Exercise Counters the Age-Related Accumulation of Senescent Cells

Group A1

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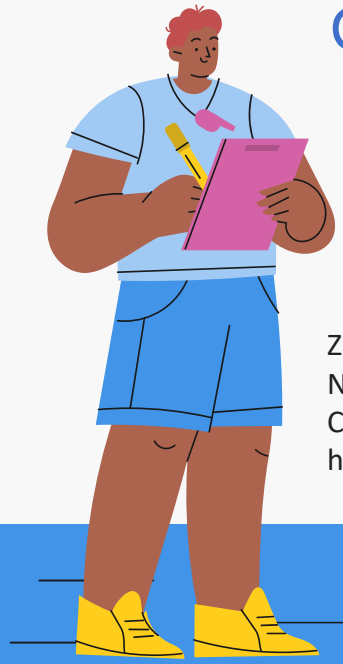
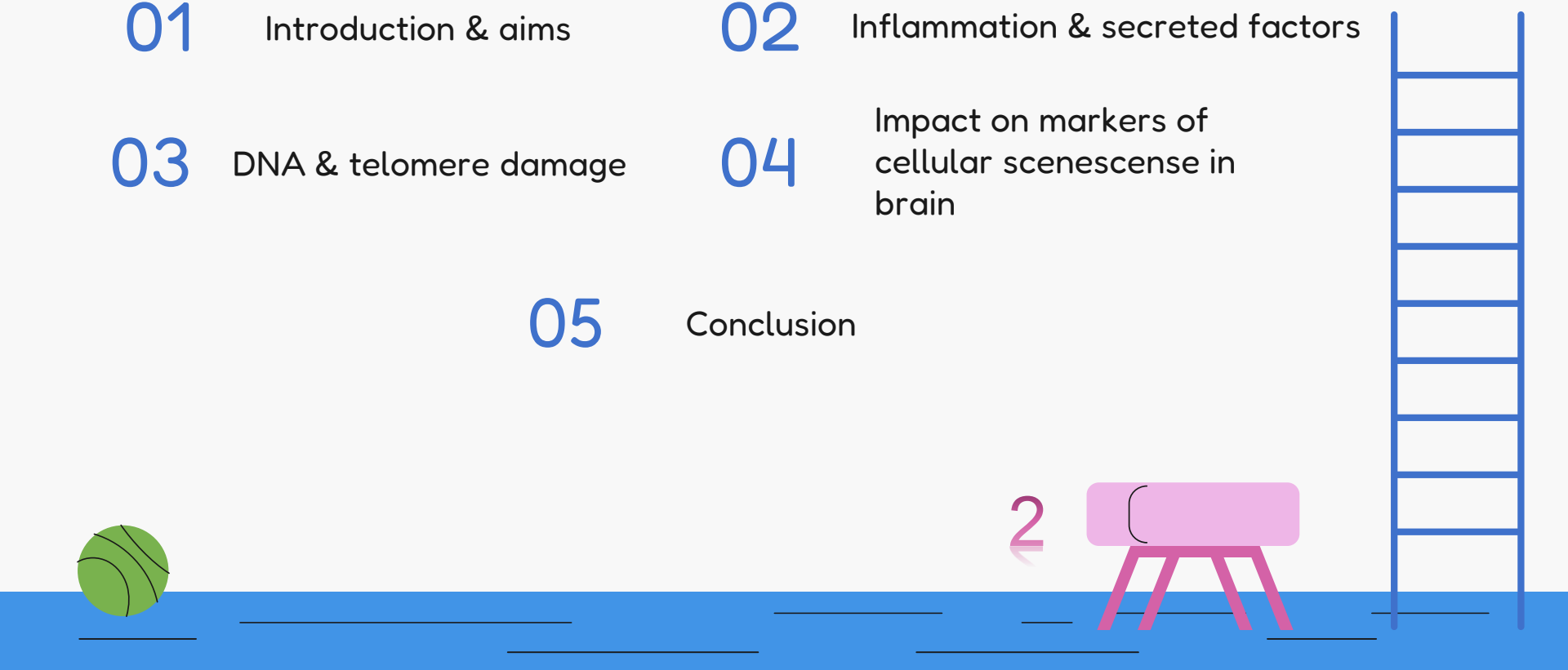


Table of contents



01

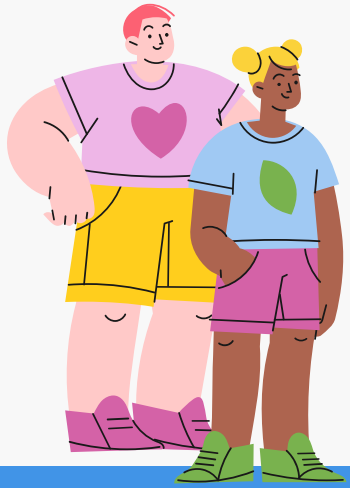
Introduction..

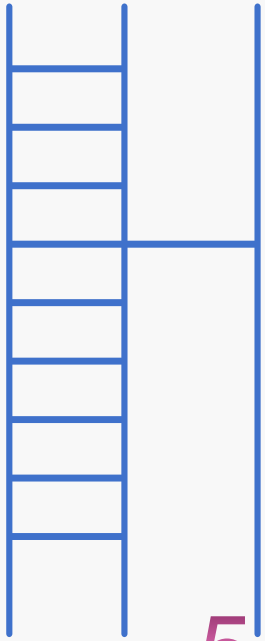
Introduction

Aging is a major risk factor for various diseases, but targeting it to prevent chronic diseases has been seen as science fiction. Advances in understanding aging biology and preclinical models have led to the geroscience hypothesis, which suggests interventions targeting key aging hallmarks could prevent, delay, or reverse age-related conditions. This could have transformative impacts on human health, extending health spans and reducing morbidity. Exercise is a highly effective means to counter aging-related conditions like heart disease, diabetes, Alzheimer's, osteoporosis, sarcopenia, cancer, and frailty. Recent evidence highlights cellular senescence as a driver of aging and aging-related conditions.

Aim

This overview underscores the accumulating evidence suggesting that **exercise acts as therapeutic mechanisms** for aging.

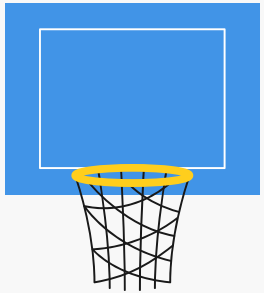




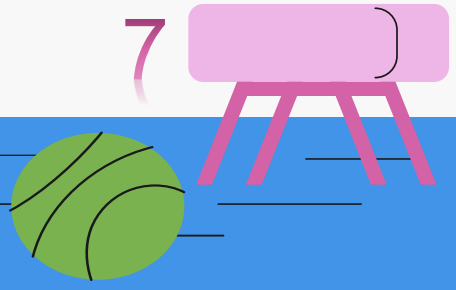
02

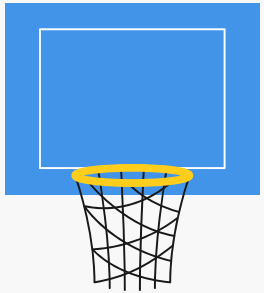
Inflammation and Secreted Factors

Method

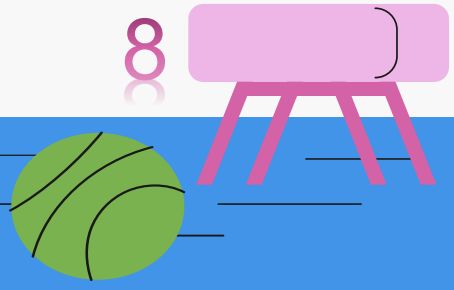


The study aimed to investigate the impact of exercise on inflammation and secreted factors, focusing on both animal models and human subjects. In the animal model, middle-aged high-fat diet (HFD)-fed mice underwent voluntary wheel running for 4 months, while in humans, older adults with an average age of 67 years participated in 3 months of progressive strength and endurance training.





Various techniques were employed to assess inflammation and secreted factors, including gene expression analysis of proinflammatory markers and components of the cGAS-STING pathway in adipose tissue and circulating CD3+ T cells. Additionally, the study evaluated the expression of anti-inflammatory mediators and neurotrophic factors.



Results

In the animal model, voluntary wheel running for 4 months resulted in a significant reduction in the expression of proinflammatory SASP factors, including IL-6, CCL2, and PAI1, in adipose tissue of middle-aged HFD-fed mice. In older adults undergoing 3 months of progressive strength and endurance training, there was a notable decrease in the expression of components of the cGAS-STING pathway in circulating CD3+ T cells.

These findings were consistent with data from several cross-sectional studies in humans, demonstrating an inverse relationship between markers of inflammation and physical activity levels and fitness.

Discussion

Advancing age is often associated with chronic low-grade inflammation, which contributes to various age-related pathologies. Senescent cells, through their SASP, are implicated as significant contributors to age-associated inflammation, both locally and systemically. Interestingly, exercise has been shown to exert a suppressive effect on sterile inflammation despite initially triggering an acute and transient inflammatory response. This suppression is evidenced by the reduction in basal levels of recognized proinflammatory SASP factors post-exercise intervention.

Moreover, exercise-induced transient elevations in IL-6 may stimulate the expression of anti-inflammatory mediators while downregulating the expression of proinflammatory cytokines, such as TNFα and IL-1β. Additionally, exercise promotes the activation and secretion of brain-derived neurotrophic factor (BDNF) from skeletal muscle, which in turn facilitates DNA repair mechanisms, potentially counteracting senescence-inducing stimuli.

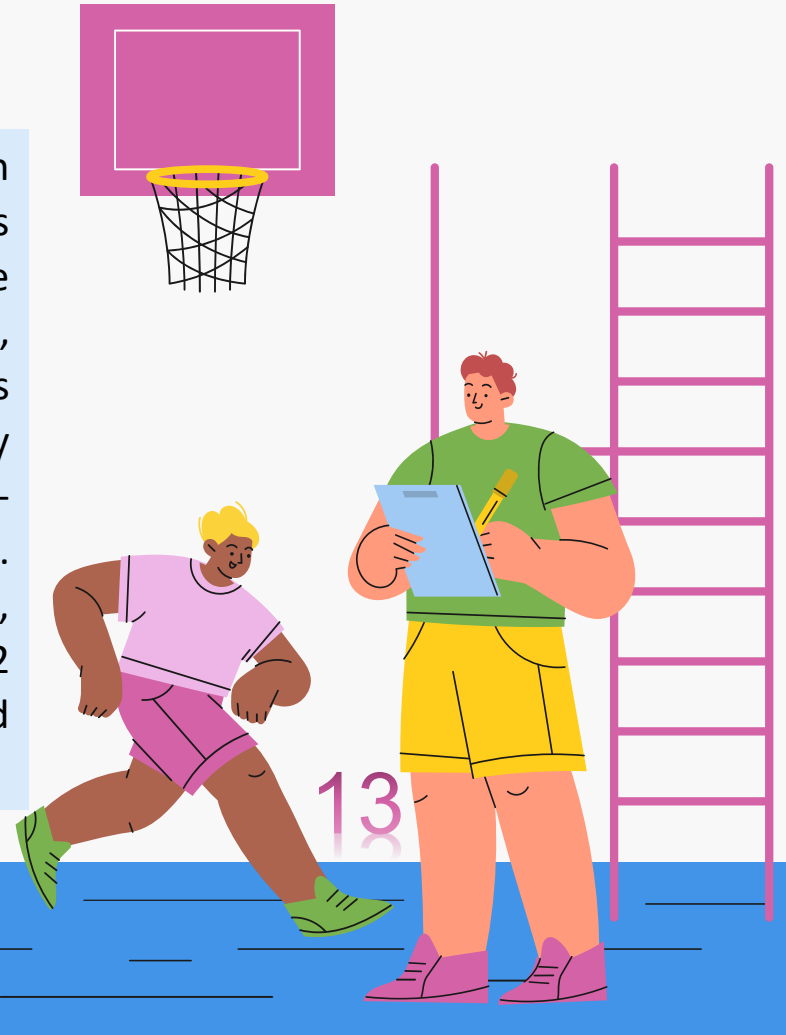
In summary, exercise appears to function as a senomorphic, targeting the SASP and mitigating its detrimental effects on inflammatory processes associated with aging. Furthermore, the acute cellular stress response induced by exercise may confer resilience to future senescence-inducing stimuli, suggesting a hormetic effect. These findings underscore the importance of exercise as a potential intervention to attenuate age-related inflammation and promote healthy aging.

02

DNA and Telomere Damage

Methods

The study investigated the impact of physical activity on DNA damage and telomere length in both animal models and humans. In the animal model, 30-month-old rats were subjected to 8 weeks of treadmill running, while in humans, approximately 100 healthy individuals aged 50–72 years were assessed. For DNA damage assessment, the study utilized techniques such as the measurement of 8-hydroxy-2'-deoxyguanosine (8-OHdG) content and the comet assay. Telomere length was evaluated using various methods, including telomere repeat-binding factor 1 (TRF1) and TRF2 expression analysis, telomerase activity measurement, and assessment of telomere length in different cell types.



Results

1) In the animal model, treadmill running for 8 weeks attenuated the age-associated increase in DNA damage within skeletal muscle, attributed to enhanced DNA repair and resistance to oxidative stress.
2) In humans, while no association was found between self-reported physical activity and DNA damage measured via the comet assay.
3) There was a positive correlation between physical activity levels (including high-intensity activity) and DNA repair in lymphocytes.

Results

4) Moderate- to high-intensity activities were associated with a trend for higher DNA repair.
5) Regarding telomere length, findings were inconsistent across studies.
6) In younger mice, voluntary wheel running did not affect telomere length in the aorta, but it increased the expression of protective factors like TRF1, TRF2, and Ku70.

Results

7) Additionally, exercised mice showed higher telomerase activity in various tissues compared to sedentary controls.

8) Professional long-distance runners, both young and middle aged, exhibited higher telomerase activity and TRF2 protein abundance compared to untrained peers.

Discussion

1) The results suggest that exercise may mitigate DNA damage and enhance DNA repair mechanisms, particularly in skeletal muscle.

2) The effects of exercise on telomere length are less clear, with inconsistencies observed in different studies.

3) Factors such as study design, duration, and tissue types analyzed could contribute to these discrepancies.

4) Exercise appears to bolster the resilience of DNA and telomeres against damage-inducing stimuli and may help prevent the accumulation of senescent cells.

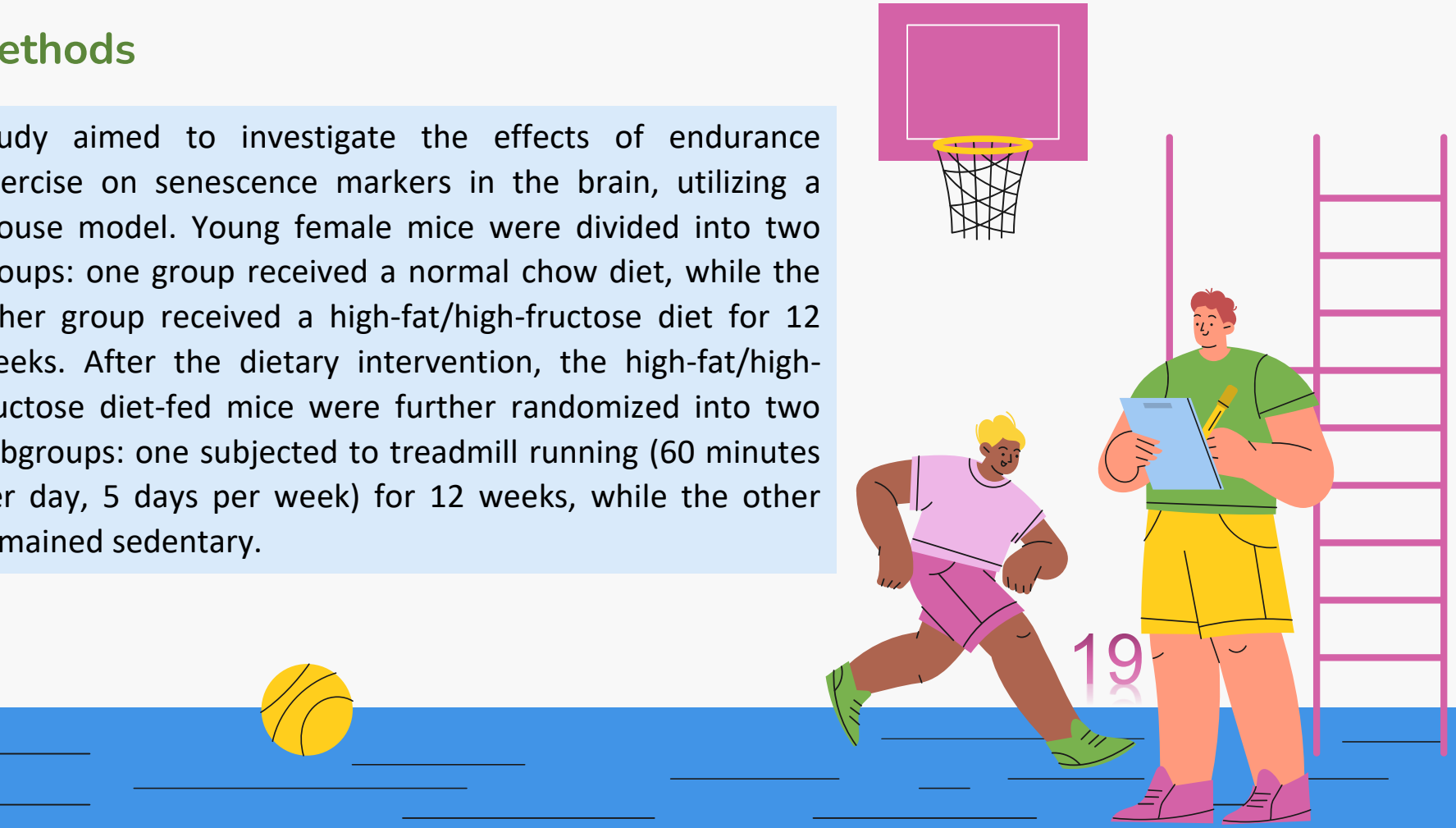
5) Further research is needed to elucidate the precise mechanisms underlying the effects of exercise on DNA damage and telomere maintenance.

03

Impact on markers of cellular senescence in brain

Methods

Study aimed to investigate the effects of endurance exercise on senescence markers in the brain, utilizing a mouse model. Young female mice were divided into two groups: one group received a normal chow diet, while the other group received a high-fat/high-fructose diet for 12 weeks. After the dietary intervention, the high-fat/high-fructose diet-fed mice were further randomized into two subgroups: one subjected to treadmill running (60 minutes per day, 5 days per week) for 12 weeks, while the other remained sedentary.



Results

The exercise intervention in high-fat/high-fructose diet-fed mice resulted in a significant reduction in the levels of senescence markers, additionally, exercise attenuated diet-induced neuroinflammation and oxidative stress in the hippocampus, consistent with previous findings.

Discussion

The findings suggest that exercise may mitigate the adverse effects of a high-fat/high-fructose diet on brain health by reducing cellular senescence and associated inflammatory and oxidative processes. These results underscore the importance of regular physical activity in promoting brain health and may have implications for the prevention and management of age-related cognitive decline and neurodegenerative disorders.

Conclusion:

Exercise is widely considered as one of the most effective methods to prolong human health span.

Recent discoveries regarding the mechanisms by which exercise enhances function and combats diseases have the potential to influence public health strategies aimed at promoting physical activity.

Additionally, these insights may uncover biological pathways that could be targeted through pharmacological means.

The literature reviewed in this context indicates that exercise not only mitigates various forms of molecular damage leading to cellular senescence but also potentially facilitates the clearance of senescent cells through immune-mediated processes.

This body of evidence supports the notion that exercise plays a role in preventing the accumulation senescent cells associated with aging.

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Thank you..