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Review Article

Who is Responsible for Aging: Life Style or Genetics or Both?

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ABSTRACT

Aging is the total outcome of interactions among genetic, environmental and lifestyle factors at a given time. Survival events such as, well-beyond average life expectancy, delayed onset of age-related diseases (before 80 years of age) and/or preservation of good health/function is very common presently may be due to improvement in health and nutritional conditions. Researchers at Yale University hooked the organs to a system that pumped in a blood substitute. Similarly researchers have revived the disembodied brains of pigs four hours after the animals were slaughtered pointing towards rejuvenation of life, Modern data analysis and in particular, AI approaches could be transformative toward identifying strategies for preservation of good health with advancing age.

Keywords: Gender paradox; Growth hormone; Thymus; Pig heart; Artificial blood; Rejuvenation

INTRODUCTION

Age is a universal feature of every organism and defined as a progressive failure of defence and repair processes that produces physiological frailty (the loss of organ reserve with age), loss of homeostasis and eventual death, since it is unavoidable and natural phenomenon of life [1]. Although a complete arrest of the aging process may be impossible, progress in developing pharmacological, dietary, and genetic interventions that lead to healthy aging might allow individuals to live longer while being less burdened by physical and/or mental decline. It's a universal truth; one who is born later or sooner will die. In fact, uncovering the biological basis of aging is one of the greatest contemporary challenges in science; nevertheless, by compiling and correlating data from various experiments in understanding the aging process. The nine hallmarks of aging are identified, they are, genomic instability, telomere attrition, epigenetic alterations, loss of proteostasis, deregulated nutrient sensing, mitochondrial dysfunction, cellular senescence, stem cell exhaustion, and altered intercellular communication [2].

LITERATURE REVIEW

How aging starts? convincing cells to die could make us stronger

Our cells are constantly dying and being replaced with fresh, healthy replacements; it's how our body as a whole outlasts its short-lived constituent parts. The majority of our cells die noble deaths (either by terminal differentiation or by apoptosis); they cease to be once they're damaged beyond repair [3]. However, some ragged cells refuse to turn out the lights, and that's where the trouble begins. These stubborn, damaged cells can accumulate in the body over time, and they can accelerate the aging process and cause the onset of disease. Tests in humans haven't yet begun, and further research into cell senescence and cell death needed. In any case, tinkering with the machinery of cell death and regeneration one of those researchers are exploring to help extend healthy life spans. If the preliminary results are any indication, however, the researchers are on the right track.

Age-related adipose involution and loss of growth hormone receptors on rat thymocytes and cartilage *in vitro* have been studied earlier by us [4-7]. This process that is under hormonal control and the hormone binding sites are declined with age [4-7], ayurvedic science also proposed the phenomenon that in every decade of human life spawn some organs of the body looses " vigour" of their activity. Aging is a complex phenomenon and many laboratories across the world are engaged to understand "aging". People's body systems age at different rates [8].

Chronological age cannot be reverted but with new experimentation there is a hope based on the experiments performed recently that there may be reversal of biological age.

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Researchers at Yale University, hooked the organs to a system that pumped in a blood substitute. Similarly researchers have revived the disembodied brains of pigs four hours after the animals were slaughtered. These experiments raise questions about the ethics of the approach [9] and, more fundamentally, about the nature of death itself [10].

The gender paradox

Researchers have found a genetic variant linked to longer life among men may be due to deletion of exon 3 GH receptor which is a marker of male-specific exceptional longevity associated with increased GH sensitivity and taller stature [11]. However, the variant was just as likely to be among women who lived past 100 years of age as it was among 70-year-old women, suggesting that there are different genetic factors at play regarding longevity in men and women scientists studying lifespans of wild mammals have found that, just like humans, females tend to live significantly longer than their male counterparts. "This whole issue has shocked us," co-author Nir Barzilai [12,13].

Long life genetics

Compared to last century the global average life expectancy humans has become more than double(13), this may be due to availability of better medical facilities and healthy nutrition and is now above 70 years. Although estimate differs among studies; based on twin studies it is found out that genetics i.e., the heritability is responsible for increase in human lifespan is only about 25%, [14]. Researchers who have conducted a genome-wide association meta-analysis have found a role for tissue-specific expression of genes on chromosome 5q13.3, 12q13.2, 17q21.31, and 19q13.32 for longevity; two recently spot out novel genomic regions — HLA-DQA1/DRB1 and LPA — linked to longevity, in addition to known links at CHRNA3/5 and APOE earlier [15].

Long life-life style

In addition, researchers found that change in life style also added to the life span. For example, quitting smoking as well as educational attainment and openness to new experiences are linked genetically to increased lifespan [16]. It can be difficult to identify the impact of one specific unhealthy behaviour for example, overeating. Instead, the researchers turned to the natural experiment. It is also true that life style changes gene expression [17]. Modifiable factors that can affect the expression of genes include diet, physical activity, tobacco smoking, alcohol consumption, psychological stress and ultraviolet radiation. Some people carry mutations in their DNA that increase appetite or make them more likely to put on weight, so researchers were able to compare those programmed to eat more with those who were not irrespective of their wider lifestyles [18].

Dr Peter Joshi said: "It doesn't mess up the analysis. You can look directly at the effect of weight, in isolation, on lifespan." Similar sets of mutations have been linked to how long people spend in education and the enjoyment they get from smoking or drinking. Prof David Melzer, from the University of Exeter Medical School, said: "An extra year of education then may have been much more important than it is now" [19]. Meanwhile, lung cancer, body fat, and smoking were negatively correlated with lifespan. The further estimated that an increase of one BMI unit reduces lifespan by seven months, while another year of education extends it 11 months [20].

Reverse aging technology

There's no limit to longevity, says study that revives human lifespan debate. Those are the words of esteemed futurologist Dr Ian Pearson, "he believes humans are very close to achieving "immortality" – the ability to never die. However, Dr Pearson tells that there are a number of different ways we could live forever – as long as you can make it to the year 2050 [21]. Epigenetic "clocks" can now surpass chronological age in accuracy for estimating biological age. Here, we use four such age estimators to show that epigenetic aging can be reversed in humans. Using a protocol intended to regenerate the thymus, we observed protective immunological changes, improved risk indices for many age-related diseases, and a mean epigenetic age approximately 1.5 years less than baseline after 1 year of treatment (2.5 year change compared to no treatment at the end of the study). . It might be possible to reverse the body's epigenetic clock, which measures a person's biological age..The participants' immune systems also showed signs of rejuvenation [22].

The latest trial was designed mainly to test whether growth hormone could be used safely in humans to restore tissue in the thymus gland. The gland is crucial for efficient immune function. White blood cells are produced in bone marrow and then mature inside the thymus, where they become specialized T cells that help the body to fight infections and cancers. But the gland starts to shrink after puberty and increasingly becomes clogged with fat. Recent *in vitro* and *in vivo* experimentations such as, thymic regeneration [23], Reconstitution of a functional human thymus [23]. Further breakthrough came from the experiments which were done recently, keeping some organs including brain live after death of the animals on artificial blood for some length of time [24].

Biomarkers of aging

Scientists construct epigenetic clocks by selecting sets of DNA-methylation sites across the genome. In the past few years, Horvath — a pioneer in epigenetic-clock research — has developed some of the most accurate ones "Because we could follow the changes within each individual, and because the effect was so very strong in each of them, I am optimistic," says Horvath [24]. Steven Horvath in 2013, for the first time proposed DNA methylation as a marking of age that measures the cumulative effect of an epigenetic maintenance system. On epigenetic level, replicative senescence and aging evoke characteristic modifications in the DNA methylation pattern, but at different sites in the genome [25,26].

CONCLUSION

The convergence of AI with aging research (epidemiological data on aging), it was possible to predict age and associate the prediction with mortality, disease, general wellbeing, or other

biological processes including DNA methylation, gene expression, microbiome, and imaging data.

REFERENCES

1. Gupta PD. Born to die: Why do we age? J Cell Tissue Res. 2018;18(2).
2. Lopez-Otin C, Blasco MA, Patridge L, Serrano M, Kroemer G. The hallmarks of aging cell.2013;153(6):1194-1217.
3. RAO KS, Zanotti S, Reddy AG, Rauch F, Mannherz HG, Gupta PD. Oestradiol regulated programmed cell death in rat vagina: Terminal differentiation or apoptosis? Cell Biol Inter. 1998;22(2): 105-113.
4. Pandian MR, Gupta PD, Talwar GP, Avrameas S. Proesence of "receptors" for growth hormone on membranes of thymocytes. Clin Trans Endocrinol. 1975;78(4): 781-790.
5. Talwar GP, Kumar N, Pandian MR, Gupta PD. Cellular and molecular correlates of the decline in responsiveness of cartilage and thymus to growth hormone in aged animals. Mol Cellular Endocrinol. 1974;1(3): 209-226.
6. Savino W, Mendes-da-Cruz DA, Lepletier A, Dardenne M. Hormonal control of T-cell development in health and disease. Nat Rev Endocrinol. 2016;12(2): 77-89.
7. Kumar N, Gupta PD. Age related changes in cartilage matrix-possible mechanism for cartilage unresponsiveness to serum growth factors. Ind J Exptl Bio. 1980;18(11): 1238-1241.
8. Peoples body systems age at different rates. 2020.
9. Farahany NA, Greely HT, Hyman S, Koch C, Grady C, Pasca SP, et al. The ethics of experimenting with human brain tissue. Nature. 2018;556(7702): 429-432.
10. Vrselja Z, Daniele SG, Silbereis J, Talpo F, Morozov YM, Sousa AM, et al. Restoration of brain circulation and cellular functions hours post-mortem. Nature. 2019;568(7752): 336-343.
11. Danny DB, Govindaraju DR, Budagov T, Fradin D, Durda P, Ott S, et al. The GH receptor exon 3 deletion is a marker of male-specific exceptional longevity associated with increased GH sensitivity and taller stature. Sci Adv. 2017;3(6): e1602025.
12. Deluty JA, Atzmon G, Crandall J, Barzilai N, Milman S. The influence of gender on inheritance of exceptional longevity. Aging (Albany NY). 2015;7(6):412-418.
13. Perls T, Kunkel LM, Puca AA. The genetics of exceptional human longevity. J Am Geriatr Soc. 50(2): 359-368.
14. Deelen J, Evans DS, Arking DE, Tesi N, Nygaard M, Liu X, et al. A meta-analysis of genome-wide association studies identifies multiple longevity genes. Nat Commun. 2019;10(1): 3669.
15. Nagel M, Jansen PR, Stringer S, Watanabe K, Leeuw CA, Bryois J, et al. Meta-analysis of genome-wide association studies for neuroticism in 449,484 individuals identifies novel genetic loci and pathways. Nat Genet. 2018;50(7): 920-927.
16. Samarakoon SMS, Chandola HM, Ravishankar B. Effect of dietary, social, and lifestyle determinants of accelerated aging and its common clinical presentation: A survey study Ayu. 2011;32(3): 315-321.
17. Alejandro JAA, Andrea B, Bollati V. Epigenetics and lifestyle. Epigenomics. 2011;3(3): 267-277.
18. We Are Programmed for Gluttony and Weight Gain. 2017.
19. Gallagher J. DNA study provides insight into how to live longer. 2017.
20. Stenholm S, Head J, Aalto V, Kivimaki M, Zins M, Goldberg M, et al. Body mass index as a predictor of healthy and disease-free life expectancy between ages 50 and 75: A multicohort study. Int J Obes (Lond). 2017;41(5): 769-775.
21. Abbott A. First hint that body's 'biological age' can be reversed. Nature. 2019;573(7773): 173.
22. Gent RV, Schadenberg AWL, Otto SA, Nievelstein AJ, Sieswerda GT, Haas F, et al. Long-term restoration of the human T-cell compartment after thymectomy during infancy: A role for thymic regeneration? Blood. 2011;118(3): 627-634.
23. Campinoti S, Gjinovci A, Ragazzini R, Zanieri L, Ariza-McNaughton L, Catucci M, et al. Reconstitution of a functional human thymus by postnatal stromal progenitor cells and natural whole-organ scaffolds. Nat Commun. 2020;11(1):6372.
24. Horvath S. DNA methylation age of human tissues and cell types. Genome Biol. 2013;14(10): R115.
25. Xia X, Chen W, McDermott J, Han JDJ. Molecular and phenotypic biomarkers of aging. F1000Res. 2017;6: 860.
26. Field AE, Robertson NA, Wang T, Havas A, Ideker T, Adams PD. DNA methylation clocks in aging: Categories, causes, and consequences. Mol Cell. 2018;71(6): 882-895.