SUCCESSFUL AGING: WHAT WE KNOW AND WHERE CAN WE GO?

LAURENCE M. SOLBERG, MD AGSF
VICE-CHAIR FOR CLINICAL OPERATIONS
CHIEF, DIVISION OF GERIATRIC MEDICINE

RUTH S. JEWETT PROFESSOR OF GERIATRIC MEDICINE
DEPARTMENT OF AGING AND GERIATRIC RESEARCH
UNIVERSITY OF FLORIDA COLLEGE OF MEDICINE
EMAIL: LMSOLBERG@UFL.EDU
OBJECTIVES

• INTRODUCTION
• MARKERS OF AGING
  • HEALTH FACTORS
  • BEHAVIORAL FACTORS
  • BIOLOGICAL FACTORS
• DOES GENETICS PLAY A ROLE?
• COMMUNITIES THAT AGE WELL
• INTERVENTIONS: HELPFUL OR HOPEFUL
INTRODUCTION

• SUCCESSFUL AGING IS COMPLEX AND MULTIDIMENSIONAL
  • PHYSICAL, BIOLOGICAL, COGNITIVE, AFFECTIVE, AND SOCIAL COMPONENTS.
• DEFINING IT HAS BEEN ELUSIVE
• A CENTURIES OLD SEARCH
PAST MODELS

• DIFFERENT MODELS PROPOSED
  • BIO MEDICAL MODEL: HEALTHY VS DISEASED
    • BASED ON ABSENCE OF CHRONIC DISEASE
  • BIOPSYCHOSOCIAL MODEL
    • HEALTH AND FUNCTIONAL STATUS LATER IN LIFE OCCUR ON A SPECTRUM
  • ROWE AND KAHN’S MODEL OF BETTER THAN AVERAGE
    • COMBINATION OF AVOIDING DISEASE, HIGH COGNITIVE AND PHYSICAL FUNCTION, AND ENGAGEMENT WITH LIFE
  • OBJECTIVE AND SUBJECTIVE MODEL
    • OBJECTIVE: FUNCTIONAL ABILITIES, PAIN, DIAGNOSED HEALTH CONDITIONS
    • SUBJECTIVE: PERCEPTIONS OF QUALITY OF LIFE AND SUCCESSFUL AGING
NEWER MODELS

• OUTCOMES MODEL
  • STRONGEST EVIDENCE IS IN PHYSICAL DOMAIN
    • MOBILITY
      • WALKING SPEED
    • PHYSICAL FUNCTION
      • STRENGTH
      • BALANCE
      • ACTIVITIES OF DAILY LIVING
  • BETTER MOBILITY = BETTER FUNCTION = BETTER HEALTH
Fig. 1. The conceptual model illustrates important factors that can affect physical function during aging and ultimately maintenance of health and independence in older adults. Biological mechanisms and behavioral factors associated with reductions in physical function are illustrated in the outer ring. Specific health conditions that contribute to reductions in mobility and physical performance during aging are displayed in the middle ring. These conditions include but are not limited to cognitive decline, dysapnea, obesity, pain, and sarcopenia. Promising interventions for enhancing mobility and physical function, which target one or more biological mechanisms, behavioral factors, or health conditions contributing to functional decline, are shown in the outer edges. The ultimate goal is maintenance of health and independence, displayed in the innermost ring, through enhancement of mobility and/or physical function. This figure is not intended to be exhaustive but rather to highlight key biological mechanisms, behavioral factors, and health conditions that can contribute to functional decline in older adults, as well as promising interventions to attenuate declines in mobility and physical function during aging. MT: mitochondria.
MARKERS OF AGING: HEALTH FACTORS

- COGNITIVE DECLINE
- COGNITIVE FUNCTIONS DECLINE WITH AGE
  - MEMORY
  - ATTENTION
  - EXECUTIVE FUNCTIONS
- COGNITIVE FUNCTIONS THAT DO NOT DECLINE WITH AGE
  - VOCABULARY
- DEMENTIA – MAJOR NEUROCOGNITIVE DISORDER – LEADS TO SHORTENED LIFE SPAN
- DELIRIUM – A TRANSITIVE EPISODE OF COGNITIVE DECLINE – LEADS TO FUNCTIONAL AND PERMANENT COGNITIVE DECLINE
MARKERS OF AGING: HEALTH FACTORS

• OBESITY
  • PREVALENCE HAS INCREASED DRAMATICALLY IN THE PAST DECADES.
  • OBESE OLDER ADULTS ARE APPROXIMATELY 33% OF THE OLDER POPULATION.
  • AGE RELATED MUSCLE MASS CHANGES ARE MORE PRONOUNCED IN OBESE OLDER ADULTS.
  • DIRECTLY LINKED TO PHYSICAL DISABILITY WITH CHANGES IN MUSCLES FROM SKELETAL MUSCLES TO ADIPOSE TISSUE (FAT).
  • ALSO CONTRIBUTES TO COGNITIVE DECLINE THROUGH MICROVASCULAR DAMAGE IN BRAIN
  • EXCESS ADIPOSITY LINKED TO INCREASES IN REACTIVE OXIDATION, INFLAMMATION, AND DAMAGING MITOCHONDRIA WHICH ACCELERATES FUNCTIONAL DECLINE
MARKERS OF AGING: HEALTH FACTORS

• SARCOPENIA
  • AGE RELATED LOSS OF MUSCLE MASS
    • INDIVIDUALS LOSE 1-2% PER YEAR AFTER AGE 50 YEARS.
  • DEFINED AS LOW WALKING SPEED AND LOW MUSCLE MASS — THE SOCIETY OF SARCOPENIA, CACHExIA, AND WASTING DISORDER
  • MUSCLE ATROPHY LEADS TO PHYSIOLOGIC CHANGES INCLUDING GLUCOSE REGULATION, HORMONE PRODUCTION, AND CELLULAR COMMUNICATION.
  • IMPAIRED LOCOMOTION IS A HALLMARK CONCERN.
MARKERS OF AGING: HEALTH FACTORS

• DYNAPENIA
  • AGE RELATED LOSS OF MUSCLE STRENGTH – TERM COINED IN 2012 BY MANINI AND CLARK (UF COM)
  • MAY OR MAY NOT BE RELATED TO CHANGES IN MUSCLE MASS
  • INCLUDES DEFICITS IN MUSCLE QUALITY AND NEUROMUSCULAR CONTROL
MARKERS OF AGING: HEALTH FACTORS

• CHRONIC PAIN
  • HIGHLY PREVALENT IN OLDER ADULTS
    • AS HIGH AS 70% IN COMMUNITY DWELLING
    • AS HIGH AS 80% IN NURSING HOME RESIDENTS
  • KNEE PAIN IS THE MOST COMMON CHRONIC PAIN IN OLDER ADULTS
  • CONTRIBUTES TO FUNCTIONAL DECLINE AND ACTIVITY LIMITATION
  • ADVERSELY IMPACTS QUALITY OF LIFE
  • INCREASES MORBIDITY AND MORTALITY
MARKERS OF AGING: BEHAVIORAL FACTORS

• UNDER/OVER NUTRITION
  • DIET INDUCED OBESITY INCREASES WITH AGE
  • WE EAT MORE THAN WE NEED AND SO GAIN WEIGHT
    • AVERAGE CALORIE INTAKE HAS INCREASED BY 300 KCAL/DAY IN THE RECENT YEARS
    • INCREASES RISK FOR FUNCTIONAL DECLINE, MORBIDITY, AND MORTALITY
  • MORE FAT DEPOSITS IN MUSCLE EVEN WITH NORMAL WEIGHT IN OLDER ADULTS
  • VITAMIN DEFICIENCIES SEEN IN OLDER ADULTS WITH DECREASED DIETARY INTAKE
    • TEA AND TOAST DIET
    • HOSPITALIZED OR NURSING HOME PATIENTS WHO DO NOT EAT ENOUGH
MARKERS OF AGING: BEHAVIORAL FACTORS

• SEDENTARY LIFESTYLE
  • Daily energy expenditures in work-related physical activity has fallen more than 100 calories per day during the last 50 years.
  • Most adults in developed countries spend more than half their waking hours in sedentary activities.
  • Inactive lifestyle is less than 150 minutes of moderate intensity activity per week.
  • Sedentary lifestyle adds to the risks of numerous pathologic conditions.
MARKERS OF AGING: BEHAVIORAL FACTORS

• POOR SLEEP
  • SLEEP PROBLEMS ARE COMMONLY UNDERDIAGNOSED IN THE OLDER ADULT
  • POOR SLEEP IS ASSOCIATED WITH REDUCED PHYSICAL ACTIVITY
  • CHANGES IN SLEEP PATTERNS ARE NORMAL IN AGING
    • EARLIER BEDTIMES, EARLIER AWAKENINGS
  • ABNORMAL SLEEP PATTERNS ARE SEEN IN 15% OF OLDER ADULTS
  • DAY TIME NAPPING IS NORMAL, BUT CAN EFFECT QUALITY OF LIFE
  • LOWER RISK OF MORTALITY WHEN PEOPLE SLEEP 6-7 HOURS PER NIGHT
MARKERS OF AGING: BEHAVIORAL FACTORS

- ENVIRONMENTAL STRESS
  - THOSE HAVE BEEN EXTENSIVELY RESEARCHED
    - AIR POLLUTION
    - EXTREME TEMPERATURE FLUCTUATIONS
    - MOBILITY BARRIERS WITHIN LIVING ENVIRONMENTS
  - OLDER ADULTS HAVE COMPROMISED IMMUNE SYSTEMS
  - REGARDLESS OF RACE AND GENDER, OLDER ADULTS ARE MORE EFFECTED BY HEAT RELATED INJURIES
  - SOCIAL ENGINEERING OF COMMUNITIES TO INCREASE AVAILABLE WALKING PATHS IS CRUCIAL
MARKERS OF AGING: BEHAVIORAL FACTORS

• DEPRESSION
  • INCREASED RISK OF DEPRESSION AS WE AGE
  • LEADING CAUSE OF FUNCTIONAL DISABILITY WORLDWIDE.
  • INCREASED SEVERITY OF DEPRESSION LINKED TO INCREASE PHYSICAL DEBILITY
  • COMPLEX PSYCH-SOCIAL RELATIONSHIP BETWEEN DEPRESSION AND FUNCTIONAL ABILITY
  • DEPRESSION IS LINKED TO INCREASING MEDICAL ILLNESS AND COGNITIVE DECLINE
MARKERS OF AGING: BIOLOGICAL FACTORS

• CELLULAR DAMAGE
  • MITOCHONDRIA PLAY A ROLE IN CELLULAR ENERGY METABOLISM AND MAINTENANCE OF CELL FUNCTION
  • MOLECULAR DETAILS OF WHY MITOCHONDRIA REDUCE EFFICIENCY
    • IT IS THOUGHT THAT REACTIVE OXYGEN SPECIES PLAY A ROLE
  • AGING SHOWS A REDUCED EFFICIENCY OF CELL MAINTENANCE, REPAIR, AND TURNOVER
    • RESULTS IN ACCUMULATION OF LIPIDS AND DAMAGED CELL ORGANELLES
  • REDUCTION IN CELL ENERGY CAN LEAD TO MUSCLE LOSS AND SLOWED WALKING SPEED

![Diagram of mitochondrial dysfunction](image)
MARKERS OF AGING: BIOLOGICAL FACTORS

• INFLAMMATION
  • THERE IS A LOW LEVEL OF SERUM MARKERS OF INFLAMMATION C-REACTIVE PROTEIN, IL-6, IL-10, TNF-ALPHA (CALLED “INFAMM-AGING”)
    • ASSOCIATED WITH IMPAIRED MOTOR AND COGNITIVE FUNCTION THUS CONTRIBUTING TO FUNCTIONAL DECLINE
    • IL-6 IS AN INDEPENDENT RISK FACTOR FOR DISABILITY, IMPAIRED MOBILITY, AND SLOW WALKING SPEED

• HORMONAL FACTORS
  • AGING INFLUENCED BY HORMONAL CHANGES
    • TROPHIC HORMONES DECREASE (GONADAL STEROIDS, ESTROGEN, TESTOSTERONE)
    • INCREASES IN STRESS-RELATED HORMONES SUCH AS CORTISOL
      • CHRONICALLY HIGH LEVELS OF CORTISOL ARE NEUROTOXIC TO MUSCLE AND BRAIN
    • OXYTOCIN MAY ALSO PLAY A ROLE AGING NEURO DYSFUNCTION
MARKERS OF AGING: BIOLOGICAL FACTORS

• NEURODEGENERATION

• CEREBRAL NEURODEGENERATION
  • EVIDENCE INDICATES THAT AGE-RELATED LOSS OF FUNCTION IS STRONGLY LINKED TO
    DEGENERATION OF CEREBRAL STRUCTURE AND FUNCTION.
  • GRAY MATTER ATROPHY IS NEURONAL CELL BODIES ASSOCIATED WITH MOVEMENT
    DISORDERS
  • WHITE MATTER INCREASE IN INTENSITY IS DUE TO DEMYELINATION WHICH IS LINKED TO
    MOBILITY
  • CHRONIC PHYSICAL ACTIVITY IS NEUROPROTECTIVE AND MAY PREVENT OR SLOW THE
    PROCESS

• PERIPHERAL NEURODEGENERATION
  • MOTOR AND SENSORY NERVE DYSFUNCTION IS LINKED TO FUNCTIONAL DECLINE
  • DECLINE IN CONDUCTION VELOCITY EFFECTS MOBILITY
  • INCREASED APOPTOSIS IN MOTOR NEURONS OF TYPE II MUSCLE FIBERS LEADING TO
    FUNCTIONAL DISABILITY
DO GENETICS PLAY A ROLE IN AGING?

• Genetic models have shown changing 1 gene out of 20,000 genes can increase life span 10 times…in a worm, C. elegans, from 20 days to 200 days.

• Mouse models have shown some genes noted for increasing life span, but no translation to humans has been noted.

• Telomere shortening causing aging.

• Genetic research continues.
COMMUNITIES THAT AGE WELL

• GEORGIA CENTENARIAN STUDY
  • PERSONALITY TRAITS ARE ASSOCIATED WITH LONGER LIFE
    • EMOTIONAL STABILITY, AGREEABLENESS, AND CONSCIENTIOUSNESS ASSOCIATED WITH:
      • HIGHER LEVEL OF COGNITION
      • HIGHER LIKELIHOOD OF ENGAGING IN VOLUNTEER WORK
      • HIGHER LEVELS OF ADLS
      • HIGHER LEVELS OF SUBJECTIVE HEALTH
    • EXTRAVERSION AND OPENNESS TO EXPERIENCE ASSOCIATED WITH:
      • HIGHER COGNITION
      • ENGAGING IN VOLUNTEER WORK
  • NO SIGNIFICANT FINDINGS IN HEALTH DISTINCTIONS
INTERVENTIONS TO AGE SUCCESSFULLY

• NO FDA APPROVED MEDICATIONS FOR THE TREATMENT OF FUNCTIONAL DECLINE

• DIET
  • DIETARY RESTRICTION TO REDUCE WEIGHT AND AVOID OBESITY
  • PHYSICAL FUNCTION IMPROVES WITH WEIGHT LOSS BUT SARCOPENIA CAN ADVANCE
  • DIETARY RESTRICTION PLUS EXERCISE HOLDS MOST PROMISE
  • MEDITERRANEAN DIET HOLDS PROMISE (STILL NEEDS MORE LONG TERM RESEARCH)
    • NON-REFINED CEREALS, FRUITS, VEGETABLES, LEGUMES, OLIVE OIL, AND FISH
INTERVENTIONS TO AGE SUCCESSFULLY

• DIET – ANOTHER CURRENT POPULAR OPTION

• KETOGENIC DIET (KD)
  • KD RELATED TO IMPROVED MITOCHONDRIAL FUNCTION AND DECREASED OXIDATIVE STRESS.
  • SHOWN TO REDUCE THE PRODUCTION OF REACTIVE OXYGEN SPECIES (ROS).
  • STIMULATES THE CELLULAR ENDOGENOUS ANTIOXIDANT SYSTEM.

• ADVERSE SIDE EFFECTS
  • MOST COMMON ADVERSE EVENTS: GASTROINTESTINAL SYMPTOMS, VOMITING, CONSTIPATION, DIARRHEA, WEIGHT LOSS, AND HYPERLIPIDEMIA.
  • MAJOR ADVERSE EVENTS: DEHYDRATION, ELECTROLYTE ALTERATION, ARHYTHMIAS ARE UNCOMMON.
INTERVENTIONS TO AGE SUCCESSFULLY

• EXERCISE
  • PHYSICAL EXERCISE IS THE ONLY INTERVENTION DEMONSTRATED TO DECREASE FUNCTIONAL DECLINE AMONG OLDER ADULTS.
  • BENEFITS OF EXERCISE NOT SEEN IN ALL INDIVIDUALS.
  • CHANGE IN PERFORMANCE IS QUITE VARIABLE.
  • EXERCISE MAY BE NECESSARY BUT INSUFFICIENT FOR PRESERVING PHYSICAL FUNCTION AND PREVENTING DISABILITY.
INTERVENTIONS TO AGE SUCCESSFULLY

• COGNITIVE TRAINING
  • TYPICALLY INVOLVE COMPUTERIZED GAMES WHICH PROGRESSIVELY TRAIN A COGNITIVE TASK
    • WORKING MEMORY, ATTENTION, REACTION SPEED, FOCUS
  • THE ACTIVE STUDY (NIH FUNDED) SHOWED SIGNIFICANT IMPROVEMENT DRIVING PERFORMANCE
  • MANY OTHER COGNITIVE TRAINING MEASURES HAVE FAILED TO SHOW ANY EFFECT ON REAL WORLD TASKS (LUMINOSITY)
  • FUTURE STUDIES WILL NEED TO FOCUS ON HOME BASED COGNITIVE TRAINING USING GAMIFIED PLATFORMS
INTERVENTIONS TO AGE SUCCESSFULLY

• EXERGAMING – COMBINING SMART TECHNOLOGIES, EXERCISE, AND COGNITIVE STIMULATION
  • VIDEO GAMES WHICH ENGAGE THE GAMING INTERFACE THROUGH PHYSICAL ACTIVITY
  • EVIDENCE SHOWS OLDER ADULTS ARE GOOD AT ADHERING TO LONG TERM HOME BASED INTERVENTIONS IMPROVING HIGH LEVELS OF ENGAGEMENT
  • VIDEO GAMES WITHOUT EXERCISE SHOW IMPROVED EXECUTIVE FUNCTION AND ATTENTION
  • EXERGAMES FROM SEATED TASKS OF DEXTERITY AND HAND EYE COORDINATION TO FULL BODY ENGAGEMENT USING SENSORS/ACCELEROMETER IMPROVE BALANCE, WALK SPEED, MOOD, FITNESS, AND COGNITION
INTERVENTIONS TO AGE SUCCESSFULLY

• NON-INVASIVE BRAIN STIMULATION
  • INTERVENTIONS SPECIFICALLY AIMED TO MODULATE ACTIVITY TO ENHANCE BRAIN FUNCTION
  • DIRECT AND INDIRECT STIMULATION METHODS
    • TRANSCRANIAL DIRECT CURRENT STIMULATION (TDCS) APPLIES A WEAK ELECTRIC CURRENT ON THE SCALP
      • STIMULATES UNDERLYING CORTEXAL AND SUBCORTICAL BRAIN TISSUE
    • MAGNETIC TRANSCRANIAL STIMULATION (TMS) APPLIES MAGNETS ACROSS THE SCALP
      • LESS INVASIVE MANNER OF BRAIN NETWORK STIMULATION – STILL IN EXPERIMENTAL PHASE
    • GOAL IS TO STIMULATE NEURAL NETWORKS TO RECONNECT NEURAL PATHWAYS
INTERVENTIONS TO AGE SUCCESSFULLY

• PHARMACEUTICAL
  • NO FDA INDICATED TREATMENT FOR AGE RELATED SARCOPENIA, COGNITIVE DECLINE, FUNCTIONAL DECLINE
    • ACE INHIBITORS WERE THOUGHT TO HAVE BENEFITS ON FUNCTIONAL OUTCOMES BUT TRIALS HAVE NOT SHOWN THIS TO BE AN INDEPENDENT TREATMENT

• NUTRACEUTICALS
  • US SPEND OVER $12 BILLION ON SUPPLEMENTS YEARLY
    • RESVERATROL – A POLYPHENOL FOUND IN THE SKIN OF GRAPES AND RED WINE
      • FOUND IN SOME SPECIES TO EXTEND LIFE SPAN – NOT YET PROVEN IN HUMANS
    • NAD BOOSTERS – NEWEST CELLULAR ENERGY BOOSTING COMPOUND
      • INITIAL STUDIES IN MICE ARE UNDER WAY IN MICE – NO TESTING YET IN HUMANS
INTERVENTIONS TO AGE SUCCESSFULLY

- HORMONAL TREATMENTS
  - THERE ARE MULTIPLE APPROACHES THAT MAY LEAD TO IMPROVEMENTS IN PHYSICAL FUNCTION AND MOBILITY
    - TESTOSTERONE
    - ESTROGEN
    - DHEA
    - GROWTH HORMONE
    - OXYTOCIN
  - NO CONCLUSIVE EVIDENCE TO SUPPORT ONE APPROACH OVER ANOTHER
INTERVENTIONS TO AGE SUCCESSFULLY

• ADDITIONAL FINDINGS

• CAR USE AND SUCCESSFUL AGING
  • ONE STUDY SHOWED CONSISTENT ASSOCIATION BETWEEN CAR USE AND SUCCESSFUL AGING
    • CAR USE IS POSITIVELY RELATED WITH LEVELS OF SUCCESSFUL AGING
    • RELATED TO INDEPENDENCE, QUALITY OF LIFE, AND SOCIAL PARTICIPATION

• SOCIALIZATION AND SUCCESSFUL AGING
  • SIZE OF THE INDIVIDUAL’S SOCIAL NETWORK IS RELATED TO SUBJECTIVE WELL BEING AND POSITIVELY INFLUENCES SUCCESSFUL AGING
SUMMARY

• SUCCESSFUL AGING IS COMPLICATED
• MANY FACTORS EFFECT AGING AND THERE ARE MARKERS THAT CAN BE USED TO FOLLOW AGING
  • PHYSICAL FUNCTION
    • MOBILITY IS KEY
  • COGNITIVE FUNCTION
• GENETICS MAY PLAY A ROLE BUT STILL INVESTIGATING
• COMMUNITIES CAN BE ENGINEERED TO HELP PEOPLE AGE WELL
• INTERVENTIONS THAT HELP ARE EXERGAMING, INCREASING QUALITY OF LIFE, AND SOCIALIZATION
REFERENCES


THANK YOU