

# Brain Health as a Key Concept in the Development of Strategies for Delaying Age-Related Cognitive Decline and Alzheimer's Disease

**Keywords:** Brain health; Aging; Alzheimer's disease; Plasticity; Environmental enrichment

## Abstract

The rapid growth of the elderly population is accompanied by a continuous increase in the incidence of neurodegenerative diseases. This demographic change has financial, social and cultural consequences although it also represents a business opportunity and a scientific challenge. There is a need for developing novel and creative strategies based in a life-course perspective aimed at the prevention of dementia. In the current paper, the approach to this objective will be based on a review of the "brain health" concept identifying public and private initiatives to promote a healthier lifestyle. We emphasize the relationship between different factors (cognitive training, nutrition, physical activity, bilingualism, stress reduction, intellectual enrichment, etc.) with brain health maintenance and enhancement. Neuroscientific research and studies about "environmental enrichment" in animal models can also help us to search new strategies for maintaining brain functionality. An innovative approach that integrates technology, neuroscience and innovation will contribute to design multi-domain lifestyle interventions. Health education and policies related to public health can aid in the promotion of all the strategies aimed to reach a healthy aging brain, increasing cognitive reserve and contributing to the prevention of age related cognitive decline and dementia.

## Introduction

Successful aging is now considered as a multidimensional concept that involves behavioral, physical, biological and social factors. All these components must be taken into consideration when designing interventions to prevent physical and cognitive impairment [1]. It is known that the pathological changes of Alzheimer's disease may be detected as early as 20 years prior to clinical symptoms. In fact, prevention is proposed as a key element in the development of strategies aimed at reducing the prevalence of dementia in our society [2]. The continuous increase in the incidence of neurodegenerative diseases is accompanied by financial, social and cultural consequences [3,4] and has a considerable impact on public health [5]. However, the aging of the population also represents a business opportunity [3,6] and a scientific challenge [7]. New and more creative strategies are needed to stop, or at least prevent/delay, the increasing prevalence of dementia.

Early recognition of cognitive decline and the start of preventive treatments at an early stage can be the best hope for Alzheimer's disease [8]. According to recent advances in the diagnostic of Middle Cognitive Impairment (MCI) and Alzheimer's disease, it would be possible to seek strategies aimed at the prevention of dementia based



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in a life-course perspective [9,10]. The ultimate goal is to maintain our physical and cognitive health while also achieving better emotional health and increased social well-being [4,11]. Promoting resilience and cognitive reserve against cognitive decline could help us pursue these aims [4]. In this paper, our main objective is to highlight the idea that the most effective approaches to prevent cognitive impairment and Alzheimer's disease are based on strategies for "health brain" maintenance and enhancement.

## What Does "Brain Health" Mean?

"Brain health" as a goal based on the implementation of different preventive strategies is an idea included in the most recent papers which address the issue of a healthier aging brain [3]. A few systematic reviews related to major initiatives focused on maximizing lifelong brain health have been recently published. These papers would be of interest in order to promote a better understanding of this perspective among healthy adults. Several recent studies and epidemiological data suggest that some risk factors for Alzheimer's disease are modifiable (obesity, hypertension and low physical activity) and that even a slight delay in the age of onset of this neurodegenerative disorder could have a significant impact on public health [12].

The definition of the term "brain health" differs between studies and there is no clear consensus on which factors or domains should be included in it. In a recent search (November 2015) performed by us in PubMed including the keywords "brain health", only three papers were recovered. However, if we use "healthy brain aging" as keywords, a total of 5051 documents were identified. This difference suggests that while the factors related to maintaining a healthy brain are present in recently published research on prevention strategies of cognitive decline and Alzheimer's disease, "brain health" is not still regarded as a "keyword" in published papers about this topic.

We need to understand what "healthy aging" means in order to get more information about all the aspects of "healthy brain aging" [13]. A better knowledge of cognitive and brain aging could also help

us to understand more in depth the development of Alzheimer's disease. It is also very important to promote neuroplasticity by cognitive and physical training [14] taking into account age-related individual differences [15]. These interventions could help us to build cognitive reserve and delay the onset of neurodegenerative disorders [12].

In recent years, several public and private initiatives have been proposed to promote brain fitness and a healthier lifestyle [16]: review papers [17,18], books (*The Sharp brains guide to brain fitness: How to optimize brain health and performance at any age* by Fernandez, Goldberg, and Michelin), brain gyms (Brain Fitness Pavilion at the Mental Health Hospital, South Florida), international initiatives aimed to dementia prevention (European Dementia Prevention Initiative; The Healthy Brain Initiative); blogs (<http://yourbrainhealth.com.au/>); brain health education programs (Healthy habits for a healthier you); apps (Peak, Brain Baseline); webs for cognitive assessment (<https://www.cogniciti.com/>) or intervention studies (Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER)). These are just some examples of different types of information available to the general public. These resources are increasing rapidly in response to society's demands.

Recently published reviews of great interest about the concepts of "brain health" and "cognitive health" [3], "brain functionality" [19], "brain fitness" [7] or "cognitive vitality" [20] and strategies based on these ideas could help advance the search for more effective treatments for Alzheimer's disease and other neurodegenerative disorders [3].

### **Interventions Aimed to Promote Successful Cognitive Aging**

Different interventions have been proposed in the last years as useful strategies aimed to obtain a more successful aging. Since there are excellent recent reviews about these topics we will mainly emphasize the relationship between each one of these factors and brain health maintenance in order to highlight some of the main conclusions of this approach.

Cognitive training is one of the strategies that involve more support in different studies. Systematic reviews indicate that cognitive training (including computerized training and video-games) can have positive effects on long-term and working memory and on subjective measures of cognitive performance although more studies are needed regarding the transfer of these gains to daily living [19]. Psycho education has also been proposed as a component that can have additive effects with cognitive training contributing to the improvement of mood, sleep functions and cognitive performance [10]. Musical training offers protection against cognitive decline and improves performance in tasks of phonemic fluency, verbal immediate recall and working memory [21] and has also been proposed as a good model for evaluating brain plasticity along life [22].

The use of video games in brain health promotion has been recently underscored [19], although there is no clear consensus with regard to their possible benefits in elderly population. It will be necessary to perform longitudinal studies in order to evaluate if gains obtained with training are transferred to daily life activities [10]. The use of technology in daily life has also been evaluated as a mean of maintaining cognitive functioning in elderly at advanced ages since it represents a challenge for them. Within this perspective, internet can

be used for conducting intervention programs (including different intervention strategies based on email use, newsletters, webs, etc.) aimed to prevent cognitive decline and promote lifestyle changes [23].

Physical activity directly promotes plasticity and neurogenesis in different brain areas, including hippocampus, and contributes to the formation of cognitive reserve [24,25]. A recent research with older men suggests that the positive effects of aerobic fitness on cognitive function may be mediated by frontal lateralization during the performance of the cognitive task [25]. Some authors have suggested the idea that "*exercise can act as a drug*" [26] or considered as "*brain food*" [27], although it would be necessary to take into account individual differences when evaluating the doses of exercise needed for different populations [26]. Increases in BDNF levels have been reported as a consequence of physical activity or changes in nutrition whereas exposure to stress decreases the expression of this neurotropic factor [28]. There is also an increasing interest in evaluating how physical environment can be considered as a form of cognitive training. In this context, the role of brain derived neurotrophic factors (BDNF) and other neurotrophic factors in aging and Alzheimer's disease has been recently reviewed in depth [28]. Animal models can also contribute to build bridges between basic research and applied science including recommendations for exercise in human subjects [24]. This approach will allow the advance of the knowledge about the mechanisms by which exercise enhances plasticity and contributes to brain health. Preclinical studies suggest that cognitive, motor, social and somatosensory stimulation involved in enriched environments can increase adult plasticity and neurogenesis [29].

Some authors use the concept "intellectual enrichment" (including factors such as: occupation throughout life, participation in cognitively stimulating activities, education, etc.) [5] as an intervention for dementia prevention. "Environmental enrichment" is a term more associated with animal models although it has also been applied in reference to complex environments in humans [30,31]. Enriched animals display improved performance in learning and memory tasks and decreased anxiety-like behavior. Studies performed in different enriched environments in rodents offer a clue for interpreting neurobiological mechanisms related to beneficial effects of different lifestyle factors (cognitive training, aerobic physical exercise, reduction of stress, etc.) and complex environments in human subjects [30-32]. This type of environments provides three key elements: social contact, physical exercise and novelty. Both experience and changes in the enriched environment may modulate adult neurogenesis [30].

Cumulative stress can have detrimental effects on cognitive aging and telomere length [33]. For that reason, developing resilience as a strategy for stress coping in chronic situations can be a useful intervention against cognitive aging [31,33]. Excess of glucocorticoids have harmful effects on the hippocampus and has been associated with the decline in cognitive functioning [31]. In animal models, environmental enrichment counteract some of the deleterious effects of stress [31] and must also be investigated as an effective intervention in human subjects both for age-related cognitive decline and for the treatment of mental disorders.

Dietary guidelines for the prevention of Alzheimer's disease had been recently published [34] and the adherence to the Mediterranean

diet appears as a pattern that can help to increase cognitive function and to decrease the risk of cognitive decline and Alzheimer's disease [35]. However, more studies are needed to implement general dietary recommendations aimed at promoting cognitive health. The cognitive benefits of the Mediterranean diet could be mediated by different factors such as the reduction of cardiovascular risk or its effects on glucose metabolism, although direct effects of specific nutrients on the brain cannot be discarded [12,35].

Many other factors such as social engagement, bilingualism or education can also have a crucial role in healthy brain aging although further evidence is needed [34,36]. We need to perform multi-domain studies that combine the effects of different lifestyle factors involving multiple resources and interventions [2,12,19]. As Deweerdt emphasizes in the title of a paper about prevention of the cognitive decline associated to Alzheimer's disease, "*Activity is the best medicine*" although more research should be done in order to determine the "dose" and "timing" of these interventions based on lifestyle changes [37].

### A Roadmap for the Future

Recent demographic trends are characterized by rapid growth of the elderly population. In this context, health education has been proposed as an effective tool to disseminate the message that physical activity, cognitive stimulation and social interaction could be factors that influence brain and cognitive health [4]. As we have reviewed in previous sections, many studies emphasize the importance of lifestyle changes in order to maintain brain health [31]. The control of modifiable risk factors for cardiovascular diseases may also have an impact on cognitive aging [38]. It has been proposed that prevention strategies and the benefits of a healthier lifestyle for brain fitness can be transmitted to the public through educational programs [4,7] and other interventions [3]. The efforts may involve different levels: individual change, community programs and policies related to public health. All these factors would help promote the "mental capital" (including both the emotional and cognitive resources) in our aging society [39].

In the absence of effective treatments for Alzheimer's disease, new therapeutic approaches that can help prevent and/or delay the onset of this disorder are considered to be essential. Different lifestyle factors such as cognitive, social and/or physical activity seem to have great potential for the prevention of Alzheimer's disease [24,40]. Therefore, understanding the mechanisms underlying the neurobiological effects of these factors is crucial in order to design better interventions. It has been suggested that lifestyle influences cognitive decline by means of neuroprotective mechanisms involved in earlier stages and of compensatory mechanisms in later stages [9]. In order to evaluate the results of these mechanisms, we need to understand the complex interactions between the aging brain and changes in cognitive functions or, in words of Lindenberger, "*how behavior influences brain aging*" and "*how brain aging influences behavior*" [15].

A lifelong trajectory perspective can be taken to promote brain health and delay the prevalence of Alzheimer's disease [7]. We support the idea that the neuroscientific research about neuroplasticity and neurodegeneration can help us to search new strategies for maintaining brain functionality [19]. An innovative approach that

integrates technology, neuroscience and innovation will contribute to design multi-domain interventions to promote "brain health" [3,19]. In this context, a multivariate approach addressing changes in lifestyles are being considered as the pathway towards a more successful aging [17]. Advances in the scientific understanding of all the factors related to the "healthy brain aging" should lead to political and social actions [41].

Throughout the literature review, we appreciate a shift in focus from the classics to the most recent papers: a disease-oriented perspective of brain aging is leading to a new perspective more based in brain health [42,43]. This change is also reflected in the research both in neuroscience [43] and in cognitive science [15]. As Richards and Hatch affirm in the title of their paper, we have "*good news about the ageing brain*" [44].

### Conclusions

It is recognized that there are some "modifiable risk factors" that can be applied to improve cognitive aging. In this way, new and more creative strategies could be proposed [44]. In all these interventions, promoting "brain health" is considered a good strategy to maintain the cognitive vitality throughout life. Public perceptions about the main risks and protective factors for cognitive decline and Alzheimer's disease frequently are not based in scientific evidence [17,45]. For that reason, public health policies could be addressed to try to get a comprehensive promotion of all these strategies aimed at promoting a successful brain aging. This will contribute to the prevention of age related cognitive decline and dementia [31]. In this context, different interventions may be useful to increase cognitive reserve contributing to brain health maintenance.

The information provided to the public must be based on scientific research [44,45]. Lifespan psychology and cognitive neuroscience can offer us a framework integrating advances in knowledge about cognitive aging and preventive strategies for Alzheimer's disease [15,19]. The better knowledge of neuroplasticity mechanisms can also help us to design better interventions for delaying cognitive aging [15,31]. From basic research, animal models of environmental enrichment contribute to the understanding of neural and behavioral changes associated with complex environments [31]. Results obtained in preclinical studies also support the idea that new and complex cognitive experiences increase neurogenesis and stimulate neuroplasticity and may have additive effects with physical activity [30,46].

We can conclude following the idea proposed by Petersen et al. that brain health not only involves cognitive fitness but also emotional well-being and general health maintenance [47].

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