The Aging Brain: What can we do about it?

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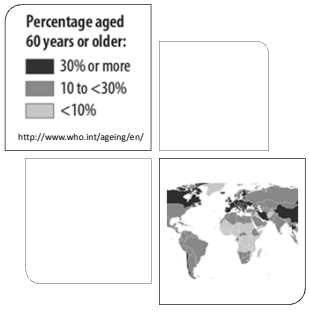
Disclosures

- No Conflicts of Interest to Disclose

99.6% Fail Rate of Investigational Drugs for Alzheimer's Disease and Other Dementia Disorders

Cummings, J. L., Morstorf, T., & Zhong, K. (2014). Alzheimer's disease drug-development pipeline: few candidates, frequent failures. Alzheimer's research & therapy, 6(4), 37.



Barnes DE, Yaffe K. The projected effect of risk factor reduction on Alzheimer's disease prevalence. *Lancet Neurol*. 2011; *10*(9), 819-828.

Objectives

1. Explain the aging brain and the cognitive functions most susceptible to decline
2. Identify factors related to increased risk or resilience for cognitive decline
3. Discuss types of activities that might promote brain health and increase quality of life
4. Understand the relationship between mental health and physical health, and how integrative treatment approaches can help

True or False?

- If you live long enough, you will eventually develop dementia?
- Older adults cannot learn new things, like a language or new instrument?
- Memory loss is a normal part of aging?
- Once you start having memory & thinking problems, there is nothing you can do about it?

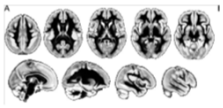
Changes in Brain Structure and Function with Age

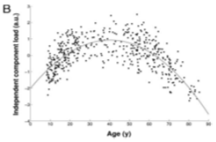
- Decreased brain volume & white matter
  - White matter > gray matter
  - Shrinkage vs. loss of neurons
- Changes in brain neurochemistry
- Changes in functional connectivity
- Changes in blood flow, plasticity & neurogenesis

Raz, N. (2000). Aging of the brain and its impact on cognitive performance: Integration of structural and functional findings. In F. I. M. Craik & T. A. Salthouse (Eds.), Handbook of aging and cognition .
Gunning-Dixon et al. (2009). Aging of cerebral white matter: a review of MRI findings. International journal of geriatric psychiatry, 24(2), 109-117.
Peters, A. (2002). The effects of normal aging on myelin and nerve fibers: a review. Journal of neurocytology, 31(8-9), 581-593.
Callaghan et al. (2014). Widespread age-related differences in the human brain microstructure revealed by quantitative magnetic resonance imaging. Neurobiology of aging, 35(8), 1862-1872..
Rizvi et al. (2018). The effect of white matter hyperintensities on cognition is mediated by cortical atrophy. Neurobiology of aging, 64:25-32

Last in, First out?

- Gray matter varies with age
- Areas last to myelinate most vulnerable
  - Frontal & Temporal Association areas
- These changes correlate highly with cognitive test performance
- But… Brain pathology does not always correlate with cognitive dysfunction





484 healthy participants (aged 8–85 years)

Figures: Douaud et al. (2014).

Raz, N. (2000). Aging of the brain and its impact on cognitive performance: Integration of structural and functional findings.
Douaud et al. (2014). A common brain network links development, aging, and vulnerability to disease. PNAS (111)49.
Ahmed et al. (2018). Physiological changes in neurodegeneration—mechanistic insights and clinical utility. Nature Reviews Neurology, 14(5), 259.

Brain Plasticity

Brain plasticity	In older adults, research suggests:
• Neurological process by which learning occurs • Represents several different processes • e.g., Stimulation of dendritic branching and/or synaptogenesis	• Learning is intact but may happen in different areas • Learning is slower and requires greater repetition • Adaptive mechanism to compensate for lost function or brain injury

Peters, A. (2002). The effects of normal aging on myelin and nerve fibers: a review. Journal of neurocytology, 31(8-9), 581-593.
Yotsumoto et al.(2014). White matter in the older brain is more plastic than in the younger brain. *Nature communications*, 5, 5504.

Compensatory Brain Activity & Plasticity

Functional Compensation
- Increases and decreases in brain activity observed in older adults†
- **Better performance** linked to
  - Compensatory bilateral activations in PFC*
  - Shifts in activations from posterior to more anterior brain regions**
- Increased functional activity in older adults is due to the process of compensatory scaffolding***

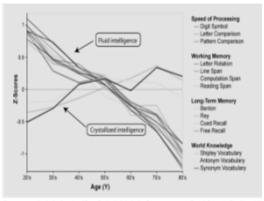
Brain Compensation Theories:
- Dedifferentiation†
- HAROLD*
- PASA**
- STAC***

Image: Cabeza (2002).

†Li et al. (2000). Unifying cognitive aging: From neuromodulation to representation to cognition. Neurocomputing 32-33, 879-890.
*Cabeza, R. (2002). Hemispheric asymmetry reduction in old adults: The HAROLD model. Psychology and Aging, 17, 85-100.
*Cabeza, R., Anderson, N. D., Locantore, J. K., & McIntosh, A. R. (2002). Aging gracefully: Compensatory brain activity in high-performing older adults. Neuroimage, 17, 1394-1402.
**Davis, S.W., Dennis, N.A., Fleck, M.S., Daselaar, S.M., Cabeza, R. (2008). Que PASA?: The posterior-anterior shift in aging. Cerebral Cortex, 18, 1201-1209.
*** Park, D.C., Reuter-Lorenz, P. (2009). The adaptive brain: aging and neurocognitive scaffolding. Annual Review of Psychology, 60, 173-96.

Cognitive Functions with Age

- "Crystallized" Intelligence
  - Knowledge does not decline, and may even improve
- "Fluid" abilities show decrease over time
  - Visual Memory
  - Working Memory
  - Executive Attention/Processing Speed



The aging mind: neuroplasticity in response to cognitive training (Park & Bischof, 2013).

What does normal cognitive aging "look" like?

- Mild changes in attention/processing speed common
- More difficulty multitasking or changing strategies
- Cognitive slowing
  - *Can you repeat that?*
  - May take longer to learn new things but learning is possible
- Memory Changes
  - "Tip of the tongue"
  - Problem is in accessing memory (recall) and not storage

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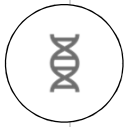
Genetic Risk Factors & Dementia

- Early Onset Familial Alzheimer's disease (AD)
  - < 5-10% of population
  - Associated with 3 genetic mutations, autosomal dominant pattern
- The apolipoprotein E (APOE) e-4 allele best known genetic risk for late onset AD
  - Not a determinant gene
  - Interactions with sex, race & age but also covaries with behavioral risk factors that are modifiable
    - e.g., Depression, vascular risk factors, & education



MacAulay et al. (Submitted). Predictors of Heterogeneity in Cognitive Function: APOE-e4, sex, education, depression, and vascular risk
https://www.alzforum.org/early-onset-familial-ad/overview/what-early-onset-familial-alzheimer-disease-efad

Which identical twin smoked?

Okada, H. C., Alleyne, B., Varghai, K., Kinder, K., & Guyuron, B. (2013). Facial changes caused by smoking: a comparison between smoking and nonsmoking identical twins. *Plastic and reconstructive surgery*, *132*(5), 1085-1092.

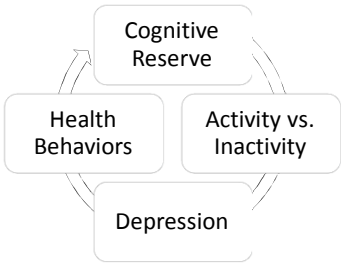
Images from: http://www.nbcnews.com/id/33385839/ns/health-skin_and_beauty/t/twin-study-reveals-secrets-looking-younger/#.Wwq3ci-ZNTY

Seven Potentially Modifiable Risk Factors for Alzheimer's Disease

1. Diabetes
2. Midlife hypertension
3. Midlife obesity
4. Smoking
5. Depression
6. Cognitive inactivity or low educational attainment
7. Physical inactivity

1. Barnes DE, Yaffe K. The projected effect of risk factor reduction on Alzheimer's disease prevalence. *Lancet Neurol*. 2011; *10*(9), 819-828.
2. Prince MJ. *World Alzheimer Report 2015: the global impact of dementia: an analysis of prevalence, incidence, cost and trends.* Alzheimer's Disease International.
3. Livingston G, Sommerlad A, Orgeta V et al. Dementia prevention, intervention, and care. *Lancet*. 2017.

If not for your heart, then do it for your brain!



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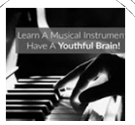
Brain Plasticity & Aging: Keeping the brain and body active!

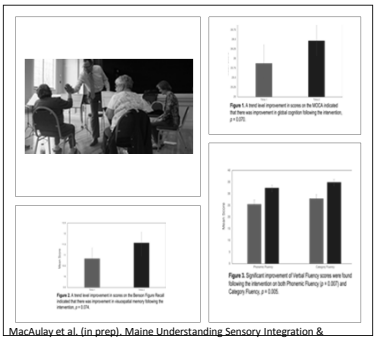
Exercise	Socializing
Physical activity	Mental activity

Promising Novel "Cognitive" Interventions

- Musicians vs. non-musicians
- Piano playing
- Choir
- Dance outperforms aerobic exercise!



Hanna-Pladdy et al. The relation between instrumental musical activity and cognitive aging. Neuropsychol. 2011; 25(3), 378.
Bugos JA. Community music as a cognitive training programme for successful ageing. Int J Com Music. 2014; 7(3), 319-331.
Moussard, et al. (2016). Life-long music practice and executive control in older adults: An event-related potential study. Brain Research, 1642, 146-153
Seinfeld et al. Effects of music learning and piano practice on cognitive function, mood and quality of life in older adults. Front psychol. 2013;4.



MacAulay et al. (in prep). Maine Understanding Sensory Integration & Cognition (MUSIC) Project: Music learning as a cognitive intervention.

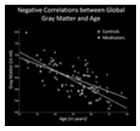
Maine Understanding Sensory Integration & Cognition (MUSIC) Project

- Learning to play a music recorder
- 12-music lessons once a week in 26 older adults
- Preliminary findings suggest improvements in neuropsychological tests associated with global cognition & frontal lobe function
- Limitations - no control group – yet!

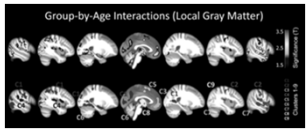
Brain Atrophy & Meditation

Link between age and cerebral gray matter in mediators vs. controls. Results suggest:

- Everyone's brain ages but…
- Less age-related gray matter atrophy in long-term meditation practitioners



aged 24 and 77 years



Luders, E., Cherbuin, N., & Kurth, F. (2015). Forever Young (er): potential age-defying effects of long-term meditation on gray matter atrophy. *Frontiers in Psychology*, 5, 1551.

Mindfulness Training

- Mindfulness is associated with improve attention in adults
- Informal and formal practices to increase awareness
- Types of Activities
  - Mindful Eating
  - Mindful Walking
  - Gratitude
  - Brushing teeth, showering, washing dishes…

Gard et al. The potential effects of meditation on age-related cognitive decline: a systematic review. *Ann N Y Acad Sci.* 2014;1307(1), 89-103.
McEwen BS. In pursuit of resilience: stress, epigenetics, and brain plasticity. *Ann N Y Acad Sci.* 2016;*1373,* 56-64.

Take-home message

More

- **Moderation**
- Laughter
- Challenges
- "Real food"
- Music
- Dance
- Smiling
- Gratitude
- Activities
- Time with people we care about

Less

- **Excess**
- "Worrying about the weather"
- Sodas & fast food
- Smoking

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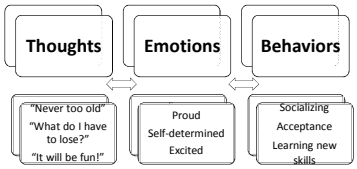
It's not just in our head: *What we think and feel matters*

Cognitive Model of Aging



Stephan, Y., Sutin, A. R., & Terracciano, A. (2016). Feeling older & risk of hospitalization: Evidence from three longitudinal cohorts. Health Psychology. Advance online publication. doi:10.1037/ hea0000335

Self Determination Theory (SDT) & Behavior Change

1. Foster Autonomy
   - Provide relevant information with personally meaningful reasons for change
   - Enable a sense of agency or choice.
2. Competence
   - Increase skills and confidence to manage health problems
   - Coping strategies to adapt to changes (e.g., how to remain active with loss of mobility or vision)
3. Relatedness
   - Goal Setting - Problem solving that includes instrumental as well as social support to address motivation factors that may maintain maladaptive health behaviors.

Deci, E. L., & Ryan, R. M. (2008). Self-determination theory: A macrotheory of human motivation, development, and health. Canadian psychology, 49(3), 182.
Ryan et al. (2008). Facilitating health behaviour change and its maintenance: Interventions based on self-determination theory. *European Health Psychologist, 10*(1), 2-5.

Integrative Practice and Precision Medicine

- Concept of disease
- Beyond one system & across the life span
- Holistic approaches to treatment
  - Exercise
  - Diet
  - Quality of Life

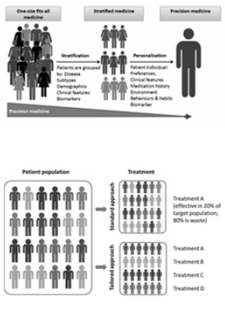


Image Credits: *Manchester Precision Medicine Institute. Retrieved from: https://evolve.community.usf.edu/2017/04/26/the-chronicles-of-evolutionary-weight-in-the-fight-against-cancer/*

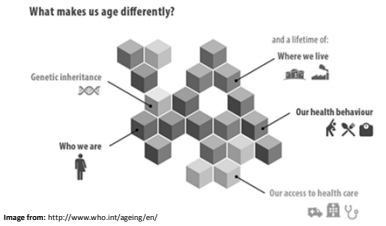


Image from: http://www.who.int/ageing/en/

Yeah, but… Time to change our approach

Future Directions & Research Needed

- Environment & Successful Aging
- Interdisciplinary work on aging
- Help Me, Help YOU
  - More community-based participatory research programs

So What Can We Do as Providers?

Psychoeducation

- Understand the psychology behind aging
- Lifespan approach to behaviors
- Use of positive replacement behaviors

Patient centered approaches

- Self-Determination Theory

Integrative treatment approaches

- Precision medicine

Thank you for your attention!

- Questions? Comments? Want to get involved?

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