The Aging Brain: How Life Changes the Brain
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Objectives

1. Identify risk factors that accelerate the aging process.
2. Differentiate normal aging from pathological aging (dementia).
3. Identify actions that slow the aging process and promote healthy brain function.

Overview

• The Brain normal development
• Aging – What is it and what accelerates it
• How aging affects the brain
• Pathological aging - Dementia (Alzheimer's Disease)
• How to slow the aging process

Watson

• 90 IBM Power 750 Servers
• 2880 Power 7 processors
• Each processor with 8 cores containing 1.2 billion transistors – 27,648,000,000,000 transistors
• 16 Terabytes of RAM
• 500 gigabytes/sec (1 million books/sec)

Watson Vs. the Brain

• Kilobyte = 1000 bytes
• Megabyte = 1000 KB or 1,000,000 bytes
• Gigabyte = 1000 MB or 1,000,000,000 bytes
• Terabyte = 1000 GB or 1,000,000,000,000 bytes
• A teraflop is 1 trillion point operations per second
• Brain holds approximately 1.25 Terabytes of data & performs at approximately 100 teraflops
• Watson holds 1 TB of data and performs at 80 teraflops
• Why did Watson win?
• Could ring in faster – In Jeopardy cannot ring in until Alex finishes reading the question – they programmed Watson to electronically ring in as soon as the switch was flipped to allow ring ins.

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Neuron

• 100 billion nerve cells
• Over 1 trillion supporting cells
• Each brain cell with up to 10,000 connections to other cells
  = 40,000,000,000,000,000
  = Forty Quadrillion

Normal Brain Development

• From birth to age 8 massive remodeling, with millions of neurons lost
• A second wave of neurogenesis, heavily concentrated in the PFC, peaks in girls at 11 and boys at 12 followed by more remodeling and neuronal loss
• White matter maturation progresses from back to front culminating around age 25
• When shown faces and asked to identify emotions, young teens activated their amygdala and limbic system, whereas in older teens activated the PFC.

Neurotrophic Factors

• Brain Derived Neurotrophic Factor (BNDF)
  – Increased by mental & physical exercise
  – Suppressed by stress
  – Activated by depression treatments
• Nerve Growth Factor (NGF)
  – Increased by physical exercise
  – Increased by lithium
  – Suppressed by lack of exercise & amphetamines
• Vascular Endothelial Growth Factor (VEGF)
  – Increased by physical exercise

What is Aging?

• Chronologically growing older?
  – God is ancient, but God is not “elderly”
• Functionally growing older?
  = Slow decline in vitality and ability

Functional Aging

• Taste/Smell
  – Slight decrease with age but remains good well into 70’s
• Bones/muscles (decreased mobility)
  – Lose mass, strength, elasticity, markedly accelerated with sedentary lifestyle
• Touch
  – Decreased sensitivity increased risk of burns
  – Decrease circulation, sweat glands, thinning skin, more difficulty maintaining body temp, easier skin breaks and increased risk of infection

Functional Aging

• Hearing impairments
  – Over 60 = 30%
  = 75-84 = 33%
  – Over 85 = 50%
• Vision changes
  – 30’s – 40’s begin to lose near vision
  – As aging continues peripheral vision decreases
  – Night vision is reduced
  – Eye muscles weaker
  – Cloudy lenses
  – Color vision changes with greens/blues harder to see
  – 7-15% of seniors with serious impairments
What Contributes to Functional Decline as we Age?

2nd Law of Thermodynamics
- Entropy – if energy isn’t put into a system it slowly decays
  - Leave your home for 20 years and return
  - Allow a car to sit for 20 years
- Human genome???
  - If mankind is disconnected from God, is there a slow, gradual entropy to our genome?
  - Are we degrading or evolving to higher forms?
  - The Bible says that when Adam sinned, “dying you will die.”

Human Genome
- An instruction manual containing a library of information
  - DNA molecules = letters
  - Clusters of these molecules = words
  - Words group to form genes = chapters
  - Chapters Genes group into Chromosomes = volumes
  - Volumes Chromosomes group into genome = library containing 3.2 Billion base pairs in 23 chromosomes

Genetic Entropy
- Mutation Type
  - Mitochondrial
  - Nucleotide substitution
  - Satellite mutations
  - Deletions
  - Duplications/insertions
  - Inversions/translocations
  - Conversions
  - Total/person/generation
- Mutations per person per generation
  - <1
  - 100-300
  - 100-300
  - 2-6% (plus)
  - 2-6% (plus)
  - Numerous
  - Thousands?
  - >1000
Genetic Mutations
- A person at 65 will have in their DNA up to 6000 point mutations that were not there at birth
- Each generation receives up to 1000 new mutations that the previous generation did not start with.
- There has not been one mutation found that has actually added genetic information or improved the species
- The human genome is slowly degrading

What is Oxidative Stress
- It is the damage to DNA, proteins and lipids (fatty substances) caused by oxidants, which are highly reactive substances containing oxygen.
- This is why we hear so much about “antioxidants” substances that prevent oxidation.

What increases oxidative stress?
- Obesity
  - Adipose tissue produces reactive oxygen species (ROS) and reduces the production of antioxidant enzymes

What increases oxidative stress?
- At age 70
- Obese
  - 8% less brain volume and look 16 years older
- Overweight
  - 4% less brain volume and look 8 years older
What increases oxidative stress?

- Obesity
- Alcohol, tobacco, drugs
  - Suppresses antioxidant enzymes, disrupts mitochondrial function, increase the production of super oxides and free radicals, activates the brain’s HPA (stress response)
- Chronic Stress, activation of fear circuits
  - Abuse
  - Violence
  - Belief in fear inducing God constructs

Over active Amygdala

- Activates sympathetic nervous system
- Which activates macrophages –
  - Why?
- Which release cytokines – IL1, IL6, TNF
- Which damage:
  - Insulin receptors, glucocorticoid receptors, interfere with NE, SHT, DA signaling
- Resulting in:
  - Increased DM, obesity, high cholesterol, MI, Stroke, depression
  - All of which increase dementia

Telomeres

- 1965 – cells with short telomeres didn’t divide in culture
- 1990 – each time a human cell divides the telomeres shorten until cannot divide
- 2006 – People with mood d/o’s have shorter telomeres
- 2011 – institutionalized children have shorter telomeres
- 2012 – telomere length predicts remaining lifespan

Telomeres

- Shorter in males than females
- Heredity accounts for 80% environ 20%
- Negative effect
  - Childhood adversity
  - Mood disorders
  - Hostility
- Positive effect
  - Healthy Diet
  - Exercise

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5th Commandment

• “Honor your father and your mother, so that you may live long in the land the Lord your God is giving you. (Ex 20:12)
• Why?
• God uses power to make it so?
• When we live in harmony with God’s design for life we are healthier & live longer and when violate God’s design we activate inflammatory cascades, shorten telomeres and age faster.

Advanced Glycation End-Products (AGE)

• Glycation is the process of sugars, in a non-enzymatically controlled way, binding to proteins and DNA significantly altering their structure and function. The altered protein/DNA is an AGE
• AGEs react with body tissues to produce free radicals and Reactive Oxygen Species (increased oxidative stress)

AGE’s Impact

• Damage collagen (skin thins, wrinkles, loses elasticity)
• Binds with oxidized LDL in endothelium (arterial walls causing inflammation and obstruction) and prevents HDL from removing the LDL

AGE’s Impact

• Damage collagen (skin thins, wrinkles, loses elasticity)
• Binds with oxidized LDL in endothelium (arterial walls causing inflammation and obstruction)
• Interact with IgG altering immune response
• Interact with cellular membranes altering membrane function
• In vitro they interact with DNA – potential to alter DNA expression
Two Primary Sources of AGEs

- Food
  - Browned, fried, & charred foods (30% absorption)

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Two Primary Sources

- Food
  - Browned, fried, and charred foods (30% absorption)
- Body metabolism (high blood sugar levels increase AGEs)
  - Hgb A1c = glycated hemoglobin
    - This why diabetics have higher CAD, and end organ damage

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What Accelerates Aging of the Brain?

- Obesity
- Alcohol, tobacco, drugs
- High oxidative stress/AGE diet
- Sedentary lifestyle
- Low education
- Lack of brain activity
- High stress life
- Relationship problems
- Lack of spirituality/altruism

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How to reduce AGE's & Slow Aging

- Reduce Consumption of Sugar
  - Average American consumes 125-150 pounds per year
- Stabilize blood sugar levels, eat complex carbs, and proteins, high fiber diet
- Eat vegetables and fruits raw, boiled or steamed
  - Water prevents sugar from binding to proteins
- Limit consumption of browned, caramelized, deep fried foods - this cooking technique creates AGEs
- Limit meat, but when used cook at low temperature and slowly cook. High temps create AGEs

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How to Reduce AGE's & Slow Aging

- Avoid high fructose corn syrup. Fructose is 10x more reactive than glucose in the body.
- Drink water. For many the greatest sources of excess sugar are soft drinks.
- Stop smoking.
  - Smoking has long been associated with cancer and cardiovascular health concerns. Recent research has clearly shown a significantly higher level of serum AGEs in smokers and especially diabetic smokers.
- Scavenger of AGE
  - Rhodiola rosea, Green Tea, Grape Seed Extract, Omega 3 Fatty Acids, carnosine, Vitamin B & Alpha lipoic acid
  - Plant sources of alpha-lipoic acid include broccoli, spinach, collard greens, chard and brewers yeast

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What Reduces Oxidative Stress and Slows Aging?

- Diet
  - Designed to reduced AGEs
    - apples, broccoli, spinach, kale, peaches, cabbage, cauliflower, tomatoes, carrots, citrus fruits, most berries and omega 3 fatty acids

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Study Neurology 2011
Nutrients Improve Brain Volume and Cognitive Function
• 3 distinct nutrient biomarker patterns (NBPs) in blood related to cognitive performance & (MRI) measures of brain aging.
• 2 Diet patterns with favorable cognition and brain volume
  – High in plasma B vitamins (B1, B2, B6, folate, and B12), as well as vitamins C, D, and E (Fruits, Nuts, Grains, Vegetables)
  – High in plasma marine omega-3 fatty acids. (Oily Fish)
• Diet with less favorable cognition and brain volume
  – A diet high trans fat pattern (fast food, junk food)

If Vegie Diet Healthier Then Why Did God tell them How to Eat Meat?
• Exodus 16 God provides manna
• Numbers 11:4 “Israelites started wailing and said, ‘If only we had meat to eat!’”
• Leviticus = God basically says: 
  = “Okay, if you insist on meat – then eat only these meats, prepared in this way and it will be least damaging to you.”

Freedom in Christ from Ceremonial Law
• We are free in Christ from ceremonial law
• Means – we can eat whatever we want and not be CEREMONIALLY unclean
• Why? Because Ceremonial Law was done away with at the Cross
• But, were the Laws of Health done away with at the Cross?

What Reduces Oxidative Stress and Slows Aging?
• Diet
• Exercise
  – IL-10 is anti-inflammatory cytokine reduces inflammation
  – Increases all neurotrophins
  – Older persons who exercise regularly saw 2% growth in hippocampus reversing effects of aging
• Fresh clean air & Hydration
• Avoidance of inflammatory substances

What Reduces Oxidative Stress and Slows Aging?
• Diet
• Exercise
• Fresh clean air & Hydration
• Avoidance of inflammatory substances
• Worship of God of love and volunteer to help others
Altruism Promotes Better Health

- Adults who volunteer (after accounting for variables such as education, baseline health, smoking, etc.):
  - Live longer, have less illness, less disability, less depression, less dementia and live independently longer than those who did not.1


How Healthy Spirituality Helps Slow Aging

- Activates PFC and ACC, calms amygdala, lowers inflammatory response resulting in improved mental and physical health
- Altruistic activities result in better mental and physical health
- Reduced anxiety and worry
- Healthier lifestyle so reduced oxidative stressors
- Healthier relationships lower stress

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What Reduces Oxidative Stress and Slows Aging?

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- Exercise
- Fresh clean air & Hydration
- Avoidance of inflammatory substances
- Worship of God of love and volunteer to help others
- Rest (physical & mental)

What unique about Loma Linda

- Heterogeneous
- SDA

From Blue Zone Website

- Lessons from Loma Linda
  - “Find a sanctuary in time to decompress. Strict observance of the Sabbath is strictly occurs from Friday to Saturday night, giving Adventists a weekly time to focus on family, friends, God and nature.”
- SDAs also:
  - Eat healthy (high percent of vegetarians)
  - Don’t smoke, use alcohol or illegal drugs
  - Exercise more than most
  - Less obesity

Ellsworth E. Wareham, M.D.

- 94 y/o heart surgeon
- Still performing heart surgery
- Vegan
- No Alc, Tob, drugs
- Exercises Regularly
- Weekly Sabbath rest
- Volunteers
- Healthy Relationships
What Reduces Oxidative Stress and Slows Aging?

- Diet
- Exercise
- Fresh clean air & Hydration
- Avoidance of inflammatory substances
- Worship of God of love and volunteer to help others
- Rest (physical & mental)
- Antioxidants:
  - N-acetyl cysteine, omega 3 fatty acids, Vitamin E (from food), Vitamin C, flavanoids (fresh fruit juices)

Pathological Aging

Dementia

What is Dementia

- A brain disease characterized by multiple cognitive deficits, including memory and one or more of the following:
  - Aphasia (language disturbance)
  - Apraxia (motor disturbance)
  - Agnosia (impaired recognition of familiar objects)
  - Executive function impairment

Alzheimer's disease (AD)

- More than 24 million people worldwide have dementia
- An estimated 4.0 million new dementia cases occur each year
- The number of dementia cases is predicted to double every 20 years
  - To 42.3 million in 2020
  - To 81.1 million in 2040
- AD is the most common cause of dementia
- AD incidence doubles every 5 years after age 65 years
- The prevalence of AD among the elderly is 67 per 1,000 persons. (Parkinson's disease is 9.5 per 1,000)
- More than 1 in 3 people aged 85 years and older receive a diagnosis of AD

Potential Pathway

- Increased Amyloid (genetic, head injury, chronic stress with increased ROS, AGEs, inflammation)
- Amyloid phosphorylates Tau
- Tau disconnects from microtubules and cell membranes causing disintegration of microtubules
- Microtubules carry negative charge, when intact hyperpolarize neuronal axonal membranes reducing excitability and influx of positively charged ions
- When microtubules breakdown, increased influx of positive ions and more cell death
- Axons contain high levels phosphatase to dephosphorylate Tau and thus protect neurons

ApoE

- Lipoprotein that transports fat vitamins, cholesterol into cells
- 3 gene variants ApoE2, ApoE3, ApoE4
- ApoE2: 7% population, increased risk of atherosclerosis
- ApoE3: 79% of population neutral effect
- ApoE4: 14% of population implicated in Alzheimer's
  - If two copies 10-30 x increased risk
  - Up to 65% of people with Alzheimer's with this gene
  - But 1/3 of Alzheimer's without this gene
**ApoE4 – Genetic Risk**
- The ApoE4 is neither necessary nor sufficient to get the disease.
- A study out of Washington University found that people with ApoE4 were not demented and had less amyloid in their brain if they had a history of exercise.
- Genetics account for only 1/3 of the risk
- What is the key?
- Inflammation is likely the key and lifestyle impacts inflammation

**4 Keys to AD Prevention**
- **Physical conditioning**
- Active animals have larger hippocampi
- Older people who walk regularly even as little as 15 minutes a day -- have a lower risk for AD.
- People who routinely exercise exhibit better cognitive abilities and actually have larger brains.
- Exercise in older adults 2% growth hippocampi reversing two years of aging

**4 Keys to AD Prevention**
- **Mental Stimulation**
- Read, write, and do a crossword: Mentally stimulating activities and certain brain-training programs are in the long term associated with lower brain amyloid levels and a decreased risk for AD, as are graduating from college or engaging in life-long learning.1,2


**4 Keys to AD Prevention**
- **Stress Management**
- Chronic stress activates inflam pathways and damages brain
- Study of 5000 individuals found that neuroticism—which included feelings of guilt, anger, anxiety, and depression—was associated with a greater risk for dementia. In contrast, conscientiousness was shown to be protective against dementia.

- Meditation on God of love reduces stress
- Altruistic activities reduce dementia risk
- Trust God with outcomes
- Be truthful — address issues and resolve them
- Forgive

http://www.comeandreason.com/article/S1064-7481(12)00031-0/fulltext
4 Keys to AD Prevention

- Physical conditioning
- Mental Stimulation
- Stress Management
- Nutrition
  - Normal weight
  - Mediterranean diet
  - Fruits, nuts, veggies, omega 3 FA
  - Avoid sugars, trans fats

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Risk Factors for Dementia

- Increasing age
- Family history
- Oxidative stress
- Trisomy 21
- Alcohol/drug abuse
- Smoking
- Sedentary lifestyle
- Toxic exposure
- Head injury
  - #1 cause head injury in USA bicycles
  - Boxing, Football
  - Soccer – more head use = more cognitive decline later in life
- Poor vascular health
- DM/glucose intolerance
- Obesity
- Western diet
- HTN (even when treated)
- Low intelligence
  - Television increases risk of dementia because it slows neural connectivity
- Low cognitive stimuli
- Depression
- PTSD
- Social isolation
- Psychological stress
- Chronic sleep deprivation

Prevention Options for Dementia

- Healthy diet
- Almonds & Vit C
- L-Methyl Folate and B vitamins
- N-acetyl Cysteine
- Curcumin
- Omega 3 Fatty Acids (DHA/EPA)
- Exercise
- Pomegranate Juice
- Sleep stabilization
- Mental activity
- Healthy Spirituality

Dr. Jennings’ Dementia Cocktail

- Namenda (memantine) 10mg b.i.d.
- Cholinesterase inhibitor
- Omega 3 fatty acids
- Vitamin E & C (Almonds not supplement)
- Baby aspirin
- L-methylfolate and NAC
- Exercise
- Pomegranate Juice 8 ounces per day
- Sleep Stabilization
- Healthy Spirituality