

Science of Wisdom in the Era of the New Pandemics

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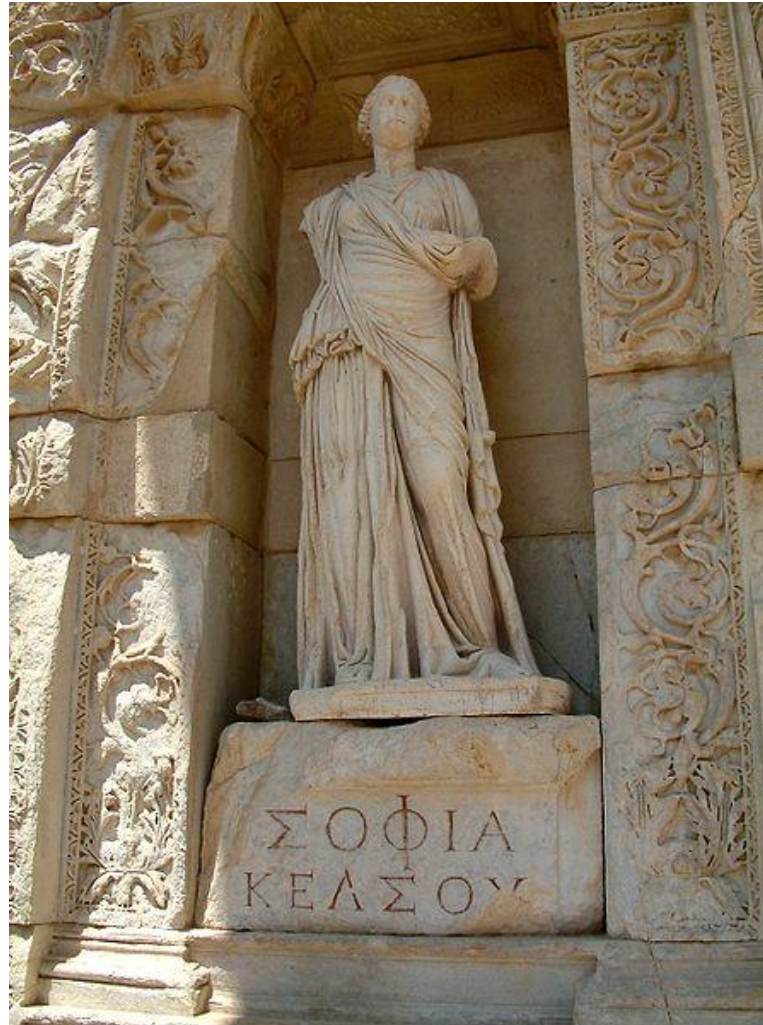


Tanya Nguyen

OUTLINE

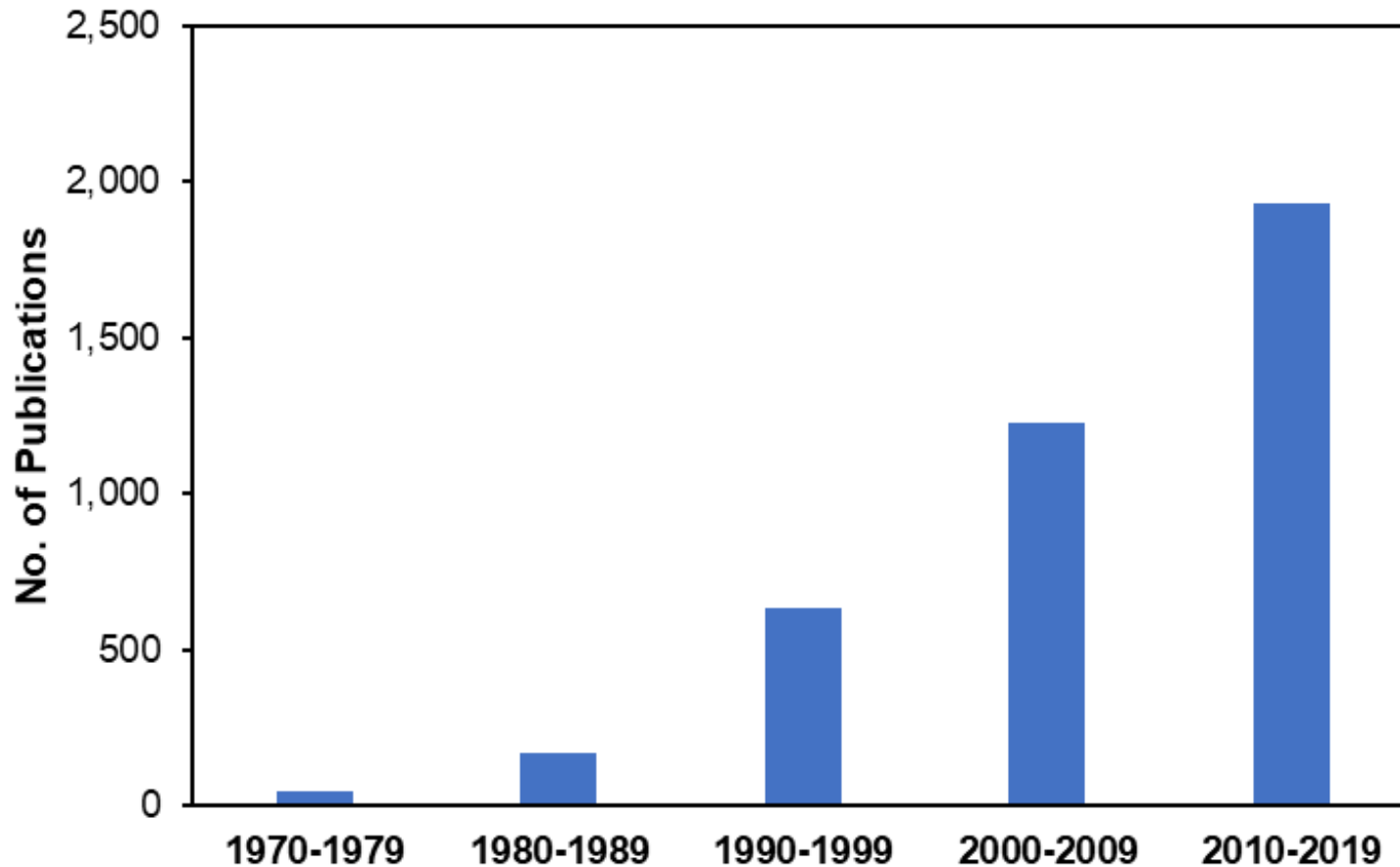
- **Wisdom: Definition, Measurement, and Neurobiology**
- **Wisdom and Aging**
- **Wisdom versus Loneliness**
- **Enhancing Wisdom**

SOPHIA: Personification of Wisdom



Published Papers on “Wisdom” by Decade

(Jeste & Lee, Harvard Rev Psych, 2019)



Defining Wisdom

- A) Wisdom in the scriptures: Mixed-methods Qualitative-Quantitative research
- B) Review of empirical literature on wisdom (which started in the mid-1970s)
- C) International Expert Consensus using Delphi (Rand Panel) method

Striking similarities in conceptualization of wisdom

(Jeste & Vahia, Psychiatry, 2008; Meeks & Jeste, Arch Gen Psychiatry, 2009; Bangen et al. Am J Geriatr Psychiatry, 2013; Montross, et al., Int'l Psychogeriatrics, 2018)

Wisdom: A Multi-component Trait



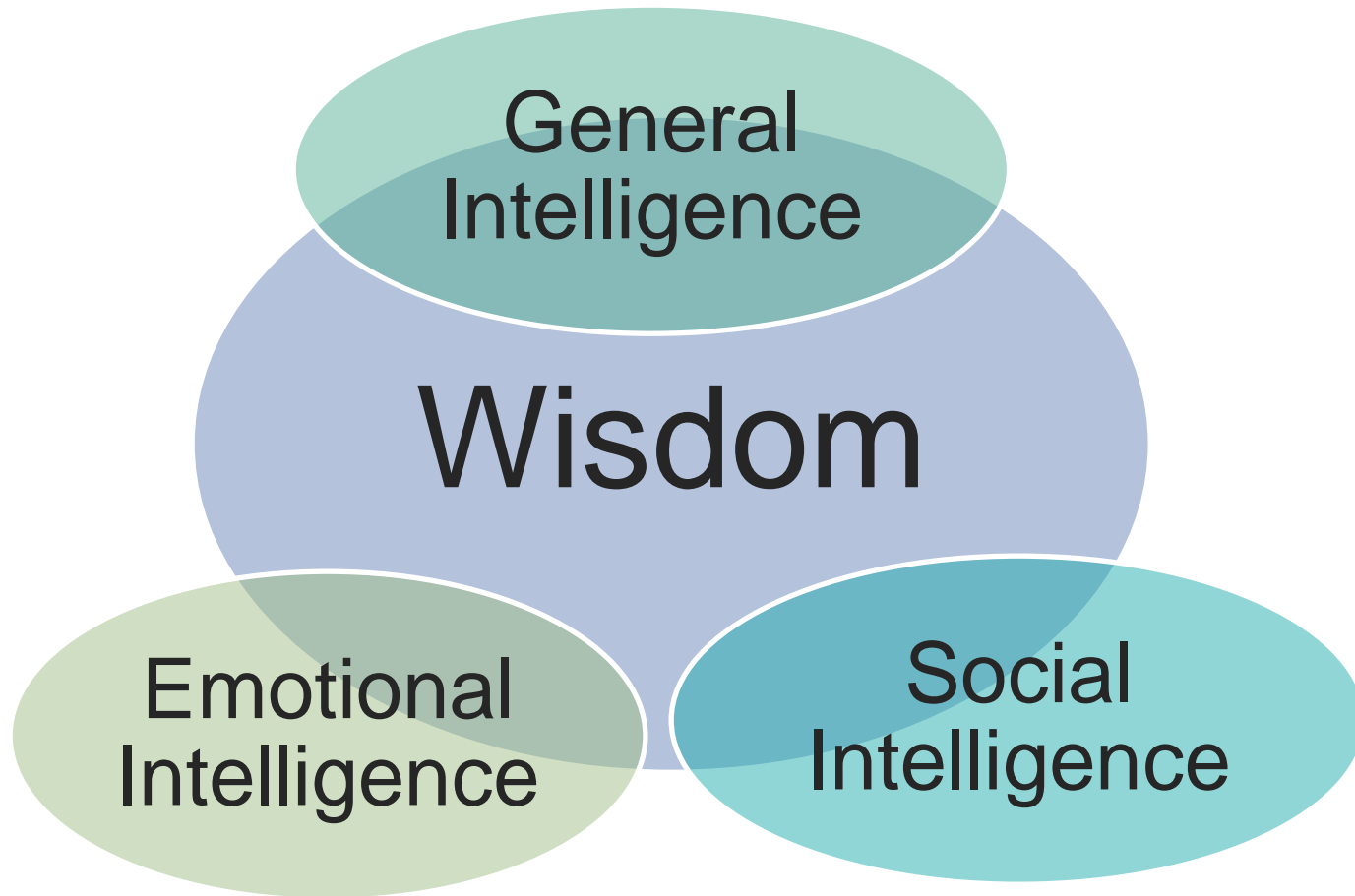
San Diego Wisdom Scale (SD-WISE)



- Total 28 items, each to be rated on a 1-5 scale (“strongly disagree” to “strongly agree”)
- Good to excellent psychometric properties
- Examples of items:
 - “It is important that I understand the reasons for my actions.”
 - “I have trouble thinking clearly when I am upset.”

(Thomas ML, et al., J Psychiatric Research, 108:40-47, 2019;
Jeste DV, et al., JPR, 2020)

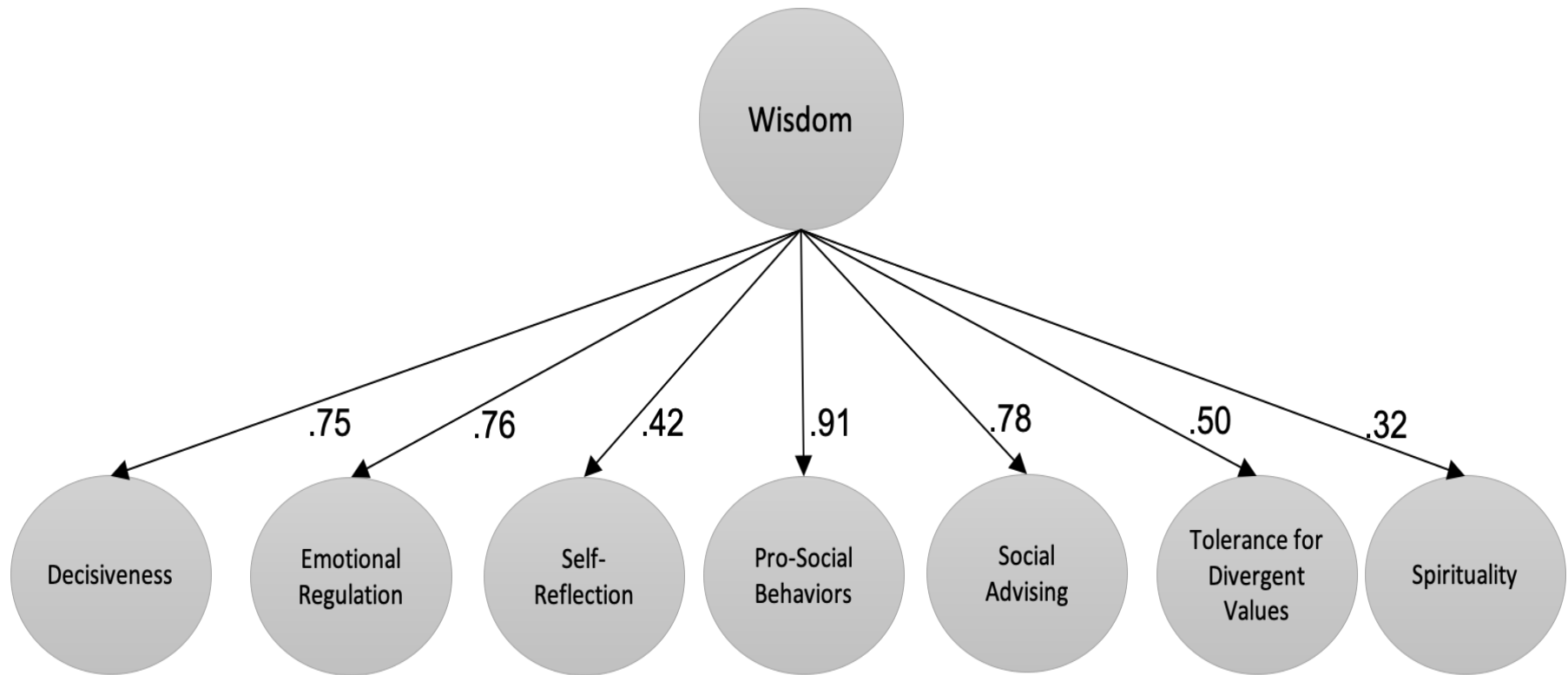
Wisdom is more than Intelligence



Factor Loadings between the Higher-Order Wisdom Factor & the 7 Subdomain Factors

(N=1,786)

(Jeste, et al., J Psych Research, 2020)



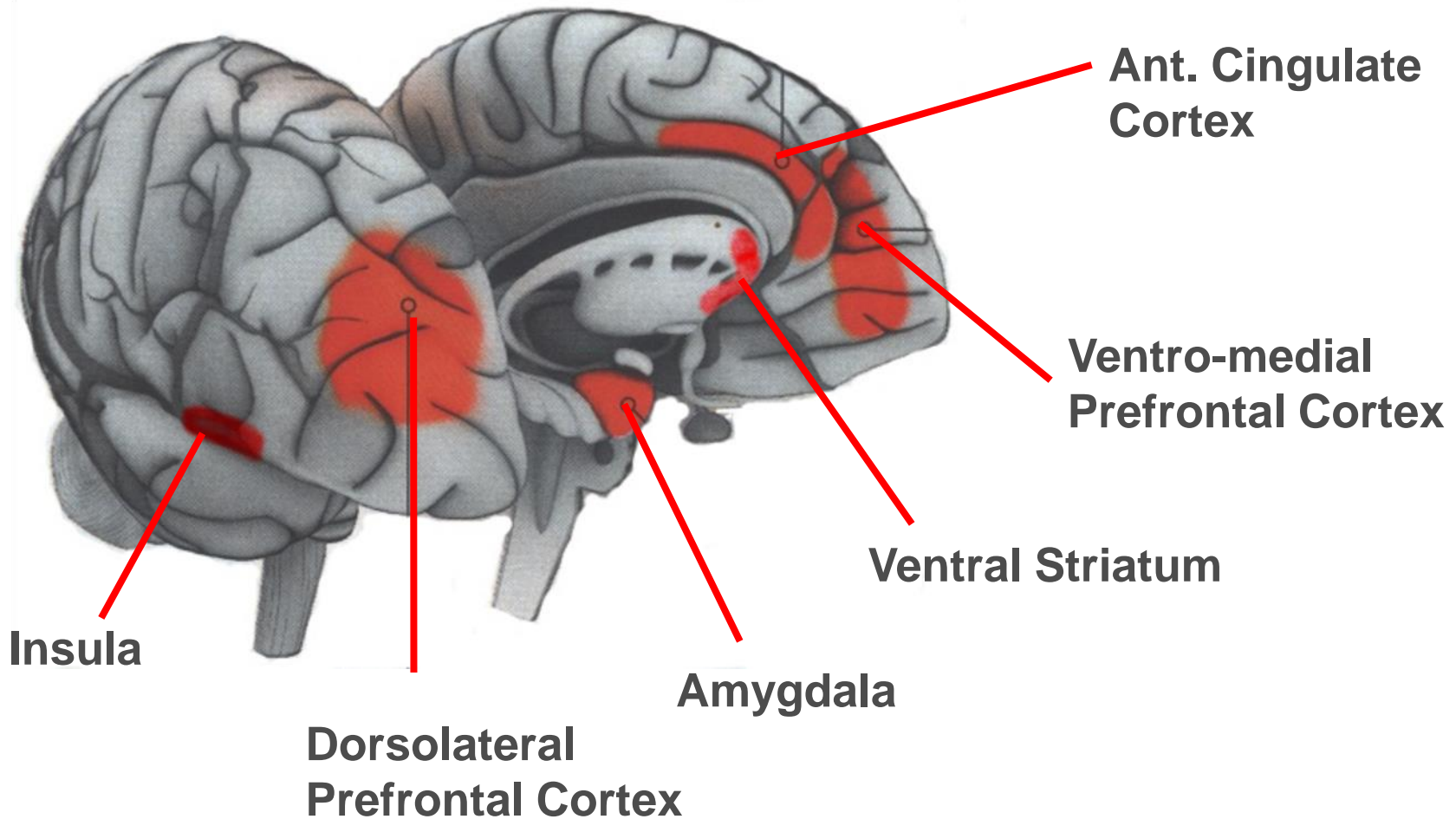
Postulating Neural Networks in Wisdom

- Basic concept of wisdom hasn't changed since ancient times, suggesting a neurobiological basis
- Reviewed literature on neurobiology of individual components of wisdom and their antitheses (e.g., antisocial personality)
- Studied “experiments of nature” – persons whose personality & behavior changed from wise to unwise following localized brain injury (e.g., Phineas Gage) or with diseases affecting specific brain areas (Frontotemporal Dementia)

(Meeks TW & Jeste DV, Arch Gen Psych, 66:355-365, 2009)

Brain Regions Involved in Wisdom

(Meeks & Jeste, Arch Gen Psych 2009)



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The Puzzle of Human Aging

Life History in Evolutionary Biology: Most vertebrates die soon after losing fertility, yet humans have very prolonged post-reproductive lifespan, inconsistent with Darwin's hypothesis of survival of the fittest

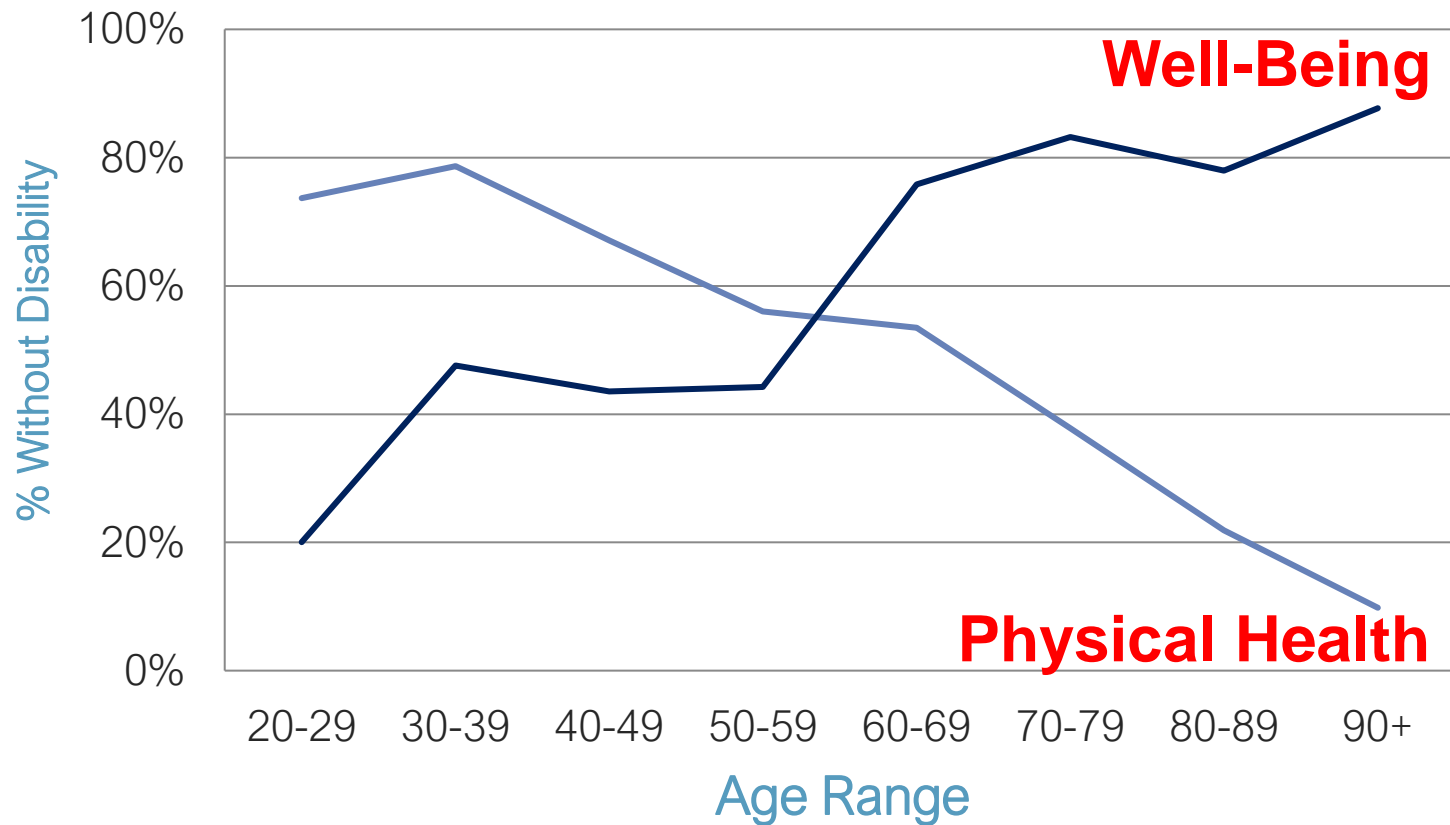
Can any aging-associated change contribute to species-related fitness?



(Foster, ET Al., Science, 2012; Lahdenpera, M., et al. Nature, 2004; Hawkes & Coxworth, Evol Anthropol, 2013; Croft, et al., Trends in Ecology & Evolution, 2015; Gopnic, 2016)

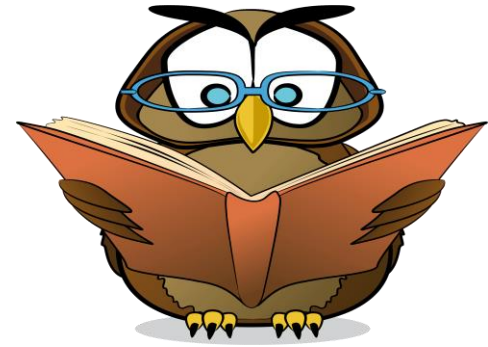
Paradox of Aging:

Health from Age 21 to 100 Years (N=1,547)



(Jeste DV, et al., Am J Psychiatry, 2013;
Thomas ML, et al., J. Clin. Psychiatry, 2016)

Abilities that Tend to be Better in Older Adults than in Youth

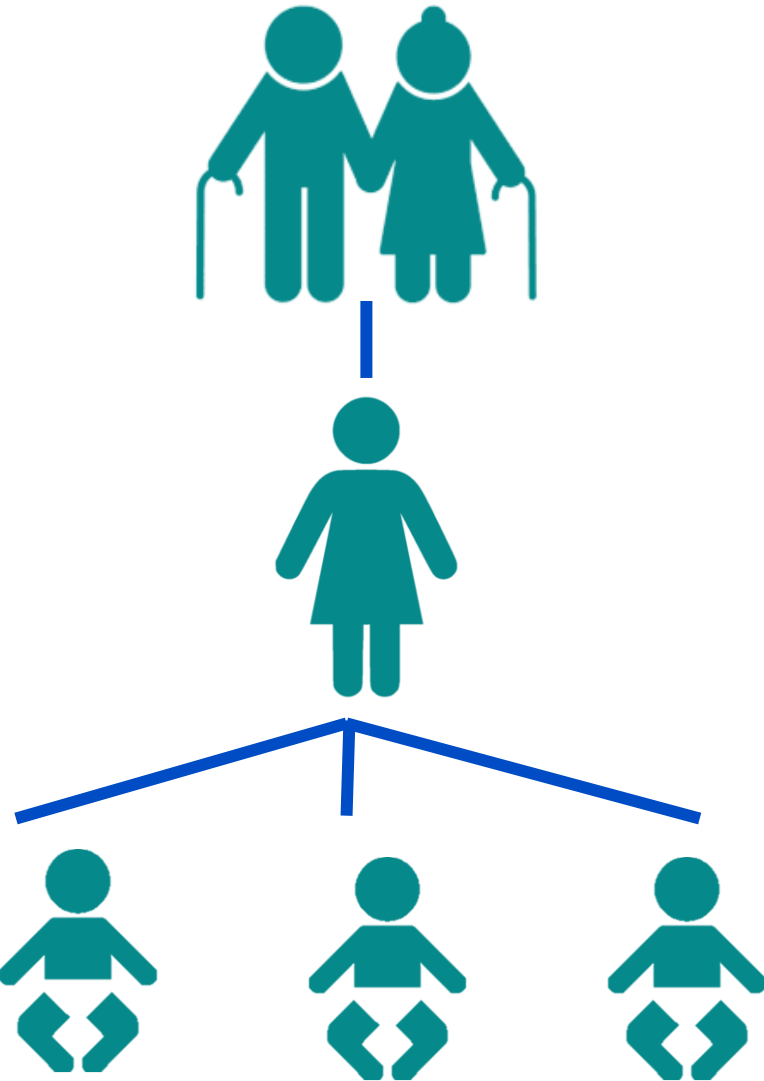


- Emotional regulation
- Positivity: Favoring positive emotions & memory
- Empathy and Compassion
- Self-reflection
- Experience-based decision making

(Carstensen et al., 2004; Mather et al., 2004, Birditt et al., 2005, Kennedy et al., 2004, Brassens et al., 2012; Meeks & Jeste, 2009; Bangen, et al., 2013; Helmuth et al., 2003; Jeste et al., 2010;

Grossman, et al., 2010; Worthy, et al., 2011)

Grandmother Hypothesis Of Wisdom



- **Grandmother involvement in raising grandchildren helps younger generations' well-being, longevity, and fertility** (Lahdenpera, et al., Nature, 2004; Foster et al., Science, 2012; Hawkes & Coxworth, Evol Anthropol, 2013)
- **Grandparent genes? - Variants of CD33 and APO-E** (Schwarz, et al., PNAS, 2015)

Effects of Grandparenting on Behavior Problems in Grandchildren

(Attar-Schwartz, et al., J Family Psychology, 23:67-75, 2009)

- 1,515 secondary school students (age 11-16) in UK
- Greater grandparent involvement was associated with fewer emotional problems, more prosocial behavior, and reduced adjustment difficulties, especially among teenagers from lone-parent and step-parent families



Inter-Generational Activities Benefit both Generations



- Experience Corps: Trained older adult served in public elementary schools
- Outcomes:
 - Improvement in children's grades & happiness
 - Enhancement of seniors' mental & physical health, biomarkers of stress & aging in blood & urine, and hippocampal volume on brain MRI

(Parisi, JM, et al., Educat'l Gerontol, 35, 867-879, 2009)

Neuroplasticity with **Active** Aging

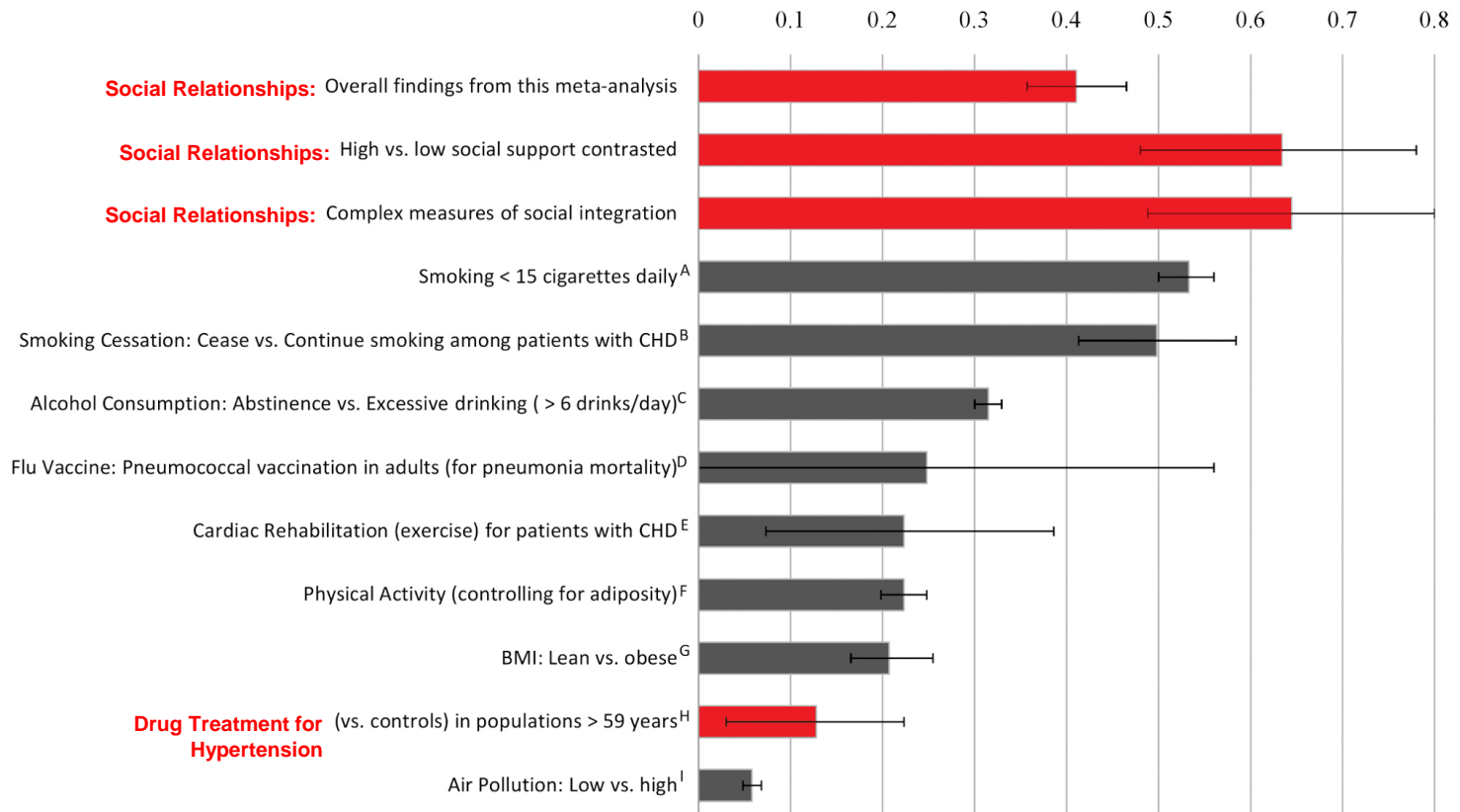
- Greater recruitment & more efficient utilization of neuronal networks (Posterior-Anterior Shift of Aging and Hemispheric Asymmetry Reduction)
- Synaptogenesis & neurogenesis in selected non-cortical brain regions
- Diminished amygdala activation with negative emotional stimuli, regret, and fear → Positivity
- Caveat: Cognitive decline begins to overwhelm neuroplasticity in older old people

(Gage, et al., 2002; Mather, et al., 2004; Dennis & Cabeza, 2008; St Jacques, et al., 2009; Eyler, et al., 2011; Brassens, et al., 2012; Bangen, et al., 2012)

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Psychosocial Determinants of Health: Odds of Reduced Mortality



Holt-Lunstad J, et al., PLOS Medicine 7(7): e1000316, 2010.
<https://doi.org/10.1371/journal.pmed.1000316>

Loneliness: A Grand Challenge for the Society



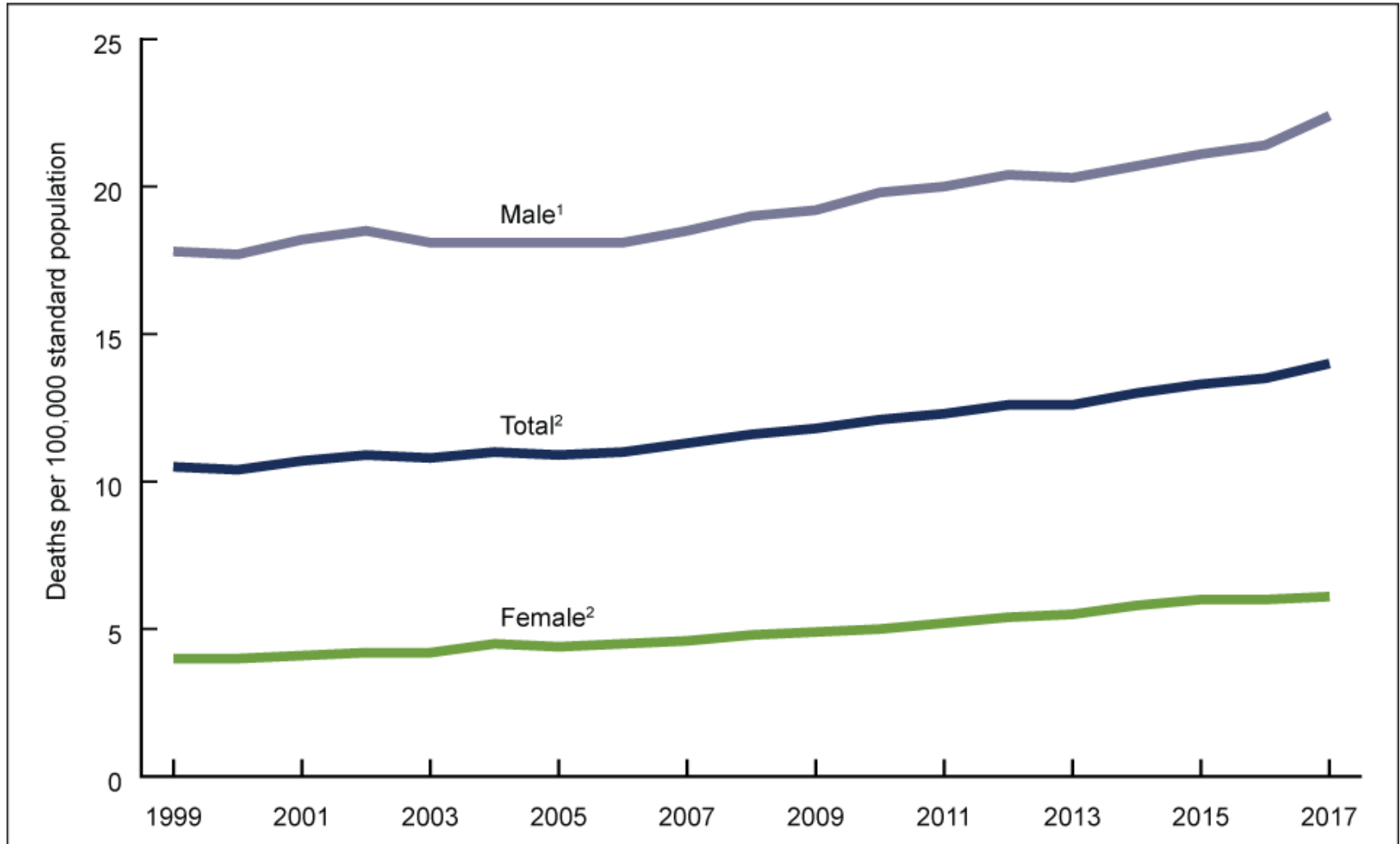
A silent killer; increases odds of mortality by 30% - as dangerous as smoking and obesity (Holt-Lunstad, et al., 2015)



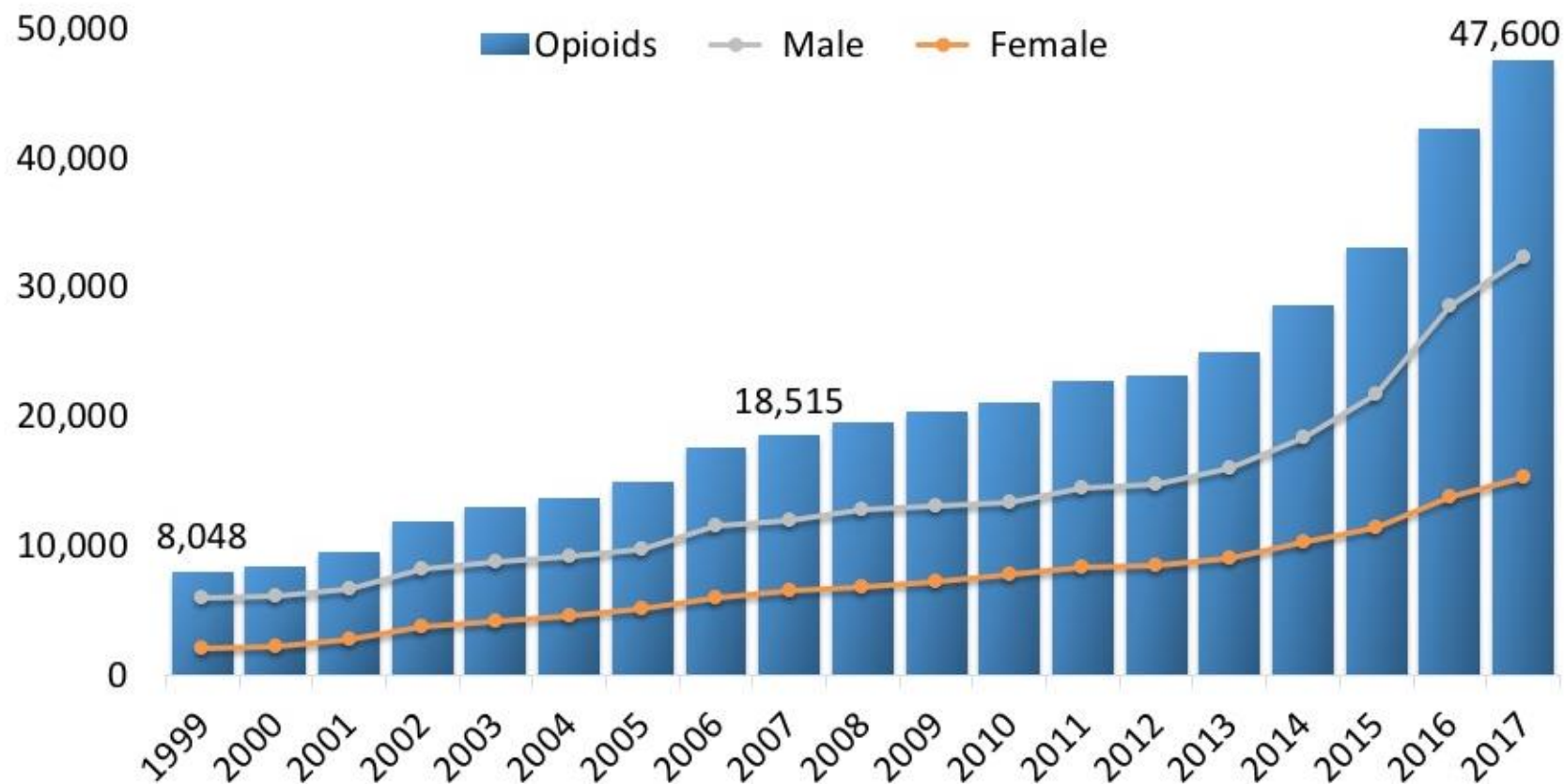
In the US, 162,000 deaths per year are attributable to loneliness – more than those secondary to lung cancer or stroke (Agency for Healthcare Research and Quality, 2019)

In the UK, a new Minister of Loneliness was appointed in 2018

US Suicide Rates Increased by 33% in 2 Decades (1999 – 2017) (CDC Statistics)

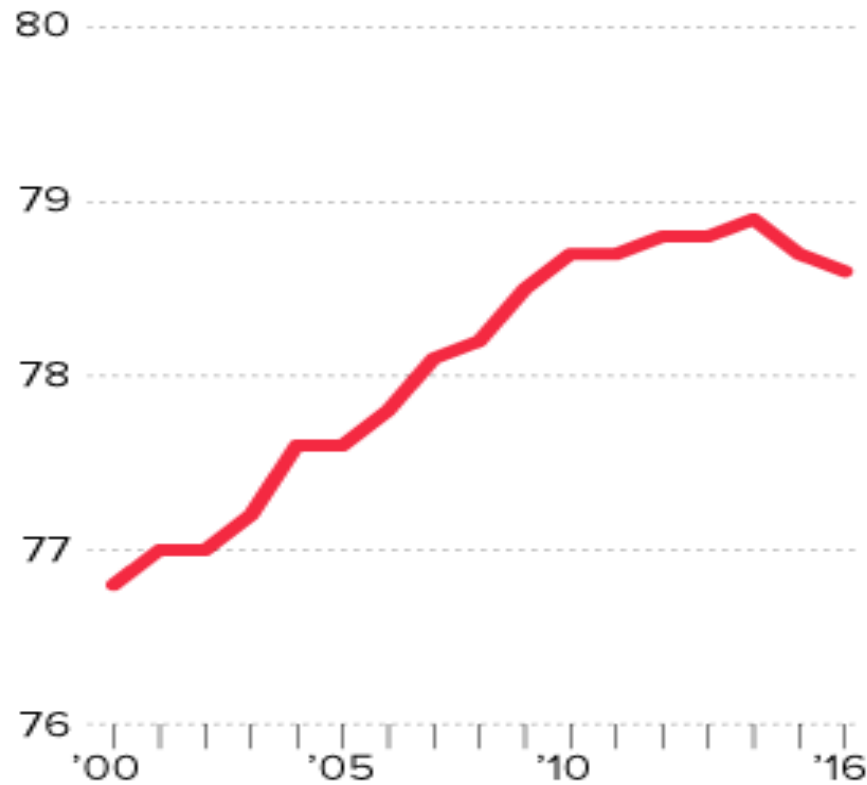


Mortality from Opioid Abuse (1999-2017)



Source: : Centers for Disease Control and Prevention, National Center for Health Statistics. Multiple Cause of Death 1999-2017 on CDC WONDER Online Database, released December, 2018

Recent Decline in Average Lifespan in the US



Genetic Basis of Loneliness

GWAS analyses for loneliness in UK Biobank study (N=452,302)



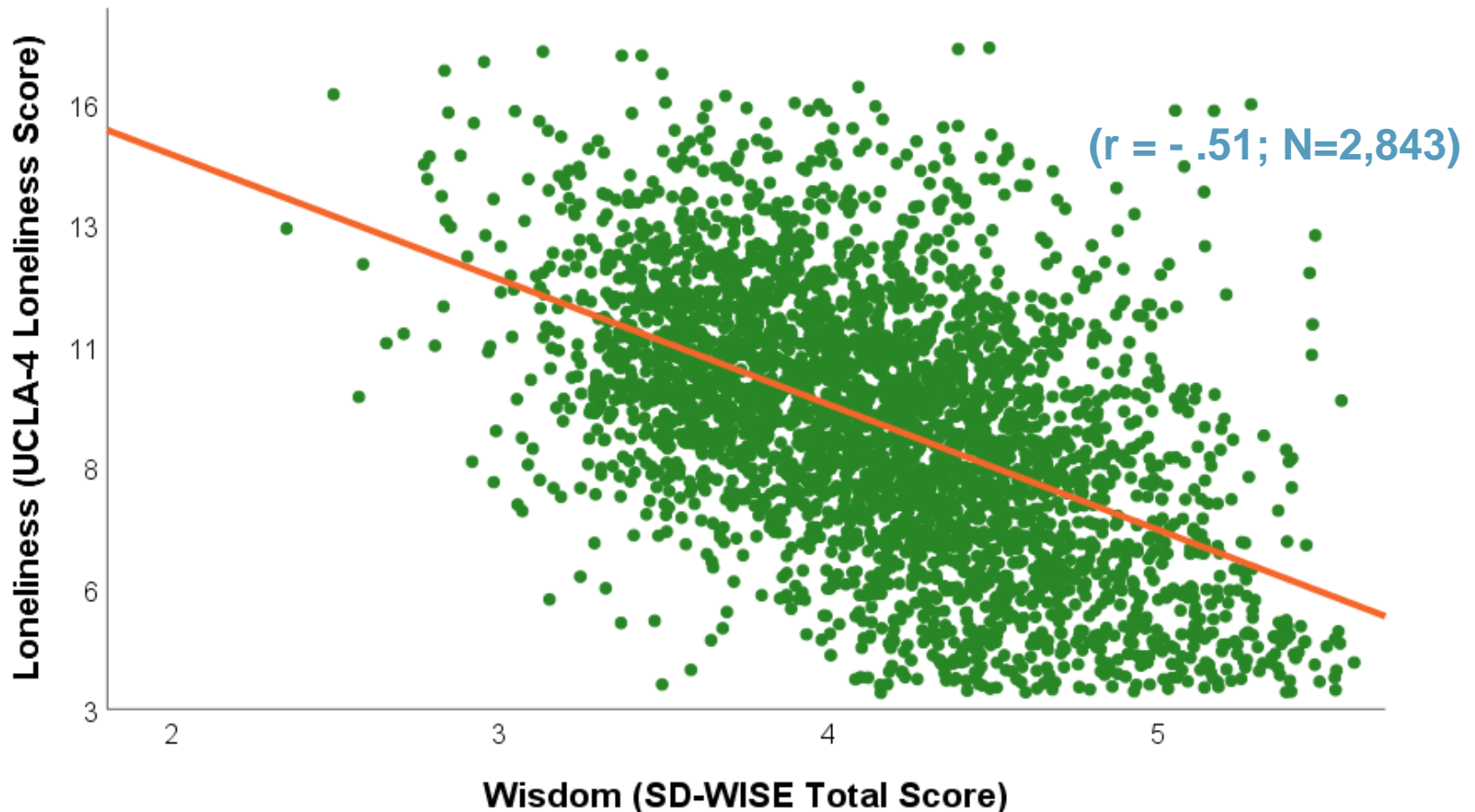
- Twin- and family-based studies found that loneliness is a modestly (37%-55%) heritable trait with a highly polygenic architecture
- Genetic predisposition toward loneliness predicts cardiovascular, metabolic, and psychiatric disorders (depression, dementias)

(Day, FR, et al. Nat Commun. 9:2457, 2018;

Gao, J, et al. Neuropsychopharmacology. 2017;42:811-8218)

Abdellaoui, A, et al., bioRxiv, Nov. 14, 2018)

Loneliness vs. Wisdom: mTurk: Amazon-based Survey (Nguyen, et al., J Clin Psychiatry, 2020)



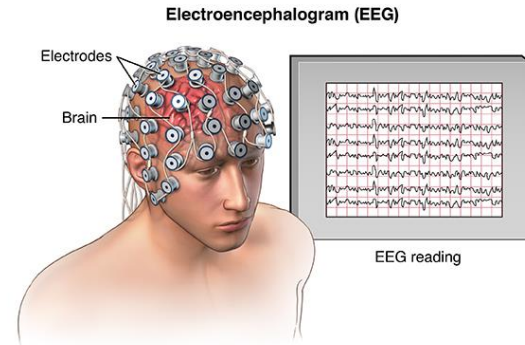
Loneliness versus Wisdom/Compassion



- Loneliness is associated with worse physical & mental health, and wisdom/compassion with better physical & mental health (many studies)
- Strong inverse correlation between loneliness and wisdom/compassion (Lee, et al., 2019; Nguyen, et al., 2020; Jeste, et al., 2020 a & b)
- Longitudinal study – Higher level of compassion predicted lower level of loneliness 7 years later (Lee EE, et al., under review)
- Intervention to increase compassion in order to reduce loneliness (funded by UCSD Sanford Institute)

EEG – Loneliness vs. Wisdom

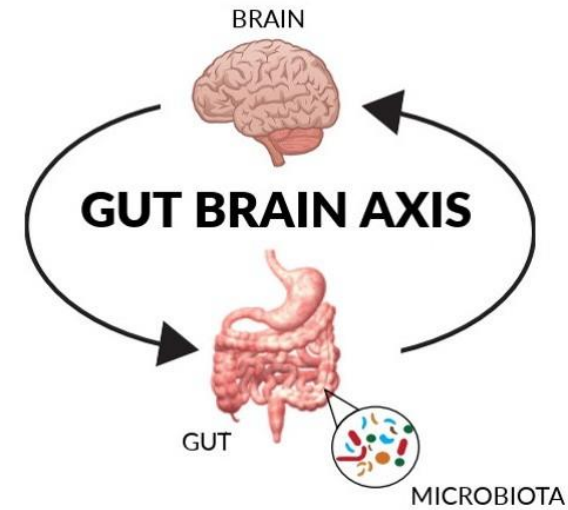
(Grannan G, et al., Cerebral Cortex, in press)



- Neural Engineering & Translation Labs
- 147 adults, ages 18 to 85
- Temporo-Parietal Junction: Loneliness was associated with greater activity in the presence of angry emotions; Wisdom was associated with greater activity in the presence of happy emotions
- Differential involvement of ventral striatum in loneliness vs. insula in wisdom

Gut Microbiome – Loneliness vs. Wisdom

(Nguyen TT, et al., Front. Psychiatry, in press)



- Center for Microbiome Innovation – 16S rRNA
- 184 adults (age 28-97 years)
- Alpha and Beta diversity measures of phylogenetic richness were associated with higher levels of compassion, wisdom, and social engagement, and lower level of loneliness

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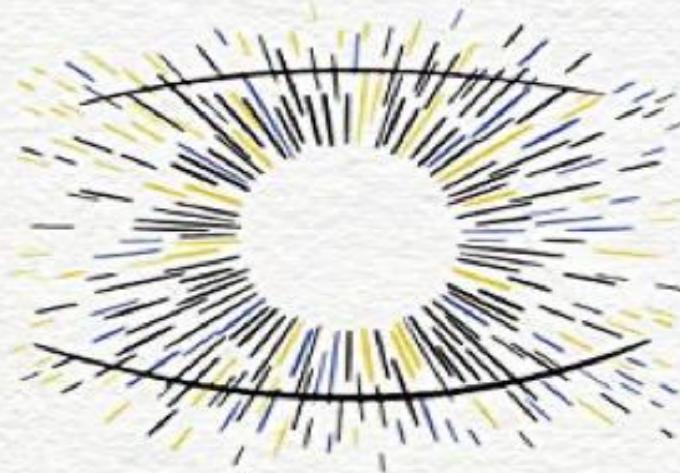
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...brilliant contribution to the emerging science of wisdom—how we define it and how we can intentionally cultivate it in ourselves and our society.”

Tara Brach, Ph.D., author of *Radical Compassion*

wiser



**THE SCIENTIFIC ROOTS OF WISDOM,
COMPASSION, AND WHAT MAKES US GOOD**

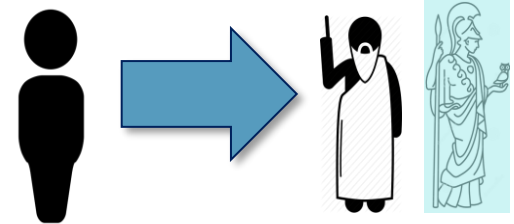
**DILIP JESTE, MD
with SCOTT LAFEE**

Can Wisdom be Enhanced?

- Most traits are only partly (35%-55%) inherited
- Wisdom may increase with aging, experience, and learning, but is reduced with specific brain trauma or disease – i.e., wisdom is modifiable
- Possible means of enhancing wisdom:
 - Psychosocial / Behavioral
 - Pharmacological / Biological
 - Technological

Interventions to Enhance Wisdom Components

(Lee, et al., JAMA Psychiatry, 2020;
Treichler, et al., Int'l Psychogeriatrics, 2020)



- **57 RCTs to enhance:**
 - Empathy/Compassion/Altruism, Emotional regulation, and Spirituality
- **Participants:** People with mental illnesses, people with physical illnesses, and those from general population
- **47% of studies reported significant enhancement of a wisdom component (moderate to large effect size)**

Biological Effects of Mind-Body Interventions

- 2-month Mindfulness-Based Stress Reduction reduced pro-inflammatory NF- κ B-related gene expression in circulating leukocytes
- Daily Meditation for 6 months increased telomerase activity; also greater white matter integrity on MRI



MRI

(Creswell et al 2012; Jacobs et al 2010; Caria et al 2007; Vinogradov, et al., 2009; Tang et al., 2010; Eack, et al., 2010)

Practical Wisdom = Wise Decision Making

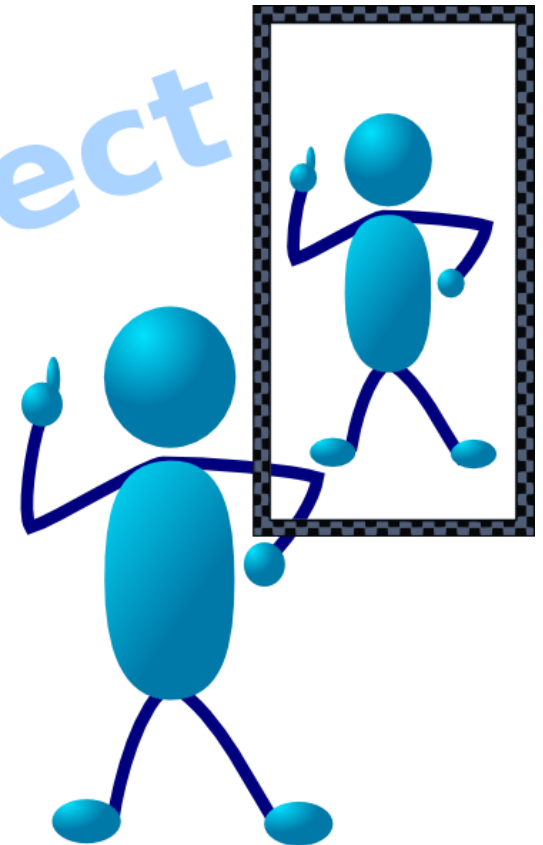
- Forming a habit of making wise decisions in daily life, affecting self and others
- Wise decisions involve self-reflection, emotional regulation with positivity, empathy and compassion, decisiveness amid uncertainty, and spirituality



First Step in the Process of Becoming Wiser is Honest Self-reflection

- Which components of wisdom am I strong in?
- Which components of wisdom am I weak in?

Reflect



Enhancing Compassion

- Role playing for hours to days as a person with Blindness, Immobility (in a wheelchair)
- Gratitude Diary
- Random acts of kindness

GERT (GERontologic Test suit)



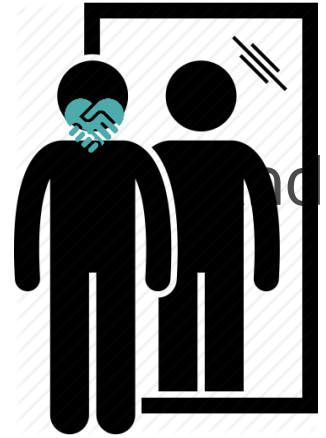
<http://www.age-simulation-suit.com/>

Strategies for Self-Compassion

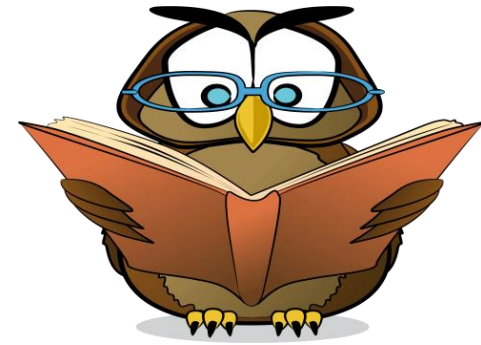
- Self-kindness: Offer yourself soothing comfort as you would to your friend
- Sense of common humanity:

Everyone makes mistakes, and faces serious challenges

- Mindfulness: I have had similar stresses in the past and survived



Future Wisdom Research



- Longitudinal studies including genomics
- Neurocircuitry with functional imaging
- Animal studies
- Biological means of enhancing wisdom – rTMS?
- Artificial Intelligence to Artificial Wisdom

Societal Wisdom



- Today's highly stressed, polarized, angry, anxious, and depressed society
- Modern pandemic of loneliness, suicides & opioid-related “deaths of despair”
- Need for teaching & rewarding “soft skills” of wisdom (compassion, self-reflection, acceptance of diverse perspectives) to students, businesses, and politicians?

International Community Campaigns



WHO Global Network
for Age-friendly Cities
and Communities

Great Southern **Compassionate Communities**



Transforming a Lonely, Distressed, and Polarized World into Happier, Healthier, and Wiser Society



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