

Metabolic Theories of Aging

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Metabolic theories of aging postulate that aging is due to energy expenditure, which ultimately results in the breakdown and eventual death of cells. Historically, within the realm of metabolic theories of aging, there have been three models: The Rate-of-Living theory, The Oxidative Damage/Free Radical theory, and the Metabolic Stability theory. All three theories maintain that aging is directly related to metabolic rate, but the theories differ in how they arrive at that conclusion.

The Rate-of-Living theory of aging is the most antiquated of the metabolic aging theories. It proposes that two factors are responsible for determining longevity in all living organisms: 1) a genetically pre-determined capacity for overall metabolic potential, and 2) metabolic rate. The first empirical evidence for this theory dates back to 1908, when Max Rubner observed increasing metabolic rates as a function of increasing body mass in five mammalian species of varying longevities (guinea pig, cat, dog, cow, and horse). Rubner reported that the animals' metabolic rates increased as a function of body mass, and that larger animals had longer lifespans.

Based on these results, Rubner postulated that longevity could be determined by calculating the pre-determined capacity for organic energy use and the rate at which the energy was being expended. Rubner's observation was supported by Raymond Pearl when he concluded that slower metabolism resulted in an increased lifespan among fruit flies and cantaloupe seeds. Despite the evidence for the Rate-of-Living theory, modern scientific developments have refuted the accuracy of the theory. The first development is the comparison of animal metabolisms with expanded species data, including mammals as well as birds. When compared, general conclusions are the

same (i.e., larger mammals expend more energy, metabolic rate declines with increases in body mass, and larger mammals live longer). However, specific conclusions, specifically that animals expend the same amount of energy per gram of tissue, have been refuted.

The strongest empirical evidence against the Rate-of-Living theory is based on comparison of birds to mammals. Within birds, there are patterns which are comparable to those within mammals (i.e., larger birds expend more energy, and the relationship is inverse for weight). However, birds of any mass have significantly higher metabolic rates than mammals of the same size. Additionally, it has been found that birds with higher metabolic rates also live longer. Given these results, it is maintained that the Rate-of-Living theory is inaccurate.

The second metabolic theory of aging, the Oxidative Damage/Free Radical theory, was first proposed in 1956 by Denham Harman. The theory posits that free radicals and oxidants, or radical oxygen species (ROS), react with macromolecules in the body and damage DNA proteins. ROS can originate from external sources such as ultraviolet radiation, but most ROS are generated as a byproduct of the process of oxidative phosphorylation within the body.

Oxidative phosphorylation is continuously occurring in cellular respiration, and is the molecular process that is responsible for the production of adenosine triphosphate (ATP), which fuels energy metabolism. Consequently, cellular proteins are under constant assault from the ROS generated during continual oxidative phosphorylation. Studies have found that although animals have protective mechanisms to defend against ROS, damage inevitably evades the defense mechanisms. As a result, the continual production of ROS has direct relationship with increased protein damage over time. Although the Oxidative Damage/Free Radical theory provides a mechanism through which the Rate-of-Living theory could operate, empirical evidence does not consistently support their interdependence.

The final metabolic theory of aging, proposed by Lloyd Demetrius in 2004, is the Metabolic Stability Theory of aging. This theory proposes that metabolic stability, or the ability of cell regulatory processes to maintain levels of metabolic homeostasis when presented with stress, is the primary cause of aging. Demetrius contends that metabolic stability may limit the amount of ROS produced through oxidative phosphorylation, thus reducing irreversible cellular damage and increasing longevity. Based on this assumption, research has proposed that caloric restriction increases metabolic stability, subsequently reducing rate of aging and increasing lifespan. However, Demetrius argues that the efficacy of caloric restriction is dependent upon the ages at which organisms in a species reproduce and die. Demetrius proposes that the effect of caloric restriction for organisms who have a late sexual maturity and broad reproduction period (i.e., humans) is negligible.

Further Reading

Demetrius, L. (2004). Caloric Restriction, Metabolic Rate, and Entropy. *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences*, 59(9), pp.B902-B915.

Olshansky, S. and Rattan, S. (2005). At the Heart of Aging: is it Metabolic Rate or Stability?. *Biogerontology*, 6(4), pp.291-295.

Speakman, J. (2005). Body size, energy metabolism and lifespan. *Journal of Experimental Biology*, 208(9), pp.1717-1730.