Editor’s Perspective

Dampening the Progression of Dementia

According to the World Health Organization, the incidence of cognitive loss and dementia is exponentially increasing with advancing age. The incidence of dementia has doubled every 5.9 years. In the age group 60 to 64 years of age, the incidence of dementia is 3.1/1000 person-years but in the age group greater than 95 years, the incidence of dementia is now 175.0/1000 person-years. Globally, 7.7 million new cases of dementia and cognitive loss are expected each year. Although peak incidence can vary around the world; the peak incidence is among those aged 80-89 years in the Americas with average survival from the onset of dementia until death estimated at approximately 4.6 years in duration.

Several factors can increase the risk for the onset of dementia and result in a large financial burden. Risk factors include tobacco use, diabetes mellitus, low education in early life, and hypertension. With regard to the global financial burden of dementia, it is estimated that costs are equal to one percent of the world’s gross domestic product and exceed $600 billion United States dollars annually. By the year 2030, these costs are believed to increase by over eight-five percent. Yet, these estimated health care costs account for a small percentage of the true costs, since informal care is most commonly provided by family, friends, and through community assistance.

With the knowledge that dementia and cognitive loss have become the leading chronic disease contributors to disability and place a significant burden on the world’s economy, new areas of investigation that may limit or resolve dementia and cognitive loss are highly warranted. The silent mating type information regulation 2 homolog 1 (Saccharomyces cerevisiae) (SIRT1) may offer one exciting new target for the treatment of dementia. SIRT1 is a member of the sirtuin family. As a histone deacetylase, SIRT1 can transfer acetyl groups from e-N-acetyl lysine amino acids on the histones of DNA to control transcription. There are 7 identified mammalian homologues of Sir2 that exist and include SIRT1 through SIRT7. SIRT histone deacetylases control post-translational changes of proteins and oversee cellular proliferation, survival, and senescence. SIRT1 also is dependent on nicotinamide adenine dinucleotide (NAD\(^+\)) as a substrate.

New work has highlighted the role of SIRT1 during dementia and cognitive loss. For example, SIRT1 in combination with transcription factors may offer protection against amyloid (A\(\beta\)) toxicity. SIRT1 may reduce oxidative stress and cell injury during exposure to A\(\beta\). In addition, in Drosophila models, absence of SIRT1 activity with a reduction in autophagy activity can lead to the neuronal accumulation of A\(\beta\). SIRT1 also may be involved in the deacetylation of tau to reduce the spread of tau in models of tauopathy. Expression of SIRT1 also may be necessary to limit cognitive dysfunction and may be tied to a reduction in endoplasmic reticulum stress. In addition, SIRT1 has been linked to the modulation and suppression of inflammatory responses that may impact cognitive function.

Clearly, multiple factors may lead to dementia and the loss of cognitive function. In this issue of Current Neurovascular Research, a number of studies address these factors. In the paper by Li et al., the authors illustrate that onjisaponin B, a bioactive ingredient from Radix Polygalae, can limit lipopolysaccharide-induced cognitive deficits. A number of cellular pathways appear to account for these results and include interleukin mediated pathways as well as the sirtuin SIRT1. The inflammatory response noted also may be tied to microRNAs. The work by Yang et al. suggests that microRNA-155 may regulate cerebral inflammatory response through autophagy pathways. In other areas, progression of atherosclerosis may also lead to a cognitive loss. The paper by Chang et al. suggests that cyclophilin A may serve as a predictive biomarker for carotid stenosis during ischemic cerebral injury. Statins also appear to play a role during dementia and may actually reduce the risk of onset of dementia. The work by Gołąd-Janowska et al. illustrates the significant role of circulating stem cells (CD133\(^+\)), early progenitor (CD133\(^+\)/VEGFR2\(^+\)) cells, and endothelial CD34\(^+\)/CD133\(^+\)/VEGFR2\(^+\) cells during stroke and found that statins may promote the presence of these stem cells. Other related areas of interest in this issue of Current Neurovascular Research include novel neuroimaging models for the prediction of ischemic disease, the neuroprotective role of bradykinin B2 receptors, the use of low dose intra-arterial tirofiban in mechanical thrombectomy, and the role of serum white blood cell levels and serum total bile acids during ischemic cerebral disease. Given the multiplicity of factors that can impact dementia and cognitive loss, this issue of Current Neurovascular Research provides an exciting glimpse into the potential new prospects for the treatments of cognitive loss that hopefully will ‘dampen the progression of dementia’.

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