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Review

Beneficial effects of dietary restriction in aging brain

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ABSTRACT

Aging is a multifactorial complex process that leads to the deterioration of biological functions wherein its underlying mechanism is not fully elucidated. It affects the organism at the molecular and cellular level that contributes to the deterioration of structural integrity of the organs. The central nervous system is the most vulnerable organ affected by aging and its effect is highly heterogeneous. Aging causes alteration in the structure, metabolism and physiology of the brain leading to impaired cognitive and motor-neural functions. Dietary restriction (DR), a robust mechanism that extends lifespan in various organisms, ameliorates brain aging by reducing oxidative stress, improving mitochondrial function, activating anti-inflammatory responses, promoting neurogenesis and increasing synaptic plasticity. It also protects and prevents age-related structural changes. DR alleviates many age-associated diseases including neurodegeneration and improves cognitive functions. DR inhibits/activates nutrient signaling cascades such as insulin/IGF-1, mTOR, AMPK and sirtuins. Because of its sensitivity to energy status and hormones, AMPK is considered as the global nutrient sensor. This review will present an elucidative potential role of dietary restriction in the prevention of phenotypic features during aging in brain and its diverse mechanisms.

1. Introduction

Aging, a naturally occurring process, is an inevitable time-dependent decline in systemic functions. It is characterized by random changes in the structure and functions at various molecular and cellular levels that increase the vulnerability to diseases and probability of death. Natural phenomenon such as greying of hair, wrinkling of skin, dementia, reduction in muscle tone and motor coordination are some of the observable features of aging. The cause of aging is multifactorial and its underlying mechanism is not well elucidated. Unraveling how these factors interplay in governing lifespan can help us to better decode the mechanism of aging. Cumulative evidence has suggested that these varied factors act in synergy to direct the aging process of an organism, mostly controlled in combination by genetic and epigenetic factors. (Sharma and Dkhar, 2014). Understanding the aging process will pave the way to novel approaches to a healthier life, even in old age. Thus, over the years researchers have proposed a number of theories of aging (Jin, 2010). The various theories have been proposed in an attempt to explain the mechanism of aging, but till date none of them appears to stand alone. Some of them such as the classical theory of programmed death by Weismann in 1891, which stated that aging evolved as an advantage for the species has become obsolete (McDonald, 2014). Later on, Weismann postulated that aging resulted as organisms allocated more energy for reproduction rather than maintaining the soma, which was then modified by Kirkwood (1977) to the disposable soma hypothesis, in which it was hypothesised that a balance must be maintained between maintenance of the soma and reproduction. We can see that the antagonistic pleiotropy theory (a factor that is important early in life may be detrimental later in life) of aging by Williams (1957) derived its basis from the mutation accumulation theory of aging by Medawar in 1952.

Hence, the theories put forward by Weissman, Kirkwood, Medawar and Williams are considered to be the classical evolutionary theories of how aging evolved. It can also be pointed out that the codon restriction theory (Strehler et al., 1971), error catastrophe theory (Medvediev, 1962; Orgel, 1963), the oxidative stress or free radical theory by Harman (1956) and the mitochondrial theory of aging (Miquel et al., 1980) revolve around the notion that is implied as in the mutation accumulation theory of aging (Medawar, 1952). These theories presume that aging occurs as a result of time-dependent accumulation of damaged biomolecules in the body. The cross-linking theory (Bjorksten, 1968; Bjorksten and Tenhu, 1990) also suggests that aging occurs due to the accumulation of cross-linked proteins with molecules like glucose (glycation) leading to the formation of aberrant non- functional proteins. Lately, the free radical theory of aging is facing some debate (Gladyshev, 2014), and the hyperfunction theory of aging (Blagosklonny, 2008) totally contempt it. Yet again, the neuroendrocrine theory (Dilman and Dean, 1992), the cellular senescence theory of

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