Alzheimer’s and Exercise

Stanford ADRC

Second Annual Patient and Research Participant Appreciation Celebration
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Stanford University
Linking Diet, Exercise and Alzheimer’s

IN HIS 40S and a self-described fitness nut, Stephen Chambers doesn’t seem like someone who would be worrying about Alzheimer’s.

But when his father was diagnosed with the disease about five years ago, he went to the Alzheimer’s Prevention Clinic in New York to see what he could do.

Though he had no noticeable memory issues, cognitive testing showed less than ideal levels in certain areas. His neurologist told him there were a number of lifestyle changes that might help his cognition and possibly reduce the risk of developing Alzheimer’s disease.

Mr. Chambers, a 48-year-old physical therapist in Jersey City, N.J., modified his sleep, diet and exercise routines. Eighteen months later, his performance on a battery of cognitive tests improved, particularly in areas like processing speed and executive function, such as decision-making and planning.

“I feel a certain sense of comfort in knowing that there are factors that I can control that can contribute to the decreased risk of me getting Alzheimer’s,” says Mr. Chambers.

Mr. Chambers is among 154 pa-
says Dr. Sabbagh of the study. “That is where the trend is going.”

Ronald Petersen, director of the Mayo Clinic Alzheimer’s Disease Research Center in Rochester, Minn., called the study encouraging but cautioned that lifestyle changes aren’t a magic bullet. “Does that mean we’re going to prevent Alzheimer’s disease?” he says. “No.” But measures that might help delay the onset are significant. “If we can postpone the onset or slow the progression of cognitive impairment and Alzheimer’s disease, that’s very important,” he says.

Mr. Chambers says he now eats blueberries or strawberries, which are high in antioxidants, at least two to three times a week. He eats more of certain kinds of fish to get more Omega-3 fatty acids, which can decrease inflammation and improve cardiovascular and brain health. And he adds powdered cocoa flavonols to his morning coffee because studies show they can combat insulin resistance and promote cognitive function.

He also listens to more music, particularly classical music, and tweaked his workouts to include more high-intensity interval train-
Alzheimer’s risk increases with aging

- Normal cognition
- Age-related cognitive impairment
- Mild Cognitive Impairment (MCI)
- Dementia

- Amyloid plaques
- Tau tangles

- Alzheimer’s disease
- Vascular dementia
- Lewy body dementia
Exercise dramatically reduces Alzheimer’s disease incidence

Exercise – how much? 30 min/day 5d/week - moderate levels

~40% reduced risk

Gomes-Osman et al Neurology 2018
WHO guidelines 2019
Jia et al BMC Geriatrics 2019
Exercise decreases amyloid accumulation and overcomes ApoE4 genetic risk

45-88 yo normals – parent-AD ± exercise past 10 years

30 min mod exercise 5d/wk

Head et al. *Arch Neurol* 2012
High physical activity – resilience to amyloid

Harvard Aging Brain Study - Rabin et al JAMA Neurol 2019
Walking reverses of Hippocampal Age-related Atrophy!

hippocampus
1-2%/yr atrophy

10 → 40 min/day walk 1 year

LEFT HIPPOCAMPUS

Volume (mm$^3$)

Baseline 6-months 1-year

Erickson et al
PNAS 2011
Exercise effects on cognition in MCI

Meta-analysis:

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Experimental</th>
<th>Control</th>
<th>Std. Mean Difference</th>
<th>IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
<td>Weight</td>
<td></td>
</tr>
<tr>
<td>Busse 2008</td>
<td>6.3 (8.9)</td>
<td>3.2 (8.1)</td>
<td>17 (6.5%)</td>
<td>0.36 [-0.36, 1.07]</td>
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<tr>
<td>Hong 2017</td>
<td>1 (3.27)</td>
<td>0.42 (4.45)</td>
<td>12 (4.8%)</td>
<td>0.14 [-0.70, 0.98]</td>
</tr>
<tr>
<td>Lam 2015</td>
<td>3.3 (3.3)</td>
<td>3.2 (3.3)</td>
<td>131 (32.9%)</td>
<td>0.03 [-0.21, 0.27]</td>
</tr>
<tr>
<td>Lautenschlager 2008</td>
<td>0.87 (3.44)</td>
<td>-1.29 (3.95)</td>
<td>52 (16.9%)</td>
<td>0.58 [0.18, 0.98]</td>
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<tr>
<td>Singh 2014</td>
<td>2.73 (3.13)</td>
<td>0.95 (3.05)</td>
<td>27 (9.5%)</td>
<td>0.57 [-0.01, 1.14]</td>
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<tr>
<td>Suzuki 2013</td>
<td>0.2 (2.42)</td>
<td>-0.3 (2.59)</td>
<td>45 (16.4%)</td>
<td>0.20 [-0.21, 0.61]</td>
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<tr>
<td>Varela 40% 2011</td>
<td>1.09 (6.5)</td>
<td>-2.27 (4.7)</td>
<td>15 (6.6%)</td>
<td>0.57 [-0.14, 1.28]</td>
</tr>
<tr>
<td>varela 60% 2011</td>
<td>0.42 (5)</td>
<td>-2.27 (4.7)</td>
<td>15 (6.4%)</td>
<td>0.54 [-0.18, 1.28]</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>321 (100.0%)</td>
<td>314</td>
<td>0.30 [0.10, 0.49]</td>
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</tr>
</tbody>
</table>

Heterogeneity: Tau² = 0.01; Chi² = 8.70, df = 7 (P = 0.28); I² = 20%
Test for overall effect: Z = 3.03 (P = 0.002)
Physical activity effects on cognitive measures in dementia: RCT meta-analysis

Mean: 183 min/week, aerobic vs social activity (AD + non-AD)
Physical activity effects on cognitive measures in dementia: RCT meta-analysis

Lais Fajersztajn (2008) 2.33 (0.64, 4.02) 4.32
Massimo Venturelli (2011) 2.42 (1.32, 3.52) 10.18
Anthea Vreugdenhil (2012) 2.47 (1.64, 3.31) 17.69
Cynthia Arcoverde (2013) 1.34 (0.36, 2.32) 12.77
Wang Ying (2014) 1.71 (0.94, 2.48) 20.62
Vjera A. Holthoff (2015) 2.26 (1.28, 3.25) 12.72
Yan Lanyun (2015) 1.56 (0.81, 2.32) 21.70
Overall (I-squared = 0.0%, p = 0.461) 1.94 (1.59, 2.29) 100.00

NOTE: Weights are from random effects analysis
How does exercise protect against Alzheimer’s?

Exercise

- Increased BDNF, other unknown factors
- Increased neurogenesis
- Increased synapse numbers and function
- Increased vascular health

Protection against Alzheimer’s disease
- Better brain health
- Increased network connectivity
- Larger cognitive reserve

BDNF (brain-derived neurotrophic factor)

Spire-Jones and Ritchie Science 2018
Developing drugs to reverse degeneration

Longo Lab, Stanford
From mice to people
Basic science and clinical care at Stanford

Stanford Neuroscience Institute 2020

Stanford Neuroscience Health Center 2016

Adult Hospital November 2019

Packard Children’s Hospital 2018