Multidimensional Aspects of Aging
– Without and With HIV

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POTENTIAL CONFLICTS OF INTEREST

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OUTLINE

- What is (Successful) Aging?
- Positive Traits and Aging: Wisdom
- Aging with HIV
- Strategies for Successful Aging
WHAT IS AGING?

Aging is not a disease to be cured or prevented
- It is a dynamic process of continually evolving balance between growth / development and degeneration, that begins at conception

CHANGING AGE PYRAMID

(United Nations, 2012)
WHAT DOES CHRONOLOGICAL AGE MEAN?: A 90-YEAR-OLD PERSON

IS THIS SUCCESSFUL LIVING / AGING?
IDA KEELING (AGE 100) SETS WORLD RECORD FOR CENTENARIANS IN 100-METER DASH
Does successful aging include being in a wheel chair for most of one’s adult life?

Is This Successful Living?

President Franklin D. Roosevelt in a wheel chair, with his granddaughter
ORIGINAL DEFINITION OF SUCCESSFUL AGING

- Absence of disease
- High physical and cognitive function
- Engagement with life

(Rowe and Kahn, Science, 1988)

AGING COMES IN DIFFERENT SIZES AND SHAPES
THE SAGE STUDY

UC San Diego
Successful AGing Evaluation (SAGE) Study


SAGE STUDY

• To study different domains of successful aging (physical, cognitive, psychosocial) in a longitudinal study of a randomly selected community-based sample
• Over 1,500 home phone users in San Diego, ages 21-103 years
• Phone interview, Mail-in survey, Saliva sample: DNA
• 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)

% Without Disability

Age Range

20-29 30-39 40-49 50-59 60-69 70-79 80-89 90+

Well-Being

Physical Health


PARADOX OF AGING: 3 DOMAINS

Decline / Improvement in Standard Deviations

1.5 1 0.5 0.0 -0.5 -1 -1.5 -2 -2.5

Physical Health  Cognitive Health  Mental Health

Stein Institute for Research on Aging
Center for Healthy Aging
HOW MEANINGFUL ARE SUBJECTIVE MEASURES OF WELL-BEING?

- A single item of self-rated general health predicted mortality (-a meta-analysis)

- Self-rated quality of well-being correlated significantly with objective indicators of quality of life in a community

- No evidence for a social desirability bias in most of the self-report measures of successful aging and physical & cognitive function

- Increasing focus on patient-reported outcomes
  
  (DeSalvo et al., J Gen Intern Med, 2006; Oswald & Wu, Science, 2010; Dawes et al., Ageing and Society, 2011)
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ABILITIES THAT TEND TO BE BETTER IN OLDER ADULTS THAN IN YOUTH: WISDOM OF AGING?

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

(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)
CONCEPTUALIZATION OF WISDOM

• Wisdom is a complex multi-component human trait, that involves dynamic but balanced integration of various components; the whole is greater than the sum of its parts

• Wisdom is purposeful – it seeks to enhance the well-being of the self and of the society

• The basic concept of wisdom seems to have remained unchanged across centuries & cultures

  (Jeste DV and Harris J, JAMA, 2010;

COMMON COMPONENTS OF WISDOM ACROSS DEFINITIONS

• Emotional regulation

• Pro-social behaviors (Compassion, empathy, altruism)

• Social decision making

• Self-understanding or Reflection

• Acknowledgement of uncertainty

• Decisiveness

• (Spirituality)

  (Meeks TW & Jeste DV: Arch Gen Psych, 2009;
NEUROCIRCUITRY OF WISDOM?

- Literature review of published cases of people who went from being “wise” to “unwise” after a localized brain injury or brain disease
- Review of studies of genetics, brain imaging, and neuropathology associated with presence vs. absence of wisdom-associated behaviors

(Meeks T & Jeste DV, Arch Gen Psych 2009)

PUTATIVE NEUROCIRCUITRY OF WISDOM
(MEEKS T & JESTE DV, ARCH GEN PSYCH 2009)
NEUROBIOLOGY OF INCREASED WISDOM WITH AGING?

- Compensation for Neuro-degeneration: Enhanced ability to recruit alternate brain networks and/or more efficient utilization of those networks, esp. in prefrontal region (PASA or Posterior-Anterior Shift of Aging; HAROLD or Hemispheric Loss of Asymmetry)

- Synaptogenesis & Selective Neurogenesis, if stimulated by physical & psychosocial activity

- Adaptive Shifts in Emotional Regulation: Reduced amygdala and frontostriatal activation with viewing negative pictures or with regret, respectively

(Mather, 2004; Bangen, 2012; St Jacques, 2009; Brassen, 2012; Gage, 2002; Dennis & Cabeza, 2008; Eyler, 2011; Bangen, 2013)

GRANDMA HYPOTHESIS OF WISDOM

- When grandparents are involved in raising their grandchildren, those children live longer, are happier, and produce more children than the grandparents did – demonstrated in bottle-nose dolphins, killer whales, and humans (Lahdenpera¨, et al., Nature, 2004)

- Evolution of “Grandparent Genes” in Humans: Specific variants of genes CD33 (→ better immune function) & APOE (→ less amyloid in heart and brain) are more common in humans than in chimpanzee – did they evolve to preserve wise grandparents and delay their cognitive decline? (Schwarz, et al., PNAS, 2015)
OTHER POSITIVE TRAITS

- **Resilience**: In physically ill patients, resilience was associated with medically desirable behaviors (self-care, treatment & exercise adherence, and health including pain), and greater longevity (Lamond et al., 2008; Shen & Zeng, 2010; Stewart & Yuen, 2011)


- **Social Engagement** (148 studies; N >300,000): 50% increased likelihood of survival among socially engaged people (Holt-Lunstad, et al. PLoS Med 2010; 7: e1000316)

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**Optimistic People Live Longer than Pessimistic Ones (Dutch Study)**

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AGING OF THE HIV POPULATION: 2015 VS. 2020

2015

> 50 Years Old, 50%
< 50 Years Old, 50%

2020

> 50 Years Old, 70%
< 50 Years Old, 30%

Centers for Disease Control, 2008; United States Senate Special Committee on Aging, 2013
AGING OF HIV+ AMERICAN ADULTS

• In 2000, a 20-year-old HIV+ adult was expected to live to age 36; today he is expected to live to 71

• Older HIV+ adults have high risks of physical comorbidity, polypharmacy, neurocognitive impairment (HAND), and depression

• Aging of HIV+ adults is associated with poverty, poor personal and social support & access to overall healthcare

(Nokes et al., 2000; Pitts et al., 2005; Lyons et al., 2010; OAR Workgroup, 2012; Skevington, 2012)

• There are many adults with HIV who are aging well with this disease despite certain personal and physical losses… Studies with an emphasis on positive psychology, hardiness, resilience, social support, self-efficacy, and spirituality are encouraged. … not only is it important to examine the problems associated with living with HIV, it is also important to encourage and translate research findings for those not successfully aging.

--- Office of AIDS Research Working Group on HIV and Aging, 2012 (High et al., 2012)
WELLNESS WITHIN ILLNESS: AIDS, SCHIZOPHRENIA, & CANCER

- Well-being increases with aging – Healthy survivor bias is not the primary explanation
- A sizable minority of the patients had scores in the “normative” range
- Well-being correlated with levels of resilience, optimism, and other positive traits, but not with other demographic or illness-related variables


SELF-RATED SUCCESSFUL AGING

![Bar graph showing proportion of the group self-rated successful aging by HIV status.](image)
GREG LOUGANIS

Four-time Olympic gold medalist; the only man to ever sweep the diving events in consecutive Olympics: ‘84 & ‘88

Tested positive for HIV at age 28

New documentary Back on Board premiered on HBO in August 2015 featuring his complex life (alcohol dependence, near bankruptcy, living with HIV)

Currently mentor for the US Olympic diving team, a motivational speaker, a best-selling author, and LGBT activist
“MAGIC” JOHNSON

What you can do to avoid AIDS

With a new introduction by Magic Johnson
“Magic Johnson’s message is still breaking barriers and making a difference. This book could help save lives.”
American Medical Association

EARVIN “MAGIC” JOHNSON

“MAGIC” JOHNSON (AGE 58)

• Won high school, NCAA, and NBA championships, and Olympic gold medal in basketball
• Announced his HIV infection at age 32
• Married, with 2 children
• Currently an AIDS activist, a TV and radio broadcaster, a motivational speaker, an entrepreneur (part-owner of LA Dodgers, Sparks, and Lakers), and a philanthropist
UC SAN DIEGO STUDY OF AGING WITH HIV: DEMOGRAPHIC CHARACTERISTICS OF THE STUDY COHORT BY HIV STATUS

<table>
<thead>
<tr>
<th>Variable</th>
<th>HIV- (n=96)</th>
<th>HIV+ (n=103)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>52 (8)</td>
<td>51 (8)</td>
</tr>
<tr>
<td>Education (years)**</td>
<td>15 (2)</td>
<td>14 (3)</td>
</tr>
<tr>
<td>WRAT-4 Reading</td>
<td>107 (15)</td>
<td>103 (14)</td>
</tr>
<tr>
<td>% Female *</td>
<td>30%</td>
<td>12%</td>
</tr>
<tr>
<td>% Caucasian *</td>
<td>67%</td>
<td>58%</td>
</tr>
</tbody>
</table>

Note. Values represent $M$ (SD) unless otherwise noted.
* $p<.05$; ** $p<.01$

ADVERSE ASSOCIATIONS OF HIV INFECTION

<table>
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<tr>
<th>Variable</th>
<th>HIV- (n=96)</th>
<th>HIV+ (n=103)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brief Symptom Inventory-Anxiety ***</td>
<td>1.4 (2.7)</td>
<td>4.1 (5.3)</td>
</tr>
<tr>
<td>Life Events ***</td>
<td>3.8 (3.3)</td>
<td>7 (7)</td>
</tr>
<tr>
<td>Perceived Stress ***</td>
<td>10.4 (6.3)</td>
<td>15.2 (8.1)</td>
</tr>
<tr>
<td>MoCA *</td>
<td>26.0 (2.9)</td>
<td>24.7 (3.5)</td>
</tr>
</tbody>
</table>

Note. Values represent $M$ (SD)
* $p<.05$; ** $p<.01$; *** $p<.001$
### POSITIVE PSYCHOLOGICAL MEASURES

<table>
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<tr>
<th>Variable</th>
<th>HIV- (n=96)</th>
<th>HIV+ (n=103)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Self-Rated Successful Aging **</td>
<td>7.8 (1.6)</td>
<td>7.1 (2.2)</td>
</tr>
<tr>
<td>Resilience **</td>
<td>33 (6)</td>
<td>30 (8)</td>
</tr>
<tr>
<td>Optimism ***</td>
<td>24 (4)</td>
<td>22 (5)</td>
</tr>
<tr>
<td>Personal Mastery ***</td>
<td>24 (4)</td>
<td>21 (5)</td>
</tr>
</tbody>
</table>

*Note. Values represent M (SD).*

**p<.01; ***p<.001

### HIV DISEASE CHARACTERISTICS BY AIDS STATUS

<table>
<thead>
<tr>
<th>Variable</th>
<th>HIV+ nonAIDS (n=42)</th>
<th>HIV+ AIDS (n=59)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estimated duration of infection (years)</td>
<td>15 (6, 23)</td>
<td>18 (10, 25)</td>
</tr>
<tr>
<td>% On ARV</td>
<td>90%</td>
<td>98%</td>
</tr>
<tr>
<td>Months lifetime ARV exposure *</td>
<td>95 (38, 187)</td>
<td>168 (82, 217)</td>
</tr>
<tr>
<td>% Detectable Plasma RNA</td>
<td>8%</td>
<td>7%</td>
</tr>
<tr>
<td>Nadir CD4 ***</td>
<td>380 (264, 681)</td>
<td>60 (14, 150)</td>
</tr>
<tr>
<td>Current CD4 ***</td>
<td>802 (577, 998)</td>
<td>421 (239, 651)</td>
</tr>
</tbody>
</table>

*p<.05; ***p<.001
POSITIVE TRAITS BY AIDS STATUS

<table>
<thead>
<tr>
<th>Variable</th>
<th>HIV+ nonAIDS (n=42)</th>
<th>HIV+ AIDS (n=59)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resilience *</td>
<td>27.5 (9.2)</td>
<td>30.9 (7.1)</td>
</tr>
<tr>
<td>Optimism *</td>
<td>20.3 (5.2)</td>
<td>22.6 (4.9)</td>
</tr>
<tr>
<td>Personal Mastery *</td>
<td>20.0 (4.8)</td>
<td>21.9 (4.4)</td>
</tr>
<tr>
<td>Compassion **</td>
<td>4.6 (1.6)</td>
<td>5.7 (1.2)</td>
</tr>
</tbody>
</table>

*p<.05; **p<.01 (t-tests)

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STRATEGIES FOR SUCCESSFUL AGING OR HEALTHY LIVING

- Healthcare: therapeutic & preventive
- Diet – Calorie restriction, “Superfoods”
- Physical and Cognitive activity
- Stress reduction – meditation, other ways
- Sleep hygiene


ACTIVE LIFESTYLE FACTORS AND NEUROCOGNITIVE IMPAIRMENT

(FAZELI ET AL., 2014 JNV)

- Self-reported participation in social, physical, and mental activities (e.g., employment = proxy for mental activity) was associated with better neurocognitive outcomes in HIV, which is consistent with the non-HIV aging literature

- Cross-sectional data, so causation cannot be determined; yet, these data support the notion that living an active life may help successful cognitive aging
**COVARIATE-ADJUSTED NEUROCOGNITIVE MEANS BY ACTIVE LIFESTYLE FACTORS**

(FAZELI ET AL., 2014 JNV)

ALF = Active lifestyle factors; *3 > 1 and 0 (p < 0.05). The y-axis is truncated for visual representation of means. Bars represent standard errors.

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**PHYSICAL ACTIVITY AND NEUROCOGNITIVE IMPAIRMENT**


- Moderate levels of physical activity (PA) were associated with lower odds of Neurocognitive Impairment or NCI (p=0.01) and better everyday functioning (p=0.04) after controlling for relevant variables
- The association between moderate PA and global NCI was driven by executive function (p=0.04)
- These cross-sectional findings suggest PA is associated with better neurocognitive and everyday functioning among older HIV+ adults
Physical Activity and Neurocognitive Impairment

Predicted probabilities for global neurocognitive impairment by moderate IPAQ scores.
Imp=neurocognitively impaired, Nml=neurocognitively normal

Interventions to Enhance Resilience

• Master Resilience Training for the armed forces
• Stress Management and Resilience Training (SMART)
• Mindfulness-Based Stress Reduction
• (Novel Biological interventions such as Training to modulate one’s own brain activity with real-time fMRI-based neuro-feedback)
  (Loprinizi et al., 2011; Rose et al., 2013; Creswell et al 2012; Caria et al 2007)
BIOLOGY OF POSITIVE PSYCH. INTERVENTIONS

• 2-month Mindfulness-Based Stress Reduction reduced pro-inflammatory NF-κB-related gene expression in circulating leukocytes

• Daily Meditation for 6 months increased telomerase activity

(Creswell et al 2012; Jacobs et al 2010; Caria et al 2007)

EFFECT OF MEDITATION

Brain Regions with Significant Fiber Integrity Increase After 11 h of Meditation (Integrative Body-Mind Training)

(Tang et al., PNAS, 2010)
PSYCHOSOCIAL STIMULATION OR PSYCHOTHERAPY

Brain on a treadmill?

NEED TO CHANGE THE PRESCRIPTION

Dx:
AIDS
Rx:
ARV

Exercise 5 x week
Fitbit
Healthy Diet
Sleep
Meditation
Reading
Volunteering

Stein Institute for Research on Aging
Center for Healthy Aging
GOAL: CHANGE “SILVER TSUNAMI”, INTO A “GOLDEN WAVE” OF HEALTHY, HAPPY, ACTIVE, & WISE SENIORS

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Thank You!
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