THE SCIENCE OF WISDOM

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OUTLINE

• What is Wisdom?
• Wisdom and the Brain
• Does Wisdom Increase with Aging? - A Developmental Model
• Interventions to Enhance Wisdom
• How Can We Make the Society Wiser?
WISDOM ALONE IS THE SCIENCE OF OTHER SCIENCES.

--- PLATO (427 – 347 BC)
“FUZZY” CONSTRUCTS LONG DISMISSED BY BIOLOGICAL RESEARCHERS

- Consciousness
- Cognition
- Emotion
- Stress
- Resilience
- Wisdom?
NUMBER OF PUBLICATIONS ON “WISDOM” IN PUBMED BY DECADE

<table>
<thead>
<tr>
<th>Decade</th>
<th>No. of Publications</th>
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<td>1970-1979</td>
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<td>2010-2017**</td>
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Jeste DV & Lee EE (in press)
DEFINING WISDOM

A) Wisdom in the scriptures

B) Review of empirical literature (which started in the mid-1970s): Mostly western studies

C) International Expert Consensus using Delphi (Rand Panel) method

D) Qualitative interviews of older adults

WISDOM IN THE SCRIPTURES


• **The Bhagavad Gita** (200-500 years BC, based on Yogas from 2,000 - 5,000 years BC): (Jeste DV & Vahia IV, Psychiatry, 2008)

• **Common Components of Wisdom:**
  Pro-social behaviors (empathy, compassion)
  Social decision making
  Self-reflection (Humility)
  Emotional regulation
  Spirituality
COMMON COMPONENTS OF WISDOM IN MODERN DEFINITIONS

• Pro-social behaviors (Empathy, compassion, altruism)
• Social decision making
• Self-Reflection (Insight)
• Emotional regulation with positivity
• Decisiveness amid uncertainty
• Spirituality

(Meeks TW & Jeste DV: Arch Gen Psych, 2009; Bangen K, et al., Am J Geriat Psych, 2013)
MEASURING WISDOM

- Self-report scales: Most measures of psychological constructs are based on self reports
- Interviews with questions or vignettes about ambiguous situations or moral dilemmas
- Rating wisdom of one’s peers
- Nominating and characterizing famous “wise” people (Mother Teresa, Abraham Lincoln, Mahatma Gandhi, Nelson Mandela)
- No objective measures at present
REPORTED ASSOCIATIONS OF WISDOM

- Well-being
- Happiness
- Life satisfaction
- Resilience
- Overall physical and mental health

CONCEPTUALIZATION OF WISDOM

• Wisdom is a complex multi-component trait, involving balanced integration of various components, with the whole being greater than the sum of its parts

• Wisdom has a purpose: it enhances a person’s well-being and also helps the society’s welfare

(Jeste DV and Harris J, JAMA, 2010)
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POSTULATING NEURO-CIRCUITRY OF WISDOM: "WISE" REGIONS OF BRAIN?

- Basic concept of wisdom hasn’t changed since ancient times, suggesting a neurobiological basis
- We reviewed literature on neurobiology / brain localization 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 (Fronto-Temporal Dementia)

(Meeks TW & Jeste DV, Arch Gen Psych, 66:355-365, 2009)
PHINEAS GAGE (1823-1860)

- Railroad construction foreman in Vermont
- “….. although untrained in the schools, he possessed a well-balanced mind, and was looked upon by those who knew him as a shrewd, smart businessman, very energetic and persistent in executing all his plans of operation” – Dr. Harlow (his physician)
- 1848: A sudden explosion caused a large iron rod to go through the back of Gage’s left eye and came out thru top of his head

Miraculously, he recovered quickly; the only major impact was on his personality (+ left eye)
“Fitful, irreverent, at times grossly profane, with little deference for his fellows, impatient of restraint or advice when it conflicts with his desires, at times pertinaciously obstinate, yet capricious and vacillating, devising .. and (then quickly) abandoning plans of future operations. A child in his intellectual capacity and manifestations, he has the animal passions of a strong man. .... His mind was radically changed, so decidedly that his friends ... said he was "no longer Gage." – Dr. Harlow

- Study of his skull using modern neuroimaging techniques showed bilateral damage to prefrontal cortex (Damasio H, et al., Science, 1994)
MODERN-DAY PHINEAS GAGE

• 26-year-old man with an exemplary academic and professional (military) record

• Penetrating head injury → Precipitous decline in social functioning - lost job, followed by multiple temporary low-level jobs, despite average to superior scores on most neurocognitive tests (e.g., Verbal IQ 119)

• 3 marital break-ups, estrangement from children

• Neuropsychological and brain imaging studies: bilateral prefrontal cortex damage, left > right

FRONTO-TEMPORAL DEMENTIA (FTD)

- Pathology restricted to prefrontal (& anterior temporal) lobes
- Slow onset of personality changes and behavioral abnormalities before age 60
- Poor social decision making, with loss of personal and social awareness
- Disinhibition, Impulsivity
- Sociopathy, Lack of empathy
- Emotional coldness, Apathy
- Poor insight, Self-centeredness
PUTATIVE NEUROCIRCUITRY OF WISDOM
(MEEKS & JESTE, ARCH GEN PSYCH 2009; JESTE & HARRIS, JAMA 2010)

Ant. Cing. Cortex)  
Conflict detection

Ventro-medial PreFrontal Cortex  
Emotional regulation,  
Compassion

Amygdala  
Strong emotions

Dorso-lateral PreFrontal Cortex  
Cold cognition, Utilitarian choices
NEW SCALE FOR MEASURING WISDOM: SD-WISE

• Based on consensus definition of wisdom
• Higher-order neuro-biologically driven model of wisdom with 4 items for each of 6 domains
• Total 24 items, each to be rated on a 1-5 scale (“strongly agree” to “strongly disagree”)
• Takes 5 minutes to complete
• Good to excellent psychometric properties
SD-WISE: ILLUSTRATIVE ITEMS

• “I avoid situations where I know my help will be needed.”
• “Others look to me to help them make choices.”
• “It is important that I understand the reasons for my actions.”
• “I have trouble thinking clearly when I am upset.”
• “I tend to postpone making major decisions as long as I can.”
• “I am okay with others having morals and values other than my own.”

(Thomas m, et al., J Psychiatr research, 2017)
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PUZZLE: HUMAN LONGEVITY MAKES NO SENSE FOR DARWINIAN HYPOTHESIS OF SURVIVAL OF THE FITTEST

- In the wild, most of large animals don’t live long after losing fertility and becoming physically disabled.
- Human life-span continues to increase, but the fertility-span and health-span have not increased.
- Persons living to age 90 spend half of their life without fertility & with increased physical disability – i.e., with no fitness benefit to the species (or to self).
- Something must improve with aging.
Rome – Dr. Rita Montalcini, a Nobel Laureate, on her 100\textsuperscript{th} birthday: “My mind is sharper today than when I was 20.”
“I think I do science better now than I did when I was younger. In science, judgment is so important, and I now have a better understanding of which problems are important and which are not.”

--- Dr. Eric Kandel, Nobel Laureate (1929 -)
SUCCESSFUL AGING EVALUATION (SAGE) STUDY AT UC SAN DIEGO’S STEIN INSTITUTE

• Longitudinal study of 3 domains of aging (physical, cognitive, psychosocial) in a community-based sample selected using random digit dialing

• > 2,000 home phone users in San Diego, ages 21-100; Phone interview, Mail-in survey, Saliva sample

• Unique focus on positive traits such as resilience, optimism, compassion, wisdom

Physical Health vs. Mental Well-Being From Age 21 to 100 Years (N=1,547)

ABILITIES THAT TEND TO BE BETTER IN OLDER ADULTS THAN IN YOUTH: WISDOM OF AGING

- Pro-social behaviors (Empathy, Compassion)
- Experience-based decision making
- Self-reflection or insight
- Control of emotions
- Positivity: Favoring positive emotions & memory

(Carstensen et al., 2004; Mather et al., 2004, Birditt et al., 2005, Kennedy et al., 2004, Brassen 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)
GRANDMA HYPOTHESIS OF WISDOM

• When Grandma (GM) helps her adult Daughter (D) in raising her Children, D lives longer, is happier, and produces more children than GM did \textbf{+ There is greater happiness, health, and longevity in all 3 generations} – reported in bottle-nosed dolphins, killer whales, Seychelles warblers, & humans (Foster et al., Science, 2012)

• \textbf{Evolution of “Grandparent Genes” in Humans:} Specific variants of genes CD33 (\textbf{\(ightarrow\) better immune function}) \& APOE (\textbf{\(ightarrow\) less amyloid in heart and brain}) are more common in humans than in chimpanzees – did they evolve to preserve wise grandparents and delay their cognitive decline? (Schwarz, et al., PNAS, 2015)
WISDOM AND LONGEVITY: CENTENARIANS IN CILENTO, ITALY

- Collaboration between University of Rome, La Sapienza (Di Somma & colleagues) and UC San Diego (Brenner & colleagues) to study centenarians and their children in Cilento, a birthplace of Mediterranean diet

- Studying lifestyle, diet, and positive traits along with diseases of aging, and multiple cutting-edge biomarkers
• 29 people over age 90 and their 51 children or other family members aged 51–75 years

• Old-old adults >90 years had better mental well-being despite having worse physical health than their middle-aged children

• Main themes from qualitative interviews: positivity, working hard, spirituality, bond with family, religion, & land, and balance between stubbornness and adaptability (decisiveness & acceptance of uncertainty) ----------- Wisdom

ARE WOMEN WISER THAN MEN? - SAGE STUDY

Cognitive

Reflective

Affective

Men (N = 441)  Women (N = 391)

*** = p < 0.001
DOES WISDOM INCREASE WITH AGING?: 6 Year-Follow-up

Men (N = 115)

- Cognitive
- Reflective
- Affective

Women (N = 106)

- Cognitive
- Reflective
- Affective

* = p < 0.05; ** = p < 0.01; *** = p < 0.001
NEUROPLASTICITY WITH ACTIVE AGING

• Greater recruitment & more efficient utilization of neuronal networks → Compensation for aging-related cognitive decline

• Synaptogenesis & Neurogenesis in selected brain regions, with physical/psycho-social stimulation → Neuro-psycho-plasticity

• Reduced dopaminergic activity in reward circuitry involving limbic striatum → Emotional regulation

• Diminished amygdala activation with negative emotional stimuli, regret, and fear → Positivity

(Gage, et al., 2002; Mather, et al., 2004; Dennis & Cabeza, 2008; St Jacques, et al., 2009; Eyler, et al., 2011; Brassen, et al., 2012; Bangen, et al., 2012-13)
DEVELOPMENTAL MODEL OF WISDOM

- **Genes**
  - Brain health
  - Longevity

- **Brain Function**
  - Wisdom neuro-circuitry
  - Neuroplasticity

- **Benefits**
  - Children’s fertility
  - Longevity
  - Well-being

- **Childhood Behavior & Environment**
  - Grandparents
  - Education

- **Adult Behavior & Environment**
  - Life experiences
  - Lifestyle

- **WISDOM**
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CAN WISDOM BE ENHANCED?

- Most traits are only partly (25%-50%) inherited, and even gene expression can be influenced by environmental and behavioral factors (epigenetics).
- Studies report increase in traits like optimism & resilience with psychosocial & other interventions.
- Wisdom is a multi-component trait that is affected by environment and behavior.
- Wisdom can increase with aging, experience, and learning, but is reduced with specific brain trauma or disease – i.e., wisdom is modifiable.
CLINICAL TRIALS FOR ENHANCING COMPONENTS OF WISDOM

• 48 randomized controlled trials to enhance one of the components of wisdom: Empathy or compassion, Emotional regulation, and Spirituality

• Participants included people with mental illnesses (e.g., depression) or physical diseases (e.g., cancer) or those from the community (e.g., children with behavior problems, bullies, stressed parents)

• Many, but not all, studies reported significant improvement in the specific component of wisdom

• Limitations of the published studies (Jeste DV, Lee EE, et al., under review)
PRO-SOCIAL BEHAVIOR INTERVENTION
(CHUNG, ET AL. NEUROPSYCHIATRIC DISEASE AND TREATMENT, 2016)

- **Subjects:** 20 adolescents w. high-functioning autism spectrum disorder

- **Intervention:** Pro-social online game version of Cognitive Behavior Therapy (Game-CBT) to improve social skills - compared to off-line CBT. During game, participants engaged in social activity via avatar by chatting, presenting virtual gifts, imitating other players to improve their own avatar, and become friends with other avatars.

- **Results:** Both therapies were equally effective in improving social communication quality, response to emotional words and emotions, but produced different areas of activation in response to emotional words on BOLD fMRI (temporo-parietal vs. cingulate-parietal).
EMPATHY INTERVENTION  
(GARAIGORDOBIL ET AL., PSICOTHEMA, 2015)

- **Subjects:** 176 adolescents in Spain (age 13-15 y.)
- **Goals:** Education on cyberbullying (identification, roles, consequences); reporting and coping strategies; improving control of anger-impulsivity, conflict resolution, tolerance of diversity.
- **Intervention:** Cyberprogram 2.0 to increase empathy and decrease face-to-face bullying and cyberbullying. Structured 19 one-hour group sessions included role-playing, brainstorming, case study, and guided discussions.
- **Control condition:** Tutoring program
- **Results:** Cyberprogram 2.0 significantly increased empathy and decreased amount of bullying and cyberbullying compared to control condition
INTER-GENERATIONAL ACTIVITIES TO PROMOTE WISDOM

• Experience Corps: Trained older adult volunteers served > 15 hours/week in public elementary schools as mentors & tutors to enhance children’s literacy development & behavioral management skills

• Outcome: Improvement in children’s grades & happiness + Enhancement of seniors’ mental & physical health and biomarkers of stress & aging in blood & urine, and hippocampal volume on brain MRI

• (Unfortunately, wisdom was not assessed)

(Parisi, JM, et al., Educat’l Gerontol, 35, 867-879, 2009)
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FUTURE INTERVENTION RESEARCH

• Larger and longer randomized controlled trials with appropriate control groups
• Use of validated measures
• Associations with other health-related measures, including biomarkers
• Family-, organization-, and community-level interventions
• Use of technology, including machine learning and Artificial Intelligence, to administer wisdom interventions and assess their effects
UCSD – IBM CENTER FOR ARTIFICIAL INTELLIGENCE FOR HEALTHY LIVING
(CO-DIRECTORS: JESTE & KNIGHT)

• 5-year, $10 million grant from IBM
• Focus: Healthy aging and Microbiome
• Bringing together researchers and trainees in AI, aging, neuroscience, and health sciences
• Goal: To advance AI technologies to help older adults live independently longer, and have a higher quality of life
RELEVANCE OF WISDOM TO HEALTH AND HEALTHCARE

• Interventions for prosocial behaviors & emotional regulation in people with neuropsychiatric disorders: brain injury, fronto-temporal dementia, autism, personality disorders

• Interventions for spirituality in people with physical illnesses; Spirituality is now a formal component of palliative and hospice care

• Teaching of wisdom in medical and other professional schools

• Impact on healthcare costs for youth & seniors
RELEVANCE OF WISDOM IN RAPIDLY CHANGING SOCIETY

• Reports of increasing levels of stress, depression, suicidality, especially in youth
• Education of children & adults should involve much more than the 3 R’s and IQ
• Inter-generational activities help all generations
• Need for teaching compassion, emotional regulation, self-reflection, and acceptance of uncertainty – i.e., Wisdom
• A country’s Wisdom Index should be more important than its GDP or even Happiness Index
PILLS FOR WELLNESS AND LONGEVITY

- HEALTHY LIFESTYLE
- WISDOM
- SOCIAL SUPPORT
1. I try to anticipate and avoid situations where there is a likely chance I will have to think in depth about something.

2. A problem has little attraction for me if I don’t think it has a solution.

3. I prefer just to let things happen rather than try to understand why they turned out that way.

4. I am hesitant about making important decisions after thinking about them.
3D-WS-12 AFFECTIVE DIMENSION

1. I can be comfortable with all kinds of people. (R)
2. Sometimes I feel a real compassion for everyone. (R)
3. I don’t like to get involved in listening to another person’s troubles.
4. I’m easily irritated by people who argue with me.
1. When I look back on what has happened to me, I can’t help feeling resentful.

2. I either get very angry or depressed if things go wrong.

3. When I am confused by a problem, one of the first things I do is survey the situation and consider all the relevant pieces of information. (R)

4. Sometimes I get so charged up emotionally that I am unable to consider many ways of dealing with my problems.