Biological Theories of Aging

Psychology of Aging

October 20, 2005
Biological Aging Defined

Aging is a complex biological process in which changes at molecular, cellular, and organ levels result in a progressive, inevitable, and inescapable decrease in the body's ability to respond appropriately to internal and/or external stressors.

Chodzko-Zajko & Ringel, 1987
## Myths About Aging – Physiological Aspects

<table>
<thead>
<tr>
<th>Myth</th>
<th>Best Available Evidence</th>
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<tr>
<td>Our physiological processes remain at a fairly constant level of</td>
<td>Most of our bodily functions reach their maximum capacity prior to or during early adulthood and begin a gradual decline thereafter.</td>
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<td>efficiency until we approach old age, at which time they undergo a</td>
<td>Age related physical changes do not occur according to a strict timetable. Adults age at different rates, and such groupings as “the elderly” are more heterogeneous than is commonly believed.</td>
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<td>drastic decline.</td>
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<td>Most adults proceed at much the same rate through a series of similar</td>
<td>Helplessness and dependency are not characteristic of old age. Some 87% of adults over 65 are able to cope more than adequately with the demands of everyday living.</td>
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<td>physical changes.</td>
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<td>Most adults past age 65 are so physically incapacitated that they</td>
<td>There are no drugs, pills, powders, vitamins, dietary supplements, or diets with PROVEN anti-aging capacities.</td>
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<td>must depend to a great extent on other people.</td>
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<td>Taking large doses of antioxidants (or ginseng, selenium, pantothenic</td>
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<td>acid or vitamin C) will extend the length of your life.</td>
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Theories of Aging have been around for more than 2000 years.

**Galen (A.D. 129 –c. 199)**
- Thought that aging was due to changes in body humors that began in early life
- These changes caused a slow increase in dryness and coldness of the body

**Roger Bacon (c. 1220-1292)**
- One of the first to suggest a “wear and tear” theory
- Aging is the result of abuses and insults to the body system
- Good hygiene might slow the aging process

**Charles Darwin (1809-1892)**
- Attributed aging to the loss of irritability in the nervous and muscular tissue
Overview of three types of modern biological theories of aging:

• Genetic Cellular theories
• Non genetic cellular theories
• Physiological System Theories
Genetic Cellular theories

Theories that attribute aging to an innate genetic program, much like a built in biological clock

Substantial evidence suggests that the life span of plants and animals is under genetic control. Mammals all seem to have relatively fixed life spans. At the same time, considerable diversity exists among different species. This marked species variability and specificity in longevity lend support to the notion of genetic control of life span.
Genetic Cellular theories

Findings that imply that cellular aging is programmed by our genes:

• Humans with long lived parents and grandparents live an average of 6 years longer than those whose parents die before the age of 50.

• Human body cells grown in tissue cultures are able to divide only about 50 times, after which they age and die.

• The reproductive capacity of cells taken from old animals is even more limited; these cells can undergo only about one half as many divisions as those obtained from young animals.
Genetic Cellular theories

- Because a direct relationship exists between the life span of a species and the capacity of its cells to divide, this suggests that age related changes are programmed into the genes of each species.
- Thus, Genetic Cellular theories attribute aging to changes in 2 kinds of molecules: deoxyribonucleic acid (DNA) and ribonucleic acid (RNA)
Genetic Cellular Theories

**DNA** – controls the formation of proteins required by the cell to maintain life.

**RNA** – transfers information from the DNA molecules to another location in the cell where proteins are assembled.
Genetic Cellular theories – DNA Damage Theory

- Damage to the DNA molecules is responsible for aging
- Caused by exposure to radiation or harmful cellular mutations
Important Contraindications:
- Mutations and radiation affect dividing cells, whereas the physiological effects of aging are due primarily to cells that are no longer able to divide. Mutations occur too slowly to account for the pronounced physiological changes that occur with increasing age.
- Damage to DNA molecules is usually reversible because most cells contain appropriate repair mechanisms.
Genetic Cellular Theories – Error Theory

• Errors in RNA transmission produce a protein or enzyme that is not an exact copy of the original, thus it cannot carry out its function in maintaining life. As a result, cells grow older and die, and so do we.

• Errors are likely because RNA molecules are relatively unstable and formed continuously, whereas DNA molecules are highly stable and maintained throughout the lifespan of a cell.

• Recent findings suggest possible relationships between somatic mutations and age related illnesses such as certain types of cancer.
Non Genetic Cellular Theories

AKA “Wear and Tear Theories”

- Attribute aging to progressive cell damage caused by the internal and external environment, rather than to an innate genetic program.
- With the passage of time, changes occur in the cells that impair their effectiveness. Thus, aging is due to progressive damage.
Non Genetic Cellular Theories
– Accumulation Theory

• Aging is caused by the accumulation of various harmful substances in the cells of an organism.
• Older cells contain a dark colored, insoluble substance called “Lipofuscin” – the amount of this material increases at a constant rate over time.
• This “Cellular Garbage” interferes with cellular functioning because it takes up space and serves no useful purpose. This may ultimately result in the death of the cell.
Non Genetic Cellular Theories – Cross Linkage Theory

• With age, our proteins, DNA and other structural molecules develop inappropriate attachments or cross-links to one another.
• These unnecessary links or bonds decrease the mobility or elasticity of proteins and other molecules.
• Proteins that are damaged or no longer needed are normally broken down by enzymes, but the presence of cross-linkages inhibits the activity of the enzymes.
• These damaged and unneeded proteins, therefore, stick around and can cause problems.
Non Genetic Cellular Theories – Cross Linkage Theory

- This model posits that cross-linkages ultimately lead to severe nutrient/oxygen deficiency and impaired waste removal.
- Cross-linking of the skin protein collagen has been shown to be at least partly responsible for wrinkling and other age-related changes in the skin.
- Cross-linking of proteins in the lens of the eye is believed to play a role in age-related cataract formation.
- Cross-linking of proteins in the walls of arteries or the filtering systems of the kidney account for at least some of the atherosclerosis and age-related decline in kidney function observed in older adults.
Non Genetic Cellular Theories – Cross Linkage Theory

- Cross-linking appears to occur when older immune systems are incapable of cleaning out excess glucose molecules in the blood.
- These sugar molecules react with proteins causing cross-links and the formation of destructive **free radicals**.
Non genetic Cellular Theories – Free Radical Theory

• This theory attributes aging to the operation of specific cross linking agents called “Free radicals”
• "Free radical" is a term used to describe any molecule that differs from conventional molecules in that it possesses a free electron, a property that makes it react with other molecules in highly volatile and destructive ways.
• In a conventional molecule the electrical charge is balanced. Electrons come in pairs so that their electrical energies cancel each other out. Atoms that are missing electrons combine with atoms that have extra electrons, creating a stable molecule with evenly paired electrons and a neutral electrical charge.
• The free radical, on the other hand, has an extra negative charge. This unbalanced electrical energy tends to make the free radical attach itself to other molecules as it tries to steal a matching electron to attain electrical equilibrium. In doing so they create free radicals and extensive bodily damage.
Non genetic Cellular Theories – Free Radical Theory

• Free radicals attack the structure of our cell membranes, creating metabolic waste products, including substances known as lipofuscins. An excess of lipofuscins in the body is shown as a darkening of the skin in certain areas, so-called "aging spots”.
• Lipofuscins in turn interfere with the cells ability to repair and reproduce themselves. They disturb DNA and RNA synthesis, interfere with synthesis of protein, lower our energy levels, prevent the body from building muscle mass and destroy cellular enzymes, which are needed for vital chemical processes.
• Free-radical damage begins at birth and continues until we die. In our youth its effects are relatively minor since the body has extensive repair and replacement mechanisms that function to keep cells and organs in working order. With age however, the accumulated effects of free-radical damage begin to take their toll. Free-radical disruption of cell metabolism is part of what ages our cells; it may also create mutant cells leading ultimately to cancer and death.
Another way of looking at free-radical changes is to think of it as oxidation, the process of adding oxygen to a substance. Another word for oxidation is rust and in a sense our aging process is analogous to the rusting away of a once-intact piece of metal.

Because forms of oxygen itself are free radicals, our very breathing and our otherwise healthy aerobic exercise generate free radicals that help along the aging process.

Free radicals form from environmental factors such as pollution, sunlight, strenuous exercise, X-rays, smoking and alcohol.
Non genetic Cellular Theories – Free Radical Theory

- Substances that prevent the harmful effects of oxidation are known as antioxidants. Natural antioxidants include vitamin C, vitamin E and beta carotene, the substance that our body uses to produce vitamin A.
Physiological System Theories

- Attributes aging to the **gradual failure of certain physiological systems** and to the resulting inability of these systems to coordinate important bodily functions.
- In order for the body to function properly, both **cellular functions and organ systems** have to be carefully integrated and coordinated.
- When one or more of the regulatory systems of the body breaks down, the organism eventually dies.
Physiological System Theories – Immunological Theory

Defines aging as a disease of the immune system

• The immune system protects us from invading microorganisms and atypical mutant cells that form within the body (i.e. cancer).

• Immune system acts in 2 ways: (1) by generating antibodies that react with the proteins of foreign organisms, (2) by forming cells that engulf and digest foreign cells

• The production of antibodies and the ability to recognize mutant cells peaks during adolescence and decreases over time
Physiological System Theories – Immunological Theories

- **Autoimmune Theory**: The body loses its ability to distinguish between foreign agents/antigens and necessary body cells. The immune system becomes self-destructive and reacts against itself.

- Examples of autoimmune disease are lupus, scleroderma and adult-onset diabetes.
Physiological System Theories – Neuroendocrine Theory

• Elaborates on the wear and tear theory by focusing on the **neuroendocrine system**: a complicated network of biochemicals that governs the release of our hormones and other vital bodily elements.

• When we are young, our **hormones work together to regulate** many bodily functions, including our responses to heat and cold, stress and sexual activity. As well, it controls our metabolic rate, glucose secretion and water levels.

• Different organs release various hormones all under the governance of the **hypothalamus**
Physiological System Theories – Neuroendocrine Theory

- When we're young, hormone levels tend to be high, accounting for (among other things), menstruation in women and high libido in both sexes. As we age, the body produces lower levels of hormones which can have disastrous effects on our functioning.
- For instance, growth hormones and testosterone that help us form muscle mass drop dramatically as we age, so that even if an elderly person has not gained weight, he or she has undoubtedly increased the ratio of fat-to-muscle.
Physiological System Theories – Neuroendocrine Theory

- Hormones are vital for repairing and regulating our bodily functions, and when aging causes a drop in hormone production, it can cause a \textbf{decline in our body's ability to repair and regulate itself.}

- For example, \textbf{type 2 diabetics} have low insulin levels due to decreased secretion by the pancreas. They rely on an exogenous supply of insulin in order to maintain optimal levels of blood sugar.

- Hormone production is highly interactive. The drop in production of any one hormone is likely to have a feedback effect on the whole mechanism, signaling other organs to release lower levels of other hormones which will cause other body parts to release lower levels of yet other hormones.
Physiological System Theories – Neuroendocrine Theory

• The functioning of the hypothalimus and pituitary gland (i.e. the hypothalimus-pituitary axis) has been the focus of much research since it is responsible for the regulation of the thyroid, adrenal gland, and the release of sex hormones (i.e. estrogen and testosterone).

• After menopause, when estrogen levels decline, biological aging appears to accelerate in women, and estrogen replacement therapy seems to slow down this process.

• Hormone replacement therapy, a frequent component of many anti-aging treatments, helps to reset the body's hormonal clock and so can reverse or delay the effects of aging.
• Some researchers speculate that our “biological clock” resides in the hypothalamus and controls the rate of aging.
Lengthening Life – Restricted Diets

• Eating fewer calories while maintaining a nutritionally sound diet – which is not discontinued when the dieter achieves his/her ideal.

• The preponderance of research evidence does support this hypothesis:

• **Rats:** fed nutritionally adequate restricted (2/3 the amount of what they would normally eat) have longer maximum and average life span than controls.

• **Monkeys:** reduced caloric intake by 30% lowers body temperature (thought to be due to lowered metabolic rate). In turn, it is thought that this enhances longevity as a result of its impact on various cellular processes such as DNA damage and repair, and the development of certain tumors.
Lengthening Life – Restricted Diets

- **Humans**: critical experiments have not yet been conducted
- **Interesting note re: humans** –
  The heaviest and thinnest of a given cohort have the shortest longevity, and those slightly above their ideal body weight live the longest.
Life Lengthening Behaviours

• Psychological and social factors are important determinants of human longevity (ex. personality, marital status, social relationships, depression etc.)

• Empirical evidence indicates that your chances of remaining healthy and living longer depend to a considerable extent on your own behaviour.