

Lifestyle Impact on Cognitive Decline and Neurodegeneration Overview

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ABSTRACT

Cognitive decline is a part of a natural phenomenon that eventually happens to almost everyone as they age. It results from a combination of lifestyle habits, genetic factors, trauma or just gradual wearing-out of one's nervous system. The effects of lifestyle and behavior which include patterns of dietary intake, physical activities as well as practicing unhealthy habits such as smoking and alcohol consumption, have been globally emphasized and embraced time and again as a crucial component to avoid serious health complications. It is also been included as an evidence-based guideline for children, adolescents and adults from diverse populations in all countries. Healthy lifestyle behaviors and therapeutic lifestyle changes were emphasized and reaffirmed as central to cardiovascular health promotion and risk reduction, respectively. Certain healthy behaviors known to combat cancer, cardiovascular disease, diabetes and may also reduce the risk of cognitive decline. Simple lifestyle changes might delay the start of cognitive decline and dementia or slow its progression. Activities that boost your body and brain are such as staying mentally active, engaging in regular physical activity and eating a heart-healthy diet. There are also evidences where people may benefit from staying socially engaged with friends, family and the community. People can reduce the risk of cognitive decline by making key lifestyle changes. There are measures which can be taken to modify their lifestyle while they still can before it's too late to stop if not to minimize the onset of neuron degeneration.

Key words: Alzheimer's disease, Lifestyle, Neuron degeneration, Cognitive decline, Dementia, Neurological deficit.

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INTRODUCTION

The term lifestyle refers to day to day behaviours, habits and functions of an individual involving their activities, job and diet. It is a way used by people from various countries or referred to the characteristics of inhabitants from a specific geographical region, economic, political, cultural and religious practices.¹ According to WHO in recent years, lifestyle behavioral pattern and habits are said to be one of the contributing factors for the onset of various metabolic diseases which can lead to serious life-threatening health conditions. It is said that more than 50% of related factors affecting the individual health and quality of life are correlated to lifestyle.² Over the past decade, with the emerging of new technologies such as the internet and virtual communication networks have led our world to a major challenge that threatens the physical and mental health well-being of millions of people. In order to keep up with the growing tech world, the interest in younger generation is strongly shifted to learning new things out of curiosity and most people do not realize that this pathway follows an unhealthy sedentary lifestyle. The link between lifestyle and general health should be highly considered as many studies revealed that amid acquiring knowledge on new gadgets and technologies, most

people get their focus deviated, eventually being unaware of the health consequences. It is evident that recent technologies which include electronic games, home computers, handheld devices, smartphones, iPods etc. play a vital role in our daily lives these days. Gadgets are popular in children as well as elders.³ It is indeed a sad reality to embrace and to say most people encounter illnesses, disabilities and even death at an early age nowadays as compared to the previous generations. Health problems like metabolic diseases, cancer, joint and skeletal problems, cardiovascular diseases, diabetes, obesity and so on, can be caused by unhealthy lifestyle habits, addiction and physical inactivity.⁴ According to a research done by Brannon and Feist, fatalities in the 20th and 21st century results from diseases strongly associated with individual lifestyle/behavior.⁵ In addition to habits, there have been many studies done on sedentary lifestyle being strongly linked with the onset of various metabolic diseases. The term cognitive decline refers to deterioration in memory or cognition which may take place as a normal process. Various research studies have revealed that lifestyle and habits can be directly related to the onset of cognitive decline leading to certain neurodegenerative conditions. Although

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there may not be any specific lifestyle or habits which trigger cognitive neuron cell death, it may be more appropriate to mention that this works accumulatively over a long period of time in certain individuals. Most often we are aware of the known fact that diseases are said to be associated with the type of diet and hereditary factors. Lifestyle defines a person and the kind of consequences that comes is a package which they have to deal with that may or may not be reversed according to the damage sustained.

Importance of Lifestyle and Behaviour

The common factors contributing to sedentary lifestyle are socio-economic status, age and gender, advancement in technologies and long working hours. Quality of life is the result of diverse factors and behavior/lifestyle is one of the most powerful determinants of good health.⁶ Most people do not realize this correlation which eventually may or may not progress to cognitive decline and other types of neurodegenerative conditions. In recent decades, researches have taken interest in lifestyle and habits as being an important factor of health and the onset of diseases. According to WHO, 60% of related factors to individual health and quality of life are correlated to lifestyle.² In recent days, we see extreme changes taking place in the lives of people regardless of age, gender and personal backgrounds. Malnutrition, unhealthy diet, smoking, alcohol consumption, drug abuse, stress and so on, are the presentations of unhealthy lifestyle that has been known to be the dominant forms of lifestyle.

The concept of sedentary behavior is a term used to characterize those behaviors that are associated with low energy expenditure. The definition of "Sedentary" in Latin which is "Sedere" means "to sit". This includes prolonged sitting at work, home, business centers, long screen time, car driving and leisure time.⁷ Despite the well-known and discussed benefits of physical activity, many adults and children continue to lead a sedentary lifestyle. It has been revealed that most urban dwellers choose to adapt sedentary lifestyles which have obvious negative health implications particularly cardiovascular diseases.⁸ The importance of healthy lifestyle behaviors has been universally emphasized and embraced as a central component of evidence-based guidelines for children, adolescents and adults from diverse populations. Health behaviors, including patterns of dietary intake, physical activity and inactivity, substance abuse like drug addiction, smoking and alcohol consumption are often one of the major root causes of serious illnesses. These unhealthy behaviors have led to various chronic diseases such as heart diseases, deep vein thrombosis, Type-2 diabetes, hypertension, osteoporosis, cancer, muscle and skin disorders also neurodegenerative diseases. It is a known fact that these diseases are among others with resultant increase in morbidity and mortality.⁹

Previous studies and evidences showed that lack of physical activity ameliorates psychological stress, vascular and metabolic risk factors (such as high blood pressure and diabetes).^{10,11} Frequent engaging in physical activity can also bring about amyloid clearance and increase the cognitive reserve, which is defined as the brain's ability to cope with damage and still function adequately.¹² Increased brain volume and elevated levels of brain-derived neurotrophic factors have also been closely associated with physical activity.^{13,14}

Variables of Lifestyle

The concept of quality of life indicates health and functional status, perceived health status, subjective health, health perception, symptoms, satisfaction, cognition, functional disability, disorder and well-being.¹⁵ Quality of living varies from each individual based on the circumstances and area of interest, ranging from those associated with the basic necessities of life, to the realization of feelings and satisfaction, even

including physical, psychological and social dimensions.¹⁶⁻¹⁸ It has already been proven that having a systematic quality life with strict diet monitoring can minimize certain types of diseases. Some of the common variables of lifestyle that influence health can be categorized as the following items:

- 1. Exercise:** This has been globally accepted and established fact through various studies that exercise plays a crucial role if not treating but minimizing general health problems.¹⁹ Continuous and regular exercise along with a healthy diet increase the health benefits especially cardiovascular circulatory. Some studies stress on the relation of active lifestyle with happiness.^{20,21} Physical activities produces beneficial effects through mechanisms that involve the physiology of the cardio circulatory system, glucose and lipid metabolism in general and the coagulation process. The present orientation is that moderate daily physical activity such as walking or biking for 30-45 min a day has the exact outcome as performing more vigorous physical activities.
- 2. Sleep:** The quality of sleep holds a significant key to a healthy life. Sleep disorders have been linked to several social, psychological unhealthy consequences. The nature of a person's lifestyle may affect the quality of sleep and this has a clear influence on mental and physical health, which may lead to neuron degeneration. Problematic or disturbed sleep has adverse effects on all individuals, regardless of age and gender; however, older people typically show an increase in disturbed sleep or reduced sleep patterns that can create a negative impact on their quality of life, mood and alertness.^{22,23} Therefore, regular exercise and good quality of sleep are excellent combination to maintain a good health not merely physically but mentally as well.
- 3. Body Mass Index and Diet:** Poor diet is also an important factor in daily lifestyle and has a direct and positive relation to health. The consequences of unhealthy diet are one of the common issues in urban societies. Body Mass Index (BMI) is the key measurement to monitor unhealthy lifestyle. Vegetables may also have a neuroregulatory role by inducing satiety and ultimately reducing the risk of obesity, which is another major risk factor for accelerated cognitive decline and dementia.²⁴ Urban lifestyle due to limited time and feasibility leaves most people with no option but to settle in for a quick bite turning to good old fast foods which is a growing trend among younger generations especially with some of the outlets offering free Wi-Fi for the customers. This is not only common amongst students and youngsters but even amidst the business-oriented people in which they have their regular meetings in these outlets. This goes on to develop imbalanced nutrition problems and increasing cardiovascular conditions.²⁵ It is now evident that the intestinal microbes influence host function well beyond the gut and it has been implicated in a variety of diseases including obesity, diabetes, non-alcoholic fatty liver disease, autism, multiple sclerosis and cardiovascular disease.²⁶ In recent research work, it was found that cognitive decline in hepatic encephalopathy is associated with the presence of specific bacteria, although there was no causality reported.²⁷ Diet is said to be an important factor which will impact on the composition of the systemic milieu and can similarly modulate stem cell ageing, adult hippocampal neurogenesis and cognition.²⁸ Therefore, modulation of adult hippocampal neurogenesis by diet emerges as a possible mechanism by which nutrition can impact on cognitive ageing either via the systemic milieu or *via* the gut-microbiota, as discussed earlier.
- 4. Substance and medication abuse:** The word abuse is related to an addiction of any substance, which brings adverse events/reactions to the human body which is considered as an unhealthy lifestyle. Smoking, drug addiction and alcohol consumption are the main substance that may result in various problems like cardiovascular disease,

asthma, liver diseases, cancer, brain injury, etc. One of the longitudinal studies has indicated that 30% of people between the ages of 18–65 years old, who smoke cigarette permanently, ultimately lead to chronic illnesses.²⁹ In addition to that, using normal medication as self-treatment, sharing medication, using medications without prescription, prescribing too many unnecessary drugs which may be harmful on prolong use goes on to disrupt the normal functioning of several organs. Drug abuse, as a social phenomenon, is one of the chronic problems of the present era that almost all the countries are dealing with globally. It has been known to have social, psychological, physical and economic effects.³⁰ The amount of drug abusers varies in different countries, races commonly in young adults and currently it is seen even in much younger generation. The range of suicidal tendencies has been very high due to drug abuse with an increased amount of early deaths.^{31,32} Chronic drug addictions in any form and excessive alcohol consumption is a known fact for the onset of neuronal cell death which eventually leads to cognitive decline and neurodegeneration.³⁴ It was also reported that drug abuse has a significant relationship with the level of education. Lower degree of education obviously has inadequate knowledge about drugs and their effects.^{33,34}

5. **Modern technologies:** Advanced technology and facilities in the current era and the misuse of technologies often result in unpleasant consequences. For example, using of computer and other devices all through the day up to midnight to wee hours of morning may affect the pattern of sleep and eye conditions. It has been reported that mobile phone addiction is related to symptoms of depression and neurological hazards due to constant exposure to radiation.³⁵ Though it has become a necessity to keep up with the tech world and devices, unfortunately this unhealthy lifestyle can result in detrimental effects
6. **Recreation:** Outdoor activities, socializing, travelling or leisure time with hobbies is a significant key factor which must be included as part of our lifestyle. This is seen usually in the urban community which reflects on how important recreation in one's life even before the onset of certain common and terminal diseases. It is a normal phenomenon whereby neglecting leisure or any form of recreation can bring negative consequences on physical and mental health. On the other hand, with disorganized planning, unhealthy leisure and lifestyle, people sometimes do endanger their health as well.³⁶
7. **Ethnicity and Socio Economic Status:** Socio-Economic Status (SES) such as parental income and education, are inversely associated with sedentary behavior. The sedentary behavior tends to be higher in low SES groups as their knowledge is very limited on health and factors affecting the human body.³⁷
8. **Sedentary lifestyles:** Reduced physical activity which characterizes sedentary lifestyle results in accumulation of excess calories and fatty acids. An individual, who leads a sedentary life, absorbs and stores a lot of calories because of reduced energy expenditure.^{38,39} These unwanted calories leads to obesity. It is an unhealthy condition associated with excess body fat.⁴⁰ Obesity has been identified as one of the emerging major problems of younger age groups and adults especially those in urban areas and developing countries due to availability of amenities and over-eating tendencies. Health problem due to obesity carries a very high morbidity and mortality rates. Some of the diseases arising from sedentary lifestyle are type-2 diabetes, hypertension, hypercholesterolemia, cancer, cardiovascular diseases, muscle and skin changes and vitamin deficiency. It has been revealed that 9 out of 10 type-2 diabetes could be prevented if some of the risk factors were eliminated, these include—overweight, unhealthy diet, smoking and physical inactivity.⁴¹ Salmon J *et al.* discovered that increased sitting time exposed most people to type-2 diabetes. WHO correlated that prolonged sitting time or inactive stage due to sedentary lifestyle

increases great risk of developing colon cancer in men whereas endometrial and breast cancer in women.⁴² Muscle fibers also undergo changes with prolonged sitting. One begins to lose the muscle fibers that are responsible for active movements. Hypercholesterolemia causes 18% of global cerebro vascular disease and 56% of ischemic heart disease.⁴³ If muscles are not used constantly with regular exercise, the fibers become gradually replaced with fat and muscle wasting eventually occur.⁴⁴

Neurodegeneration and Cognitive Decline

It is predicted that by 2050, there will be an increase in the ageing population presenting significant economic, social challenges, burden for healthcare systems and on society will rise. According to the studies, by 2050, the likelihood of developing neurodegenerative diseases, such as Alzheimer's or Vascular Dementia (VD) will increase by 45%.⁴⁵ Cognitive function tends to improve over the first 18 years of life, peak during the next few years and then deteriorate steadily thereafter.^{46,47}

Neurodegenerative diseases result from gradual or progressive loss of structure and function which in the end leads to cell death of neurons (cells responsible for the nervous system functions). This degeneration can affect movements of the body and brain function, with or without causing dementia (progressive or chronic decline of cognitive function that affects memory, thinking, behavior, calculation, learning and emotion capacity and should never be associated with a normal aging process).^{16,48} The major problem is that these disorders are normally detected behindhand and restricting the efficacy of the treatment options. Neurodegenerative diseases have major impact at professional, social and family level that can lead to a complete inability to carry out any type of daily activity. Some of the common associated signs are motor, breathing difficulties, cognitive problems or gradual memory loss (possibly affecting the memory of all that has been learned over a lifetime).

The brain is affected in several ways in the process of aging, from the cellular to functional level. Changes associated with age manifest themselves as decline and deterioration in several abilities, including sensory, motor and higher cognitive functions.^{49,50} Most evidently, there has been certain specific diseases strongly related to age causing lesions in the brain that exacerbate the physiological changes which occur during normal aging. Cognitive decline is a classic example of this interaction between aging-related changes and age-related diseases in older people. The decline includes a large spectrum of clinical manifestations, which ranges from intact cognition through mild cognitive impairment (MCI) and finally, dementia. The term dementia is characterized by progressive deterioration in multiple cognitive domains that is severe enough to interfere with daily functioning.⁵¹

Although the most consistent risk factor for developing a neurodegenerative disorder, especially AD or PD, some cognitive decline is expected with age, the reason is not yet known on how this may directly relate to dementia. Neurodegenerative diseases are multifactorial debilitating disorders of the nervous system that affect approximately 30 million individuals worldwide (Table 1). Neurodegeneration is not an acute or sudden phenomenon but a gradual process which involves many factors and lifestyle habits is most certainly is a part of contributing factor.⁵² Alzheimer's, Parkinson's, Huntington's and Amyotrophic Lateral Sclerosis make up a group of neurodegenerative diseases which are characterized by specific etiologies with different morphological and pathophysiological features. It is the consequence of misfolding and dysfunctional trafficking of proteins.⁵³ Reactive oxygen species (ROS) which are naturally generated chemical molecules within the biological system have been implicated in the pathogenesis of neurodegenerative diseases. It plays an important role in mediating cellular activities such as inflammation, cell survival and stressor responses as well as many diseases

Table 1: Examples of Neurodegenerative Diseases.⁶⁴⁻⁶⁸

Examples of Neurodegenerative Diseases	Characteristics
Alzheimer's disease and other dementias	Memory loss, personality changes, mood swings, impaired gait, language difficulties, problems with attention and orientation, low energy
Parkinson's disease and PD related disorders	Tremors, rigidity, gait difficulties, dystonia, mask like facial expression
Amyotrophic lateral sclerosis	Weakness in hands, leg, feet, clumsiness, difficulty in walking, tripping, falling, muscle cramps, twitching in arms, shoulder, slurred speech
Huntington's disease (Lou Gehrig's Disease)	Uncontrolled movement of the arms, legs, head, face and upper body, decline in thinking and reasoning skills, including memory loss, concentration, judgment and ability to plan and organize, depression, anger, anxiety
Prion disease	Rapidly developing dementia, changes in gait, hallucinations, muscle stiffness, confusion, fatigue, difficulty speaking
Motor neurone diseases (MND)	Weakening grip, which makes it hard to pick up and hold things, fatigue, muscle shrinkage, cramps, slurred speech, weakness in the arms and legs, clumsiness and stumbling, difficulty swallowing, shortness of breath, inappropriate emotional responses, such as laughing or crying, weight loss
Spinocerebellar Ataxia (SCA)	Problems with coordination and balance (ataxia) uncoordinated walk, poor hand-eye coordination, abnormal speech (dysarthria), involuntary eye movement, vision problems, difficulty processing, learning and remembering information
Spinal Muscular Atrophy	Muscle weakness and twitching, difficulty breathing and swallowing, changes in the shape of the limbs, spine and chest due to muscle weakness difficulty standing, walking and sitting.
Creutzfeldt-Jakob disease	Personality changes, anxiety, depression, memory loss, impaired thinking, blurred vision or blindness insomnia, difficulty speaking and swallowing, sudden jerky movements
Gerstmann-Straussler-Scheinker disease	Progressive ataxia, clumsiness, unsteadiness, cognitive dysfunction leading to bradyphrenia (slowness of thought processing) and dementia of different degrees, dysarthria (slurred speech) nystagmus (abnormal eye movements) spasticity (rigid muscle tone) visual disturbances, deafness
Lewy Body disease	Visual hallucinations, movement disorders, depression, insomnia, fluctuating attention, cognitive problems, apathy
Multiple Sclerosis	Walking (Gait) difficulties, fatigue, numbness in face or extremities, vertigo, vision problems, spasticity, bladder disorders, sexual problems, cognitive and depression. Speech problems, seizures and tremors

including cardiovascular disorders, muscle dysfunction, allergy and cancers. In addition to that, mitochondrial dysfunction and/or environmental factors strongly associated with age have also been a contributing factor in causing neurodegeneration.⁵⁴⁻⁵⁷

Alzheimer's disease, the most common form of dementia, is one of the nation's largest public health crisis. Alzheimer's is known as an irreversible neurological condition that impairs cognition, orientation and functional capacity.⁵⁸ Moreover, it is one of the most common causes of fatality in the United States that cannot be prevented, cured or even slowed. The brain is an organ with high metabolism rate, oxidative stress is a common phenomenon in its neural tissue.⁵⁹ The two main types of antioxidant compounds which are involved in oxidative stress regulation in the body are antioxidant enzymes, that neutralizes reactions against free radicals and reactive oxygen species and the other is antioxidant nutrients, which help as co-factors in catalytic activities.^{60,61} Some neurodegenerative disorders such as Alzheimer's, Parkinson's and Amyotrophic Lateral Sclerosis have a clear familial occurrence, suggesting a genetic basis. Among these affected families, the disease runs as an autosomal dominant trait, as in HD less frequently, the disease runs as an autosomal recessive trait, X-linked trait even a maternally inherited trait. Besides these "pure" genetic neurodegenerative diseases, others are sporadic but show a small contingent of patients in whom the illness is inherited. This is true for PD, AD and even ALS, of which about 10% of all cases are familial. In case of truly sporadic, which is the majority of patients; it appears that the genetic contribution to the neurodegenerative process is minimal.⁶² Most elderly individuals exhibit mild motor and cognitive alterations reminiscent of those found in neurodegeneration. This observation coincides with a popular believe that aging might

be a "benign" form of neurodegeneration. This idea was supported and widely accepted until recently, that normal aging, like neurodegeneration, is inevitably associated with neuronal death. From as early as 1950s, decreased numbers of neurons in different regions of the brain were reported in aged humans with no overt neurological or psychiatric conditions which might have led to a neurodegenerative condition. Subsequent studies have estimated these losses to be as high as 100,000 neurons per day, which could easily explain the cognitive decline and decrease in brain weight traditionally associated with normal aging.⁶³ A person might have a gene that makes him or her more susceptible to a certain neurodegenerative disease, but whether, when and how severely the person is affected depends on what environmental factors and lifestyle habits he or she is exposed to during life.

Inadequate nutrition and with existence of several diseases, cognitive function in 'healthy' individuals will be detrimentally fretful during their lifetime. Most people will encounter disease at some stage of their life, with majority of diseases associated with some form of negative consequences in cognitive function.⁶⁹ However, over the years evidence is accumulating that cognitive decline during normal ageing can be attenuated by a wide variety of factors, such as improved nutrition, appropriate dietary supplementation, lifestyle modification with increased physical exercise and performance of mental exercises.^{70,71} Research work conducted with humans and on animals has demonstrated that the brain is sensitive to stress and is especially vulnerable during early childhood and old age.^{72,73} Exposure to Early-life Stress (ES) is associated with lasting changes in the structure of the adult brain and accelerated cognitive decline. Being exposed to stress of any kind in early life will in turn lead

to unhealthy sedentary lifestyle which eventually affects the cognitive functions as it has been discussed above.

Role of Free Radical in Development of Neurodegenerative Disorders

Free radicals are metabolic by products produced naturally in our body through oxidation and it is said to be highly reactive and unstable molecules. In addition to being generated from a normal metabolic process in the body, it is also produced due to exposure to carcinogens and toxins in the environment such as ultraviolet light and tobacco smoke.⁷⁴ The term oxidative stress is used to describe the oxidative damage resulting from unfavorable and critical imbalance between free radical generation and antioxidant defenses.⁷⁵ Oxidative stress is a harmful condition that occurs when there is an excess of free radicals and/or a decrease in antioxidant levels. It can be the cause of environmental factors such as pollutants, chemicals and radiation.⁷⁶ The brain, spinal cord and peripheral nerves which comprise the nervous system is rich in both iron and unsaturated fatty acids. The nervous tissue is particularly susceptible to oxidative damage due to high lipid content coupled with its high aerobic metabolic activity. There is substantial evidence that oxidative stress is a causative factor in the pathogenesis of major neurodegenerative diseases, including Parkinson's disease, Alzheimer's disease and amyotrophic lateral sclerosis (ALS, "Lou Gehrig's disease") also in cases of stroke, trauma and seizures.⁷⁷ The proof to date for oxidative stress in Parkinson's Disease, Schizophrenia, Alzheimer's Disease and different neurodegenerative ailments is strongly persuasive. Clinical research exhibit that a range of events associated with Alzheimer's are capable of stimulating production of free radicals and depletion of antioxidant levels. Additionally, free radical injury is observed in the form of elevated lipid peroxidation and oxidation of DNA bases among patients with Parkinson's Disease.⁷⁸

CONCLUSION

It is fundamental to understand the relationship between sedentary behaviour and health, modifying these behaviors in order to reduce the morbidity and mortality rates caused by the health complications which follow. Sedentary lifestyle leads to and exposes individuals (both old and young) to various non-communicable and devastating diseases. Neurodegenerative disorders remain an important source of morbidity and chronic suffering globally which has a strong link on lifestyle habits as discussed earlier. Hence, it is essential to promote healthy lifestyle, raising public awareness, understanding about diseases particularly on neurodegeneration and its possible root cause arising from one's lifestyle and habits particularly in the low socioeconomic community. Expansion of educational programs for general prediction, based on psychological empowerment in lower age groups (children and teenagers) could also be effective in reduction of drug abuses. Neurodegenerative disease can be associated with risk factors, for example, vascular risk factors (commonly hypertension and high cholesterol). Over the years we have come to know that most of the metabolic diseases specifically hypertension, diabetes and hypercholesterolemia are due to high consumption of high sodium substance commonly found in fast food. Frequent visits and excessive intake of processed or fast food are commonly practiced among the working urban community. According to most of the studies that has been done, it can be said that lifestyle has a significant influence on physical and mental health of humans. It is indeed crucial to encourage healthy behaviors, lifestyle modifications, physical and mental activities on a daily basis that contributes to cognitive ability and the maintenance of healthy mental functioning, such as exercising the mind, being social, healthy eating, stress reduction and appropriate sleep. It is also evident that in addition to reducing the risk of cognitive decline and

dementia, these lifestyle modifications will delay the possible onset of neurodegeneration.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

ABBREVIATIONS

AD: Alzheimer's disease; **ES:** Early-life stress; **PD:** Parkinson's disease; **ROS:** Reactive oxygen species; **MCI:** Mild cognitive impairment; **VD:** Vascular dementia; **ALS:** Amyotrophic lateral sclerosis; **HD:** Huntington's disease.

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