Brain+Body Healthy Aging: A Community-Based, Scalable, Total Lifestyle Program to Reduce Alzheimer's Dementia Risk

November 13, 2020
Presenters

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- **Chelsea Stillman PhD**, Research Assistant Professor, University of Pittsburgh, Department of Psychology cms289@pitt.edu

- **Carol Zernial MA**, Senior Vice President Social Responsibility and Foundation Executive Director; WellMed Medical Management, Inc. czernial@wellmed.net
DISCLOSURES

Paul Bendheim is the founder and has an equity position in Brain Savers Inc.

The other presenters have no disclosures.
Paul E Bendheim, MD
Clinical Professor of Neurology

THE UNIVERSITY OF ARIZONA
College of Medicine
Phoenix

Founder, Brain Savers®, LLC

BrainSavers®
BECAUSE GRAY MATTERS™
Objectives

• Describe the spectrum of age-associated cognitive decline, Alzheimer’s disease (AD) & other dementias.

• Describe the principles of neuroplasticity & cognitive reserve.

• Highlight the basic & clinical science research results that i) revolutionized our understanding of the aging brain, ii) provide the scientific basis for evidence-based, healthy brain aging programs.

• Identify lifestyle components - socialization, nutrition, cognitive & physical activities, stress reduction, sleep - that influence the aging brain & reduce the risk of AD & vascular dementia.

• How evidence-based programs to engage “the worried well” – the 100+million at risk for age-related cognitive impairments – have been implemented.
The Goal: HEALTHY BRAIN AGING Reduced Risk of AD & All-Cause Dementia
Two fundamental principles are the scientific basis of the New Science of the Aging Brain

**Brain Plasticity = Neuroplasticity**
*The adult brain is malleable and changeable: it can actually generate new cells and new connections even in the later decades of life.*

**Brain Reserve = Cognitive Reserve**
*A personal insurance policy of a stronger brain. A brain that is more resistant to the wear & tear of the aging process and that is less vulnerable to Alzheimer’s disease and other dementias.*
MAJOR BRAIN STRUCTURES

FRONTAL Lobe
TEMPORAL Lobe
HIPPOCAMPUS
PARIETAL Lobe
OCCIPITAL Lobe
CEREBELLUM
The Most Incredible Object in the Universe

- 100 billion neurons connected by synapses
- 100 trillion synapses
- 100 billion - 1 trillion glial cells (housekeeping)
- 2.5 million miles of mini-cables (axons and dendrites)
- Grows at the rate of about 250,000 nerve cells per minute throughout the course of pregnancy.
- “Functions of the brain and specificity with which these are assigned to one or another type of cell or small location are stunning in their complexity.”
- How is such an intricate network constructed in the first place?

Ackerman S. The Development and Shaping of the Brain
Synapse formation on neurons born in the adult hippocampus

Ramon y Cajal ~1895

Supplementary Figure 1. Dendritic spines from new neurons are apposed to perforant path axonal boutons. a. Confocal projection of the dentate gyrus showing perforant path axons in red and new neurons in green. Scale bar, 100 μm. b. Confocal projection of GFP⁺ neurons and RFP⁺ axons. Scale bar, 50 μm. c. Confocal projection of GFP⁺ dendritic spines contacting perforant path axonal boutons. Scale bar, 2 μm.
Abnormal Brain Aging: The Spectrum of Age Related Cognitive Decline

• Age-Associated Memory Impairment = Normal Aging

• Mild Cognitive Impairment (MCI)
• Dementia: Mild – Moderate – Severe

Dementia

• Not a specific disease - A group of symptoms
• Loss of memory, thinking & reasoning skills
• Severe enough to reduce a person's ability to perform normal everyday activities
• Behavioral & psychiatric symptoms may be present
• Progressive worsening over time
• Many diseases/conditions can produce dementia
• Some are reversible
Dementias & Conditions That Mimic

**Progressive dementias**
- Alzheimer's disease
- Vascular dementia
- Lewy body dementia
- Frontotemporal dementia
- Mixed dementia

**Disorders linked to dementia**
- Huntington's disease
- Traumatic brain injury (TBI)
- Creutzfeldt-Jakob disease
- Parkinson's disease
Treatable / Reversible Dementias

- Infections & immune disorders
- Metabolic problems & endocrine abnormalities
- Nutritional deficiencies
- Medication side effects
- Subdural hematomas
- Toxins
- Brain tumors
- Hypoxia
- Normal-pressure hydrocephalus

Modified from: https://www.mayoclinic.org/diseases-conditions/dementia/symptoms-causes/syc-20352013
# Normal Aging vs. Dementia

<table>
<thead>
<tr>
<th>Normal Aging</th>
<th>Dementia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not being able to remember details of an event from a year ago</td>
<td>Not being able to recall details of recent events or conversations</td>
</tr>
<tr>
<td>Not being able to remember the name of an acquaintance</td>
<td>Not recognizing or knowing the names of family &amp; friends</td>
</tr>
<tr>
<td>Forgetting things &amp; events occasionally</td>
<td>Forgetting things or events more frequently: <strong>impairs daily activities</strong></td>
</tr>
<tr>
<td>Occasionally have difficulty finding words</td>
<td>Frequent pauses &amp; substitutions when finding words</td>
</tr>
<tr>
<td><strong>You are worried</strong> about your memory: your relatives are not aware of any problems</td>
<td>Your relatives are worried about your memory, but <strong>you are not aware</strong> of any problems</td>
</tr>
</tbody>
</table>

Alzheimer Society of Canada
The Alzheimer’s Epidemic
Normal Aging vs. AD
Amyloid Plaques & Neurofibrillary Tangles

Plaques
Alzheimer’s

Tangles

Normal

Courtesy of Harry Vinters, MD, and Pierre Tariot, MD.
The Problem & The Opportunity

Alzheimer’s Disease is a Massive Unmet Medical & Societal Need

- Greatest risk factors: advancing age and **unhealthy lifestyle practices**.
- 6th leading cause of death
- 1 in 3 seniors will die with AD or other dementia.
- 2020 - new case of AD diagnosed every 65 seconds.
- Since 2000, heart disease deaths are down 9%, **AD deaths are up 145%**.
Alzheimer’s Disease

5.8 million Americans have Alzheimer's disease today
2020 - new case every 65 seconds

At Risk:
• ~ 77 million baby boomers + ~ 35 million seniors

Costs 2020:
• Direct = $305B (AD & other dementias)
• Medicare = $206B
  “Costs” not included: Caregivers ($244 billion in 2020), Veterans Administration, private & long-term healthcare insurance.

Projected 2050:
• Direct = $1.1 trillion
• Medicare = $758B

More information: 2020 AD Facts & Figures
Risk Factors for Alzheimer’s Disease

Unmodifiable

Modifiable

Modifiable

# A New Paradigm

## Traditional Pharma Solutions Remain Elusive

"Another Promising Alzheimer’s Drug Trial Ends In Failure: ‘This One Hurts.’” Biogen / Eisai; Aducanumab  
- March 21, 2019

**Another Alzheimer's Drug Fails as Lilly, Astra Halt Tests.** Lanabecestat - June 11, 2018

"Alzheimer's Drug Fails in Another Crushing Disappointment: Merck Announces Discontinuation of APECS Study Evaluating Verubecestat (MK-8931) for the Treatment of People with Prodromal Alzheimer’s Disease”  
- Feb 13, 2018

“Eli Lilly’s Alzheimer’s drug fails in late-stage trial, dashing hopes.” Solanezumab - Nov. 2016

“Trials for Alzheimer’s Drug Halted After Poor Results.” Pfizer / Johnson & Johnson; Bapineuzumab - Aug 6, 2012;

"By one count, more than 190 Alzheimer drugs have failed in trials. Spending on care for people alive in the U.S. right now who will develop the affliction is projected to cost $47 trillion over the course of their lives, according to a report in March (2018) from the Alzheimer’s Association.”

## Lifestyle as Preventive Medicine

“Sufficiently strong evidence that regular physical activity, a healthy diet, life long learning/cognitive training and management of cardiovascular risk factors may reduce the risk of cognitive decline and may reduce the risk of dementia.” - Institute of Medicine / National Academies of Science 2015; Baumgart et al, 2015

“A gold-standard clinical trial provides evidence that diet, exercise and an active social life can help prevent cognitive decline.” – Sci Am; April 2017


“A 2 year multidomain intervention of diet, exercise, cognitive training, and vascular risk monitoring versus control to prevent cognitive decline in at-risk elderly people (FINGER): a randomised controlled trial” – Lancet March 2015
Evidence for the Effects of Lifestyle Behaviours on Neurocognitive Health

Chelsea Stillman, PhD
Research Assistant Professor
University of Pittsburgh

NANASP Webinar
November 13, 2020
Health Neuroscience

“...a new field that is at the interface of health psychology and neuroscience. It is concerned with the interplay between the brain and physical health over the lifespan.” (Erickson et al., *Curr. Dir Psy Sci*, 2015)

“... how the brain affects and is affected by health behaviors” (Stillman & Erickson, *Ann. NY Acad Sci*, 2018)
We are aging.
A top concern about getting older is declining cognitive capacity.

The PARADE/Research!America Health Poll Charlton Research Company, 2005
Schaie, 1994

Salthouse, 1996
Kennedy, Erickson, Rodrigue, Voss, Colcombe, Kramer, Acker, Raz, 2009 2009
At least 1/3 dementia cases are attributable to modifiable risk factors.

Strategies to promote successful aging
Strategies to promote successful aging

**Stay connected** “Steady social contact protects cognitive function as you age.

**Benefits of exercise** “Can exercise give a memory boost? You bet!”

**Stay intellectually challenged** “Intellectually challenging activities keep your brain agile.”

**Benefits of food** “Is there a diet to cut the risk of Alzheimer’s? Yes—by as much as 50%!”

**Recapture needed sleep** “… sleep essential for memory”

**Release unwanted stress** “Chronic stress can have damaging effects on key areas of the brain”
Strategies to promote successful aging

**Stay connected** “Steady social contact protects cognitive function as you age.

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Guiding Questions

1. What are the effects of exercise interventions on cognition?

2. Does exercise predict subsequent cognitive functioning in late life?

3. What other strategies promote neurocognitive health?
1. What are the effects of randomized exercise interventions on cognition?
Older sedentary adults

Baseline assessments

Randomization

Aerobic Exercise (e.g., Brisk Walking)

Stretching/Toning control

Fitness MRI
Cognitive testing
Blood biomarkers

6-months or 1-year of treatment

Follow-up assessments

**Both groups** receive physical activity

**Both groups** receive laboratory based treatment in groups

**Both groups** come to the lab 3 days per week for 30-45 minutes

**Differences:** Intensity and type of physical activity
Exercise Interventions Improve Cognition.

Cognitively Normal Older Adults

Sanders et al., 2019
Exercise Interventions Improve Cognition.
How does exercise affect cognition?
Mechanisms of Exercise

Stillman et al., *Frontiers in Human Neuroscience*, 2016
Mechanisms of Exercise

Evidence-Based Mechanisms (Only Those Confirmed by Randomized Controlled Trials) of Exercise That Contribute to Its Salutary Effects on Cognition

- **Level 1**: Cellular and molecular signaling pathways
  - Young children (>6 years)
  - Children (6–13 years)
  - Adolescents (14–17 years)
  - Young-middle aged adults (18–50 years)
  - Older adults (>50 years)
  - BDNF

- **Level 2**: Brain structure and function
  - Hippocampal volume
  - Mood
  - Mood
  - Mood, sleep

- **Level 3**: Mental states and higher-order behaviors
  - White matter and brain function
  - Hippocampal volume, cortical volume, white matter, brain structure

Figure 1. Evidence is presented across three different levels of analysis and separated by age group to highlight emerging patterns and existing gaps in evidence. While there are complexities in defining specific age ranges for developmental periods such as adolescence, age group is used to simplify the presentation of the studies discussed here. Level 1 refers to cellular and molecular signaling pathways. Level 2 refers to brain structural or functional pathways, and Level 3 refers to psychosocial pathways which are defined as higher-order behaviors or mental states. Abbreviations: BDNF, brain-derived neurotrophic factor; IGF-1, insulin-like growth factor 1.
The hippocampus

- Region shown to be highly sensitive to environmental enrichment in animal models
- Is one of the first regions to show deterioration in certain neurodegenerative diseases
- Shows neurogenesis throughout life in humans
- Central to memory function
Effects of exercise on hippocampal structure

- Erickson et al., *PNAS*, 2011
  - 120 cognitively normal, sedentary older adults
  - Aerobic walking or stretch/tone
  - 12-months
  - Baseline assessments (incl. structural MRI)
Erickson, et al., PNAS, 2011
Hippocampus

A.

Caudate Nucleus

B.

Thalamus

C.

Erickson, et al., PNAS, 2011
2. Does exercise predict subsequent cognitive functioning?
Physical activity is associated with reduced risk for cognitive impairment.

<table>
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<tr>
<th>Study or Subgroup</th>
<th>Weight</th>
<th>Risk ratio IV, Random, 95% CI</th>
<th>Risk ratio IV, Random, 95% CI</th>
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<td>Ho et al., (M)</td>
<td>2.7%</td>
<td>0.53 [0.25, 1.12]</td>
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<tr>
<td>Ho et al., (F)</td>
<td>5.8%</td>
<td>0.53 [0.32, 0.87]</td>
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<td>Laurin et al., (M)</td>
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<tr>
<td>Schuit et al.,</td>
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<td>Yaffe et al.,</td>
<td>20.5%</td>
<td>0.74 [0.60, 0.91]</td>
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<tr>
<td>Pignatti et al.,</td>
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<tr>
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<td>Sumic et al., (M)</td>
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<tr>
<td>Sumic et al., (F)</td>
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<td>Middleton et al.,</td>
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<td>Niti et al.,</td>
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<tr>
<td>Etgen et al.,</td>
<td>3.9%</td>
<td>0.46 [0.25, 0.85]</td>
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<tr>
<td>Total (95% CI)</td>
<td>100.0%</td>
<td>0.62 [0.54, 0.70]</td>
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</table>

Heterogeneity: $\tau^2 = 0.01$; $\chi^2 = 16.94$, df = 14 ($P = 0.26$); $I^2 = 17\%$

Test for overall effect: $Z = 7.49$ ($P < 0.00001$)
Physical activity is associated with reduced risk for Alzheimer’s Disease.

Beckett et al., 2015

**Figure 2 Caption:** Physical activity and the reduction of risk in developing Alzheimer’s disease.
3. What other strategies promote neurocognitive health?
Multidomain Interventions

**Stay connected** “Steady social contact protects cognitive function as you age.

**Benefits of exercise** “Can exercise give a memory boost? You bet!”

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The FINGER Study

- Finnish cohort study to prevent cognitive impairment and disability
- Two-year multi-domain intervention (N = 1260):
  - Intervention group: diet, exercise, cognitive training, vascular risk monitoring
  - Control group: health advice
- Primary outcome: cognitive performance
- Secondary outcomes: dementia, depression, disability, vascular risk

Results: The FINGER Study

• Dropout rates low (~12%) and adherence high
• Compared to the control group, participants in the intervention group scored:
  • 25% higher on a test of general cognition
  • 83% higher on executive functioning
  • 150% higher on processing speed
• More to come…

Summary & Open Questions

• It is never too late!

• RCTs provide causal evidence we can induce changes in aging brains in a matter of months

• Exercise is a lifestyle behavior backed by the most science to date

• Multi-component interventions may offer more bang for your buck than singular components
  • BUT, still need to better understand how they work
Thanks for your attention.

The Brain Aging and Cognitive Health Research Group

University of Pittsburgh, Pittsburgh,
Paul E Bendheim, MD
Clinical Professor of Neurology

THE UNIVERSITY OF ARIZONA
College of Medicine
Phoenix

Founder, Brain Savers®, LLC
“A growing body of research supports the protective effects of late-life intellectual stimulation on incident dementia.” JAMA 2002
How to Achieve Healthy Brain (and Body) Aging

BrainSavers® Brain+Body Total Fitness Program

Social Engagement
Physical Fitness
Cognitive Fitness
Stress Management
Quality Sleep
Healthy Nutrition
BRAINSAVERS® SYNAPSE
STAYING CONNECTED

The Fitness Program To Remember™
BrainSavers Brain+Body Total Fitness Program

• Stimulating curriculum on the 6 components.

• Organized, structured, instructor-led 1 hour classes.

• **Brain exercises** including memory, other cognitive functions. Cognitive movement activities – all designed to strengthen 20 “brain muscles”.

• **Physical exercises**: stamina, balance, strength and flexibility.

• **Social activities** for promotion of social engagement.

• Improve **nutrition, reduce stress**, and achieve **memory consolidating sleep**.

• “**World Brain Gym**” out-of-class leisure activities for incorporating program knowledge into activities of everyday life.
Be Your Own “Healthy Brain Doctor”

BUILD BRAIN RESERVE

STRESS REDUCTION

ATTITUDE

SLEEP

EXERCISE

SOCIALIZATION

MENTAL STIMULATION

NUTRITION
Brain+Body Healthy Aging: A Community-Based, Scalable, Total Lifestyle Program to Reduce Alzheimer's Dementia Risk

NANASP
November 13, 2020
WellMed Charitable Foundation

Established in 2006 by Dr. George Rapier

- Independent non-Profit, 501(c)3 Foundation
- Philanthropic partner of WellMed Medical Management

Mission

- Support programs that serve seniors and their family caregivers
22,000 Providers Strong, Serving 868,531 Patients.

This includes both commercial and FFS lives with WellMed and USMD

Changing the Face of Health Care Delivery for the Nation

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WellMed Charitable Foundation

What we do in addition to philanthropic giving:

19,117 Caregivers

16 States

6 Caregiver Resource Centers

11 Senior Centers (TX, FL)

45,243 Members

Stress-Busting Program For Family Caregivers

Wellness, Information, Support and Education

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<th>Senior Centers</th>
<th>Square Feet</th>
<th>Clinic Y/N</th>
<th>Members Since Opening</th>
<th>2019 Members YTD</th>
<th>Average Daily Attendance</th>
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<td>Y</td>
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<td><strong>Totals</strong></td>
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<td><strong>11,724</strong></td>
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</table>
Senior Centers: Owned and Contracted

Owned Centers: 11

- Miami, Florida – 3
- San Antonio – 3
  - Partner: City of San Antonio
- Austin – 1
- Lower Rio Grande – 2
  - Partner: Area Agency on Aging
- Corpus Christi – 1
  - Partner: City of Corpus Christi
- Dallas – 1
  - Partner: City of Dallas Park & Rec

Contracted Network Centers: 113

- San Antonio – 51 City + 7 YMCA
- Corpus Christi – 5 City sites
- Dallas – 41 Dallas Park & Rec sites
- El Paso – 4 El Paso Park & Rec sites
- Miami – 4 Miami Park & Rec sites
- Tampa – 1 site
Senior Center Eligibility

- Age 60 and over
- No Cost
- Open to the community
Why Senior Centers?

• Realization that health and behavior change don’t happen in the clinic
• It’s one thing to say go exercise – another to have a vibrant senior center right outside the clinic door
• Ideal venue to address social determinants of health
• Our WellMed Charitable Foundation senior centers may be one of the few locations where we own the senior center data AND can compare to health care outcome data
"There is great potential to leverage the infrastructure of community resources such as senior centers to deliver effective interventions to improve health outcomes in lower income and minority individuals"
Published 2018 NIH Study on Diabetic Control of WellMed Patients Who Use Senior Centers: Results

Regardless of whether patients or providers initiated the discussions; the study findings were consistent with other research that physician discussion or encouragement of lifestyle change is associated with health benefits.
In 2019, we pulled the names of 10 senior center members/WellMed patients from 2 WCF centers and 1 City of San Antonio center.

Dr. Derick Young analyzed key health data from the time they joined WellMed:
- Body Mass Index (BMI)
- Blood Pressure (BP)
- A1C (blood sugar)
- PQH9 (depression)
- Overall
# Results by Measure

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<th></th>
<th>Stable</th>
<th>Improved</th>
<th>Worsened</th>
<th>Total % Positive</th>
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<tr>
<td>Overall</td>
<td>61%</td>
<td>27%</td>
<td>12%</td>
<td>88%</td>
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<tr>
<td>BMI</td>
<td>69%</td>
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<td>58%</td>
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<td>A1C</td>
<td>62%</td>
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<tr>
<td>PQH9</td>
<td>54%</td>
<td>27%</td>
<td>19%</td>
<td>81%</td>
</tr>
</tbody>
</table>

*Stability is king.* – Derick Young, MD
- 50% improved in at least one measure
- 23% stable in all measures
Why BrainSavers?

• Addresses the common fear of getting Alzheimer’s or dementia.
• 82% of people say it’s important to check their thinking or memory.
• Attracts new participants, and often younger participants
• Only program that has all of the proven components of brain health: exercise, nutrition, socialization
• Builds on existing programs
BrainSavers Reach

• Sites
  – All WCF senior Centers
    • San Antonio, Corpus Christi, Austin, Lower Rio Grande Valley, Miami
  – City of San Antonio Senior Centers
  – Dallas Park & Recreation
  – Madonna Senior Activity Program
  – Good Samaritan Programs
  – YMCA Schertz
Success with Programs

- Smaller centers that need to attract new members
- Large centers that need to offer new programs
- Younger members who have just retired
- Leveraging popular instructors
- Building upon existing healthy lifestyle programs
- Complete Online Version for COVID
Refer Our Patients

San Antonio Area Senior Center Resources

Patient Name ________________________________
Provider Name ______________________________

Enjoy a full range of classes and events to help improve your health, at no cost. Your provider may suggest the following:

<table>
<thead>
<tr>
<th>Staying Strong</th>
<th>Lifetime Learning</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exercise Equipment</td>
<td>BrainSavers</td>
</tr>
<tr>
<td>Dancing</td>
<td>Socialization</td>
</tr>
<tr>
<td>Chair Fitness</td>
<td>Nutrition/Healthy Eating</td>
</tr>
<tr>
<td>Tai Chi</td>
<td>Support for Family Caregiving</td>
</tr>
<tr>
<td>Zumba</td>
<td>Money Management Counseling</td>
</tr>
</tbody>
</table>

Fitness Studio Equipment | Getting Social
Cardiovascular | Movie Day
Strength Training | Arts & Crafts
Range of Motion | Social Events

Bring this referral sheet to obtain your complimentary “welcome” gift!

For more details on our Senior Activity Centers, visit WellMedCharitableFoundation.com.

Stay active, be healthy and build relationships at your local Senior Community Center.

Join us at any Senior Community Center location:

Alicia Trevino Lopez Senior Center
8353 Culebra Rd.
San Antonio, TX 78251
210-558-0178

Elvira Cisneros Senior Community Center
517 S.W. Military Dr.
San Antonio, TX 78221
210-927-9328

Doris Griffin Senior Center
6157 N.W. Loop 410, Ste 120
San Antonio, TX 78238
210-780-7444

Membership is not required and there are no fees to use our Senior Community Centers or to attend classes. Not all classes are offered at each location. Call ahead for a full list of classes and times.

WellMed does not discriminate on the basis of race, color, national origin, sex, age, or disability in its health programs and activities. ATTENTION: If you speak English, language assistance services, free of charge, are available to you. Please call 888-781-WELL (9655). ATENCIÓN: Si habla español (Español), hay servicios de asistencia de idiomas, sin cargo, a su disposición. Llame al 888-781-WELL (9655).
What does brain health look like?
## Virtual Senior Center

- **Type** | **Number of Videos** | **Views Per Type**
- Fitness  | 100            | 60,248       
- Craft    | 36             | 6,709        
- Health Tips | 30          | 34,716       
- **Totals** | **166**        | **101,673** 

+ BrainSavers

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Questions??
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www.wellmedcharitablefoundation.org