

Review Article

The Continuing Challenge of Cognitive Decline: An Individual Process of Aging?

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Abstract

During the modern gerontology the cognitive decline were generally considered as an inevitable and natural accompaniment of aging. Over the past decade, the distinction between normative from non-normative changes remains difficult. The purpose of this review is to present a synthesis and integration of the current knowledge of cognitive decline by interdisciplinary perspectives. The theories of cognitive decline based on neuroplasticity and the predictors of cognitive decline are also discussed. In addition, highlights current strengths and limitations of the cognitive decline studies are critically analyzed.

Current researches are contesting the discouraging perspective that assumes that the cognitive decline is related to normal process of aging across the life span. The view that aging is a synonym of cognitive decline is being replaced by the recognition that it is a multidimensional and multidirectional process. However, cognitive decline is still not well understood.

Presently, firm conclusions about if the cognitive decline is a part of the normal process of aging or just an individual process do not exist, there are only speculations. The empirical findings are heterogeneous and the resolution may reside on interdisciplinary robust research.

Keywords: Cognitive decline; Aging; Risk factors; Protective factors; Neuroplasticity

Abbreviation

SCG: Subjective Cognitive Complain; AD: Alzheimer's Disease; MCI: Mild Cognitive Impairment; DSM-5: Diagnostic and Statistical Manual of Mental Disorders - Fifth Edition.

Introduction

The well-known demographic changes on Western societies related to the aging of the population due to the progresses in medical advances and technology used to treat a vast variety of problems, which have increased the average of the life expectancy [1]. This will change dramatically the age distribution in the next fifty years, where the people of age 65 and older constitute a substantial part of the population. For this reason, life course changes in the cognitive abilities are an emergent phenomenon and a high priority scientific challenge [2].

It is widely agreed that cognitive decline is a reduction in cognitive abilities known as a normal part of aging [3] which has a negative influence on personal life and family functioning, as well as health status, economic and healthcare repercussions [4,5]. Understanding how to prevent and delay cognitive decline is important because these decline can herald older adult who will suffer from dementia in the next decades and contribute significantly to the reduction of costs of caring for the individual, the family and the government [4,5].

The changes in cognitive function in human aging is not uniform across the whole brain or all cognitive abilities, neither across all older adult [6-8].

The cognitive reserve hypothesis and the theories of cognitive based on neuroplasticity suggests that the brain has the capacity to adapt to the process of aging, namely the response to the decrease of cognitive abilities and sensory-motor, but also to the physical, cognitive and social environment changes [9-12]. There is a growing tendency to consider that the brain displays certain plasticity. For this reason, some older adult maintain a good cognitive performance, others experience decline in certain cognitive abilities [5,9,13].

In addition, the theory of biocultural co-constructivism consider that the structure and function of the human brain is shaped with the reciprocal action of co morbidities, the genes, the physical, the cognitive and the social environment [9,13], and also to disclose that each personal variables will interfere in the rate of changes as well as affect differently the process of aging [6-8,14,15]. In fact, the reasons regarding cognitive decline has still not been fully understood.

In this review, we will critically discuss the emerging trends and the developments of interdisciplinary research aiming to explore if the cognitive decline is a part of the normal process of aging or just an individual process, characterized by the individual specificities.

Overview of the cognitive decline in neuroscience and psychology

Aging, brain and cognition: Aging is an inescapable natural biologic process, regulated by genetic factors and influenced by environmental factors [13,15,16]. Successful aging for older adults is defined as the absence of physical and mental disease or disability that is associated with subjective perspectives of aging well [17].

There is an ample evidence that life course concerns neuroanatomical, morphologic biochemical and functional changes who are intimately tied to alterations in cognitive function at different stages in lifespan [16]. These processes can lead to damage from oxidative stress, diminished ability to detoxify free radicals, decline in mitochondrial function, accumulation of amyloid- β peptide and tau protein, decrease integrity of neuronal membranes, loss of neurons and synapses, altered metabolic functions to cell death [18-21]. The vast majority of imaging studies have suggested that notable changes with healthy aging occurs markedly in frontal regions, but in whole brain, particularly white matter volume, the prefrontal cortex, hippocampus, sub cortical regions (thalamus, putamen, caudate, nucleus accumbens) and parietal and temporal lobe volume, as well as ventricular expansion, that is correlated with poor cognitive performance [12,18,22]. These changes may be related to gender. In men, the frontal and temporal lobes are the most affected [23]. Whereas in women is the hippocampus and parietal lobes [18]. The reduction of neurotransmitters has been also incorporated in the normal aging process. This reduction on dopamine and acetylcholine seems to be related with difficulties in planning and small declines in memory, respectively [12,19]. Studies using brain imaging techniques and postmortem are considering the presence of inter individual variability and providing evidences of neurodevelopmental arrests in adulthood [23].

Over the past few years, a considerably evidence has been accumulated suggesting that advancing chronological age is associated by a systematic decline in many cognitive abilities that play a prominent role. Over time, some cognitive abilities stabilize and other may even increase. The fluid abilities are the most affected cognitive abilities by advancing of age [24]. As a matter of fact, significant changes in cognition can occur in multiple domains, including the well-established episodic memory, attention, verbal fluency, processing speed, explicit memory, executive functions, attention, working memory and language, which suffer a substantial decline thought much of adult age range [24]. Another important consideration is that some aspects of cognition remains stable, or even improves, across lifetime [25]. This is the case of crystallized intelligence and emotion regulation [26]. For example, semantic memory can remain stable throughout the life trajectory or, in some cases, develop with age. In contrast with has been mentioned above, the amygdala's function is preserved in healthy older adults and shows a minimal atrophy, as compared to other brain regions [12,26]. Relatively spared until late in life are knowledge-based verbal abilities and verbal production, implicit memory and autobiographical memory [27].

So far, the search of the study of this relationship between volumetric cortical loss and cognitive decline aging has contradictory results. It has been proposed that education and brain volume are measures of cognitive reserve and predict slower progression to cognitive decline [9,25]. Education, or intelligence itself, is also an important protect factor for age-related changes that can impair cognition [28]. In terms of life-course perceptible there is a continuum between cognitive deficits, childhood intelligence quotient and brain cortical thickness [2], which may be a predictor of a successful cognitive aging future and also reduce the chance of developing vascular dementia [29]. For this reason, higher education level is

accompanied with greater cognitive performance [28], particularly in executive and processing function [22]. This suggests that individuals with successful coping with normal age-associated cognitive decline are assumed to have higher cognitive reserve and develop a more brain efficiency throughout a more efficient use of brain networks [16]. The opposite occur in the female gender, with less school years, less levels of physical activity and depression [28,30]. There is the hypothesis, that education may influence the cognitive trajectory by promoting health consciousness, more physical exercise, better stress management, meaningful social network and mentally-stimulating activities [9,10,28].

The potential harbingers for future cognitive decline can be the Subjective Cognitive Complain (SCG). The SCG may represent a higher risk of progression to objective cognitive impairment or neuropathologies and it is the earliest manifestation of Alzheimer disease [31,32]. Recent findings support that an objective decline, whether self- or informant-based, are correlated with greater psychological distress and could be an early indicator of cognitive decline [31]. In fact, the clinical significance remains highly controversial because these complains are correlated with psychological factors or are related to abnormal cerebrospinal fluid biomarkers of Alzheimer disease [33]. These correlations make this complain a clinical challenge to interpret. Apparently clinically normal older adults with SCG can represent a unique opportunity to study the natural course and history of Alzheimer disease but also represent an important clue for early detection and preventive interventions [31,32].

The complexity of brain, neural and cognitive function makes the exact mapping of this cognitive decline extraordinarily difficult. In fact, cognitive decline does not occur uniformly, whereas some cognitive abilities are more susceptible affected than others to effects of aging [23]. The etiology of the change, the chronological point when this becomes evident, its magnitude and rate of progression varies with cognitive function and among individuals [19]. Accordingly, some older adults experience cognitive decline, others perform as well or better than younger adults and the same individual may perform differently in different domains. The functional neuroimaging studies reveals that owing to the normal processes of aging, the older adults when compared to young people, exhibit more activity in the right hemispheres, the ventral or dorsal prefrontal cortex during memory tasks and the frontal and parietal throughout attention tasks [7,8,12]. According to the theories of neuroplasticity, it's thinkable that older adult may over recruited areas to compensate the weakness ones [11,12]. Another possibility is that bilateral activation represents a greater attentional effort a less selective cognitive processing or can be related to an inefficiency of sensory and perceptual abilities [22]. An understanding of such processes not only are important to the inferring neural plasticity and to how the development of brain function across life, but can also be a source of insight into the ways of this aging changes support the prism of adaptation. Another controversial issue resides in neuronal regeneration. It is hypothesized the development of dentate gyrus cells on hippocampus [34]. However, the precise function and survival of these new cells is still unknown.

The relationship between age-related changes in brain structure, function and cognition are not uniform across the whole brain neither

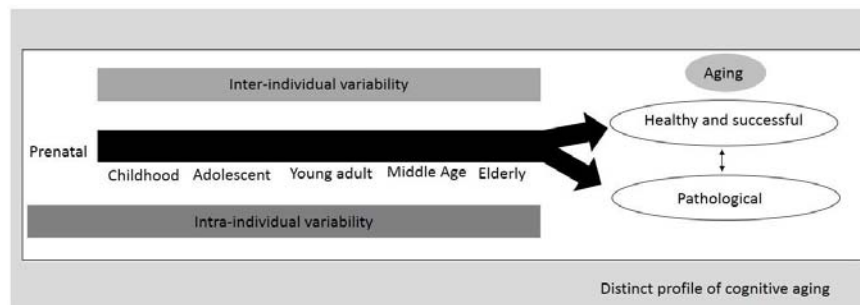


Figure 1: Overview of individual cognitive decline for healthy and successful aging.

across all older adult [6-8]. The debate still exists to identify what is cognitive decline and what is the underlying mechanism responsible for those changes.

Predictors of cognitive decline: Several decades of research revealed that biological, psychological, social engagement and lifestyle can be regarded as predictors of cognitive decline [10,35].

The most cited risks factors are age, gender, education, objective and subjective difficulties like memory, reduced hippocampal size, mood, personality (neuroticism), amyloid deposition, carrying one or two apolipoprotein e4 alleles, presenilin-1 and presenilin-2, sensory difficulties, sedentary lifestyles, multiple medical comorbidities, and finally, innumerable medical problems (hypertension and diabetes) [20,21,36].

Relevant longitudinal and cross-sectional studies indicate that chronological timetable aging is absent and the diseases processes are independent of normal aging. It is noteworthy that aging increase the risk for neurodegenerative diseases, vascular diseases (vascular and micro vascular changes) [37], APOE-ε4 allele, stress-related corticosteroid levels, lipid levels (cholesterol pathway) and chronic inflammation, which is associated as common brain abnormalities in older adult [20]. Although changes in the bodies exists and were marked by the decline over the time and these modifications do not inevitably lead to diseases such as diabetes or hypertension [38,39].

Besides that, the link between this variable and cognitive decline has not been clarified. It is plausible that the cognitive performance decrements are associated with high arterial blood pressure, diabetes mellitus, dyslipidemia, hypercholesterolemia, smoking, alcohol, incident stroke or small vessel disease [36-39]. The association of risk factors, brain lesion and cognition is complex. However, the treatment of vascular risk factors can actually prevent or postpone the cognitive decline and for the smokers the risk might be limited to specific cognitive domains [37]. Preventing and diagnosis metabolic and cardiovascular diseases might be essential to promote cognitively healthy aging, but their applicability to research and clinical practice is somewhat restricted.

Common or individual differences in cognitive decline: Implicit in the concept of healthy and successful aging is the idea that the cognitive decline forms are continuum, so cognitive changes associated to aging usually are in mild and do not interfere with normal daily activities [17]. Often, the distinction of normative from non-normative changes remains difficult. On the one hand the recognition of the predementia symptomatic stage of impairment

resulted in the identification of the Mild Cognitive Impairment (MCI), as a transitional stage between normal aging and Alzheimer's Disease (AD) [40]. On the other hand, in dementia research there is a long debate about if AD is an extreme of these continuum (continuity view), presented in the revised diagnostic guidelines [3], or a category different from normal ageing (discontinuity view) [5]. Recently, reinforced by longitudinal studies, investigators started to consider that the heterogeneity in cognitive decline across life time can reflect a variety of underlying neuropathological conditions. For this reason, predicting the progressive to MCI, then to AD, versus the remittent course of MCI in the primary care is so important. However, the concept of MCI into clinical diagnostic algorithms, such as the Diagnostic and Statistical Manual of Mental Disorders - Fifth Edition (DSM-5) [41], remains questionable, because three-quarters of patients with MCI stayed cognitively stable or even improved within 3 years [42].

Cognitive decline cannot be considered unavoidable, it is not known whether is, or not, an inevitable consequence of the advancing of age [7,8,15]. The view that aging is a synonym of cognitive decline is being replaced by the recognition that many individuals maintain mental acuity even with the advance of age [7]. However, firm conclusions about the etiology of the normal changes do not exist, and there are only speculations.

It is abundantly clear that cognitive functioning are overlap and interactive in a complex way and the evolution of cognitive performance over the life-span is not a uniform process, but instead is heterogeneous [7,8,15]. As summarized in (Figure 1), this variability makes it difficult to predict a single profile of cognitive aging [43].

Current research is contesting that discouraging perspective and claiming that significant cognitive decline cannot be attributed to age alone [16]. The answer for the biggest question for the aging researchers is what accounts for this multidimensional and multidirectional process of cognitive decline is the enormous inter-individual variability (diversity) and intra-individual variability (dispersion) [6,44]. In cognitive performance the diversity has been associated with education, social engagement, economic resources and genetic factors, whereas dispersion has been associated with demographic, health and individual characteristics [44].

The biocultural co-constructivism theory suggests that the brain and cognition abilities are shaped continually, not only in early development, but also in adult life span [45]. This emerging trend of interdisciplinary research are making the first steps in

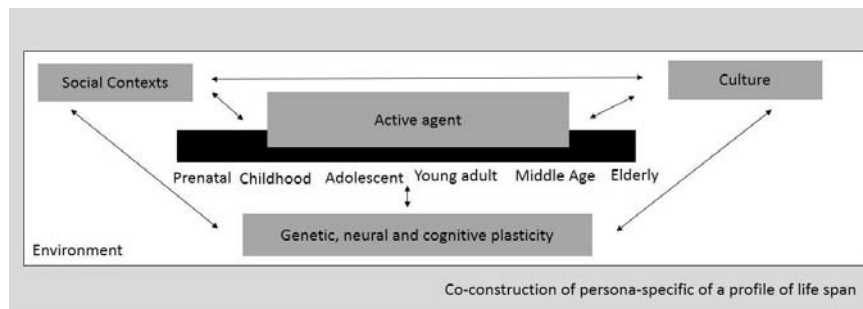


Figure 2: Life span development by the view of biocultural co-constructivism theory.

the understanding that life span is co-constructed [46-48]. In fact, according to this view, neurobehavioral development across the life span are a reciprocal co-constructive interaction between environment, culture, social context, behavioral, genetic, neural and cognitive plasticity, and occurs simultaneously in the different time scales (i.e., moment-to-moment micro genesis, life span ontogeny, and human phylogeny) and encompassing multiple levels (i.e., neurobiological, cognitive, behavioral, and socio cultural), which implies the diversity in the form of inter-individual difference [48] (Figure 2). For this reason, the individuals are not passive recipients of their biological, ecological and cultural inheritances [46]. Instead they are active agents and their behavior, memory plasticity, plasticity of the functional organization of cognitive and cortical processes and dopaminergic system influence the development and organization of their brain functional architecture [49]. The brain is an open, dynamic and adaptive system that was personalized through lifespan [47].

The biocultural co-constructivism theory has been accumulating empirical evidence; however details about reciprocal co-constructive interactions are still not well understood [49].

The complex of the life span development and the large number factors that influences the rate of the cognitive aging between and within individuals on an interactive and distinct way. Much of the research continues to investigate the common factors that may explain the overall population shift and those that differentially affect individuals [13,15]. Likewise, assume that cognitive decline has clear generalities and common principles, but attributes this to variability from individual to individual [6-8,14,15].

Limitation in cognitive decline studies: The determinants of the cognitive aging across the life span are mainly explored by diverse scientific areas like biomedical and psychological science. The rapid and immense progress in the last decades have probably provided findings with several limitation, specifically, (a) samples of convenience have small sizes, which lessen the validity of any statistics derived from them, (b) latent variables are commonly reported, (c) group data poorly replicates the information about the individual patient, (d) clinical groups with heterogeneous characteristics, (e) reduced construct validity of the neuropsychological tests (measuring more than one cognitive function), (f) short follow-up, and (g) the possibility of undiagnosed the stage of pathological cognitive impairment or reverse causation are present [2], [5,13,15].

The solution for those limitations may be in the addition of more disciplines, not only, medicine and psychology, but also

genetics, sociology, economics, epidemiology, education or even communication [13]. Future research would benefit with the development of translational research methodologies, able to transfer the results from a controlled laboratory studies to real life scenario. In turn, this will improve each discipline and provide ambitious and promising advance in understand deeper the complexity and diversity of the life span.

Conclusion

At present, there are a number of questions that remains open. The differences between successful aging and age-related diseases are poorly understood or have depressingly few answers. The reasons for individual differences on aging are a matter of considerable debate. The key question phenomenon of cognitive decline needs some agreement among the different theoretical perspectives of aging, in order to determine the best methods to establish the dynamic relationship between demographic, biological, social, environment and personal factors. In view of the large limitations reported in the study of cognitive decline, it seems necessary to explore and generate new research hypotheses.

Firm understanding of the title of this article, The continuing challenge of cognitive decline: an individual process of aging?, hints to another important direction for the future research of cognitive abilities in later adult life: the extraordinary opportunity to the development of an cross-disciplinary investigation with the integration or expansion of contemporary prospective cohort studies with longer follow-up, in order to create a different epidemiological study that may integrate a world-wide database about the course of the evolution of human cognition. A better understanding has potential targets like the interventions that could positively affect several aspects of the life course changes in cognitive, prevent age-related diseases and to improve active life expectancy and promote longevity free of disease and disability. Besides engagement in physical, social and cognitive activities, aging has potential for continued successful development.

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