of an oral medication compared to placebo in subjects with mild to moderate AD. Subjects 55-85 who are currently receiving or were previously treated with an ACE inhibitor may be eligible.
Memory in Alzheimer's Disease and Mild Cognitive Impairment	Healthy adults, MCI, AD	This study seeks to better understand why patients with AD and MCI frequently remember things that never happened and to find ways to reduce false memories in patients with dementia. Subjects between 65 and 90 years old may be eligible to participate.
Aerobic Exercise, Neurotrophins, and fMRI	Healthy adults	This study is investigating the effects of exercise and cardiovascular fitness on cognitive processes, brain function, and levels of certain proteins in the blood. Eligible participants will be randomized to either an aerobic or non-aerobic exercise program for 12 weeks. You may be eligible if you are a healthy, sedentary adult aged 18-35 or 55-85.
Memory Benefits of Sleep in Healthy Young, Elderly and Mild AD Patients	Healthy adults	The goal of this study is to examine the effects of sleep on memory processing for healthy young adults and healthy elderly individuals. Volunteers participate in a daytime nap study or an overnight study. Participants may be eligible if they are between the ages of 65 and 80, are in good physical and mental health and do not have any sleep complaints.
Health Pathways	Healthy adults, Caregivers	The Health Pathways study looks at how caring for a person with dementia affects physical and emotional health. Participants attend four annual face-to-face interviews in which they are asked questions about their health and about the person they care for. They also complete lab work. Participants may be eligible if they have no memory concerns and are age 60 or older.
Impact of Physical Fitness on Cognition and Brain Function	Healthy adults	The focus of the study is to determine whether physical fitness and activity levels have a positive impact on cognitive abilities and function in older adults. Volunteers between ages of 55 and 85 may be eligible.
STUDY TITLE	CURRENTLY RECRUITING	STUDY DESCRIPTION
Cardiovascular Integrity Risk for Cognitive Decline in Aging (CIRCA)	Healthy adults, MCI	Both AD and cerebrovascular disease can cause changes in the brain that are associated with changes in memory, thinking and organizational skills. This study is looking closely at how brain structures relate to cognitive changes and how risk factors for cerebrovascular disease may affect individuals with and without MCI. Volunteers may be able to participate if they are between the ages of 45 and 85 and have MCI or no memory concerns.
Cerebrovascular Contributions to Brain Aging and Dementia	Healthy adults, MCI	This study is examining the characteristics of normal aging and changes in the brain associated with aging and cognitive impairment using brain imaging. Volunteers may be eligible if they are between 60 and 80 years old and are healthy adults or have been diagnosed with MCI.
Mitochondrial Abnor- malities and Repair in Psychiatric Illness	Healthy adults, AD	This study is recruiting people with AD and healthy controls in order to learn about the structure and function of cells and mitochondria of persons with brain illness. The study is designed to collect smal skin and blood samples from ill and healthy subjects and can be completed in one visit of about 2 hours Interested volunteers between ages 55 and 89 may be eligible.

Interested? Contact the BU ADC recruitment coordinator at 617-414-1078 or joinADC@bu.edu.

Major NIH Research Grants awarded to BU ADC Investigators

• Ann McKee MD

UO1: CTE and Posttraumatic Neurodegeneration: Neuropathology and Ex Vivo Imaging

Bob Stern PhD

U01: Detect, Define and Measure the Progression of Chronic Traumatic Encephalopathy

• Benjamin Wolozin, M.D., Ph.D. (Zenith award)

Stress Granules and the Biology of TDP-43

• Wendy Wei Qiao Qiu, M.D., Ph.D.

Plasma Amylin, Cognitive Function and Brain Imaging in the Framingham Heart Study

Sudha Seshadri MD

AD Gene Discovery: Exome Chip, New Endophenotypes & Functional Studies in CHARGE

• Jesse Mez, MD (K 23 award)

Genetic and Neuropsychological Heterogeneity in Alzheimer's Disease

Lindsay Farrer PhD

Alzheimer Disease Genetic Architecture in African Americans

Recent Research Grants funded by AA to BU ADC investigators

• Rhoda Au, Ph.D

Framingham Cognitive Aging Study: Impact of Vascular Metabolic Risk Factors

• Thor Stein, M.D., Ph.D.

<u>Genetic Risk Factors Underlying Chronic Trauma and AD Pathology</u>

• Tsuneya Ikezu, M.D., Ph.D.

Exosome Pathway as a Novel Therapeutic Target of Tauopathy

- Benjamin Wolozin, M.D., Ph.D. (Zenith award)
- It Takes TIA to Tangle: The Role of RN A Binding Proteins in AD
- Wendy Wei Qiao Qiu, M.D., Ph.D.

Setting up a challenge diagnostic test for Alzheimer's disease

• Richard Sherva, Ph.D., M.P.H.

<u>Genetics of Rate of Cognitive Decline in a Clinical Trial of Alzheimer's Disease</u>

• Jesse Mez, MD

New Investigator grant for targeted sequencing in the UNITE football players