Deep Science Publishing
https://doi.org/10.70593/978-93-49910-64-5_6

Chapter 6: Aging's impact: Physical, mental, and emotional changes over time

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Abstract

Aging leads to widespread effects across biological, physiological, and cognitive systems, resulting in a gradual decline in overall function and resilience. At the cellular level, aging is marked by increased DNA damage, mitochondrial dysfunction, and impaired proteostasis, contributing to reduced regenerative capacity. Physiologically, aging affects almost every organ system, leading to decreased cardiovascular efficiency, weakened immune responses, slower metabolism, and reduced bone density. Cognitive functions, including memory, learning, and processing speed, also tend to decline with age. These changes increase susceptibility to chronic diseases such as cancer, diabetes, neurodegenerative disorders, and cardiovascular disease. Understanding the effects of aging is critical for developing strategies to enhance healthspan, maintain functional independence, and improve quality of life in older populations.

Keywords: Aging consequences, Cardiovascular Aging, Chronic Diseases, Physiological Decline, Cellular Dysfunction, Memory Loss, Musculoskeletal neural degeneration, Quality of Life

6.1. Introduction

Aging is a natural and inevitable biological process that affects every living organism. As individuals grow older, their bodies undergo a wide range of physical, physiological, and cognitive changes that reflect the gradual decline in cellular function and systemic efficiency.

These changes—commonly referred to as the effects of ageing—manifest at multiple levels, including the molecular, cellular, organ, and behavioral levels. The effects of ageing are not uniform and can vary greatly depending on genetic factors, lifestyle choices, environmental influences, and healthcare access.

While some changes are benign or even positive, such as accumulated wisdom and emotional resilience, others contribute to an increased vulnerability to disease, reduced physical performance, and diminished quality of life. Understanding the diverse effects of ageing is essential for promoting healthy aging, improving elder care, and developing interventions that can enhance longevity and well-being in later life.

6.2. At organ system level effects

Due to the fast growth in the ageing population globally, researchers are interested in identifying treatments that would delay the physiological, metabolic, and functional decrease in various systems, organs, and tissues of the body as they age.

Ageing is a complex process and decline in function of organ specific nature is necessary to analyze in this process. Organs are believed to have a certain ability to withstand perturbations and return to homeostasis which is known as "organ reserve." This reserve turns down with age and can explain some functional deterioration in the elders like decrease in strength, balance and cognition. In fact, it has been noted that reserve capacity in a healthy young adult is 7 to 11 times greater than the average demand, but, as age reaches to 85, organ reserve has been diminished to 50% of its original capacity. Ageing affect different organs of the body and change their functions in different ways.

6.2.1. Effects on heart

As people age, there is a small enlargement in heart size developing thicker walls and slightly larger chambers. The increase in size is basically due to an increase in the size of individual heart muscle cells. The age-related stiffening of the heart walls causes the left ventricle to remain empty and can sometimes lead to heart failure called diastolic heart failure, mainly in old age people with other diseases such as high blood pressure, obesity and diabetes.

During ageing, the elasticity of arteries and arterioles decreases, hence they cannot relax as quickly during the rhythmic pumping of the heart. Due to this there is an increase in blood pressure when the heart contracts (during systole) sometimes above normal than it do in younger people. Abnormally high systolic blood pressure is very common among older people and causes a disorder called isolated systolic hypertension (Howlett, 2010).

Many of the effects of ageing on the heart and blood vessels can be reduced by regular exercise. Exercise helps people maintain cardiovascular fitness as well as muscular fitness as they age.

According to Howlett (2010), during exercise, ageing has important effects on cardiovascular performance. With age, there will be a reduction in aerobic capacity in individuals with no evidence of cardiovascular disease is attributable in part to peripheral factors, like reduced muscle mass, increased body fat, and a decline in O_2 extraction with age (Figure 6.1).

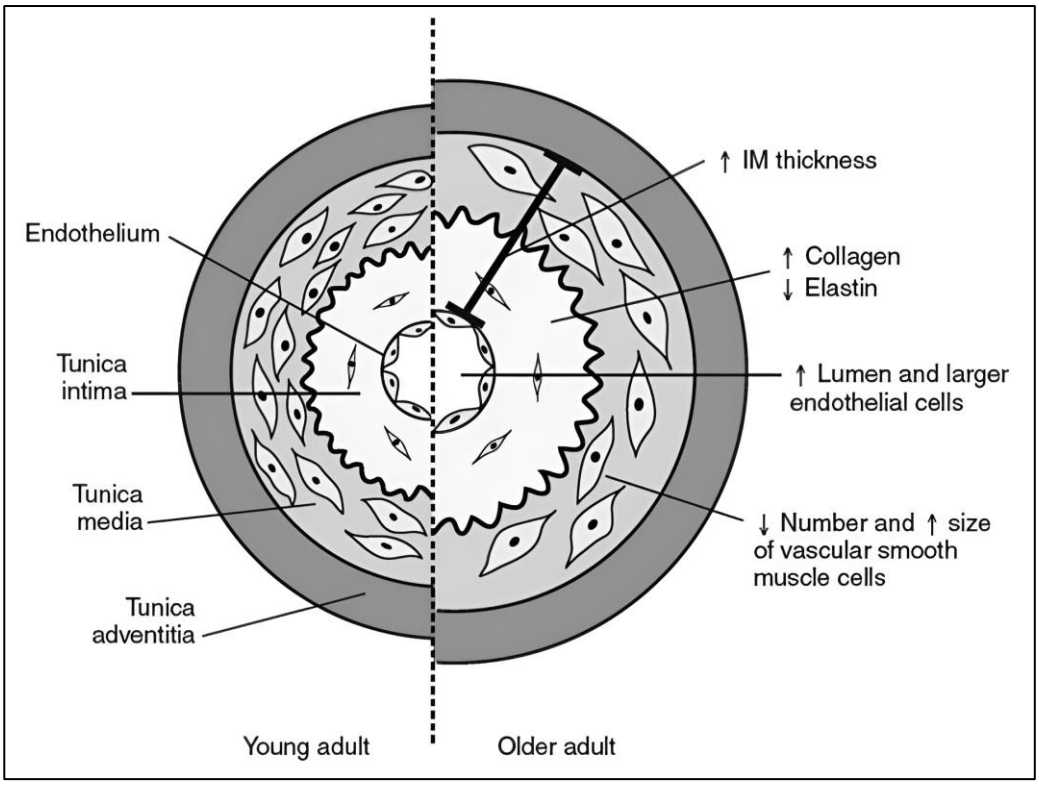

Figure 6.1. Remodeling of the central elastic arteries with age.

The layers of the arterial wall are labeled as indicated. There are significant changes in central elastic arteries as a consequence of the ageing process. As ageing proceeds, there is an increase in the lumen diameter. Elastin decreases and collagen deposition elevation are responsible for intimal remodeling in ageing arteries. In the tunica media, number of vascular smooth muscle cells decreases, while rest of the cells hypertrophy.

In ageing, arterial stiffness increase due to the increased content and cross-linking of collagen. Other factors such as elastin content reduction, fragmentation of elastin, and increased elastase activity also are factors which increase stiffness in ageing arteries. Changes in the endothelial regulation of vascular smooth muscle tone

and changes in other aspects of the arterial wall and vascular function also may add on to the increase in arterial stiffness with ageing.

6.2.2. Effect on sense organs

As people age, there will changes occurring in sense organs too. The following symptoms occurring in eyes are stiffening, denser, yellow colored lens. Less fluid is produced by the eyes, making them feel dry. This change occurs because the number of cells that produce fluids to lubricate the eyes decreases. Tear production may decrease.

Older people might visualize more tiny black specks moving across their field of vision called as floaters. They are bits of normal fluid in the eye that have solidified. The appearance of the eyes changes in several ways: The sclera of the eyes may turn slightly yellow or brown. A gray-white ring (arcus senilis) may appear on the surface of the eye which is made of calcium and cholesterol salts. It does not affect vision. The lower eyelid may hang away from the eyeball because the muscles around the eye weaken and the tendons stretch. This condition called ectropion may make the eyes dry (Besdine, 2019).

Due to ageing, hearing high-pitched sounds becomes very difficult and may result in hearing loss or presbycusis. Even when other people speak more loudly, older people still have difficulty understanding the words (NIH, 2018). As people age, there will decrease in sensitivity of taste buds on the tongue. This change affects tasting sweet and salt more than bitter and sour. The ability to smell reduces because the nose lining becomes thinner and drier and the nerve endings in the nose deteriorate. However, the change is slight, usually only subtle smells are affected. Because of these changes, many foods tend to taste bitter, and foods with subtle smells may taste bland.

The mouth tends to feel dry more often, partly because less saliva is produced. Dry mouth further reduces the ability to taste food. The gums recede slightly as people age. As a result, the lower parts of the teeth are exposed to food particles and bacteria. The tooth enamel also has a tendancy to wear away. These changes and a dry mouth make the teeth more susceptible to decay and cavities (caries) and most likely tooth loss occurs (Besdine, 2019).

Major observable changes during ageing are changes on skin. The skin becomes thinner, less elastic, drier, and finely wrinkled. However, exposures to sunlight over the years greatly contribute to wrinkling and make the skin rough and blotchy. The skin tearing occurs during ageing as they produce less collagen and elastin. The fat layer under the skin thins. This layer acts as a cushion for the skin which support and protect it. The fat layer also helps conserve body heat. When the

layer thins, wrinkles are more likely to develop, and tolerance for cold decreases. The number of nerve endings in the skin decreases. As a result, people become less sensitive to pain, temperature, and pressure, and injuries may be more likely.

There will be a decrease in the number of sweat glands and blood vessels and blood flow in the deep layers of the skin also decreases. Consequently, the body is less able to move heat from inside the body through blood vessels to the surface of the body. Hence, there is an increased risk of heat-related disorders, such as heatstroke. Also, when blood flow is decreased, the skin tends to heal more slowly.

6.2.3. Effect on brain

The number of nerve cells in the brain typically decreases. However, the brain can partly compensate for this loss in several ways: As cells are lost, new connections are made between the remaining nerve cells. The brain will have more cells than it needs to do most of the activities—an attribute called redundancy. Major changes take place in the quantity of the chemical substances involved in sending messages to the brain. Nerve cells might ay lose some of their receptors for messages and blood flow to the brain decreases subsequently. Because of these age-related changes, the normal functioning of brain gets affected. According to Besdine (2019), older people may react and do tasks somewhat more slowly, but given time, they do these things accurately. Some voluntary actions may get reduced especially after the age of 70. After about age 60, the number of cells in the spinal cord begins to decrease. Usually, this change does not affect strength or sensation.

6.2.4. Effect of ageing on digestive system

Overall, the digestive system is less affected by ageing than most other parts of the body. The muscles of the esophagus contract less forcefully, but movement of food through the esophagus is not affected. Food emptying from stomach is a little bit slow and it cannot hold as much food because it is less elastic. But in most people, these changes are too slight to be noticed.

Certain changes cause problems in some people. The digestive tract may produce less lactase, and hence, older people are more likely to develop intolerance of dairy products like lactose intolerance. People with lactose intolerance may feel bloated or have gas or diarrhea after they consume milk or milk products. In the large intestine, materials move through a little more slowly. In some people, this slowing contributes to constipation (Besdine, 2019).

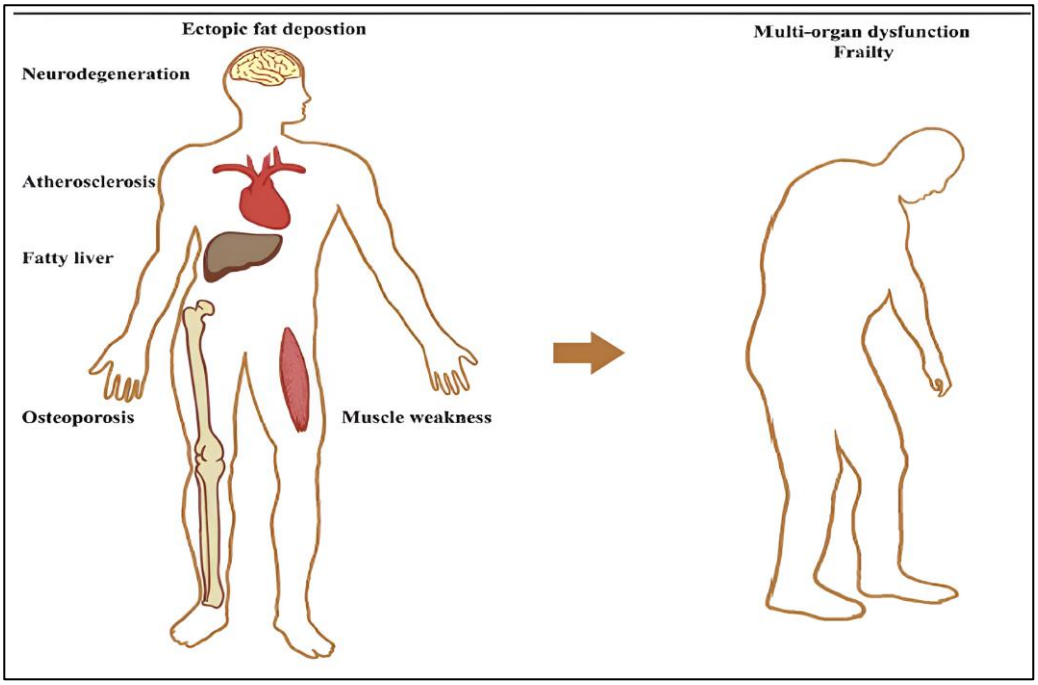

Figure 6.2 Ectopic fat depositions during ageing in human.

6.3. Tissue level

Even though numerous studies have been done in the relation between ageing and effect on organs and cells, meager studies have explored the connection of tissues with ageing phenomena. Yu et al. (2019) reviewed relationship between adipose tissue and ageing and found that the decreased expression of adipokines such as PPARg and CCAAT/enhancer-binding protein-a with ageing occurs at different rates in different depots, with particularly affected being the subcutaneous depots. A rise in the proinflammatory factors with ageing are troublesome to insulin receptor signaling in adipocytes and are associated with development of diabetes and other metabolic diseases (Gregor and Hotamisligil, 2011). There is a condition called as ectopic fat deposition during ageing as shown in Figure 6.2.

Based on various studies, several strategies have been proposed and or practiced to improve life quality and extend health span with interventions of adipose tissue. Restriction in an increase in calories has been extensively promoted as a noninvasive way to reduce weight, control diabetes, improve health, and increase longevity in both animals as well as humans (Ciobanu et al. 2017). Another study by Allyson and Kirkland (2016) explained the adipose tissue dysfunction with ageing and ectopic fat deposition and inflammation as shown/given in figure 6.3 and table 6.1.

Table 6.1 Effects of aging on different systems.

System Affected	Effect of Aging
Cellular/Molecular	DNA damage, telomere shortening, senescence
Musculoskeletal	Muscle loss, bone weakening, joint stiffness
Nervous System	Cognitive decline, memory loss
Cardiovascular	Stiffer arteries, higher BP, heart risk
Endocrine/Metabolic	Hormone changes, slower metabolism
Immune System	Weakened response, increased infection risk
Psychosocial	Mood changes, social isolation, life adjustment

Another review by Wang and Wu (2019) summarized the recent findings and potential mechanisms of the modulating effect of dietary supplementation and topical application of different classes of fatty acids and sterols on skin ageing. The mechanism is represented in figure 6.3 and 6.4.

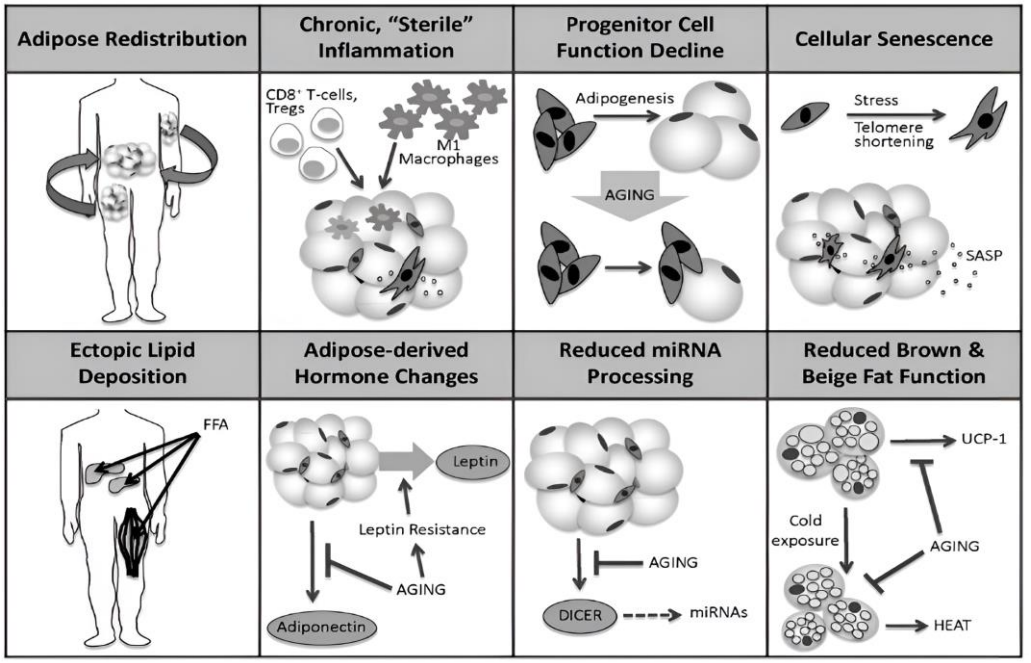

Figure 6.3 Adipose tissue dysfunction and ectopic fat deposition, inflammation during with ageing in human.

Glaucoma, a very common and chronic neurodegenerative disorder caused due to tissue stiffening was observed in aged people and Liu et al. (2018) studied the molecular and cellular events associated with it. The review by Liu et al. (2018) underlined the role of age-related ocular stiffening in the trabecular meshwork, lamina

cribrosa, retina, sclera, cornea, and Bruch membrane and conferred their potential role in glaucoma progression. An improved understanding of the interplay between age-related tissue stiffening and biological responses in the trabecular meshwork and optic nerve head could potentially lead to the novel therapeutic strategies for treatment of glaucoma and thereby relate it to ageing process.

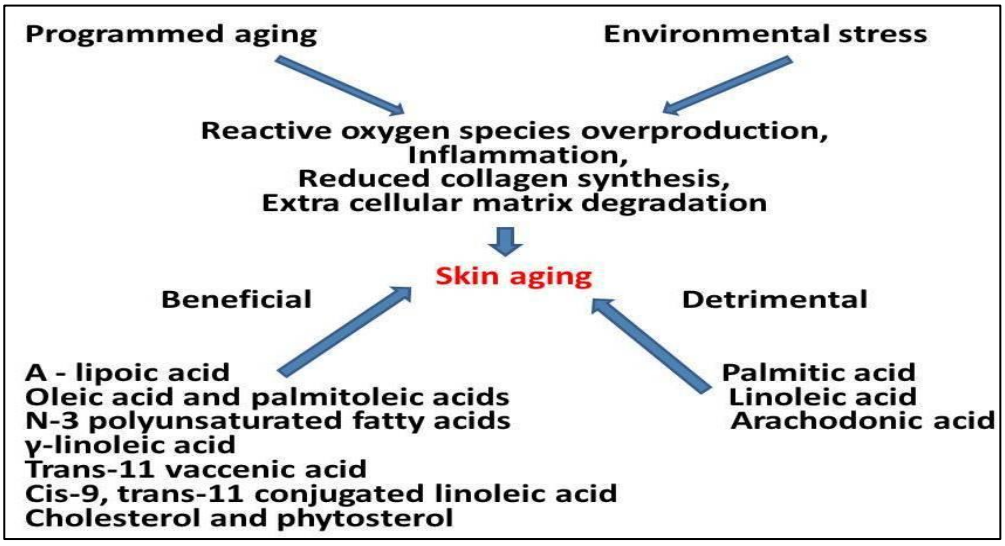

Figure 6.4 Skin ageing process as a function of dietary supplementation and topical application of different classes of fatty acids and sterols in human.

6.4. Effects of ageing at cellular level

Elevated levels of reactive oxygen species and enhanced mitophagy are associated with ageing at cellular level (Richter et al., 1988). Ageing initiates a set of cascade reactions involved in various cell biological activities (DiLoreto and Murphy, 2015).

Regulation of cellular health is managed at diverse points inside the cell starting from chromosomal integration within nucleus, regulation of RNA and protein synthesis, autophagic recycling of cell organelles, cytoskeleton integrity, regulation of cell signaling and upholding extracellular matrix. Each controlling system collects signal from every other system, ensuing in complex regulatory pathway of cellular ageing. Replicative senescence, affecting the chromosomal integrity within nucleus, is one of the most common causes of natural senescence, which is a consequence of telomere shortening after each cycle of DNA duplication (Richer and von Zglinicki, 2007). Stretch of telomere is linked with lifespan of the species in various studies e.g. Zebra fish has short telomeres and thus has a short lifespan and so are mice (Heidinger

et al., 2012; Vera et al., 2012) and long telomeres in some long lived organisms to long lifespan (Heidinger et al., 2012).

Telomere shortening is also involved in many age associated complications such as low level of innate immunity (Effros and Pawlec, 1997; Effros et al., 2005) and also associated with Alzheimer's disease (Panossian et al., 2003). At cellular level, proteins such as Sirtuins (*e.g*. SIR3 and SIR4) are reported to be linked with nuclear integration in Baker's yeast (Kaeberlein *et al*., 1999). In aged worms, nuclear shape disintegrates (Haithcock et al., 2005) while it is decelerated in insulin/ Insulin growth like factor IIS mutants (Signaling mutants) (Haithcock et al., 2005). Premature ageing is also observed with disorganization of lamin proteins at nuclear membrane (Broers *et al*., 2006). Progressive damage to nucleoporins i.e. proteins of Nuclear pore complex (NPC), further contributes in cellular ageing (D' Angelo et al., 2009).

Regulatory pathways which are involved in gene expression during stress and nutrient availability play major role in cellular senescence (Kaeberlein and Shamieh, 2010). Genes involved in cellular processes of longevity are controlled via highly conserved signaling pathways at transcriptional level (Kenyon, 2010).

Autophagic recycling of cell organelles is one among various crucial steps in maintaining cellular health (Kilonsky and Emr, 2000). It involves macroautophagy (cell organelles are trapped in double membrane and sent to lysosome for digestion, Cesen et al., 2012), macroautophagy (cytosol is directed towards lysosome in large amount (Massey et al., 2006) and chaperon-mediated autophagy (Specific proteins are trafficked to lysosome, Cuervo *et al*., 2005; Massey et al., 2006; Mizushima et al., 2008). Inhibition of autophagy results in accelerated cellular ageing (Cuervo et al., 2005; Rubinsztein et al., 2011). In *C. elegans* daf-2 mutant mitophagy and mitochondrial biogenesis is extended with age (Pinkston-Gosse and Kenyon, 2007). Cellular ageing also attributes cytoskeleton disruption (Gourlay and Ayscough, 2005). The actin filament e.g. SM22 which is a cross linking protein (Prinjha et al., 1994) is reported as biomarker of ageing in various organisms including *Saccharomyces cerevisiae* , *Drosophila melanogaster* and *Homo sapiens* (Prinjha et al., 1994; Camoretti-Mercado et al., 1998).

Regulation of Extracellular matrix (ECM) is significant in many aspects including cellular health (Kulms et al., 2002). Irregular ECM due to disruption or stress

leads to abrupt cellular shape and integrity (Kulms et al., 2002; vetterkind et al., 2005). For example, expression of collagen is declined in aged *C. elegance* (Tullet et al., 2008; Ewald et al., 2015), Glycosylation and proteomic damage occurs in ECM proteins in ageing humans (Brownlee, 1995; Kristic et al., 2014). Understanding effects of such cellular processes during senescence will also provide insight into many neurodegenerative disorders like Alzheimer's disease (Keck et al., 2003) and Parkinson's disease (Alvarez-Erviti et al., 2010) and help in prolonged quality of life of people at high risk of these neurodegenerative diseases (Devi and Anandatheerthavarada, 2010).

Conclusion

The effects of ageing are broad and multifaceted, influencing nearly every system of the body as well as psychological and social well-being. From cellular changes like DNA damage and telomere shortening to functional declines in the cardiovascular, immune, and nervous systems, ageing brings about a gradual reduction in the body's ability to maintain homeostasis, respond to stress, and repair itself. While some age-related changes are inevitable, many can be managed or delayed through healthy lifestyle choices, medical interventions, and social support. Understanding these effects is key not only to improving individual quality of life but also to addressing the challenges of an ageing population at the societal level. In conclusion, ageing is a natural part of life, but with the right knowledge, care, and attention, it is possible to age healthily and gracefully, maintaining dignity, independence, and well-being throughout the later years.

Author Contributions: "Conceptualization, methodology, software, validation, formal analysis, investigation, resources, writing—original draft preparation, and editing: SM and SVM. The authors have read and agreed to the published version of the manuscript.

Funding: SVM deeply acknowledges the support and encouragement and necessary facilities provided by Dr. Asha Rajiv, Director, School of Sciences, Jain (Deemed-to-be) University, JC Road, Bangalore, Karnataka. We acknowledge the funding provided by School of Sciences, Jain (Deemed-to-be) University, Bangalore, Karnataka under the seed money project scheme (Ref: JU/MRP/SOS/19/2022). "The APC was not funded by anyone"

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: All data are published in this article. The authros declare that this manuscript is an original work, prepared with the consent and contribution of all listed authors. It has not been submitted to, nor published in, any other journal or platform. All figures and

tables are drawn using appropriate Creative Commons platforms with proper attribution. We as authors declare that there are no conflicts of interest related to this work.

Acknowledgments: SM acknowledges and expresses gratitute to the Management, administration and Academic officials of MUIT, Noida Campus for their valuable support during preperation, and submission of the manuscript.

Conflicts of Interest: “The authors declare no conflict of interest.” “The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript, or in the decision to publish the results”.

Citation: Mathur S, Menon SV (2025) Aging’s impact: Physical, mental, and emotional changes over time. *In*: Paital B (ed) *Defy the Clock with Slow Aging*, 1st edn. Deep Science Publishing, USA, pp. 44-54, https://doi.org/10.70593/978-93-49910-64-5_6