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“*BRAIN WALKING GREEN*”

A pilot study on a preventive protocol of combined physical activity and cognitive stimulation in a group of older adults coming from Marche.

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Abstract

Background. Today we live more, but not necessarily better. The percentage of elderly people in the general population increases year by year, and the importance of adopting a bio-psycho-social approach in both treatment and prevention is becoming significant in preventing neurodegenerative conditions to broaden the concept of well-being and considering health not as "absence of disease", but as quality of life experienced and perceived. *Purpose of the study*. The present work aims to test the efficacy of a preventive intervention protocol consisting in multiple sessions of combined cognitive stimulation and Nordic Walking training within a group of healthy elders coming from central Italy (Macerata, Marche). The program is called: "Brain Walking Green", and it strives to improve cognitive performance, quality of life, physical wellness, satisfaction of the present living status and, in general, well-being. *Methods*. Subjects coming from the central Italy (Macerata, Marche) followed 90 minutes of intervention two times per week across a month. It consisted of 45 minutes of Nordic Walking training and 45 minutes of cognitive stimulation tasks. Pre and post-operative evaluations were carried out using 7 tools, aimed at evaluating general cognition, health and quality of life (QoL): 1) Addenbrooke's Cognitive Examination (ACE-R); 2) Cognitive Reserve Index questionnaire (CRIq); 3) Free and Cued Selective Recall Reminding Test (FCSRT); 4) Geriatric Depression Scale (GDS); 5) World Health Organization Quality of Life Scale (WHOQOL-BREF); 6) Short Form Healthy Survey (SF-12); 7) Motivation for Change - Physical Activity (MAC2-AF). Physical state was assessed with the following tools: 1) Tinetti scale; 2) Conley scale; 3) 6-minutes'walk test, adapted for this study testing 1 minute only. The study included an inactive control group (n = 11). *Results*. Cognitive outcomes resulted to be significantly modified by the intervention. Significant improvements were reported in general cognitive performance in the experimental group, while memory performance resulted to be improved in both experimental and control group. Post-training blood pressure values resulted significantly decreased only in the experimental group. No significant differences were detected in other secondary outcomes**.** *Discussion*. Even if there were not reported significant differences between pre and post intervention, participants revealed themselves as more confident and engaged after the protocol. General mood, trust, and self-awareness raised at the end of the intervention. The study doesn't lack of limitations, principally due to the presence of an unbalanced small sample. *Conclusion***.** Few significant results emerged on the protocol efficacy in this study**.** However, participating in multimodal interventions appeared to enhance the quality of life and the general motivation towards well-being and social engagement. Future research could include more participants, balancing gender, enlarge the total number of sessions, evaluate the role of individual differences, and test the effect of an active control group.

Introduzione. Oggi viviamo di più, ma non necessariamente meglio. La percentuale di soggetti anziani nella popolazione generale aumenta di anno in anno, e con questa il rischio di sviluppare patologie neurodegenerative tra cui, in ampia misura, le diverse forme di demenza. Adottare un approccio bio-psico-sociale multifattoriale sia in fase di trattamento che di prevenzione è fondamentale per ampliare il concetto di *ben-essere*, considerando la salute non come "assenza di malattia", ma come qualità della vita esperita e percepita. *Proposito dello studio*. Scopo di questo studio è stato valutare l'efficacia di un protocollo di stimolazione cognitiva abbinata ad un'attività fisica specifica, vale a dire il Nordic Walking. Il protocollo si chiama "Brain Walking Green" e ha lo scopo di migliorare la performance cognitiva generale, lo stato di salute fisica e il benessere esperito e percepito in un gruppo di anziani sani proveniente dall'Italia centrale (Macerata, Marche) con la finalità di preservarli dal declino cognitivo. *Metodi*. Un gruppo di 11 soggetti dai 60 anni su hanno seguito il "Brain Walking Green" nell'arco di tempo di un mese, 2 volte a settimana per 90 minuti, di cui 45 dedicati al Nordic Walking e 45 a degli esercizi di stimolazione cognitiva. Sono state effettuate delle valutazioni pre e post intervento utilizzando 7 strumenti, volti alla valutazione della situazione cognitiva, della percezione della propria salute e della qualità di vita: 1) Addenbrooke's Cognitive Examination (ACE-R); 2) Cognitive Reserve Index questionnaire (CRIq); 3) Free and Cued Selective Recall Reminding Test (FCSRT); 4) Geriatric Depression Scale (GDS); 5) World Health Organization Quality of Life Scale-BREF (WHOQoL-BREF); 6) Short Form Healthy Survey (SF-12); 7) Motivazione al Cambiamento – Attività Fisica (MAC2-AF). Lo stato fisico è stato valutato mediante: 1) scala Tinetti; 2) scala Conley; 3) 6-minutes' walk test. Nello studio è stato incluso un gruppo di controllo inattivo (n = 11). *Risultati*. Gli unici risultati significativi sono emersi nelle prestazoni cognitive generali nel gruppo sperimentale, e nella performance di memoria sia nel gruppo sperimentale che in quello di controllo. Soltanto nel gruppo sperimentale è stato possibile rilevare una diminuzione significativa dei valori della pressione sanguigna post camminata alla fine dell'intervento. Nessun altro outcome secondario è risultato significativo. *Discussione*. Nonostante non siano state riportate differenze significative tra il pre e il post-intervento, i partecipanti hanno mostrato maggiore fiducia nelle proprie capacità e propensione al contatto sociale, con progressivi miglioramenti a livello di tono dell'umore e di percezione generale dello stato di salute. La loro performance cognitiva è migliorata, e con essa l'autoefficacia individuale. Il presente studio non è privo di limiti, primo tra tutti la presenza di un campione piccolo e non perfettamente bilanciato. *Conclusioni*. Il protocollo ha prodotto pochi risultati significativi. Nonostante questo, la partecipazione ad interventi multimodali, sia pure per gli aspetti questionabili dovuti all'impossibilità di pesare i singoli effetti, sembra amplificare il benessere, la qualità della vita e il livello di motivazione generale. In futuro, studi simili a questo potrebbero ampliare il numero di partecipanti, bilanciandoli adeguatamente per genere, aumentare il numero totale delle sedute complessive di training, approfondire il ruolo delle differenze individuali e testare la presenza di un gruppo di controllo attivo.

Keywords: aging; wellbeing; physical activity; cognitive function; walking; nature; engagement; prevention; elderly health

CHAPTER 1

THE AGING PATH: LIVING LONG AND LIVING WELL

"Do not go gentle into that good night,
Old age should burn and rave at close of day;
Rage, rage against the dying of the light".

(Thomas, 1952)

The poet Dylan Thomas composed these verses, with the name of "Do not go gentle into that Good Night", one of the most famous poems of the 20th century (Thomas, 1952). He gave to his readers some advice for getting older and, specifically, the imperative of going beyond the failing of body, mind and, first, of soul. He realized that death could be challenged, and that people have more chances than they believe to face the complexity of old age: this could be a good starting point to talk about the many vicissitudes that have occurred within years in the field study of *aging*. On one hand, aging could be described as a socially constructed phenomenon (Teater & Chonody, 2020), since the way it is perceived and experienced by people varies basing on the type of culture, social expectations, and individuals' lived experiences (Chonody & Teater, 2018). Why it is so important to study aging? According to the 2019 United Nations report (United Nations, 2019), over 60 population ages faster than other age groups, and more than one fifth (20.3 %) of the EU population is made up of people 65 aged and over. In addition, life expectancy has gone from being around 73 years old to 80 years old, with serious risks regarding autonomy and preservation of general cognitive abilities including, for example, the faculty of remember (Krivanek et al., 2021; United Nations, 2019). Several studies in recent years showed that more than a half of people over the age of 65 have medium or severe memory problems and the prospect of memory loss is one of the most frightening aspects of aging itself (French et al.,2012; Page et al., 2019).

For what concerns Italian framework, the over 60 aged population is constantly increasing and statistics of the main demographic indices calculated on the resident population, such as the old age index, prove that the number of elderly people is much higher than the number of young people (http://www.tuttitalia.it/statistiche/indici-demografici-struttura-popolazione). Therefore, even only to better interpret these numbers, understanding the phenomenon of aging and its evolution over time seems of fundamental importance. According to the Life Span Psychology Perspective (Baltes et al., 1999), development is considered a life-long process, that starts with conception and goes on until death. In this view, development is not simply declined in terms of growth-maturity-decay but is expressed through more flexible stages, each of them contemplating moments of growth and decline, and, above all, the existence of considerable individual variability. Earlier studies are trying to identify the effects of normal aging, free from disease, as distinct from aging characterized by physical disease, like cancer, diabetes, or neurodegenerative conditions, such as major neurocognitive disorders. In this chapter will be discussed these differences and will be introduced an overview about old age and the aging process, using gerontological, psychological, and sociological theories, with the aim to explore and synthesize the existing research.

1. **What does "Aging" mean?**

Psychology, sociology, and gerontology have tried through years to find a common definition of aging, including mental, physical, and social aspects because, with the beginning of twenty-first century, aging population has emerged as a preeminent worldwide phenomenon with the confluence of lowered fertility and the improvement of health and longevity. The role played by the body can be considered fundamental in the management of late years, since aging is essentially a metabolic process, characterized from the progressive loss of functions. The underlying expression can help to understand this issue (Anton et al., 2005):

[genotype] + [(diet, lifestyle, and environment)] = [phenotype]

This conceptualization highlights the presence of a high level of plasticity within our genes, that is an important factor for modifying life trajectories and behaviors, considering aging as something that can be prevented or even reversed. These mechanisms act to keep the goal of survival and to take advantage of molecular processes like DNA repair and antioxidant systems that require strong metabolic resources. These theories are first steps to understand the process of aging, in terms of genes action and evolution (Kirkwood, 2000. Figure 1).

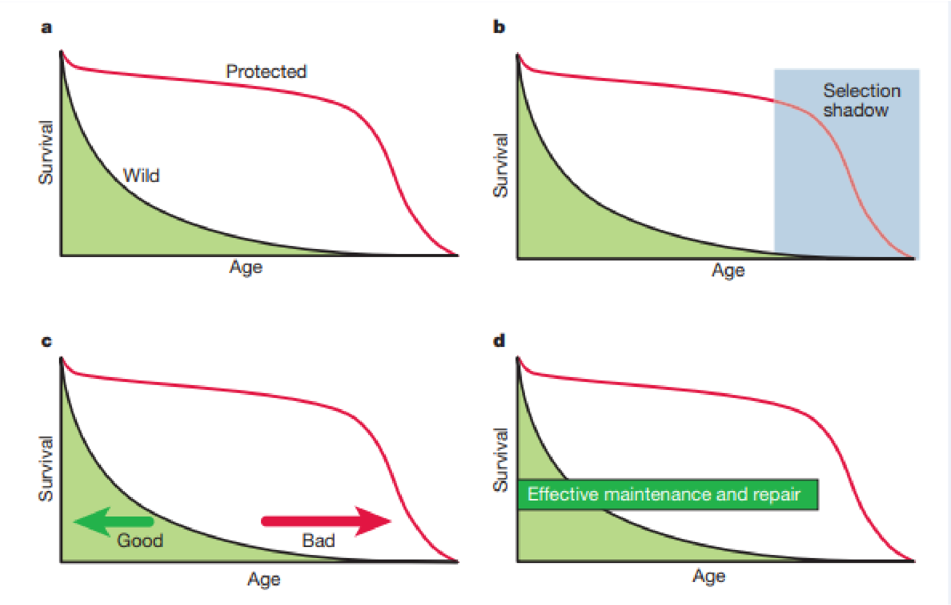


Figure 1 (a-d). Evolutionary theories of biological ageing (Kirkwood, 2000, p.234). a) Representation of ageing-gene evolution: protective factors preserve the best genes for each environment. b) Representation of the "selection shadow", the most important ingredient to permit the accumulation of late-acting deleterious mutations (mutation-accumulation theory). c) Representation of pleiotropic genes, which can be favored by selection in later life even if they have bad effects on the organism (antagonistic pleiotropy model). d) Metabolic and repair resources against selection pressure, with the goal of keeping balanced the whole organism as required from its environment (disposable-soma theory).

With aging, most of human functions are modified. The association between bodily aging and biological decline defines it not only as a biological fact, but also as a cultural one. In fact, research on aging has always emphasized losses, even if the role of aging can be described, for human beings, in terms of lifestyle, habits, diet and psychosocial factors (Rowe & Kahn, 1987): as an example, the aging body is quite always considered a malfunctioning system and this is proved by the vocabulary used to describe its characteristics, like defective, deleterious, abnormal, faulty (Ferrucci et al., 2020). A great deal of research analyzed the role of aging in the construction of social and self-identity (Gilleard, 2022; Jaggers et al., 2022): a life-course perspective is nowadays considered fundamental to increase opportunities for old age and stimulate people to view their own life course more critically.

1.1. **Age-related dysfunctions**

Aging keeps with itself a huge number of changes that are associated with alterations in dynamic biological, physiological, environmental, psychological, behavioral, and social processes. Advancing age is the major risk factor for different diseases in humans because perceptual and cognitive mechanisms undergo a reduction linked to the structural modification of the sensory organs. The most reliable marker of aging decline is vision. The conditions that can cause vision loss are macular degeneration, glaucoma, and cataracts. Age-related changes mainly take place in the muscle fibers surrounding lens: less elasticity means slower speed of processing causing the gradual slowing down of vision. The most interesting thing of this process is that brain can adapt its pattern-recognition systems: in fact, retina signals correct the input stream to complete perception and categorize stimuli (Huang et al., 2020), and the pattern-matching brain could slow down after forty and become less efficient in making vivid representation. In association with this, one of the main optical characteristics of an aged eye is the fact that it reduces spatial contrast sensitivity, increasing intraocular light scatter and demonstrating the great influence of neural factors on older adults' photopic contrast sensitivity lacking. Although there can be detected "general principles" in the aging process of visual function, individual differences play a key role: lifestyle, genetic, and environmental exposures during life-course can have different impacts on the brain structure and functions. The second most common failing that depicts the process of aging is hearing. Despite the widespread of significant hearing loss in elderly people, only 20% of them uses hearing aids (Tsimpida et al., 2022). The Age-Related Hearing Loss (AHRL) phenomenon is the result of pathologic processes related to a lack of hair cells' conduction at level of the basilar membrane, which leads to a progressive bilateral sensorineural hearing loss that impacts on older adult communication and daily functioning (Lee et al., 2010). Like the ultraviolet rays of the sun damage the eye lens, environmental factors can damage hair cells, like occupational and recreational noise, solvents, ototoxic drugs, metabolic syndrome, and exposure to loud sounds (Mishra et al., 2022). Hearing loss brings negative consequences not only on physical functioning, but also on mental health and social relations. In fact, presbycusis starts with difficulties in following conversations in noisy environments, forcing people to mobilize working memory to interpret the speech and understanding the partially percept auditory message: this aspect leads to mental fatigue and increases cognitive load. During time, people gradually reduce social interactions, becoming at high risk for depression and cognitive decline (Cosh et al., 2018; Nkyekyer et al., 2018; Yu & Liljas, 2019). Kim and colleagues (Kim, 2017) considered a group of older adults with hearing threshold ≥ 60 dB in both ears or ≥ 80 dB in one ear and ≥ 40 dB in the other. They used an audiometric assessment and diagnosed depression using the International Classification of Disease (WHO, 2019). From results emerged a strong correlation between depression and hearing loss: the greater was the severity of the hearing impairment, the greater became the risk of developing depressive symptomatology. These findings underline the importance of early aural treatment, rehabilitation and configuring of new devices to encourage recovery, because forms of audibility facilitation can contribute to well-being and improve quality of life (Maruqes et al., 2022). The sense of touch is another component that declines with age. Some forms of touch perception are particularly affected by aging (e.g., pressure sensitivity), while other ones seem to be preserved (e.g., texture discrimination). Many studies have documented a loss of tactile sensitivity with increased aged (Liu et al., 2022; Peters et al., 2016) due to decreased blood flow to the extremities (hands and feet) that can impair receptors action: sensors that are in the pads of the fingers can deteriorate and produce a loss of sensitivity, enhanced with other pathological conditions, as arthritis, making painful to move fingers and toes. Few treatments have been identified to manage these forms of sensory decline, so that scientific and technological advances would be important to improve studies and new policies aimed at treating these impairments and decrease aging complications. Also smell and taste losses are common in the elderly and could be part of normal aging process or being caused from surgery, trauma, malnutrition, and cumulative exposures to toxins. Olfactory disfunctions can manifest themselves in different ways, like *hyposmia*, that is a reduced sense of smell, *anosmia*, which means the complete loss of the ability of smell, and *dysosmia*, an altered perception of smells (Seiberling & Conley, 2004). Figure 2 shows how sensory information can represent a prognostic tool in the prodromic phase of dementia. In the clinical one, on the contrary, sensory testing could potentially be affected by other impairments, not resulting fully efficient (Brai et al., 2020). The olfactory system results to be impaired in Alzheimer Disease (AD), especially in the asymptomatic phase of the disorder: monitoring the olfactory sensitivity level can help to beforehand detect the incoming decline, together with other medical evaluations (MacDonald et al., 2018).

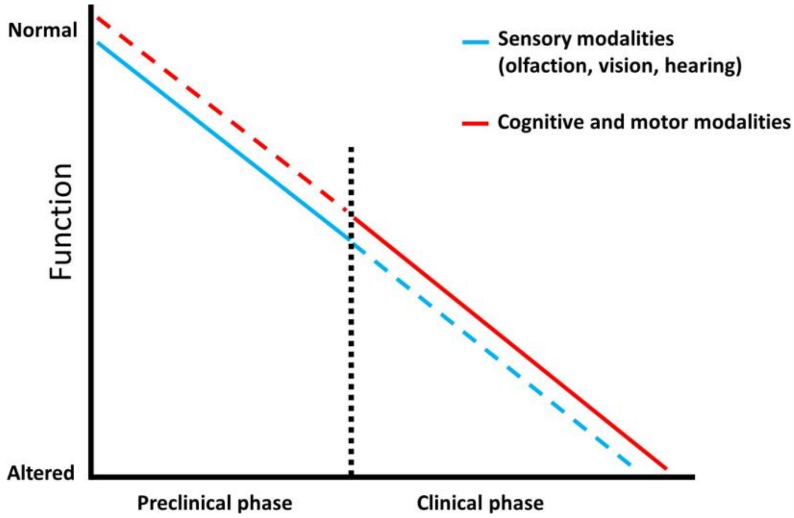


Figure 2. Sensory modalities vs cognitive and motor modalities characterizing dementia (Brai et al., 2020, p. 3).

Alongside smell, also taste perception declines during the aging process, bringing many adults to tell that food lacks flavor, and this can be interpreted both as a decline in functioning of receptors, and as a result from diseases or medications. As an example, studies of taste perception in medicated and non-medicated older individuals showed that the amount of loss was strictly associated with the number of prescribed drugs (Schiffman, 2018). There can be found fundamentally three taste disfunctions brought by age: 1) *ageusia*, that is absence of taste; 2) *hypogeusia*, that causes a decreased sensitivity of taste; 3) *dysgeusia*, i.e., the distortion of normal taste (Braun et al., 2022; Schiffman, 2000). Aging could also affect the gut (Parker & Chapman, 2004) and the motor function of the gastrointestinal tract (Rayner et al., 2000), altering the level of food intake. Poor food consumption can also result, at least in part, from the isolated living and lack of social interaction that many older people face. Optimizing the sensory, social, nutritional, and emotional aspects of food and eating could be a good instrument to improve a satisfactory food environment in late life and promote better intervention strategies (Spence & Yussef, 2021).

2. **Pathological and healthy aging: frontiers in the study of older adults.**

As argued until now, old age has often been considered as a period of withdrawal and disengagement from social interactions and activities. Studies from the biology of aging using laboratory animals, now extended to humans, have led to the conclusion that there is not a single paradigm to understand and explain aging and that nowadays the rate of this one can be slowed, reducing the burden of numerous diseases and increase *healthspan* (that portion of life spent in good health). During last decades, bio-psycho-social factors have been considered more and more in the analysis of successful aging, with a new conceptualization of healthy aging, defined as "living a long productive, meaningful life, and enjoying a high quality of life" (White House Conference on Aging, 2015). If aging is represented by an acceleration of inflammation and depletion, appropriate individualized actions could help to compress the morbidities and to slacken the onset of chronic conditions. To better understand the entire process of aging it is needed to focus the attention on the differences between "normal" aging and "pathological" aging. Evans and Rosenberg (Evans & Rosenberg, 1991) were quite the first to purpose a list of physiologic biomarkers that can gradually arise during aging: 1) loss of strength; 2) reduced flexibility; 3) decreased cardiovascular endurance; 4) increased body fat (with consequent loss of lean muscle, or sarcopenia); 5) reduced resting energy expenditure; 6) lower kidney clearance; 7) reduced cell-mediated immunity; 8) increasing hearing threshold; 9) reduced vibratory sensation; 10) compromised near vision and dark accommodation; 11) reduced taste and smell acuity; 12) increased autoantibodies; 13) altered hormone levels. During the whole life the body actively repair itself, thanks to DNA and protein mechanisms. In the normal course of aging, this action gradually slows down, becoming more exposed to free radical's damage and deprived of Vitamin E, the one that can help cells to deal with them.

Anton (2015) purposed three models to analyze normal aging and pathological one: 1) a conceptual model; 2) a pathophysiology model; 3) an intervention model. The first one (Figure 3) resumes all the physical and cognitive conditions that contribute to reduce autonomy and tries to show how health conditions can affect and reduce the effects of cognitive decline and physical performance decrease. At the center of the circles there is the most important goal that must orient and implement intervention, that is the preservation of independence and, therefore, self- integration.

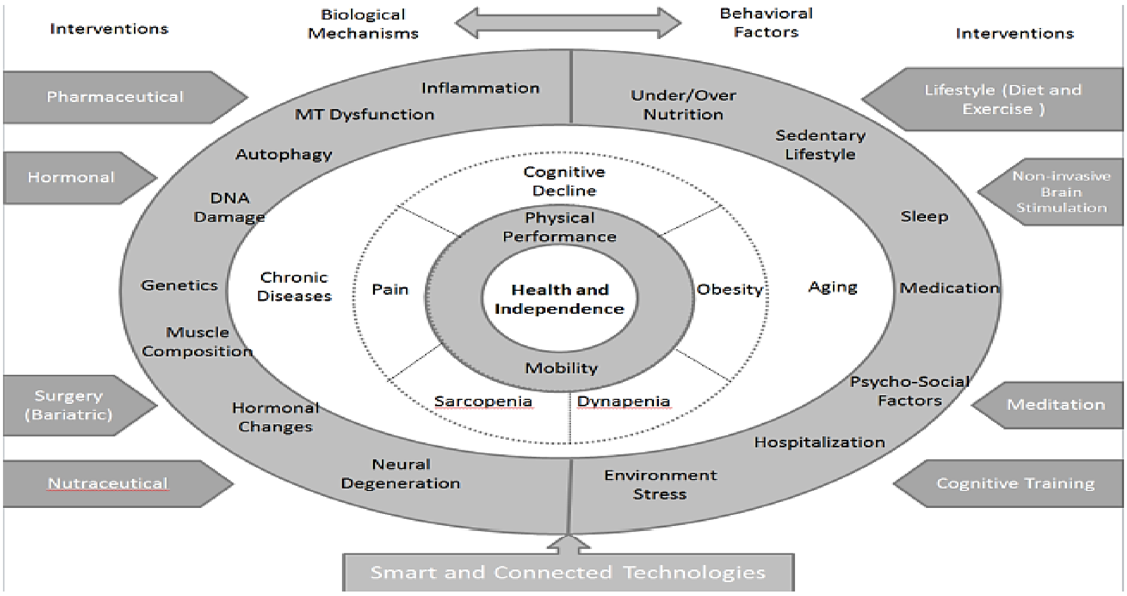


Figure 3. Factors that can affect physical functioning during aging (Anton et al., 2015, p.67).

The intervention model (Figure 4) shows the different effects that intervention have on biological and behavioral outcomes through a multiple variability of mechanisms. Dotted lines represent theoretical connections, while the solid lines are the ones that receive major clinical support. As an example, interventions like exercise programs can positively influence behavioral mechanisms, like sedentary lifestyle, and have a direct effect on counteracting cognitive decline, sarcopenia, and even obesity.

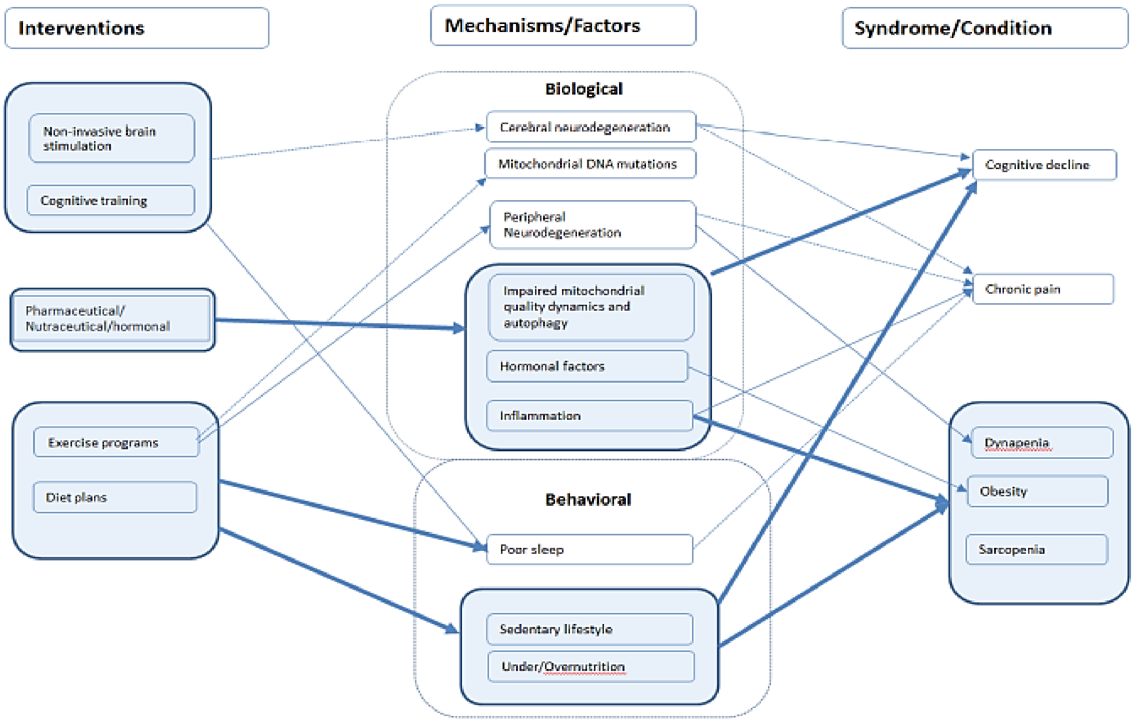


Figure 4. The intervention model. Effects of different treatments on different systems (Anton et al., 2015, p. 69).

These models, taken together, support the need of an inter-disciplinary approach, that can provide consensus within the definition of new types of intervention. The pilot study object of this work embraces this idea, converging evidence of both physical and cognitive outcomes to promote and support independence. Nowadays theorists and researchers are trying to concern with what can be done with older adults who want to live long and, most important, as well as they can, with the need to shift the focus from ‘‘how long’’ to ‘‘*how well*’’ to live as an older adult. Hereafter will be discussed some frameworks representing aging-well in the gerontological discourse that led to the conceptualization of Successful Aging (SA) model.

2.1. **From the Activity theory to the concept Successful Aging.**

The Activity Theory was developed in 1960s by Havinghurst (1961; Havinghurst et al., 1963). It supports the idea that elderly people who maintain a high level of social activity and engagement are more likely to experience a good mood and a better general level of personal adjustment. In 2018, a group of Finnish researchers (Rantanen et al., 2018) concretely tested the association between health, health behaviors, functional abilities and social support with active aging and wellbeing. A cohort of 1000 participants were firstly interviewed about their ideas on aging, wellbeing, disability, and social support. Then, they were monitored for 7 days with wearable sensors, making functional tests including muscle strength, exercise tolerance and mobility. It was made a complete clinical examination through an electrocardiogram, measurement of orthostatic regulation, tests of blood pressure and of C-reactive protein, in addition to a series of tests for chronic and acute conditions. Test results were compared with previous ones of a cohort examined in 1989-1990 and showed that the advantage of Active Aging theory is the fact of giving the possibility to include in studies both physical, psychological, and social parameters, building up new sets of evaluative biomarkers of aging (Figure 5).

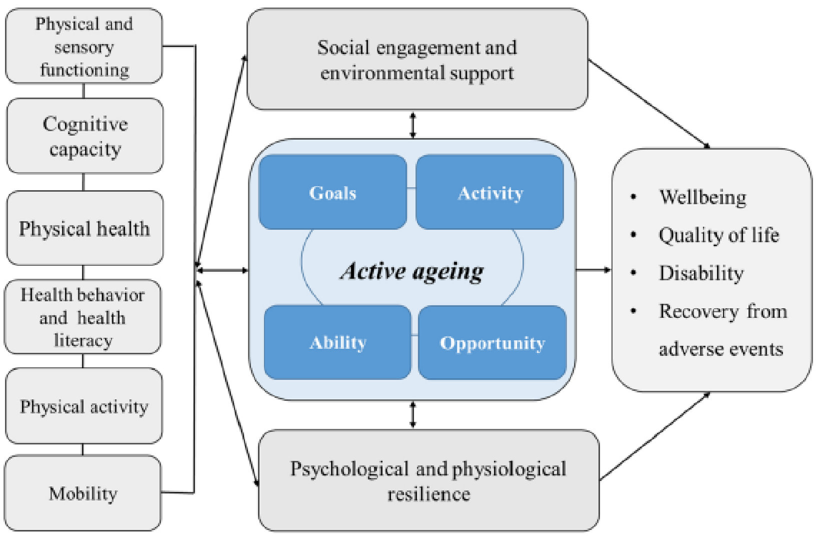


Figure 5. Conceptual framework of Rantanen analysis about Active Ageing (Rantanen et al., 2018, p. 3).

If Active Aging encourages a propositional and engaging lifestyle for elderly people, the disengagement theory states a mutual withdrawal of society and individuals. This brings to a sort of social restriction that considers sufficient the support of immediate friends, family, and the closed private sphere, making an individual quite totally self-centered (Marshalla & Clarke, 2007): aging well can be defined, in this theory, as the achievement of full self-integration by an individual. Nowadays institutions often encourage and enforce older adults' disengagement: pensions, retirement plans, and old-age support policies potentially reward older people for disengaging from society, with the improvement of their quality of life and self-esteem. An original response to the disengagement theory is the interpretative approach of Socio-Environmental theorists. In this framework, the individual is capable of exercise and choice and is defined as a real agent during all life. The theory was developed between 1960s and 19070s by Jay Gubrium, and is fundamentally built around two aspects (Gubrium, 1972): 1) environmental effects on an individual (e.g., social homogeneity, local protectiveness, residential proximity); 2) personal resources (e.g., behavior, health, education). This attention to environment and social context, brought to the development of the Continuity Theory, which argues that aging can be considered as a personal evolution, in which the past represents a resource to influence new adaptations (Atchley, 1989). The Continuity Theory defines aging as the individual predisposition and motivation toward both internal and external continuity: the first one refers to the persistence of a precise psychic structure, temperament, affect, preferences, and disposition, while external continuity is represented by external pressures, as the expectations of the external world, other people, and contexts. Instrumental and social independence purposed by the theory are the keys of an adequate sense of *be-longing* and could potentially support physical and mental modifications. For these reasons, continuity is a preferred strategy for dealing with aging, maximizing strengths, and minimizing weaknesses.

The Selective Optimization with Compensation (SOC) model formulated by Margaret and Paul Baltes (Baltes & Baltes, 1990), analyzes how individuals strategically accommodate changes and modify their interactions in different social contexts. They considered the definition of successful development as the maximization of desirable outcomes and minimization of undesirable one: later-life events and transitions could require more energy and capability to be managed, and a person can differ from another for the investment or the optimization of socio-emotional resources. Within the last decade, a huge part of research on SOC at work was conducted: studies demonstrated that the SOC model can explain the successful coping with changes related to age in occupational contexts (Moghimi et al., 2017; Muller & Weigl, 2017), demonstrating its association with competency, performance. and work-family balance. Our brains are always changing in response to pressures from genes, culture, and opportunity: the Successful Aging (SA) theory focuses on remaining free from disease and disability fails, staying physically and socially active. SA is a multidimensional concept that aims to expand functional years in later life (Annele et al., 2019), and involves physical, cognitive, and social aspects considering, as starting point, the whole environment of an individual. The definition of SA has often been used interchangeably with several concepts like "active ageing", "healthy aging" and "productive aging" (Figure 6), and has been interpreted from different perspectives, evolving through the work of various researchers over the last 50 years (Martin et al., 2015). It represents more than absence of disease: of course, this is a component of it, together with the maintenance of functional capacities, but SA involves a high level of quality of life and engagement with social and self-care.

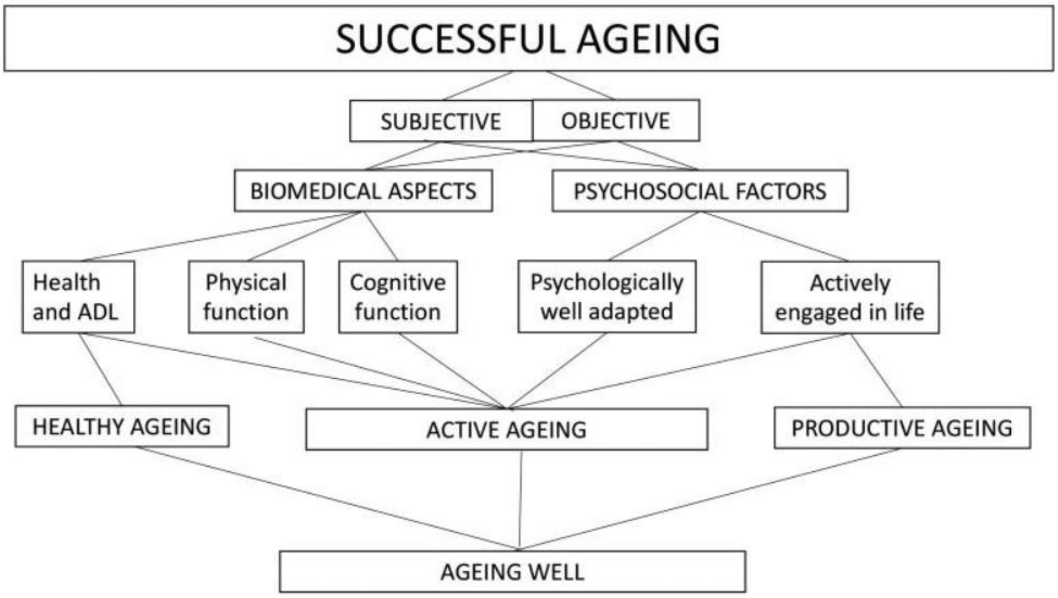


Figure 6. Dimensions of SA (Annele, 2019, p. 360).

SA promotes activity and positive features of aging and, according to Rowe and Kahn (Rowe & Kahn, 2015), it includes three components: 1) low risk of disease and disease-related disability; 2) maintenance of high cognitive and physical functions; 3) engagement in life and high social activity. To evaluate and measure SA Kim (Kim, 2008) developed a 31-item instrument on a 5-point Likert scale, comprising items about autonomous life, self-realization, active participation in life, satisfaction with children, self-acceptance, and acceptance of others, while Phelan and colleagues (Phelan et al., 2004) developed the SA questionnaire, which is composed by 20 factors that include social, physical, psychological, and functional health. These instruments help to assess different views of aging experience, based on gender, culture, health status, engagement, and self-satisfaction. Moreover, Kim (2017) identified four domains that can concretely operationalize SA that are: 1) avoiding disease and disability; 2) keep a high mental/cognitive/physical function; 3) maintain an actively engaging in life; 4) being psychologically well adapted in later life.

These dimensions enlarge the original Rowe and Kahn's definition through a holistic perspective of well-being: remaining active in late life, practicing hobbies, travelling, journaling, writing, volunteering, and experiencing cultural activities are identified as important factors to achieve SA (Reichstadt et al., 2010). According to SA, staying healthy in old life is the ability to take care of oneself, keeping independence, and maintain good physical mobility: the use of a narrative approach can be advantageous to explore direct experiences of older people and encourage experts to better discover, using the SA principles, what are the meaningful aspects that positively support the process of aging in late life (Teater & Chonody, 2020).

3. **The aging brain and neuroplasticity modifications.**

Biological and genetic markers, associated with imaging technology, allowed to characterize the process of healthy and pathological aging from a cerebral point of view, and this interdisciplinarity can be considered a proof of the dynamic and optimizing processes of the aging brain. Adults experience a gradual reduction in brain volume after thirty-five years old, in the measurement of about 5% per decade through the age of sixty and a speeding up of decline after the age of seventy (Hedman et al., 2012), with a decrease in the efficiency of synaptic connections that leads to a general slowdown of mental processes. Dopamine levels, that are integral to cognition for their role in regulating attention and modulating contextual stimuli response, decrease of about 10% per decade, along with serotonin and brain derived neurotrophic factor (BDNF) (Rollo, 2009; Miranda et al., 2019). Another important factor related to brain decline is myelin, a multifunctional protein that permits the transmission of axonal signals in the brain within the white matter. Unlike the grey matter, which shows a gradual reduction over time starting by hippocampus and caudate nucleus (Koini et al., 2018; Sodums & Bohbot, 2020), white matter starts to decline between the ages of seventy and eighty (Gunning-

Dixon, 2009), with the greatest structural deficiency observed in anterior frontal regions of the brain. Cognitive and brain aging decline are frequently associated with loss of cortical neurons. First studies (Brody, 1955, 1970) demonstrated that, with aging, people potentially lose 50% of their cortical neurons, but in 1980s, Haug (1985) produced contrary evidence, showing that many of the loss of cortical neurons could be due to the differential shrinking of myelin between young and older people, and concluding that there is no significant loss of neurons from the human cerebral cortex with age. Chronic conditions like Alzheimer's disease can bring to a significant amount of neuron loss, but this is not so common as early reports would suggest. The brain has specific regions and circuits devoted to mental activities, and age-related changes in brain volume have direct consequences for cognitive function. As an example, prefrontal cortex is involved in impulse control, decision-making and attention, and it is the first cortical region to show wear and tear as an individual gets older, causing the incapability to keep track of thoughts, prevent interferences and being engaged with daily activities (Nyberg et al., 2010). The development of mental abilities is an intricate path that involves DNA instructions, brain topography and environmental stimulation: this means, in other words, that cortical development depends on experience. Neuroplasticity can be defined as the ability of the brain to change itself (Demarin & Morović, 2014) reorganizing its structures, functions, and connections through the modulation of dendrites, axons, and synapses, but also as a mediator of responses to neuronal injury (Jellinger & Attems, 2022). It is an intrinsic property of the brain during lifespan, but its mechanisms could vary with aging. With the purpose of recognize and understand the brain functional reorganization and its role in strengthening existing connections, Park and Reuter-Lorenz (2009) purposed the Scaffolding Theory of Cognitive Aging (STAC), which assumes that functional changes occurring with aging are part of the lifespan (Figure 7).

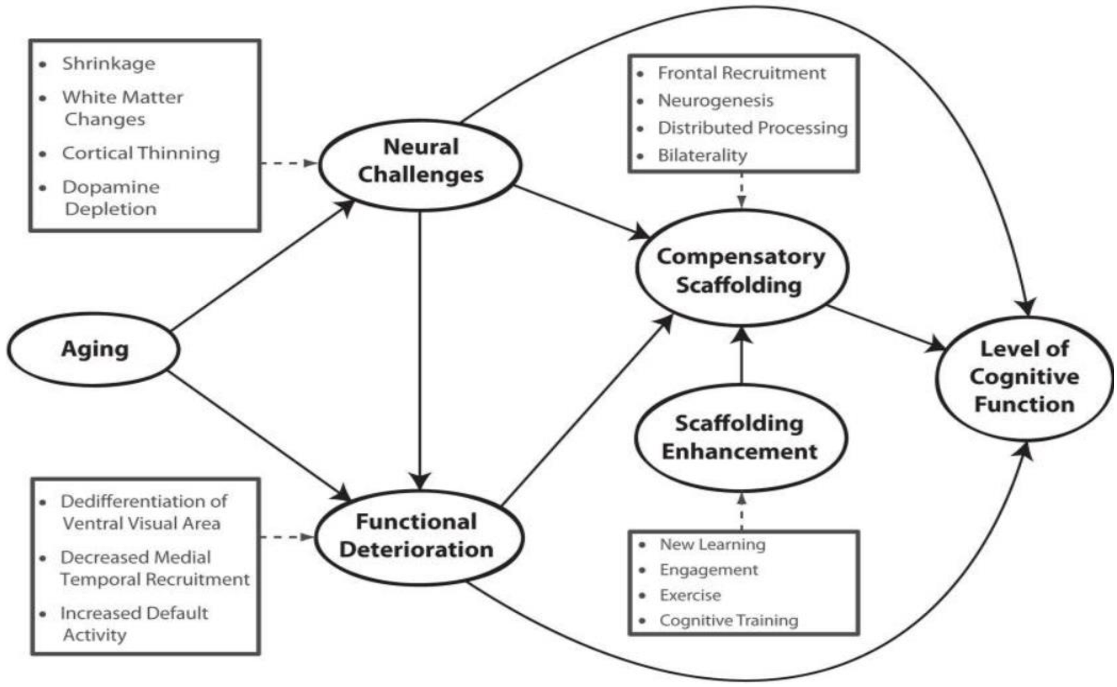


Figure 7. Graphic representation of the STAC model (Park & Reuter-Lorenz, 2009, p. 184).

The process of compensation acted by cognitive scaffolding could alleviate the progress of decline through adaptive activations of the brain and alternative neural circuits. This model is supported by findings of functional imaging techniques and their structural data (fMRI, PET), that reported the association between prefrontal bilaterality of hemispheres and higher cognitive performance in older adults compared to young ones (Cabeza et al., 2002): in category-learning tasks, older adults showed more parietal bilateral activation than young adults, proving the beneficial effect from engaging both left and right hemispheres. Moreover, aging alters the Default Mode Network (DMN), situated across frontal, parietal, and mediotemporal lobes, posterior cingulate, middle frontal cortex, lateral parietal region, and lingual gyrus (Raichle et al., 2001). The failure in shifting from a rest state to an activity one by the DMN could be another explanation for the increased activity of prefrontal cortex during aging (Reuter-Lorenz & Cappell, 2008). STAC suggests that, despite neural challenges and functional deterioration, additional neural circuitry could enhance the efficiency of brain networks.

The scaffolding process cannot be defined as the brain response to normal aging, but it is the normal adaptive response of the brain to challenges during the whole lifespan. From a neurobiological point of view, the scaffolding capacity of the brain could be limited with aging, with difficulties for plasticity and reorganization processes; in fact, scaffolding processes in the aging brain reside in prefrontal cortex and, as said before, when an under activation of this structure occurs the flexibility of circuits of becoming supplementary and complementary is extremely reduced. The essence of this model can be resumed in two words: plasticity and challenge. Multiple factors are determinant for compensatory scaffolding, and this vision of a lifelong neuroplastic brain can be an additional issue to interpret successful and productive theories of aging. There is an extensive amount of knowledge about how cognition changes with. Many aspects of memory, speed of processing, language and inhibitory function become less efficient, while other aspects of functioning, like implicit memory and knowledge storage, are relatively protected from aging. External factors could potentially explain why some individuals are more capable to compensate for age and disease-related cognitive difficulties than others. Cognitive Reserve (CR) is one of the most efficient mechanisms that protects an individual from neurocognitive damage (Stern, 2003): it is based on knowledge about brain plasticity and explains how individuals can use pre-existing resources to face age-related changes and clinical condition pathologies (Stern, 2002) by adopting strategies to compensate for their decline (Stern, 2002; Stern et al, 2020). Education, occupational attainment, and engagement in leisure and social activities can significantly reduce the risk of developing neurocognitive disorders, or slow down their speed of progress, improving SA and reducing clinical changes in traumatic brain injury (Suchy et al., 2011), Parkinson's disease (Poletti et al., 2011), multiple sclerosis (Poletti et al., 2011), and HIV-related dementia (Foley et al., 2012).

3.1. **The construct of Cognitive Reserve (CR)**

Several models tried to describe differences between younger and older adults' performance in cognitive task through the modulation in brain activation patterns, like the Compensation-Related Utilization of Neural Circuits Hypothesis [CRUNCH] (Reuter-Lorenz & Cappell, 2008), the Hemispheric Asymmetry Reduction in Older adults' theory [HAROLD] (Cabeza, 2002), and the Posterior-Anterior Shifting in Aging [PASA] (Davis et al., 2008). Recent interpretations of the original Stern's model suppose that CR counteracts the age-related depletion of attentional or working memory resources (Lojo-Seoane et al. 2020). CR could act as an additional resource to basic cognitive functions, and this is demonstrated by its role in positive influencing working memory performance (Casino et al., 2020), and in enhancing processing speed, inhibitory and attentional control (Lojo-Seoane et. al., 2020). Within normal aging, a higher CR level is associated with higher network efficiency, while in MCI condition it guarantees the preservation of functions (Figure 8), slowing down the passage to AD diagnosis (Barulli & Stern, 2013; Stern et al., 2020).

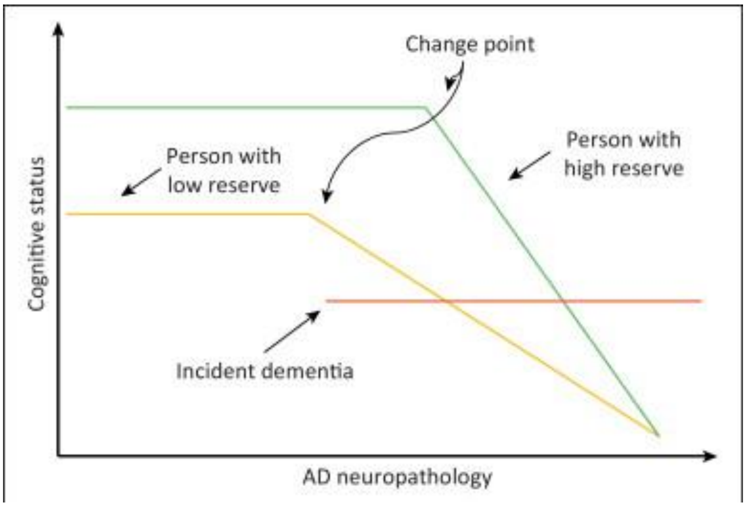


Figure 8. Representation of how CR may mediate between AD pathology and its clinical expression (Barulli & Stern, 2013, p.503).

The mechanisms in which CR could delay the onset of dementia is explained by an optimization of functional brain networks and an increasing efficiency of information transfer (Li et al., 2021). Krivanek and colleagues (2021) sustained this point, affirming that boosting both cognitive and brain reserve can be essential to shift the trajectory of decline and allows individuals to cross the threshold to worst clinical conditions later in life, despite recent evidence revealed that genetic risk for dementia could interfere with protective effects of CR (Li et al., 2021). Much of cognitive loss in middle life is nowadays considered reversible, since the number of studies that include training sessions to improve cognitive function are constantly growing. Park (Park et al., 2009) reported a summary of studies that considered results in different cognitive tasks to a sample of 20-89 aged people. The group used three measures of perceptual speed, two of visuospatial working memory, and two of verbal working memory. Results show the gradual age-related declines in speed, working memory, and long term-memory, with only the verbal ability preserved from age differences (Figure 9).

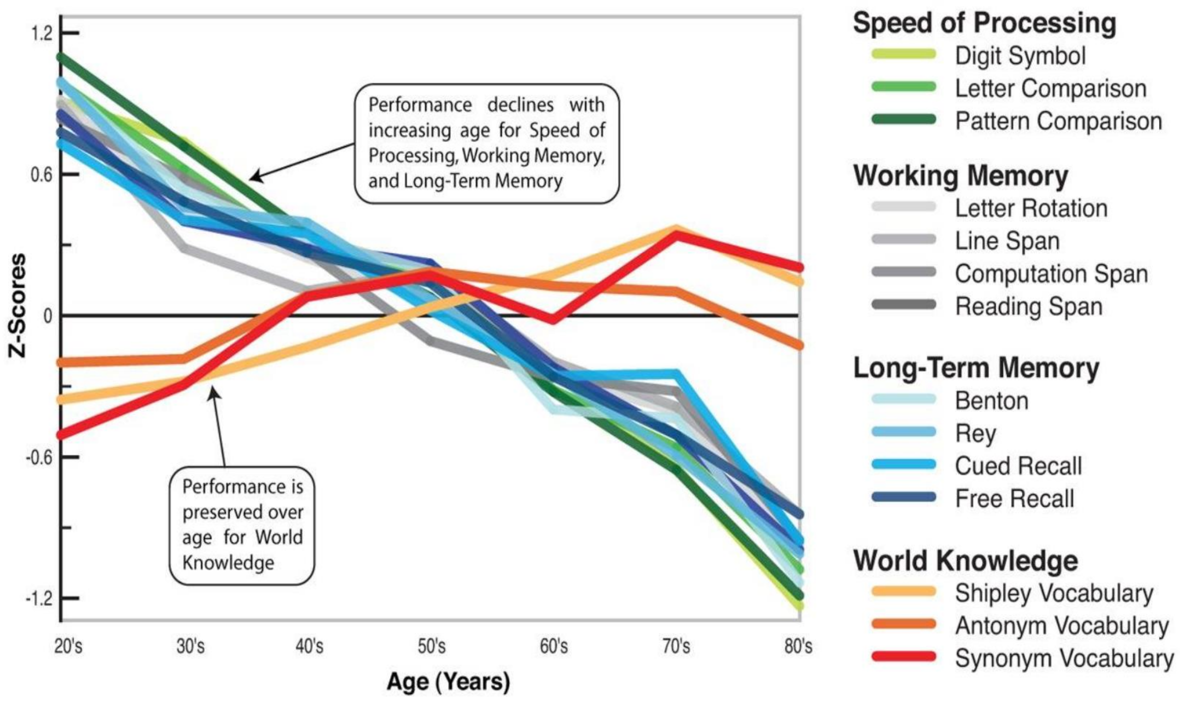


Figure 9. Decline of functions in cognitive aging (systematized by Park & Reuter-Lorenz, 2009, p. 197).

The dynamic relationship among cognitive abilities has been object of research during last years, trying to provide a growing understanding of the processes that changes during lifespan to avoid cognitive physical decline and increase mental sharpness. The present analysis is going to deepen in the impact of aging on three of the main domains that depict cognition: 1) processing speed; 2) language; 3) memory systems.

3.1. **Processing speed.**

Different behavioral approaches demonstrate the role of processing speed as the rate reached by people to perform motor, perceptual, and decision-making tasks (Eckert, 2011). Processing speed represents one of the strongest predictors of performance in cognitive tasks within older adults and an accurate indicator of their independence level (Salthouse & Ferrer-Caja, 2003). It can also be defined as a fundamental property of the nervous system because it provides the efficient implementation of overall cognitive functions. The processing-speed theory (Salthouse, 2000) defines processing speed as the fundamental factor the contributes to age-related negative effects in fluid cognition, since it causes a generalized slowing in the perception of available information and reduction of both qualitative and quantitative dimensions of performance. Cognition tasks are useful to assess and score the processing speed ability and to evaluate its impact on aging. Finkel and colleagues (Finkel et al., 2007) explored the role of processing speed as indicator of cognitive decline by considering four cognitive variables (verbal abilities, spatial abilities, memory, and processing speed) independently using data from the longitudinal Swedish Adoption/Twin Study of Aging (SATSA; Finkel & Pedersen, 2004). They included 806 nondemented individuals from 50 to 88 years old and examined age changes in cognitive functioning for each of the cognitive factors with a univariate dual change score model. Furthermore, they used a bivariate dual change score model to detect the relationships among the four cognitive abilities.

The univariate analysis revealed an acceleration of decline during years especially for spatial and speed factors, while a moderate trajectory emerged for the memory capacity and a modest one for the verbal capacity. Bivariate analysis, on the other hand, reported a valuable predictive capacity of speed factor to changes in memory and spatial factors. The inverse relationship, on the contrary, resulted to be untrue, and this supported the prominent role of processing speed in age change. Processing speed and prefrontal cortex are extremely related (Albinet et al., 2012; Eckert et al., 2010) and age-related differences in the total volume of grey matter can be considered influent in its alteration (Chee et al., 2009). The capability of switching between functional networks require attention to a task and a good self-referential thinking: this substantially vary in children's and adult's task performance but is surely impaired in older adults (Grady et al., 2006).

3.2. **Language**.

The relationship between language and age has been an active research area since early experimental investigations (Craik & Masani, 1967; Riegel & Riegel, 1964). Language is an aspect of cognition that seems to be resistant to age-related decline, and its components require the action of most of complex cognitive processes, such as working memory, semantic memory, attention, and memory binding. As an example, word's retrieval and other semantic processes could show little changes with aging, especially in their phonological aspects (Burke & Shafto, 2004). Another dramatic word production failure is the Tip-Of-the-Tongue (TOT*)* phenomenon, that represents the incapability to produce a word when certain to know it. TOTs can occur in everyday life, but studies have demonstrated that they happen more frequently in older adults than in younger ones (Burke et al., 1991; Heine et al., 1999). TOT' states are associated with reduced grey matter in left insula and anterior cingulate cortex (Shafto et al., 2007) and are related to the processes of error-monitoring and attention and explaining the difficulties in retrieving phonological information.

For what concerns spoken language comprehension, bilateral temporal cortex is important for auditory and single-word processing, and it involves the role of left lateral temporal cortex and inferior frontal gyrus for the elaboration of sentence-level material (Peelle et al., 2010). Peelle (Peelle, 2019) analyzed changes in normal aging concerning word perception, sentence comprehension, and perceptual listening by exploring differences in brain regions activations related to different language functions in older and young adults. In an experimental protocol, Erb and Obleser (2013) administered two types of spoken sentences, normal or acoustically degraded, to older and young adults: older ones reported greater activation in dorsal anterior cingulate cortex towards degraded speech, and individual differences in this area resulted to be positively related with word report scores. Moreover, they showed activations in middle frontal gyrus, anterior cingulate, and visual cortex, relying on executive attention mechanisms more than younger adults did. Older adults report difficulties in processing sentences and, sometimes, in interpret expressions and words without a reference context. This brings to a reduced use of grammatical complexity in production and different time response to comprehension tasks (Wingfield et al., 2003). Elderlies with reduced grey matter in left inferior frontal gyrus and left middle temporal gyrus showed increased activity in right hemisphere homologues of these regions, producing a more bilateral pattern of activation compared to younger ones. This aspect is a demonstration of the compensatory activity observed in older adults, which becomes useful to face cognitive demand (Figure 10) in difficult situations. Speech production is frequently associated to naming tasks, which requires object recognition for being successfully completed. Older adults result to show more difficulties in producing correct names when in front of a picture, and this aspect is related to specific differences in brain activity.

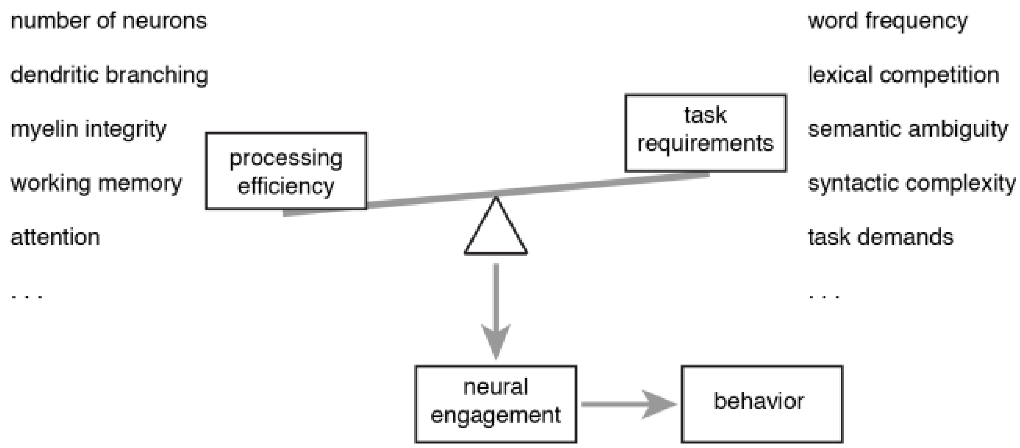


Figure 10. The role of neural networks in supporting language processing (Peelle, 2019).

Increasing linguistic difficulties in late life can also be observed in discourse production. Sentence production can be assessed by the analysis of diaries and written compositions, demonstrating that writing complexity decreases over the time (Kemper et al., 2001). These studies highlight how adult and old age are relevant in understanding the role of individual cognitive and perceptual differences in influencing language processing during late life.

3.1.3. **Memory systems.**

Tulving's memory classification comprises 5 major memory systems with different characteristics that work with different type of information: 1) procedural memory; 2) perceptual representation system; 3) working memory; 4) semantic memory; 5) episodic memory (Tulving, 2000). Madan (2011) schematized memory systems (Figure 11) using as reference previous theoretical accounts. Semantic memory results to be quite resistant to aging, even if the action of recalling names results typically impaired, while episodic memory, which can be considered strictly related to the semantic one, shows the greatest age-related modification, and unifies three concepts: self, autonoetic awareness and subjectively sense of time.

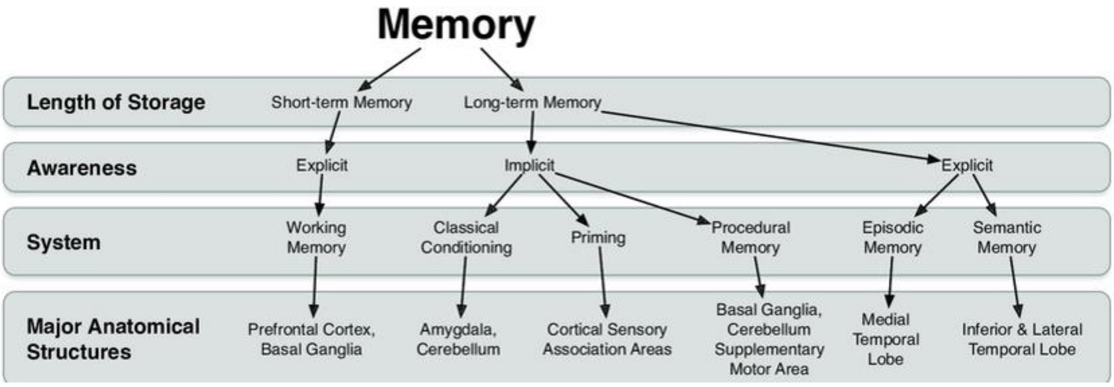


Figure 11. Memory systems general scheme (Madan, 2011, p. 39).

Different memory tasks can be used to test memory individual's capacity, and aging influence depends on the type of information that must be processed. Free recall tests are age-related, but also associative learning tasks can be accurate to detect memory frailty. Also, prospective memory tasks are interesting, because participants must carry out a task and keep in mind an action to execute in a future time. It has been demonstrated a relationship between free recall and prospective memory (Zeintl et al., 2007) strongly influenced by individual differences and implying more mental energy than other elaboration processes. The loss of inhibition can affect memory functionality because it influences the information management and the distinction between relevant and non-relevant elements even if the process of retrieving memories and practice inhibition strategies reflect independent mechanisms of action regulation. Gazzaley and colleagues (Gazzaley et al., 2005) conducted an experiment in which participants were asked to remember faces and ignore scenes, or vice versa, from a short sequence of alternating faces and scenes (Figure 12). After the sequence, it was presented a blank screen (9 seconds) and then participants were tested on the faces or the scenes.

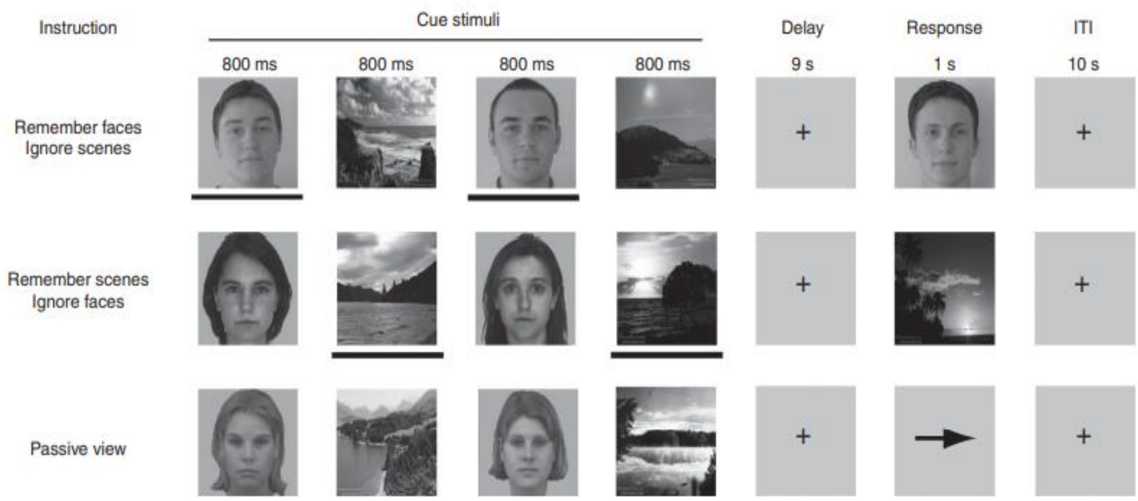


Figure 12. Experimental framework of Gazzaley's group about the impact of aging on top-down feature organization due to working memory performance. The three lines below the reported stimuli indicate the task relevance in this picture but were not present in the effective task (Gazzaley et al., 2005, p. 1298).

The study compared younger and older adults brain activations, showing that older adults seem to report deficits in suppressing task-irrelevant information, and did not show differences between the passive-view condition and the scene-specific one, aspect that is strongly associated with the previously explained notion of control. Studies have demonstrated that practicing encoding techniques and receiving adequate support, can gradually improve memory performance in older adults (Greene et al., 2021). It is fair to point out some elements of autobiographical memory system, as it is closely related to the "sense of self", of being, and to the experiences that shape an individual. The ability to take a subjective perspective is closely related to the ability of linking the past to the present: the ongoing sense of a subjective experience is what makes an individual alive and is to recognize that experience as a self-one that an individual must create a personal timeline, in which events are temporally organized (McAdams, 2006). In case of cognitive impairment or Alzheimer's disease, autobiographic memory results to be weakened and, therefore, self-concept is compromised (Martinelli et al., 2013).

In general, development is shaped by internalized age-relevant beliefs, and these can affect performance, influencing perceptions of an individual's ability. Hertzog and Hultsch (Hertzog & Hultsch, 2000) reviewed literature about aging and metacognition, and distinguished between the categories of implicit beliefs and self-referent beliefs (Figure 13).

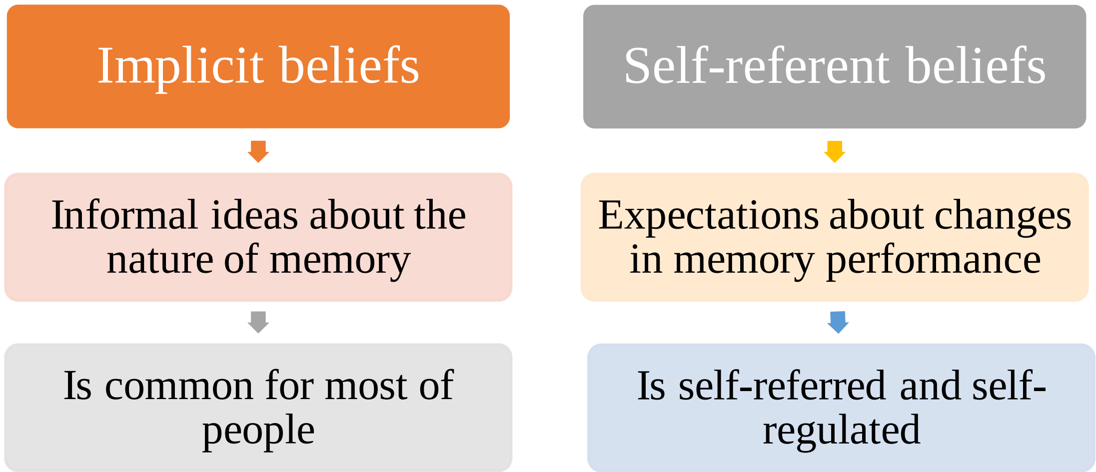


Figure 13. Negative beliefs within older adults (freely adapted by the author of this work from Hertzog & Hultsch conceptualization).

The authors suggest that these conceptions have strong influence on controlling memory performance, and stereotypes are associated with negative self-cognitive attributes, senile behavior, and forgetfulness. The ability to think about how own's memory works and to consequently adjust our behavior is known as metamemory (Rhodes, 2016), which is strictly related to the concepts of memory awareness and responsible remembering (Mieth et al., 2021). Future research could expand this evidence, to provide a broader definition of context-related influences in the studies of aging and memory.

3.4. **Neurocognitive Disorders (NCDs).**

As previously discussed, an aging population represents both an opportunity and a form of threat for society: this last paragraph will examine the cluster of neurocognitive disorders, their subtypes, and their relationship with aging. With "Neurocognitive Disorder" (NCD) is meant a deterioration of intellectual abilities, memory, and learning, often associated with behavioral alterations, that prevents patients from carrying out common daily activities, maintaining normal productive interpersonal relationships, communicating, and leading an autonomous life (Ganguli et al., 2011). There are various forms of neurocognitive impairment, similar in manifestations, but induced by various mechanisms. All of them are characterized from the presence of brain damage that can occur acutely (as in the case of stroke) or being accumulated gradually during decades and becoming evident when a certain threshold is exceeded, over which the still healthy parts of the brain are no longer able to compensate for the cognitive functions that have failed due to the severity of the lesions. In this second case, it is possible to talk about cognitive decline associated with aging, which can be mild and well manageable for several years or represent the first phase of a neuronal degeneration that will lead to more severe consequences in a short time. The definition process of NCDs has been particularly intricated. The fourth edition of DSM-IV (APA, 1994) included a chapter about neurocognitive disorders entitled “Delirium, Dementia, and Amnestic and Other Cognitive Disorders”: in this case, the definition of dementia was made up by multiple cognitive deficits, due to different etiologies, such as effects of substances and general medical conditions. Decline must affect the general level of functioning, causing significant impairment in social and occupational activities. The lack of this definition was the fact that it did not considered elements related to the pre-dementia syndrome state, but it defined analogue conditions, like age-related cognitive decline and amnestic disorders (Rodrìguez-Testal et al., 2014).

The limitations of DSM-IV prompted the revision of the fifth edition, the DSM-5, in which the introduction of the mild neurocognitive disorder is essential, because it is distinguished by the major neurocognitive disorder, that corresponds to the old definition of “dementia”. Mild neurocognitive disorder, well-known as Mild Cognitive Impairment (MCI), is a condition that allows people to still perform daily chores and look after themselves, but with difficulties in memory and possibility of misplacing things (Petersen et al, 1999; Petersen, 2004). The term *mild* is used to represent the continuum from normal brain aging to severe impairment followed by neurocognitive disorders: in fact, in about 50% of patients, MCI leads to Alzheimer’s Disease (AD), and, for this reason, it can be considered an early warning sign for it (Morris & Cummings, 2005; Petersen, 2009). It is extremely complex to find a single cortical region with a heterogeneous neuroanatomical base to locate the origin of MCI, because it arises from copious brain abnormalities (Stephan et al., 2012). A group of Chinese neuroscientists (Qian et al., 2018) used the resting-state fMRI (with 93% of accuracy) to identify an intrinsic frequency for a specific brain network that represents differences between MCI individuals and people undergoing normal aging. In MCI group they found a higher BOLD signal in limbic and paralimbic regions, but also in subcortical regions, like amygdala, anterior cingulate gyrus, orbital frontal gyrus, an area that is close related to olfaction function, hippocampus, parahippocampus, putamen and thalamus. Besides, it was highlighted a dysfunction in the precuneus and in the medial superior frontal gyrus, regions of the default mode network (DMN). Neurocognitive Disorders Work Group, appointed by APA, classified neurocognitive disorders in the actual DSM-5 cluster by identifying six domains (Figure 13).

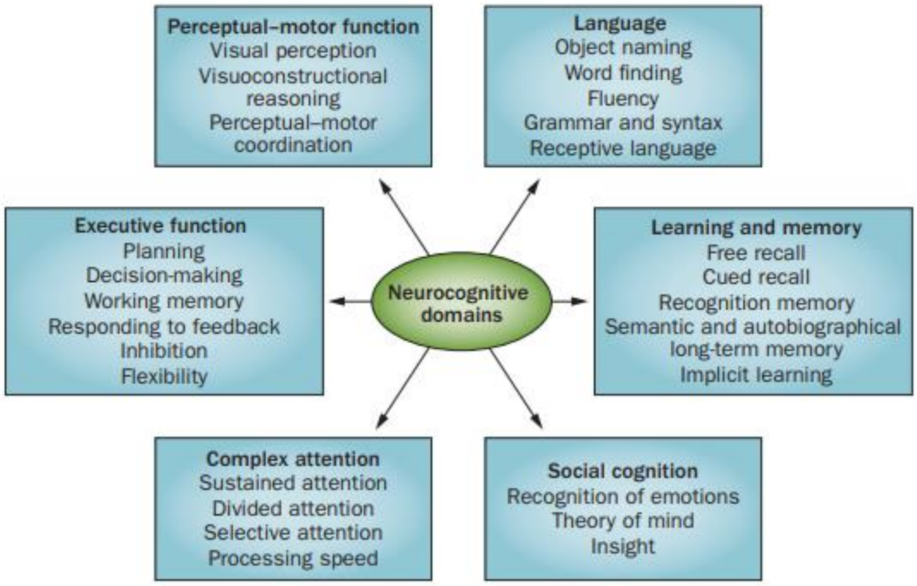


Figure 13. The DSM-5 domains of cognitive functioning (Sachdev et al., 2014, p. 3)

The social cognition domain is an extension compared to DSM-IV and defines social cues as important features to evaluate the general condition of an individual. Basing on the previously reported domains, DSM-5 (APA, 2013) provides different sets of diagnostic criteria for mild and major neurocognitive disorder. MCI has been broken down into the following subtypes: 1) amnestic; 2) non-amnestic; 3) single-domain; 4) multi-domain (Winblad et al., 2004), but a 20-year retrospective study published in 2020 debated this classification, affirming that the distinction between single-domain and multi-domain is not a significant predictor of MCI conversion in other neurocognitive disorders. Out of a total of 1188 individuals affected by MCI they found few patients presenting single-domain MCI, especially in the form of the amnestic one, while the difference between amnestic and non-amnestic MCI reported almost a 2-fold-risk of progression to major neurocognitive disorder in the case of amnestic MCI [32% developed a major neurocognitive disorder (n = 251: Alzheimer's disease; n = 102: mixed vascular and Alzheimer's disease; n = 14: other types of neurocognitive disorders), 62 % remained stable, 68% returned to normal condition].

An Alzheimer's brain is easily recognizable by its hippocampus and from the outer layers of cerebral cortex, other than from the accumulation of β-amyloid plaques, the ones that effectively cause the death of neurons, and neurofibrillary tangles, which disrupt neural transmission thanks to the β-amyloid, which is a particular protein that destroys synapses and causes neural death. Other biological biomarkers are Presenilines [PSEN1 and PSEN2] (Ledo et al., 2021) and the expansion of Huntingtin gene [HTT] (Ridler, 2018). A 2020 study (La Joie et al., 2020) recognized that the presence and location of τ protein in the brain may predict future brain damage and help with predicting the Alzheimer's progression. By the analysis of 32 brain scans of people affected by Alzheimer's disease, researchers concluded that τ might play a more influent role in brain damage than beta-amyloid: they noticed that earlier disease onset is more associated with higher τ burden, and this represent the direct cause of a more rapid atrophy. In Figure 14 it can be seen the general brain atrophy due to AD (left side), which includes cortical thinning, volume loss, white matter degeneration, and sulcal widening. The morphometric brain scan (right side) shows the progressive ventricular enlargement and AD brain atrophy, which is typically associated with the effective decline in cognitive functioning.

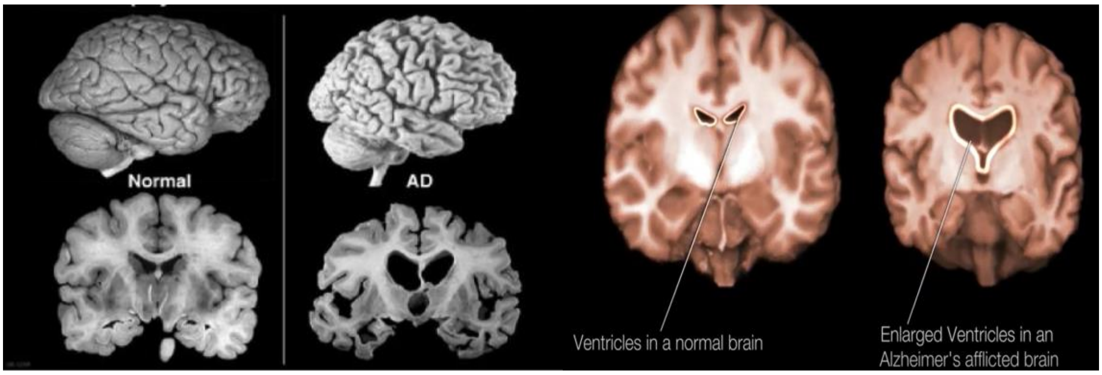


Figure 14. Differences between a normal brain and an atrophic advanced AD and a modeling of the dynamic degenerative brain process (USC Stevens Neuroimaging and Informatics Institute).

If the environment can modify gene-expression epigenetics, the context within which a person lives is critical to understand. The 2020 report of Lancet Commission (Livingston et al., 2020) purposes to improve attention on wellbeing as main goal of neurocognitive disorders' care and adopts a new framework, in which life course becomes fundamental in reducing modifiable risk factors (Figure 15).

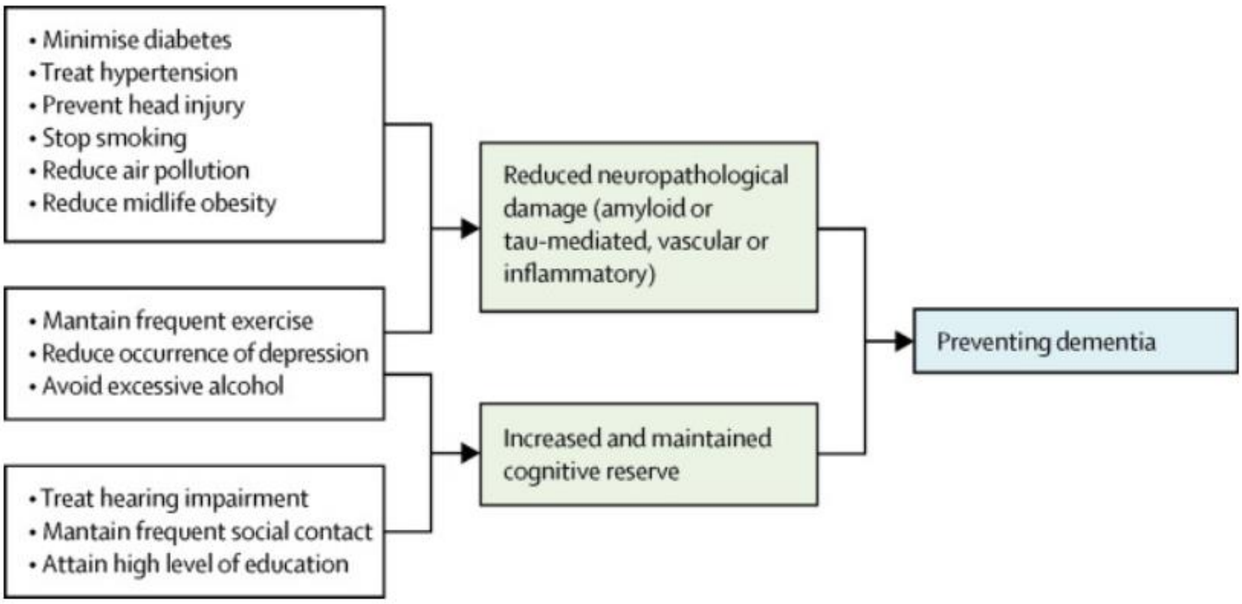


Figure 15. Mechanisms to support the role of modifiable risk factors in dementia (Livingston et al., 2020, p. 416).

The 2/3 of the overall Alzheimer's risk factors comes from genes, with the remaining 1/3 associated with environmental factors, such as a possible history of depression, head injuries, lifestyle, and quality of life: "*Dementia is by no means an inevitable consequence of reaching retirement age, or event of entering the ninth decade. There are lifestyle factors that may reduce, or increase, an individual's risk of developing it. in some population dementia is already being delayed for years*" (Livingston et al., 2017, p.3). What is the effective role of prevention, intervention, and good quality care during lifespan? To try to find an answer to this question, it is necessary to move on chapter two.

CHAPTER 2

PREVENTION AND KEYS OF HEALTH PROMOTION IN OLD-AGE

"There is a fountain of youth: it is your mind, your talents, the creativity you bring to your life and the lives of people you love. When you learn to tap this source, you will truly have defeated age."

(Sophia Loren)

The emerging issue of cognitive aging as a lifelong process is significantly influencing the public health systems and pressing communities to improve actions to maintain the general wellbeing of older adults. Cognitive aging can be influenced by modifiable and nonmodifiable factors, including genes, culture, education, medical comorbidities, physical activity, and further environmental aspects. The primary goal of prevention science is to understand the linkage between generic risk factors and clinical disorders, using both data of healthy and clinical population. New issues for the study of human development need to be incorporated in the models for preventing chronic conditions, and new multilevel perspectives about the relationship between risk and protective factors must be considered.

1. **The construct of prevention: models and theories**.

The definition of prevention has changed over the time, with many attempts by researchers to converge evidence and has expanded its meaning in the context of health and well-being only in the last few decades to become a sophisticated instrument of analysis for different variables associated with chronic disorders. The word *prevention* itself derives from Latin and means "*to come before*", referring to the sense of anticipating and take precautions against a danger or evil situation, and in the sense of "*to increase*" (Oxford English Dictionary, 1971).

Researchers started to think in term of “risk factors” in 1998, year in which the World Health Organization expressed the concept of prevention as something that <<*covers measures not only to prevent the occurrence of disease, such as risk factor reduction, but also to arrest its progress and reduce its consequences once established*>> (WHO, 1998). Different perspectives within theories become from the fundamental distinction between disease and illness themselves. Indeed, disease can be defined as an objective diagnosis made by health professionals, with specific signs and symptoms that require specific treatment, while illness can be defined as a subjective experience (Helman, 2007; Kleinman et al., 1978): as Kleinman (1978) would have said, physicians and doctors diagnose the disease, patients experience illnesses. The meaning itself of illness changes the conception of the patient, which becomes central in the explanatory models regarding diagnosis or treatment in different biomedical categories: some disease may have no symptoms that can be perceived from patients so that they can declare not to be, or, in case of neurodegenerative and psychopathological conditions, they could not be aware of what is happening inside them. With the progress of medicine and science the understanding of illness surely changed, bringing to develop different strategies of treatment specifically disease dependent. The necessity to identify risk factors introduced a new perspective in clinical medicine for epidemiologists (Beaglehole et al., 2004; Brotman et al., 2005), that brought to the evolution of the so-called *preventive medicine*, the practice of promoting preventing health care to patients to improve well-being. To define risks and protective factors, it can be said that the first ones can rate the probability of onset, severity, and duration of the pathology, while the second ones, on the contrary, refer to conditions that can improve individual resilience to risk factors (Serin et al., 2016).

An increasing world focus is on achieving equity in health (Jong-Wook, 2003) by recognizing the main challenges for intervention to reduce illness, that can be resumed with essentially four general goals (Figure 16).

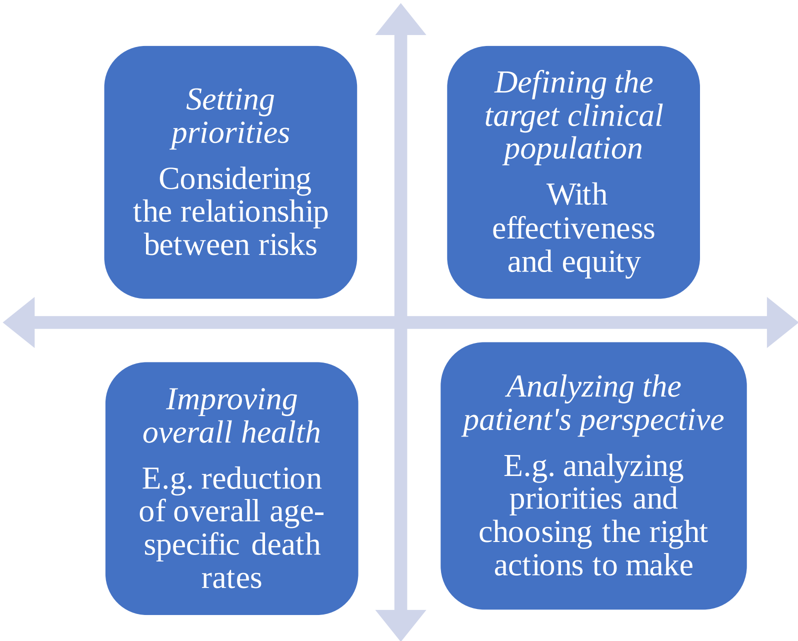


Figure 16. Schematic representation of health improvement process intended as the action of reducing risk factors within the general population.

Advantages and disadvantages of alternative strategies vary in function of the specific disorder and of population because prevention requires a coordination of multiple actions in each functioning domain. In this sense, the presence of multimorbidity in individuals brought to a new conception of care that can be defined as *patient-centered* (Gérvas & Perez Fernandez, 2006). Multiple components interventions consider risk factors in different domains with a comprehensive community organization that includes educational, governmental, health and human issues, as recent socio-ecological plans and perspectives could demonstrate (Caine, 2020; McKenzie et al., 2022). Jamoulle proposed a model (Figure 17) in which is well represented the relationship between patient and doctor side of disease and illness in the different frameworks of primary, secondary, tertiary, and quaternary prevention (Jamoulle, 1986; Kuehlein et al., 2010). For example, a patient that is having an infarction doesn't only have risk factors for it but has also developed one: this means that he has the highest risk level that can be potentially developed in the future, so that doctors must provide all preventing measures according to life circumstances and patient's will.

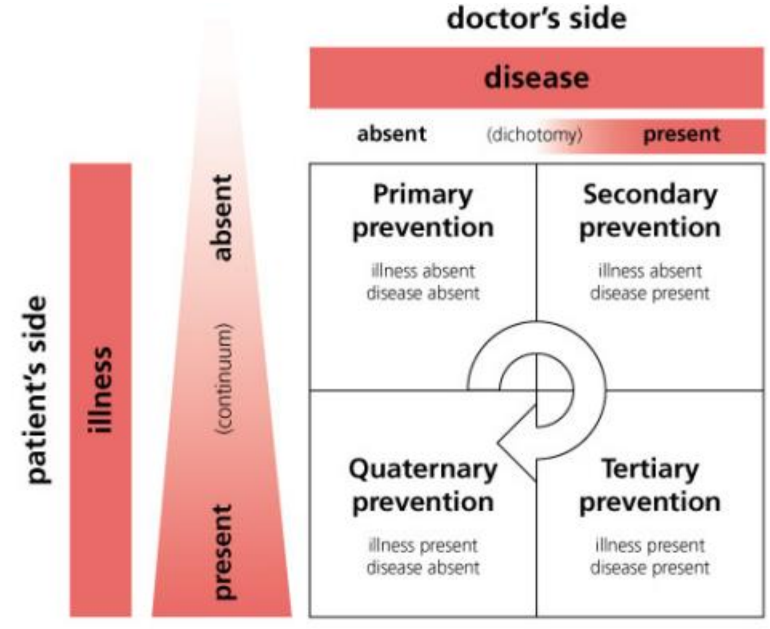


Figure 17. Different types of prevention in the relational model doctor-patient in the 2x2 Jamoulle model (Kuehlein et al., 2010, p.4).

Primary prevention does not include neither illness nor disease, while secondary one includes risk factors that don't imply necessarily the effective development of complications they are at risk for. As can be seen, tertiary prevention is the only one in which illness and disease effectively coincide. The concept of "*primum non nocere*" in modern medical practice is an ethical approach that should drive every plan of intervention and encourage clinicians to protect people from the excess of medicine, and this aspect can be considered one of the most relevant goals of quaternary prevention (Wagner, 2015). In recent years, health promotion supports the idea of an ecological theory of disease (Getz et al., 2018; Sallis et al., 2018), in which illness and health are outcomes that involve factors at micro and macro levels (e.g., biophysiology, environment, pollution, individual lifestyle, behavior). The concept of primary prevention is related to different aspects of treatment, rehabilitation, and general care. Indeed, the main goal of primary prevention is to anticipate the major number of predictable problems to protect healthy functioning and promote desired goals in basically two macro contexts (Schonert-Reichl et al., 2014): 1) universally, by being useful for everyone's benefit; 2) selectively, since it is an action that can be oriented to groups with potential high or low risk. According to Bloom and Gullotta (2014), primary prevention involves multiple levels, groups, persons, and communities underlying that protection of healthy functioning and the promotion of psychosocial wellness require constructive issues in social and physical environments, with major competence within political-economic context.

1.1. **Secondary and tertiary prevention against NCDs.**

The direct connection to primary prevention is the idea of reducing the disability due to a disorder: secondary prevention, in this sense, refers to the actions that can be worked to identify disease or negative health status as soon as possible. General health checks can be good examples of secondary preventions, such as mammograms and blood pressure measurement, because the onset of new pathological conditions must not to be underestimated: it is important for the patient to associate with the effective therapy a set of good daily practices, which contribute to lower the risk of developing new symptoms. The achievement of secondary prevention approach depends on the availability of inexpensive and scalable methods to detect preclinical and prodromal dementia states (Ojakäär & Koykev, 2021). Digital technologies and blood-based biomarkers for AD are examples of how these diagnostic instruments are becoming more and more rapid, giving the possibility of monitoring large at-risk groups.

These checks can bring to different kind of harms, such as overdiagnosis, overtreatment, injury from invasive follow-up tests, distress due to false positive test results, false reassurance due to false negative test results, possible continuation of adverse health behaviors due negative test results, and psychosocial consequences. Reducing the chronic effects of a disease by minimizing the functional impairment, like preventing further complications of Alzheimer's disease is the main goal of tertiary prevention, which includes rehabilitation practices. For what concerns MND, meta-analytic reviews highlight the potential of cognitive interventions, demonstrating their effectiveness in improving aspects such as memory, attention, executive functions, and processing speed (Cotelli et al., 2012). The dose and frequency of cognitive therapy must evaluate essentially three components: 1) the intensity, or the time (minutes/hours) of each treatment session; 2) the duration, that is for how long the cognitive therapy must be protracted; 3) the frequency, that is how many times per week the patient must be submitted to the single sessions. Even those treatments designed to support the family of patients, who after diagnosis may find themselves disoriented and confused must be considered to complete the intervention in a holistic and comprehensive way. Since contemporary medical practices could be invasive and with bring to many chances of harm, the general model of prevention considers a fourth class, the quaternary one, which expresses the need to protect individuals from overmedicalization (Jamoulle, 1986). Quaternary prevention moves into the center of the axes between illness and disease because the risk to incur in false-positive diagnoses and being exposed to strong follow-up procedures intensifies the risk of impair quality of life in healthy people (Martins et al., 2018).

2. **Primary prevention in action against cognitive decline and its relationship with well-being.**

As can be perceivable, primary prevention aims at build adaptive strengths: this issue introduces the concept of wellness enhancement (Cowen, 2000) in contrast with the simple disease-prevention and it is established evidence that different causation models can provide multiple perspectives to better understand disease models (Bloom, 1981). In case of MND, the efficacy of primary preventions stands in treating specific risk factors, interpreting early signs and symptoms to detect the disease. As an example, predictive factors of MND can be classified in sociodemographic (e.g., sex, age, education), health factors (e.g., diabetes, hypertension, diabetes), and bio-behavioral factors (e.g., smoke, alcohol, level pf physical activity), and primary prevention results fundamental because it helps to identify situations that can increase the likelihood of symptoms' occurrence (Brooks & Lowenstein, 2010). Several intervention studies focused on primary preventions are ongoing, especially in Europe, with the aim to detect pathophysiological hallmarks and potential strategies to protect people from cognitive decline. One of the most famous experimental cohort studies of the last years is the Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability [FINGER] (Kivipelto et al., 2013), in which it was tested a multidomain intervention on quality of life, depressive symptoms, disability, use of health care services, and vascular risk factors. There were involved 1200 participants 60-77 aged with an increased risk of cognitive decline, and the RCT protocol showed that a multidomain intervention that includes diet, exercise, cognitive training, and an active monitoring of vascular risk for two years significantly improved cognitive functioning. Basing on these results, the attention toward cardiovascular disease was further tested to be efficient by the Prevention of Vascular Dementia by Intensive Care (PreDIVA) trial, in which it was conducted a multicomponent intervention focused on vascular care on 3500 cognitively healthy participants from 70 to 78 years old. Contrary to expectations, the intervention didn't result related to dementia incidence reduction, with no effects on mortality, disability, and cardiovascular disease, even if it was reported an improvement in systolic blood pressure in people who followed the protocol (van Charante et al., 2016). In U.S.A. the ACTIVE study is a good example of cognitive-related intervention (Jobe et al., 2001). It is a program in which were included over 2800 healthy participants over sixty-five aged, who attended ten group sessions for six weeks in which they received memory, reasoning, and speed of processing training. Results showed that domain-specific trails maintained high the level of cognition in the targeted domain. Performance was maintained at a 5-year follow up, with beneficial effects in ADL and IADL, but the most significant result of the protocol was the fact that at ten years from the study dementia rates were lower in participants that received the speed of processing intervention (Edwards et al., 2006). Recommendations to the general population on how to manage a good lifestyle and to check their own health status can contribute to encourage public health and interventions focused on multiple domains contribute to reduce the overall burden of neurocognitive disorders and could be offered to individuals by analyzing their own condition and the exposition rate to risk factors of each one (Crous-Bou et al., 2017). Lifestyle interventions are assuming more and more support in last years, starting from Bredesen purpose (2014) of a multicomponent protocol on 10 MCI patients that demonstrate progresses in the 2-years follow-up phase. The intervention included modifications on diet, physical activity, stress reduction, and the assumption of vitamin supplements. Results suggested the concrete possibility to reverse the trajectory of cognitive decline, and actively engaging participants and in a meaningful manner resulted to be fundamental in implementing these types of interventions.

3. **Risk and protective factors from cognitive decline.**

Health promotion focuses its energies on a variety of levels, and a remarkable amount of progress has been made in identifying risk and protective factors relevant to cognitive decline and neurodegenerative conditions, so that most randomized trials of risk factors modification have been mixed to reduce the risk of impairment. Neurocognitive disorder is a multi-factorial disorder, and growing studies support the contribution of modifiable environmental factors. Epidemiological studies identified risk factors for this class of disorder, especially for what concerns Alzheimer's disease (Lashley et al., 2018; Reitz & Rosenblum, 2014). Primary risk factors for AD are genetic ones, such as the presence of APOE4 genotype, or environmental ones like head injury, low education, family history or low participation to cognitive stimulating activities (Reitz et al., 2011; Mielke et al., 2014). Sienski and colleagues (2021) investigated how *APOE4* affects lipid metabolism in brain cells, discovering that APOE4 astrocytes can process lipids and they demonstrated that by manipulating lipid metabolism it is possible to alleviate the consequences of carrying this type of allele. Also, dysfunction in vascular functioning is one of the primaries focuses of research during last years for neurocognitive disease (Nelson et al., 2016): neurovascular units guarantee many important functions for cerebral biological activity, such as blood flow, blood-barrier exchange, immune surveillance, homeostatic balance and maintains trophic functions thanks to the production of growth factors provided by glia and neurons. Trophic interaction is substantial in supporting the movement of axons and vessels: after a brain injury, growth factors can be released from cells like the brain derived neurotrophic factor (BDNF), assuring the proper functioning reprise of each neurovascular units after damage (Snapyan et al., 2009). Nevertheless, it is true that genes play a daily role in encoding protein sequences that instruct the body in everything it does to keep it healthy and alive, but genetic causes can influence early-onset cases in under 60 aged individuals, with an accounted percentage of 1 of total cases (Bekris et al., 2010). This means that other investigable factors are modifiable and can influence people's life, health care systems, and societies (Brookmeyer et al., 2007). In this chapter will be analyzed the role of diet, physical activity, and social engagement in hindering cognitive decline: maintaining an optimal bio-psycho-social balance in late life when bodies are less resilient is important to achieve the maximum benefit and a longer living.

3.1. **Diet.**

Even if this factor was not directly considered in the current pilot study, food is one of the most important, day-to-day, and intimate contacts between our DNA and the outside environment, and for this reason it is important to understand how nutritional interventions represent some of the alternative strategies that could slow and even stop neurodegeneration**.** Food and dietary patterns are the sum of biochemical interactions among nutrients, with specific mechanisms that can reduce neuroinflammation and increase brain defenses throughout life. The dominant medical model does not always put in foreground the mutual influences of brain and mental issues on the gastrointestinal system, even though it is possible to find numerous molecules and peptides that act in an interdependent way at a neurogastroenteric level (Rehfeld, 2014). Dietary compounds can cross the blood-brain barrier (BBB) and play effects on microglia and CNS' cells inflammation level. Several diets have been tested to explore the relationship between nutrition and cognitive decline prevention. The most mentioned are: 1) Mediterranean diet (*MeDi*. Scarmeas et al., 2006); 2) Dietary Approaches to Stop Hypertension diet (*DASH*. Appel et al. 1997); 3) Mediterranean-DASH Intervention for Neurodegenerative Delay diet (*MIND*. Morris et al., 2014). The Mediterranean Diet [MeDi], followed by people that live on the Mediterran Sea' shores, includes the high consumption of vegetables, legumes, fruits, cereals, potatoes, whole-grains, beans, seeds, fish, and extra virgin oil (Mazza et al., 2018), with a moderate quantity of alcohol, red meat, fried foods, sweets, and white flour products intake. Fats can derive from extra virgin olive oil and dried fruit, so that several studies found an improvement of cognitive function associated with these foods (Valls-Pedret, 2015). Scrameas (2006) considered 2258 health individuals evaluated for 4 years and investigated the connection between the adherence to this diet and the incidence of Alzheimer's disease, finding out that after 4 years of MeDi there were 262 cases of AD, with a 40% reduction of total incidence. Different chemical and biological mechanisms could be purposed to explain the association between nutrients of Mediterranean diet and better brain health, but the most important are related to the antioxidant properties of the food included in Mediterranean style and to a significant reduction of general inflammation levels (Panagiotakos et al., 2009). The *Dietary Approaches to Stop Hypertension* [DASH] diet was initially addressed to treat and prevent hypertension. It is characterized by a low consumption of saturated fats, total fats, and cholesterol, with a quantity of proteins moderately high, and a rich supply of minerals and fibers (Appel et al., 1997). In this nutritional approach is important to choose rich in potassium, calcium, magnesium, fiber, and protein foods, low in saturated fats and in sodium. A study on 923 elderly people proved lower rates of AD thanks to DASH adherence (Morris et al., 2015), and it was specifically conceived to slow and prevent the age-related loss of memory function promoting the reduction of oxidative stress and the formation of beta-amyloid plaques. MIND, as the union of MeDi and DASH, involves the assumption foods rich in carotenoids, vitamins, and flavonoids, which may benefit also on heart pathologies (Golzarand et al., 2022), obesity (Aminianfar et al., 2020), and certain cancers (Soltani et al., 2022). In a cohort of participants with history of stroke, people who followed MIND resulted to have a slower rate of cognitive decline in a 6 years' follow-up (Cherian et al., 2019), and another cohort of Puerto Rican 45-75 aged adults showed better cognitive functioning after 8 years of higher adherence to MIND

(Boumenna et al., 2022). Also, caloric restriction revealed itself as an adequate behavioral model to prevent cognitive decline and maintain good health. It consists in a diet regimen that reduces food intake without incurring in malnutrition: previous evidence showed that the complexity of caloric restriction stands in a variety of biological and chemical patterns, including metabolic, neuroendocrine, and apoptotic responses, highlighting that general effects on cognitive functions could vary among species (Bok et al., 2019). Improvements in cognitive function in healthy older subjects were reported due to caloric restriction implying multiple metabolic pathways, modulation of mitochondrial activity and reduction of oxidative damage (Leclerc et al., 2020). Researchers purposed that an adherence of at least three months is needed to elicit the protective action and the counteraction to age impairment (Dhurandhar et al., 2009; Žlibinaitė et al., 2020) bringing to an improvement of synaptic plasticity, thanks to the brain derived neurotrophic factor (BDNF). Finally, an elevated quantity of saturated fatty acids could cause negative effects on age-related cognitive decline and on MCI, which can be: 1) saturated; 2) trans; 3) monounsaturated; 4) polyunsaturated. The first ones can be found in eggs, meat, and whole-fat dairy products, the second ones in fried foods and some commercially baked goods, the third ones are the main components of olive and canola oil, while the last ones are the main components of nuts, fish, and vegetable oil. Considering the central nervous system, omega-3 fatty acids, like eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) may play an important role, although they are not directly produced by the body. DHA is vulnerable to oxidative damage, and this implies the need of assuming a polyphenol integration from the age of 60, to maintain active the neuroplastic capacity (González et al., 2012). The consumption of flavonoid-rich foods during life can reverse age-dependent memory architecture deterioration. In fact, flavonoids may induce neurogenesis, in a direct or indirect way, using signaling or peripheral vascular effects: an example of a valuable polyphenol with a wider acceptance in the diet is cocoa

(Monahan et al., 2012), which promotes blood supply to the brain and increased health and flexibility of blood vessels. Neuroprotective effects of cocoa flavonoids could produce angiogenesis, neurogenesis, and changes in neuron morphology, particularly in regions involved in learning and memory (Caruso et al., 2021; Sokolov et al., 2013). Polyphenols have also been associated to a significant reduction of diabetes, obesity, and cardiovascular disease (Guo et al., 2017; PREDIMED, 2016). Limited research and data on the antioxidant status of healthy elderly people is present, but recent evidence is focusing on developing treatments that can use lipid properties to prevent MCI (Ali et al., 2022; Nantchai et al., 2022)

3.2. **Physical Activity (PA).**

The best way to maintain the whole health and well-being of the organism is treating brain and body together. There are many effects that benefit both mental health and body structure and increasing experimental evidence during years is explaining how physical activity influences the preservation and improvement of cognitive abilities. The idea that physical activity and properties of human body could influence the brain is well represented by the theory of embodied cognition (Foglia & Wilson, 2013; Goldman, 2012): it considers humans as ecologically and genetically embedded social agents who shape and are shaped by their environment. A constant growing number of studies describe the effects of physical activity (PA) on angiogenesis, neurogenesis, and up-regulation of neuroprotective molecules, which might significantly act upon brain structures and functions (Anderson et al., 2010; Erickson et al., 2022). PA is recommended as a non-pharmacological treatment for different chronic conditions, but also an instrument to maintain general health status and, by calculating population attributable risks, physical inactivity is defined as not doing twenty minutes of vigorous activity for at least three days per week or thirty minutes of moderate activity for at least five days per week. Indeed, exercise improves cardiovascular health (Mangione et al., 2022), reduces body mass index preventing obesity (Liaw et al., 2019), and shows beneficial effects on cerebrovascular and cognitive functions (Rêgo et al., 2019). Different training programs demonstrated that anti-inflammatory effects and regular exercise can reduce the general risk of infections: an interesting demonstration of this issue derives from last research conducted in the post COVID-19 pandemic period, with consistent effects in decreasing hospitalization and death, such that it has become one of the most recommended activities to prevent the infection. A systemic meta-analysis of 2018 has examined the role of PA in MCI adults, demonstrating its beneficial effect on memory and global cognition, delaying the onset of neurocognitive disorders, Alzheimer's disease, and Parkinson's one (Loprinzi et al., 2018). A biological explanation of these mechanisms involves the increase of circulating growth factors (e.g., IGF-1) and neurotrophins (e.g., BDNF), which have effect on plasticity in young and adults' brains, influencing the course of aging, the level of damage, and the epigenetic effects due to DNA methylation (Ahuja et al., 2022; Schaeffer et al., 2022; Shobeiri et al., 2022).These molecules cross the blood-brain barrier (BBB) into the brain capillaries and influence the level of functioning of glial cells, modifying neurotransmission in different brain areas and activating different pathways of gene expression. Both endurance and resistance exercise influence the long-term potentiation of synapses (LTP) which can be defined as the physio-biological base component for learning and memory (Figure 18. Di Liegro et al., 2019). In quite all mammals, neurogenesis takes place in the hippocampus' dentate gyrus and in the sub-ventricular one of the lateral ventricles, and new neurons born in the sub-granular zone differentiate and integrate themselves in the neural hippocampus' networks.

Considering that hippocampus is fundamental for memory system, especially for episodic memory and spatial one, hippocampus-dependent learning could be strongly influenced from the regulation of local neurogenesis (Zhang et al., 2020). This is the reason why environmental stimulation in rats can support the survival of neurons, and physical activity can be considered as a good proxy to increase hippocampal neurogenesis in aged mices (Wang et al., 2021).

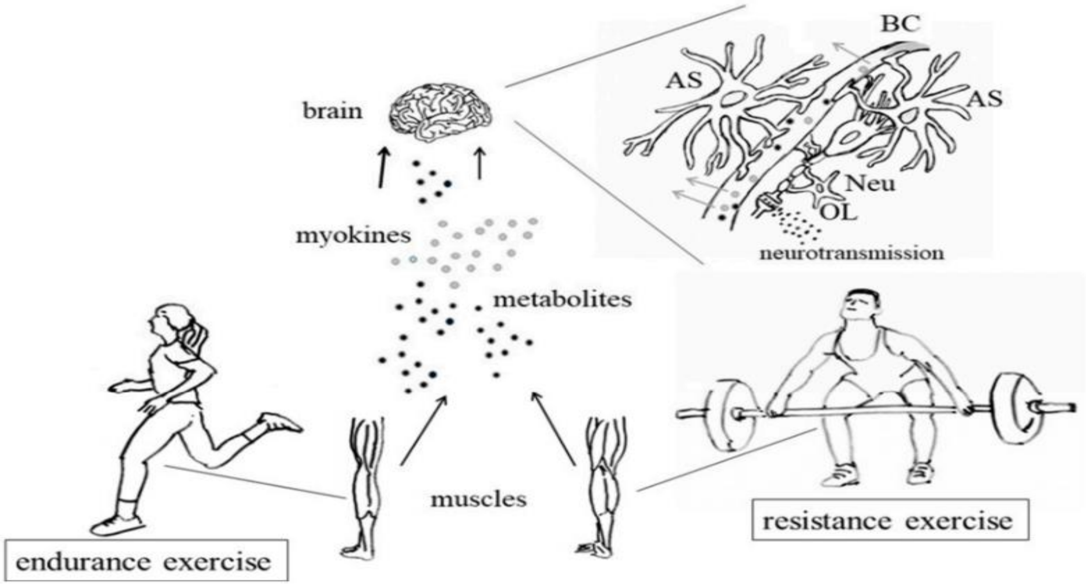


Figure 18. Role of exercise in enhancing cognitive functioning from a biochemical point of view (Di Liegro et al., 2019, p.4).

In human brains electrophysiological measures demonstrate that PA induces transient and permanent changes in the aging brain (Niemann et al., 2014). Voxel-based morphometry (VBM) and image segmentation of high-resolution brain scans report a reduction of grey and white matter loss in frontal, prefrontal, and temporal regions associated with cardiorespiratory fitness training in older adults (Colcombe et al., 2006), like yoga sessions, and attenuates motor symptoms in chronic diseases, such as Parkinson (Johansson et al., 2022), and multiple sclerosis (Leavitt et al., 2014).

Erickson and colleagues had undergone 165 healthy older adults to MRI, finding out that higher fitness levels were associated with both left and right hippocampus' enlargement, and this result correlated with improvements in spatial memory performance (Erickson et al., 2009). Longitudinal studies that considered as risk factors lipids, hypertension, diabetes, APOE status and history of stroke confirm the importance of physical activity in reducing dementia risk (Hamer & Chida, 2009): in a study conducted on 2492 older Germans, any type of PA was associated with a 20% of dementia onset risk reduction over the next five years (Luck et al., 2014). PA might protect against the adverse consequences of Aβ and τ deposition, which causes an acceleration of cognitive decline and the consequent development of AD. A longitudinal investigation of cognitively normal individuals conducted by Harvard Aging Brain Study reported that an increased baseline physical activity was associated with a reduction of the negative impact of Aβ burden on cognition and cerebral atrophy (Rabin et al., 2019). As explained below, BDNF serum levels, which promote neuroplasticity, synaptic growth, and hippocampal neurogenesis, increase quite immediately after exercise: a study on nineteen older adults highlighted that BDNF immediately increases after a 35-minute session of physical activity compared to other potential brain-healthy activities like cognitive activity and meditation (Håkansson et al., 2017). More investigation is required to achieve a complete understanding of the effective potential of PA in protecting the brain from age-related effects, but evidence has demonstrated its impact on some factors that alter neurocognitive integrity. A recent review (Lautenschlager et al., 2022) synthesized guidelines and indications for physical activity in old age, underlying the importance of motivating elderly people with MCI or Subjective Cognitive Impairment (SCI) in starting a PA program and maintain it in the long term, by strategies to enjoy physical performance and explanation of the goals from significant others, trainers, and health professionals, like participating in aerobic activity for at least 150 minutes, engaging progressive resistance training with consideration to factors like health problems, physical capacity and environment. These recommendations confirm previous literature but underline the necessity of studying on a large-scale multi-modal intervention trial in population at risk of cognitive impairment, to promote the effective utility of healthy lifestyle protocols. PA can essentially be aerobic or anaerobic. Aerobic one is any activity that involves large muscles groups and can be maintained thanks to its rhythmic in nature and that involve oxygen consumption (e.g., swimming, cycling, running, dancing, walking). A meta-analytic review of RCTs considered twenty-nine studies conducted between 1966 and 2009, with more than two thousand older aged participants, found that individuals who were assigned to the experimental group and trained aerobic exercise showed improvements in attention, processing speed, executive functions, and memory (Smith et al., 2010), suggesting that physiological mechanisms that support cognitive enhancement need to be fully and better understood. Table 1 resumes some results of brain and physical benefits due to aerobic activity in elderly subjects.

Authors	Activity	Time	Sample	Age	Benefits
Colcombe et al., 2008	Aerobic activity with a motor driven treadmill (1h per session)	6 months (1h per session)	59 sedentary community-dwelling volunteers	60-79 y.o.	Improvements in general executive control and increase of brain volume
Albinet et al., 2010	Aerobic training consisting in walking, circuit-training, step and gradually running	12 weeks (1h per session, 2 times per week)	24 healthy sedentary men and women	65-78 y.o.	Improvements in executive control and increases in vagal-HRV mediated parameters

Voss et al., 2010	Aerobic activity (walking with increasing intensity rythm)	12 months (30 minutes per session)	32 cognitive and physically healthy men and women	55-80 y.o.	Increasing connectivity in DMN and frontal executive network
Alfini et al., 2020	Aerobic exercise (moderate intensity cycling)	30 minutes of exercise	32 physically active, cognitively normal older adults	55-81 y.o.	Enhanced intrinsic functional connectivity of amygdala and hippocampus with improvements in mood quality.

Table 1. Aerobic PA and its effect on physical and brain outcomes.

On the other hand, anaerobic activity helps to build muscles endurance and ability to withstand fatigue, decreasing body fat with beneficial effects on cardiovascular risk and lipid profile. One of the leading contributors to functional decline and loss of independence in older adults is sarcopenia, that is the damage of muscle tissue like osteoporosis for bones, but luckily it has been demonstrated to be reversable (Larsson et al., 2019). In one study eight weeks of resistance training brought to significant improvements in frail nursing home residents 90-96 aged, with walking speed improved of 50% and a 174% gain in strength (Fiatarone et al., 1990). High intensity interval training (HIIT), a short workout composed by 30 seconds-1 minutes of running, cycling, or climbing stairs, followed by a minute of cool-down activities, such as walking or pedaling, repeated for ten minutes, can be a good alternative to aerobic or anaerobic exercise and a solution to gradually start moving and mobilize heart rating avoiding the monotony of traditional programs (Keating et al., 2020).

A meta-analysis of 39 RCTs that considered 45-60 minutes per session of vigorous or moderate PA in cognitively healthy adults older than 50 years showed global cognitive improvements due to aerobic exercise instead of other type of training, like yoga practice (Northey et al., 2018). Longitudinal studies are not much common in the context of PA, because of the differences in sex, social class, and culture, but there is a 44-year trial (Hörder et al., 2018) that involved 191 Swedish women (38-60 y.o.) training cycling exercise at different intensities that demonstrate that low practice brought to a higher probability of developing dementia (PA levels: low = 32%; medium = 25%; high = 5%).

3.2.1. *Effects on mood and mental wellbeing.* One more factor that has been detected in PA studies is the relationship with psychological depression and mood modification, which is clinically present in 10-15% of older adults, often due to social isolation, low income, and health decline. Aerobic exercise resulted to be positively correlated with lower depression scores, reduced anxiety, and improved quality of life in both healthy and medically ill older adults (Barbour & Blumenthal, 2005). A recent work (Boolani et al., 2021) tested 11 participants on 6 minutes of self-paced walking. It was asked participants to answer some questions about mood and motivation using the 30-item Profile of Mood Survey-Short Form (POMS-SF; Curran et al., 1995) before and after the exercise sessions (3 days of testing in total). Results demonstrated that a short 6-minute bout of physical activity can help improve feelings of energy, increasing motivation to perform physical tasks and decreasing feelings of fatigue or confusion among healthy older adults (≥ 65 y.o.). Healthy elderly adults were evaluated also in another moderate walking exercise program (Hatta et al., 2018), consisting in 80–120 minutes of self-paced walk with no fixed distance to achieve approximately 7,000–10,000 steps in one walk in which were compared general mood, stress response and executive functions before and after the intervention through a self-report survey, the Wisconsin Card Sorting Test, and the collection of salivary α-amylase immediately before and after the walking.

Results showed improvements in mood and positive behavior, with lower tension-anxiety, anger-hostility and confusion scores after self-paced walking. These effects were not reported in executive functions, which seemed to temporarily decrease with the increase of α-amylase. The interesting role of psychophysiological biomarkers in evaluating the relationship between PA and well-being states improvements was analyzed by Strahler and colleagues (Strahler et al., 2010), confirming that regular PA reduces sympathetic and hypothalamic-pituitary-adrenal axis hyperactivity in elderly people, and this is indicated by the low levels of salivary α-amylase and cortisol in more active subjects. Promoting good health for everyone and for all age groups through the culture of movement, respecting individual abilities, is the fundamental goal that the World Health Organization (WHO) as always looked at, together with education, environment, welfare, and citizenship rights. Unfortunately, Italy has one of the most sedentary populations in Europe, with 60% declaring to not practice PA, against a European average of 42% (Hallal et al., 2012). For what concerns over 65 aged people, PA should go on with at least 150-300 minutes of moderate aerobic training, or intense one for 75-150 minutes, with the supplement of multicomponent strategies that incorporate muscle strengthening ad balance training, at least three days a week, to improve muscles mobility and preventing falls (Di Pietro et al., 2020; King et al., 2019). The most common chronic diseases, such as diabetes or hypertension, are not a limit for PA: suggested motion levels are similar to non-sick peers, within the limits of what is compatible with individual physical abilities. In general, the principle that less is better than nothing is always valid, and, in conclusion, older adults should check with their doctors, or professional trainers, which kind of activity results to be better for their individual condition, respecting own's body limits and considering the whole class of age-related factors.

3.3. **Social engagement and life with people.**

One of the keys for a long health span is social connectedness. Loneliness is usually associated with early mortality (Hawkley & Cacioppo, 2010) and medical problems, such as cardiovascular incidents, personality disorders, psychoses, and, of course, cognitive decline, doubling the likelihood of developing AD and increasing the production of stress hormones, which can lead to diabetes, neurocognitive disorders, and higher risk of suicide attempts. Some researchers affirm that loneliness can be worse for health than smoking fifteen cigarettes per day, with a die rate that goes up by 30% (Klinenberg, 2018). The last COVID-19 pandemic period has confirmed these estimates: reports underlined the negative impact that isolation produced on mental and physical health (Brooks et al., 2020; Morley et al., 2020), especially for people at risk of developing neurocognitive disorders, such that it has been included in the list of the potential risk factors for dementia (Livingston et al., 2020). Social participation has been described as the engagement in religious, sports, cultural, recreational, volunteer, and community organization (Vozikaki et al., 2017). For instance, data report that volunteering is associated with a significant reduction of depressive symptoms, a major sense of self-worth accomplishment, fewer functional limitations, and even lower mortality (Anderson et al., 2014). In 205 people 30-64 aged and followed up until 66-88 years, travel, social outings, art, reading, and speaking a second language were associated with a strengthened and well-acted cognition (Chan et al., 2018), while another review on a longitudinal cohort study of 102.035 participants found that high social contact was associated with better late-life cognitive functioning both in males and females (Penninkilampi et al., 2018). Protective effects of social participation in elderly people are considered as a stimulus to increase the level of physical activity and cognitive function (Abe et al., 2022; Sepúlveda-Loyola et al., 2020), and interaction with other people can stimulate sensory systems, self-esteem, affectivity, emotional and psychological support (Hari et al., 2015; Tomioka et al., 2015), since during social contacts people receive both conscious and unconscious cues from the interlocutor expressions, gestures, postures, and actions. This means that the interaction starts from a bodily synchrony and then continues as a common orientation of interest and attention. There is difference between loneliness and social isolation. While the second one is the objective fact of having few interactions with people, loneliness is a subjective experience, and refers to an emotional state. Social isolation could be calculated, in terms of number of interactions per week, while loneliness is the feel of being detached from meaningful relationships, with lack of intimacy towards people. These two concepts are strictly related, because social isolation can lead to loneliness and both these factors can increase in old age due to a variety of circumstances. More frequent social contact in middle age can reduce dementia risks and other chronic conditions, as demonstrated in a 28-year follow-up study in which 10.308 London civil departments employees from the Whiteall Cohort were assessed by self-report questionnaires about the frequency of contacts with relatives and friends between the period of 45 and 55 years (Sommerlad et al., 2019). More social contacts were related, at the age of 60, to a lower dementia risk, with a major significant association between contacts shared with friends instead of relatives. The rise of communication and technology can be a strong cause of loneliness within aged people, since the last several years Facebook, Instagram, Twitter, and other emergent social networks are taking the place of human contacts, establishing and fulfilling online communities rather than real ones, but at the same time information and communication technologies (ICT) themselves are becoming object of study to prevent social isolation. ICT could overcome social and spatial barriers of communication by enabling easy and affordable communicative activities between elderly people (Chen & Schulz, 2016). Mellor and colleagues (2008) showed that computer and Internet's usage made by elderly people increased their social connectedness at a 3-month stage of intervention, but not at 6/9-month stage, a result that could depend on the quality and the quantity of interactions in which individuals were engaged. From a neurobiological point of view, social isolation and loneliness are associated with reduction in glutamate neurotransmitter, one of the most abundant neurotransmitters in vertebrates and an important resource for transmitting signals in the brain (Campagne, 2019). Proper brain functioning depends on keeping low levels of glutamate in the extracellular fluid, because high levels can lead to cellular death. Oxaloacetate and glutamate-pyruvate transaminase neutralize glutamate molecules to maintain its levels low, and brain membranes promote homeostasis of chemical levels in the whole structure of the brain. Inclusive and accessible social opportunities for elderly could improve motivation and self-efficacy by amplifying their contribution to community. The Canadian Longitudinal Study on Aging (Raina et al., 2009), which involved 50.000 Canadians aged between 45 and 85 years old, reported that 30% of women over 75 affirmed to be and feel lonely. Elderly people consider being engaged in life as related to feeling valuable, with a sense of satisfaction and purpose in life (Nimrod & Ben-Shem, 2015), in accordance with the construct of self-efficacy, that describes the belief that one can exert control over environment and social context. In 2017 was published a systematic review (Kelly et al., 2017) in which were considered 39 studies about the impact of social activities, social networks, and social support on global cognition of elderly individuals. There were included 3 RCTs (576 participants), 34 observational studies (87.509 participants) and 2 twin studies (189 pair of participants), considering databases from 2000 to 2017. In general, the strongest relationships were found between, executive functioning, working memory, verbal fluency, reasoning, and attention. Social network usage resulted to improve global cognition, but not episodic memory, attention, or processing speed while, on the other hand, social support enriched episodic memory and verbal fluency. These aspects will be considered in the pilot study object of this work because the influences of sociability and social activities on overall memory, fluency, reasoning, and visuospatial abilities still need to be explored. In the review were considered as social activities experiences that involve social participation or engagement, like meeting friends, attending events or functions, or participating in group recreational activities. Social activity was most consistently associated with improvements in global cognition, and genetic studies included in the review demonstrated an association with some (e.g., working memory) but not all executive functions. An innovative project was purposed by the Palo Alto Medical Foundation and is called "linkAges" (note the play on words on either *link ages* or *linkages*). It is a way to create a health online ecosystem in which can be shared services and opportunities for older adults, that can post online something they want help with and benefit from the support of an entire community (https://www.commonwealthfund.org/sites/default/files/documents/___media_files_publications_innovation_profile_2015_sep_1835_hayes_linkages_v2.pdf). Other types of interventions could involve different social-cognitive activity, like purposed in a RCT on 44 individuals 65 aged (Cohen-Mansfield et al., 2015). The study had the main goal to compare three interventions, such as group-based cognitive training, health promotion classes, and a social engagement-promoting book club. All three interventions resulted as significant in the improvement of cognitive performance, and all the three resulted in a reduction of loneliness measured with the UCLA Loneliness Scale-8 ULS-8: Hays & DiMatteo, 1987). The only variable that reported significant differences between the three treatments is the self-report evaluation of memory struggles, in which the cognitive training reported higher scores than the other two. In conclusion, beneficial effects of social activities and interactions influence the development of brain and behavior in old age. Encouraging research to promote care and non-pharmacological intervention could overcome limits for self-and-other's acceptance and adaptation, promoting trajectory for successful aging and life management in advanced aged.

CHAPTER 3

"*BRAIN WALKING GREEN*". A PILOT STUDY WITHIN AN ADULT GROUP COMING FROM MACERATA (MARCHE, ITALY)

1. **Converging evidence on multimodal interventions**.

This last chapter will report the results of the "Brain Walking Green" pilot multicomponent study, which can help to unveil new practical perspectives for changing lifestyle and enlarge the conception of prevention, that could potentially be appliable in different contexts. Since many older individuals are affected by chronic diseases, preventive programs focused on multiple domains become an efficient strategy to reduce morbidity, disability, and mortality. Pathologic conditions among older adults consist in multiple issues and, for this reason, the more a program results to be well-structured the better will be the impact of the intervention on the individual. Adherence to effective long-term preventive therapies is a major limiting factor in the success of these kind of interventions. Interventions to change behavior have the main goal to provide knowledge, because if people effectively understand the causes of diseases, they can change their behavior and prevent them. The Health Belief Model (Janz & Becker, 1984), the Theory of Planned Behavior (Ajzen, 1991), and the Theory of Reasoned Action (Fishbein, 1979) are examples of socio-psychological theories of behavior which demonstrate the role of the individual in governing health-related behaviors, and nowadays their guidelines are still followed to reduce morbidity and mortality, promoting social and environmental support. Cognitive health, as largely explained, is an important component for performing everyday activities, even if it represents only one of the aspects of overall brain health, that includes motor, emotional, and sensorial functioning.

A study found that older people who learned quilting or digital photography had a greater memory improvement than those who only socialized or performed less cognitively demanding activities (Park et al., 2014). Some of the emergent research on engagement in activities such as music, theatre, dance, and creative writing has shown promising results for improving the quality of life and well-being in the elderly, memory, and self-esteem with consequent reduction of stress and an increased level of social interaction. A recent and comprehensive report found no clear evidence that these types of activities have a beneficial and lasting effect on cognition (National Academy of Sciences, 2017), but further research is needed to definitively understand whether these activities can help reduce decline or maintain healthy cognition. Literature reports that multimodal interventions, which include more than one behavioral or lifestyle intervention, can influence, with a high likelihood, neurobiological systems (Burgener et al., 2008; Eckrot-Bucher & Siberski, 2009). Céspon and colleagues (2019) explored the role of non-pharmacological interventions in enhancing cognitive performance and preventing neurodegenerative conditions, providing suggestions to maintain functional plasticity: it emerged that multimodal interventions promote complementary neuroplasticity mechanisms, acting in a synergic way within different cortical pathways. The pilot study object of this work is based on recent evidence that demonstrated the effect of combined cognitive and physical interventions that may benefits more in cognition rather than one (Bamidis et al., 2014; Fissler et al., 2013). Multicomponent interventions can be conducted in separate times, or simultaneously administered, to study the interaction between cognitive and physical outcomes and evaluate participant's response on the final combined effect. The duration of the protocol, its intensity, and organization depends on previous studies that examined the same variables, on the characteristic of the sample, and on the specificity of each physical activity, as demonstrated by the results of a 2016 meta-analysis, which revealed that the frequency of intervention is significantly related to the group heterogeneity, and that age could affect the final effect of these type of interventions (Zhu et al., 2016). Another meta-analysis found that intervention acted five or more sessions per week showed less efficacy than intervention conducted less than 5 times per week (Lampit et al., 2014), because they can cause less adherence and high stress levels in participants. Comparison conditions are needed to verify the effect of an intervention, but evidence demonstrated that multicomponent trials with active control groups revealed smaller effect than those with passive ones (Law et al., 2014). The characteristics of "Brain Walking Green" are based on this evidence, including cognitive and physical exercise to improve beneficial effects in elderly. The cognitive-walking program addresses Eggermont's issue of non-relevant effects of single walking exercise to improve cognitive function, especially in MCI individuals (Eggermont et al., 2006), and it was aimed to influence health-related quality of life, physical status, and cognitive performance as important tools for prevention in healthy individuals.

2. **Nordic Walking for health as a "brain friendly" activity.**

Physical activity programs for health promotion in elderly are being implemented, through a special focus on aerobic, resistance and flexibility exercises (Phineiro et al., 2022). Nordic Walking (NW) is an outdoor form of exercise that implies the use of poles as an adaptation from cross-country skiing poles (Kocur & Wilk, 2006). It combines the work of the upper and lower part of the body engaging 90% of body muscles, and for this reason it results to be ideal for certain types of medical conditions. More than 65% of general population falls at least once a year (Ramsey et al., 2022) and the risk of falling is strictly associated to gait performance, structural changes in the brain, and diminished cognitive functions: patients suffering from neurological disorders exhibit structural cerebral changes, like a loss of hippocampal volume (e.g., Parkinson's disease and dementia), an increase in gait variability, and a decrease in gait speed.

Results of the beneficial effects of NW were reported in both skeletal conditions (Rodrigues et al., 2021), like arthritis or osteoporosis, and neurological disorders, especially in patients affected by Parkinson's disease (Bombieri et al., 2017; Cugusi et al., 2015). A NW observational study of 8 weeks (40 minutes of walking, 3 times per week) in six male subjects with Parkinson's disease resulted to be related to an increment of independence and quality of life (Baatile et al., 2000), while a RCT which trained 90 Parkinson's patients for 24 weeks (70 minutes, 3 times per week) showed effects of NW on walking speed, distance, and blood pressure (Reuter et al., 2011). According to these results and comparing NW with other type of walking, evidence strongly confirmed the superiority of NW, although this result cannot be extended to the general population (van Eijkeren et al., 2008). For what concerns healthy subjects, the first observational study was conducted in 1995, with the goal to compare short-term effects differences between NW and brisk walking without poles (Rodgers et al., 1995) in 10 female participants. 30 minutes of NW at a submaximal intensity (6.7 km/h) resulted to lead to an 11% greater mean oxygen consumption (VO_2), an 8% higher peak heart rate and to a raised respiratory exchange ratio of 5%. Schiffer (2006) assessed cardiorespiratory parameters in 15 healthy women during NW, traditional walking, and jogging sessions, observing that the previously reported values were higher only in NW group. Besides, at a comparable speed (up to 8.5 km/h) VO_2 and heart rate were increasingly better than jogging condition. Functional elements of NW are particularly good for older people, and can be preventive against illness, improving independence for longer (Bullo et al., 2019). Even if traditional walking is an optimal way to ensure the muscles in the lower body and cardiovascular system to work well, it does not engage the upper part of the body.

NW, on the contrary, works on strength, flexibility, balance, endurance, and general mood (An et al., 2020): the repetitive required coordination proves both relaxing and stimulating, with significant effects on positive emotions, especially if coupled with being outdoor in a social environment. Taking NW in a community breaks down barriers and help to integrate people of different ages and cultures (Zurawic, 2020). But, with these ones, the most important reason that establish NW as a very good practice for active aging is that it can be performed quite anywhere, encouraging elderly to challenge themselves and promoting a sustainable lifestyle change. NW resulted to be related also to weight loss: a RCT (Figard-Fabre et al., 2010) examined 11 obese women (BMI: 33.1) in a 4-weeks training (12 sessions) of 5 minutes walking exercise (4 times per week) with and without poles (4 km/h) and various inclinations. The use of poles increased HRV, and energy expenditure compared to walking without poles. The same author in a later RCT (2011) protocol showed NW effects on 23 obese women (BMI: 33.3) associated to a decrease in body mass index and blood pressure (timing: 30 minutes, 3 times per week), with a general toning up of muscles and reduced waist measures. NW amplifies the movement of ordinary walking to produce gains in speed: it is needed to walk looking straight ahead, opening the ribcage to improve breathing, and the use of walking poles helps to pick up the pace. The walker places the poles in turn on either side of feet, so they can land in the middle of their stride, and their angle oriented to the ground makes a propulsion movement, which, grip the poles tightly to control the push forward. The first rule in NW practice is to always remain relaxed and move naturally, to follow the natural balance and dynamic composition of the body. Teut and colleagues (Teut et al., 2016) tested 64 participants aged between 18 and 65 years with moderate/high distress levels in 8 sessions of mindful walking in 4 weeks (40 minutes walking, 10 minutes mindful walking and 10 minutes discussion): results reported that subjects following the program showed reduced psychological stress symptoms with improved quality of life compared to no study intervention. Most Nordic walkers find they can clear their minds quickly once starting train, and to focus exclusively on body's gait. The double-pendulum effect, that is the act to swing the arms from the shoulders (Figure 19), is an example of how important is to avoid tense and assume a correct posture.

Figure 19 (a-b). **a**) The double-pendulum effect played by a federal instructor during a warm-up session near Maddalena Mount (Brescia, Italy). Note that a correct arm swing causes the poles to stay correctly parallel to the ground. **b)** The act of gripping the poles, with the correct triangulation arm-hand-pole.

One of the most important checks involved in the first stages of practice is the coordination one: to achieve this it is important to lead arm and leg to opposite sides, without forcing the poles' grips: gaining grip control is essential in helping to achieve a good NW technique, because it implies the correct positioning of the articulations (Figure 19b). Some areas could show improvement very quickly (Stewart, 2014): a) posture enhances noticeably from the very first few sessions; b) waist area results to be improved by the combination of posture and calories burnt; c) thighs and buttocks tone up; d) the backs of the arms and shoulders result more defined, bringing to general fitness and weight loss. The higher complexity of neural circuitry involved in NW may contribute to slow down cognitive deficits (Murray et al., 2014; Monteiro et al., 2017; Pellegrini et al., 2018). Moreover, joining a group with an instructor or a leader promotes sociability and social support. Different type of walks can be chosen from subjects, like workout walks, adventure walks, well-being walks, and weight loss walks. The well-being walks, aimed at prevention or health management, and designed to improve balance, strength, mobility, and general fitness are becoming more and more common during last years. Including them in a structured protocol of both physical and cognitive training activity could be an interesting research perspective for future preventive studies, and the in the next paragraph will be examined the results of a young purpose which can be considered one of the first examples of this promising match.

3. **“Brain Walking Green”: an experimental preventive protocol for older adults.**

The project “Brain Walking Green” consists in a multicomponent prevention program for subjects aged 60 and over, aimed at protecting elderly individuals by promoting responsibility, consciousness, and care for psycho-physical health. Previous studies used cognitive stimulation and NW training as different outcomes to compare within different activity groups (Passos-Monteiro et al., 2020; Temprado et al., 2019) or to test the effect of NW on general cognitive functioning (Guszkowska et al., 2022), especially in subjects with disease rather than healthy ones (Górniak et al., 2021; Warlop et al., 2017).

Figure 20. A NW session of "Brain Walking Green" in action.

This study is the first attempt to fill this research gap combining cognitive stimulation exercise and NW training and making use of a wide set of both physical and cognitive evaluations in a group of healthy elderly. Modifications in cognitive functioning, especially in memory and language fluency domains, physical health, and general mood were expected after 12 cognitive stimulation sessions coupled with Nordic Walking activity, described so far as a holistic training that promotes well-being of the entire body, enjoying nature and human contact. The main hypotheses tested in this study were: 1) presence of a significant difference in general cognitive performance, memory, and fluency level, QoL and physical state between pre and post intervention; 2) presence of correlation between QoL and cognitive outcomes post-intervention; 3) cognitive performance as predictive of a better physical status at both t0 and t1 or vice versa; 4) memory performance as predictive of the general QoL perception.

3.1. **Materials and methods**.

3.1.1. *Study design and procedure*. The present protocol is a pilot study with an active experimental group and an inactive control one. The protocol took place in San Lorenzo di Treia, in the province of Macerata (Marche), from the 1st of July up to the 9th of August (12 sessions, 6 weeks). The intervention timing and its length were chosen and adapted following as reference previous protocols aimed at testing similar hypotheses (De Andrade et al., 2013; Shatil, 2013). The place of intervention was chosen for the width of space, which consented to easily work with two different subgroups in each session. A covered, but outdoor, area was used to play the cognitive stimulation, while NW was trained within trees and wide green areas. The protocol was organized in stages, which can be summarized as below:

a. Time 0: participants' health status assessment through a neuropsychological screening and a clinical interview about general well-being and mood. In addition, it was purposed an evaluation of physical functioning aspects, such as muscle strength and balance.

b. Training: 12 outdoor sessions of 90 minutes, in contact with nature and in a group context. During each session, 45 minutes of Nordic Walking were played with a federal instructor and 45 minutes were committed to cognitive exercise conducted by a psychologist and the author of this work.

c. Time 1: re-evaluation and clinical interview after 12 protocol sessions. At conclusion of the study, participants received a written report which resumed their results, evaluating the comparison between time 0 and time 1.

3.1.2. *Ethical aspects*. Participants of both groups read and signed an informed consent before participating, and all the assessment was conducted by professional figures placed in Macerata (Marche) thanks to a productive teamwork. Data were collected in anonymous format and were treated according to Italian law concerning general data protection.

3.1.3. *Participants and sampling.* The sampling procedure took place from 15 June to 28 June 2022. The protocol was promoted through flyers spread online and physically on the territory, thanks to the fruitful collaboration with the *Associazione Familiari Alzheimer Marche* (AFAM) and the social enterprise *Cambiamenti 2020*, a young reality which was born in 2020 with the aim of providing prevention and assistance to the elderly and their families by promoting a person-centered. On fifteen individuals who to took part to the protocol, only eleven were effectively considered for the study, according to the following eligibility criteria: 1) age: ≥ 60; 2) no evidence of dementia or cognitive impairment as indicated by Mini-Mental Status Exam (MMSE) score within 2.5 standard deviations of the mean for their age and education level (Santangelo et al., 1995); 3) absence of clinical condition that limited or contraindicated the practice of exercise; 4) availability to follow at least the 75% of training sessions. An inactive control group was included in the study and recruited in the same way of the experimental one, according to the following criteria: 1) age: ≥ 60; 2) no evidence of dementia or cognitive impairment as indicated by a Mini-Mental Status Exam (MMSE) score within 2.5 standard deviations of the mean for their age and education level (Santangelo et al., 1995); 3) general good physical state.

3.1.4. *The intervention: cognitive stimulation***.** The cognitive part of each session lasted for 45 minutes. At least two sessions regarded a specific cognitive domain, arranged as following (an example of the entire session can be seen in Appendix 2): 1) general attention; 2) divided and alterne attention; 3) working memory; 4) long-term memory; 5) visual memory; 6) language; 7) language; 8) executive functions; 9) executive functions; 10) "Treasure hunt" of cognitive functions (Appendix 2), a conclusive session in which participants were tested on their cognitive abilities and on their capability of recognizing which function they had to use to solve each task. In the last three sessions, there were integrated metacognitive exercises, in which participants must concentrate on finding which cognitive domain they were using while making exercises. Prospective memory tasks were also included: in some sessions it was asked participants to keep in mind that, when a certain song started, they had to do something, like take a sheet and write down three reasons why they are grateful for. As can be seen, memory training took up more space instead of other cognitive aspects: this choice is a consequence of what emerged in the clinical interviews, since participants expressed anxiety and worry toward the possibility of developing memory impairment. They referred to notice whether they could or not remember phone numbers, shopping lists, anniversaries, and scheduled dates. To actively operate on this issue, the first 10 minutes of each session were aimed to properly clarify how the different cognitive functions work, what is their impact on the brain during age and some tips to daily exercise them.

3.1.5. *The intervention: exercise training.* The Nordic Walking training was conducted by a federal instructor which organized each session (45 minutes) with different purposes and types of exercises. At the beginning of each session participants received the poles, with integrated straps and sharks. They were required to wear comfortable outfits and fitness walking shoes, to better enjoy the whole session and avoid physical injuries. The instructor started with 3 warm-up lessons, in which participants gained the basic NW movements, walk mode, foot strike, and how to drag the poles. Moreover, these first lessons stressed the idea of adopting a correct breathing technique, which is fundamental for coordination and cardiac rhythm. This phase required more time because the attempt to simultaneously engage upper and lower body results to be difficult for non-practitioners at the first approach. Subsequently, the training focused on uphill and downhill routes, trying to maintain the full-body workout as required by the instructor and the practice itself. At the end of each session was practiced a set of rest and stretch exercises, to promote mobility of the full body. The instructor chose time by time different trails: first ones were exclusively on paved road, while close to the end of the protocol he endorsed paths always more wooded. During each walk he was accurate in describing movements' ratio and the type of benefit that they could produce.

3.1.4. *Study instruments*. Participant's cognitive performance was measured with the Italian version of Addenbrooke's Cognitive Examination Revised [ACE-R] (Siciliano et al., 2016), a short cognitive assessment which allows to measure the general cognition status by five subdomains: 1) attention and orientation (AO); 2) memory (ME); 3) verbal fluency (F); 4) language (L); 5) visuo-spatial skills (VS). Scores are ranged from 0 to 100, corrected for age, gender, and schooling level, with higher ones indicating better cognitive functioning. It is possible to obtain a MMSE score by administering the test, collecting the subscores of eleven selected items (Magni et al., 1996). The Cognitive Reserve Index Questionnaire [CRI-q] in the Italian version (Nucci et al., 2011) was used to assess the level of cognitive reserve (CR), a construct that, as explained before, can be defined as the "brain resilience capacity" because it maximizes brain performance against losses and damages. The questionnaire contains an initial demographic set of questions, then the items are divided in three sections: 1) CRI-Education (r = 0.77) CRI-Working Activity (r = 0.78); 3) CRI-Leisure Time (r = 0.72). Each aspect of an individual's lifetime is recorded as a subscore, and activities are evaluated according to the number of years spent in practicing. The total CRIq score is represented by the average of the three dimensions. Basing on this evaluation, CR can be classified in 1) Low (≤ 70); 2) Medium-Low (70-84); 3) Medium (84-114); 4) Medium-high (115-130); 5) High (≥ 130). This index allowed to have a complete framework of each person by collecting information about lifestyles, abilities, and experiences. The Free and Cued Selective Reminding Test [FCSRT] (Frasson et al., 2011) was used to assess the level of memory encoding and retrieval. It is divided in two parts in which participants must point and name 12 items corresponding to a specific semantic category given by the examinator. Then, they must recall the items in a free and cued way, immediately and after 30 minutes. Scores are corrected for age, education, and gender, and cutoff scores can be used to interpret them. Quality of Life (QoL), considered as a multidimensional construct which includes physical, material, social, and emotional wellbeing, with development and activity (Felce & Perry, 1995), was estimated through three instruments:

a. Geriatric Depression Scale [GDS] (adapted from Sheikh et al., 1986). The quaestionnaire is composed by 15 items that detect the potential presence of depressive symptomatology elderly people. The sum of each Yes-No answers corresponds to the total score, that expresses the depression level as classified in: 1) Normal (3 ±2); 2) Mild (7±3); 3) High (12 ±2).

b. World Health Organization Quality-of-Life Scale [WHOQOL-BREF] (Girolamo et al., 2000). The instrument produces a quality-of-life profile and encompasses a larger number of domains that are integral to define the quality of life if compared to other forms of evaluation, with a particular focus on social relationships and environment domains. It contains 26 questions that evaluates 4 dimensions: 1) physical (7 items; r = 0.80); 2) psychological (6 items; r = 0.75); 3) social relationships (3 items; r = 0.65); 4) environment (8 items; r =0.73). There are also two items examined separately: a question asks about an individual's overall perception of QoL and the other one asks about an individual's overall perception of general health. The mean score of items within each domain is used to calculate the domain score. Then, mean scores are multiplied by 4 to make comparable results with the scores used in the original WHOQOL-100 version. The total score corresponds to the sum of each domain. In the analysis it was considered the average score of each participant for quantitative evaluations, while qualitative marking also considered the single scores obtained in the four domains.

c. Short Form 12 Health Survey [SF-12] (Apoloni et al., 2015; Ottoboni et al., 2017). This instrument has been considered in this study as a supplementary worksheet of scores emerged from WHOQOL-BREF. It is composed by 12 items, that can be divided in the two dimensions of Physical Component Summary (PCS) and Mental Component Summary (MCS). As a qualitative evaluation, it was considered the medium score obtained by both PCS and MCS. The questionnaire is based on SF-36, of which it is a reduced version. This version was chosen because the SF-36 could have been repetitive, evaluating some aspects already analyzed through the WHOQOL-BREF. It is considered a valid and reliable measure that can be used with confidence for the evaluation of these outcomes in older adults (Resnick & Parker, 2001). The main strengths of the questionnaire are its brevity and ease of administration. Each dimension is composed by 6 items and can be divided in sub items, as following:

➔ *PCS* (r = 0.89): 1) physical activity; 2) physical health level; 3) physical burden; 4) general physical health.

➔ *MCS* (r = 0.76): 1) vitality; 2) social activities; 3) emotional status; 4) general mental health.

After this accurate evaluation, participants were screened for their physical condition by a physiotherapist using essentially 3 tools:

1) Tinetti Mobility Test (TMT) [Tinetti, 1986], an instrument to prevent falls' risk in elderly people through with two measurements of balance and gait. The total achievable score is 28, and the fall's risk can be High (≤18), Medium (19-24), and Low (≥25).

2) Conley scale (Conley et al., 1999) composed by six items with a maximum achievable score of 10 and consisting of two parts in which both the patient's previous falls and the presence or absence of cognitive deterioration are investigated. The first three questions will be asked to the patient or caregiver in case he is not objectively able to answer, and the last three questions instead are based on the interviewer's observational ability. Values between 0 and 1 suggest a minimal risk of falling, while the ones between 2 and 10 indicate a risk of falling from low to high.

3) Six-minutes' walk test [6 MWT] (Rikli & Jones, 1998), a basic motor task to evaluate aerobic functionality which measures the maximum distance that an individual could traverse in a given time. The test was already used in previous pilot studies aimed at verifying the role of NW in geriatric rehabilitation (Dalton & Nantel, 2015; Figueiredo et al., 2013; Muollo et al., 2019). In this protocol it was chosen to test

participants for 1 minute and were considered the number of rounds made by them. Before and after the walk blood pressure and saturation were measured by the physiotherapist who carried out the physical evaluation. Participants walked on 30 meters flat ground.

Another interesting aspect to test was the participants' level of motivation for change. This construct has been explored in the context of counseling and outpatient interventions. The importance of knowledge about motivational traits of subjects aims to bring out and strengthen their predisposition to make a choice of improving their quality of life in accordance with premises, values, and personal goals. Many motivational assessment tools have been developed in clinical practice, and quite all of them refer to the Readiness to Change (RTC) concept, as described and introduced by Prochaska and DiClemente in the Stages of Change model (Prochaska & DiClemente, 1982). To deepen into these aspects, to each participant was administered, before starting the training, the Motivation for Change-Physical Activity questionnaire [MAC2-AF] (Spiller et al., 2009), which was oriented to the motivation towards physical activity lifestyle modification and divided into 18 sentences to be replied on a 7-point Likert scale, in order to assess 9 factors (2 items for each): 1) precontemplation; 2) contemplation; 3) determination; 4) action; 5) maintenance; 6) self-effectiveness; 7) temptation; 8) inner-fracture; 9) importance. Each subject obtained an average score which represented the availability to actively change their lifestyle and, at the end of the experience each participant filled out an evaluation questionnaire in which he/she could make a general evaluation of the protocol, trying to self-rate the level of change and the hypothetical health effect achieved.

3.2. **Data analysis.**

Data were analyzed using R Studio software (R Core Team, 2017). To describe socio-demographic characteristics of respondents, frequency, percentage, mean, and standard deviation were computed. Basing on the sample size, paired t-tests were used to analyze the intervention effect, comparing the scores' means of each test at t0 and t1. Effect sizes (Cohen's method) were calculated for each mean comparison, and classified (Cohen, 1988) as negligible (0.0-0.20), small (0.2-0.5), moderate (0.5-0.8), and large (0.8 or more). Correlations were conducted only in the experimental group through Pearson's method, which provides a p-value of the evaluated relation with 95% of confidence level, after the verification of kurtosis, asymmetry, and normality of each couple of distributions with: a) Mardia test; b) Royston test. Confidence intervals (CI) were reported with correlations to demonstrate if within the population the emerged relationship could be appreciable. Linear models were used to qualify and quantify predictive hypotheses on different variables: before applying each linear model, the requirements of normality, homo-scheduling and error independence were verified respectively with: 1) Shapiro test and one-sample t-test; 2) Breusch-Pagan-Godfrey test; 3) Durbin-Watson test. Significance level adopted was $\alpha = 0.05$ for all tests, but in some cases borderline significance was anyway considered (until 0.07). Multivariate Analysis of Variance (MANOVA) was used to verify the value of different variables on different outcome measurements (Bathke et al., 2018; Friederich et al., 2019).

3.3. **Results**

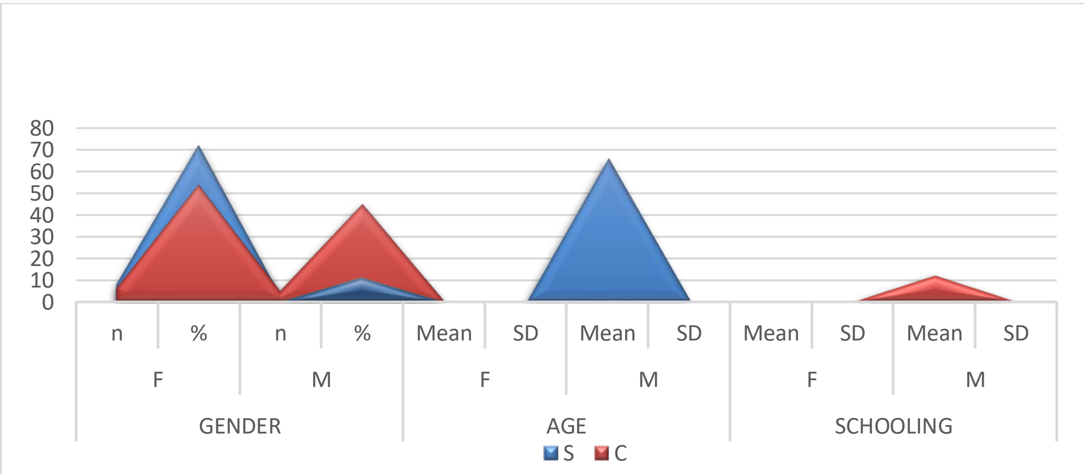
Demographic characteristics (age, gender, schooling) of the 22 participants at baseline are summarized in Table 2 and visually represented in Graphic 1. The experimental group consists of 11 subjects, 72% women (n = 8) and 27% men (n = 3).

Both women and men have an average age of 66, and a schooling level respectively of 16 and 14. The control group consists of 11 subjects, 54% women (n = 6) and 45% men (n = 5). The average age of females is 64 years, while males' one is 62 years.

	GENDER				AGE				SCHOOLING			
	F		M		F		M		F		M	
	n	%	*n*	%	*Mean*	*SD*	*Mean*	*SD*	*Mean*	*SD*	*Mean*	*SD*
S	8	72	3	27	66.25	4.62	66	6.24	16.38	3.29	14.33	2.30
C	6	54	5	45	64.12	5.28	62.50	3.53	16.80	0.52	12	4.18

	TOTAL SAMPLE				
	PARTICIPANTS	AGE		SCHOOLING	
	n	*Mean*	*SD*	*Mean*	*SD*
S	11	66.18	4.77	15.81	4.03
C	11	63.80	4.85	14.40	3.09

Table 2. Demographic data for the total sample and collapsed by gender.



Graphic 1. Demographics results for both experimental and control group.

Table 3 (split in two parts) shows the mean scores corrected at t0 and t1 of MMSE, ACE-R (with memory and fluency subtests), FCSRT (divided between Immediate Free Recall and Delayed Free Recall), WHOQOL-BREF, GDS, Tinetti and Conley scale, 1-minutes' walk test, minimum and maximum arterial pressure post walk, and the WHOQOL-BREF' subscale regarding physical activity corrected mean scores at t0 and t1 with t-tests for paired sample analysis results.

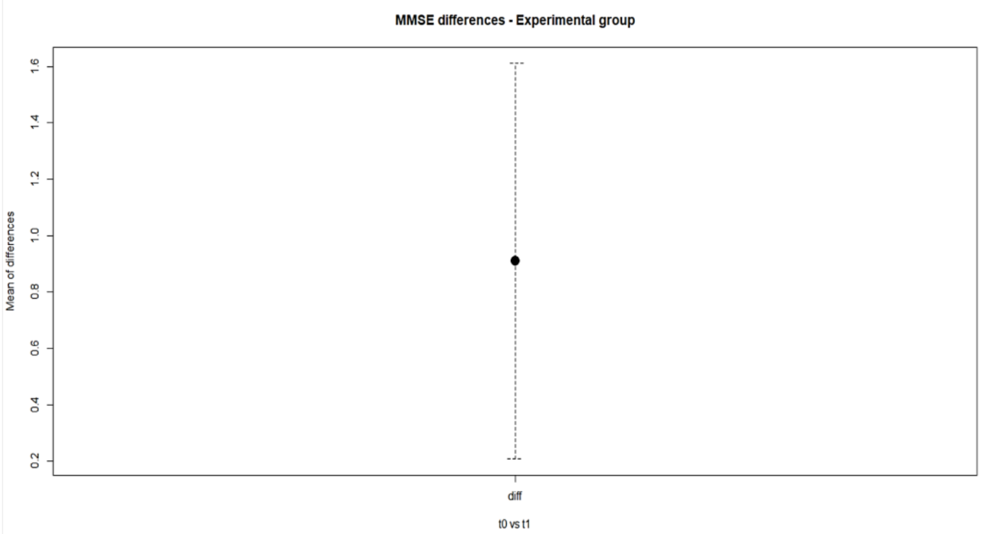
	MMSE						ACE-R					
	T0	SD	T1	SD	p-value	d (Cohen)	T0	SD	T1	SD	p-value	d (Cohen)
S	26.48	18.48	27.94	21.47	0.01*	0.84	91.66	22.32	94.93	61.17	0.02*	-0.65
C	27.98	20.66	27.47	21.33	0.13	0.33	92.46	21.09	91.88	20.56	0.34	0.08
	IFR						DFR					
S	27.66	9.76	31.50	6.78	0.14	0.58	9.57	23.82	11.41	31.56	0.07*	-0.78
C	29.16	7.50	28.16	8.89	0.70	0.14	10.86	29.84	10.83	23.86	0.94	0.02
	TINETTI SCALE						ROUNDS (1-minute walk test)					
	T0	SD	T1	SD	p-value	d (Cohen)	T0	SD	T1	SD	p-value	d (Cohen
S	27.55	8.34	28	7.84	0.13	-0.69	2.85	1.83	3.41	1.19	0.07*	1.20
C	27.82	8.39	25.45	8.44	0.37	0.42	3.09	2.27	4.02	3.31	0.37	-0.46
	MINIMUM ARTERIAL PRESSURE						MAXIMUM ARTERIAL PRESSURE					
S	81	8.66	75	19.90	0.16	0.62	147.3	15.31	133.3	66.67	0.02*	1.17
C	84.09	20.67	81.82	21.12	0.57	0.10	122.50	24.58	120.10	37.80	0.78	0.07
	MEMORY						FLUENCY					
	T0	SD	T1	SD	p-value	d (Cohen)	T0	SD	T1	SD	p-value	d (Cohen)
S	22.60	4.59	23.78	3.94	0.06*	-0.45	11.12	3.91	11.94	3.85	0.12	-0.40
C	23.79	4.50	25.22	4.37	0.04*	-0.63	11.09	2.93	10.92	3.69	0.76	0.07
	WHOQOL-BREF						GDS					
S	85.93	12.88	80	8.79	0.11	0.51	3.70	9.18	3	10.19	0.12	-0.81
C	89.64	9.48	87.91	10.38	0.14	0.17	2	9.96	1.54	10.18	0.76	0.07
	CONLEY SCALE											
	T0	SD	T1	SD	p-value	d (Cohen)						
S	0.73	0.20	1	0.45	0.34	-0.28						
C	0.63	0.23	0.64	0.57	1	0						
	PHYSICAL SELF-EVALUATION											
S	107	32.80	96.73	22.47	0.20	0.44						
C	109.6	21.10	107.2	19.27	0.18	0.21						

Table 3. T-tests for paired sample results of both physical and cognitive outcomes. As already explained, it was also highlighted the borderline significances considering the low number of participants.

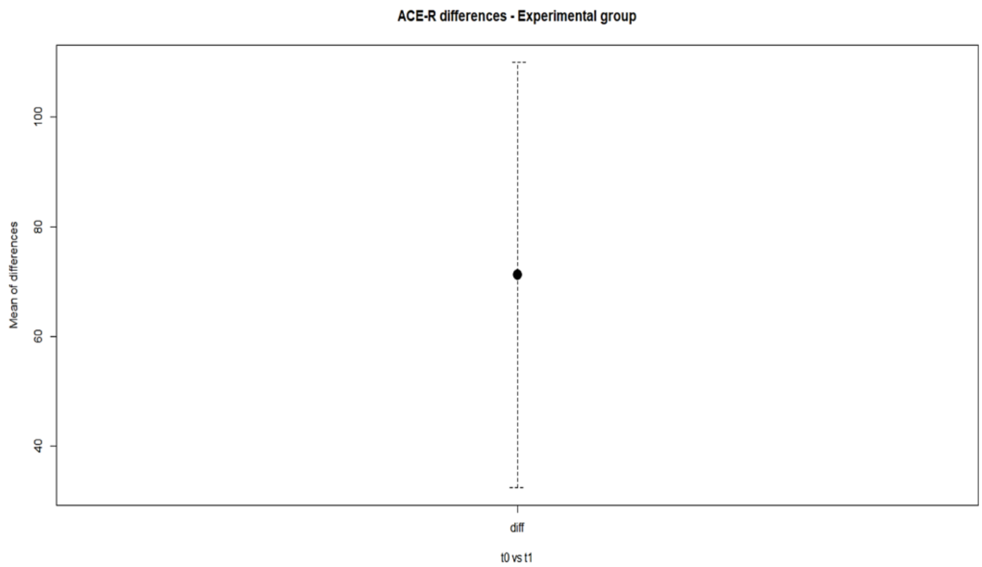
Before treatment, the experimental group obtained an MMSE average score, corrected for age and schooling of 26.48 while the control group obtained on average a starting MMSE score of 27.98. At t1 the experimental group scored on average 27.94 at MMSE, while the control group reached a score of 27.47. Of ACE-R test were considered the overall score and the scores obtained at memory and verbal fluency subtests, as two of the most exercised cognitive abilities during training and most representative of the general cognitive functioning of an individual (Gonzalez-Burgos et al., 2019; Kelly et al., 2017).

As previously explained, MAC2-AF can't be considered in an inferential way, because it was not provided of a precise cut-off, but of all the dimensions, the importance one resulted to be high averaged (M = 30.54). It was assessed exclusively at t0, in which experimental group obtained an average score of 5.90, with a minimum of 2.80 and a maximum of 24 (SD = 6.20), and the control one of 3.04 (SD = 0.59), with a minimum of 2.16 and a maximum of 4.27. For what concerns QoL and general well-being measurements, at t0 the experimental group collected an average WHOQOL-BREF score of 85.93, and a GDS one of 3.70, while at t1 participants collected an average of 88 points for WHOQOL-BREF and 3 for GDS. It was considered unfitting to assess the significance dividing both experimental and control sample by gender, as the subgroups would have been too small, leading to unreliable results. Paired t-test showed a significant difference in MMSE performance after the treatment only in the experimental group [t (11) = -2.93; p = 0.01], with a large estimate effect size (d: -0.84). Significance was also observed in ACE-R scores at the follow-up, in which experimental subjects resulted to be improved [t (11) = -2.80; p = 0.02] with a medium estimate effect size (d: -0.65). There were not identified significative differences in immediate and delayed free recall (IFR, DFR) for both control and experimental group, while a borderline significance emerged for ACE-R's *memory* subtest both in the experimental group [t (11) = 2.14; p = 0.06] with a negligible effect size, and in the control group [t (11) = -2.38; p = 0.04] with a medium effect size (d: -0.63). Significative differences in Tinetti, WHOQOL-BREF (including its subscales), and Conley test didn't emerge. For what concerns the six-minutes' walk test, adapted in this protocol testing 1 minute only, the experimental group showed a significant difference in blood pressure values after the training [t (11) = 2.01; p = 0.02], with a large effect size (d = 1.17), while for the control group values were not significantly different. Moreover, the difference between number of rounds before and after the protocol resulted to be at a borderline significance only for the experimental group [t (11)

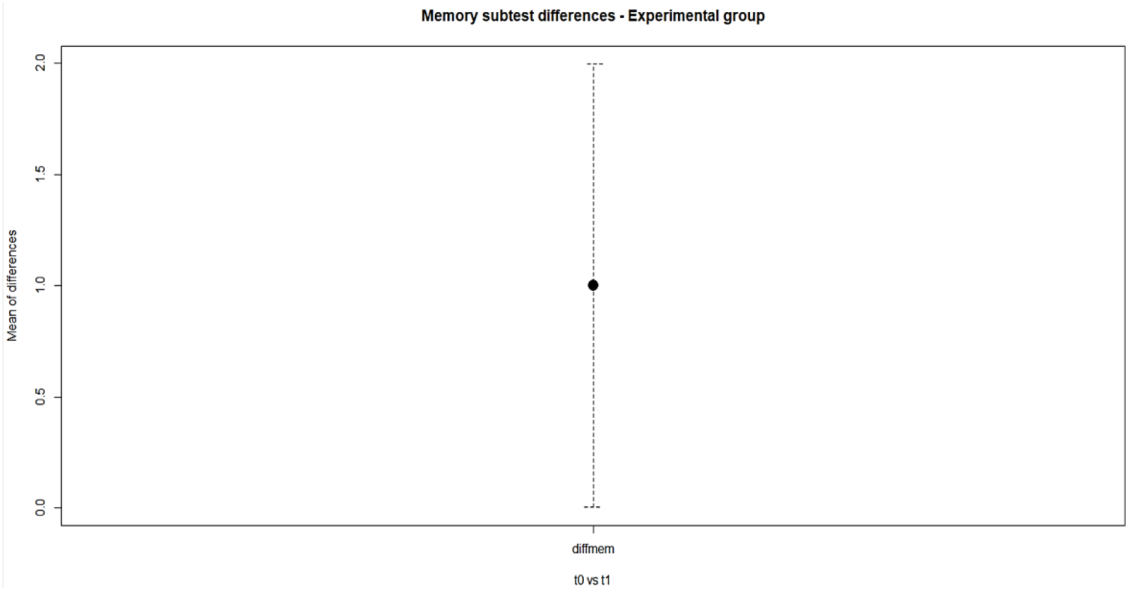
= -2.02; p = 0.07], with a large effect size (d = 1.20). Graphics 2-5 represent the of Confidence Intervals (CI) between pre and post intervention means for cognitive variables in the experimental group. To each interval has been associated the error margin of means' differences (*wd: average estimated width*), which is sensitive to the correlation between measurements (n.b. graphical differences reflect metric differences of measurements' units).



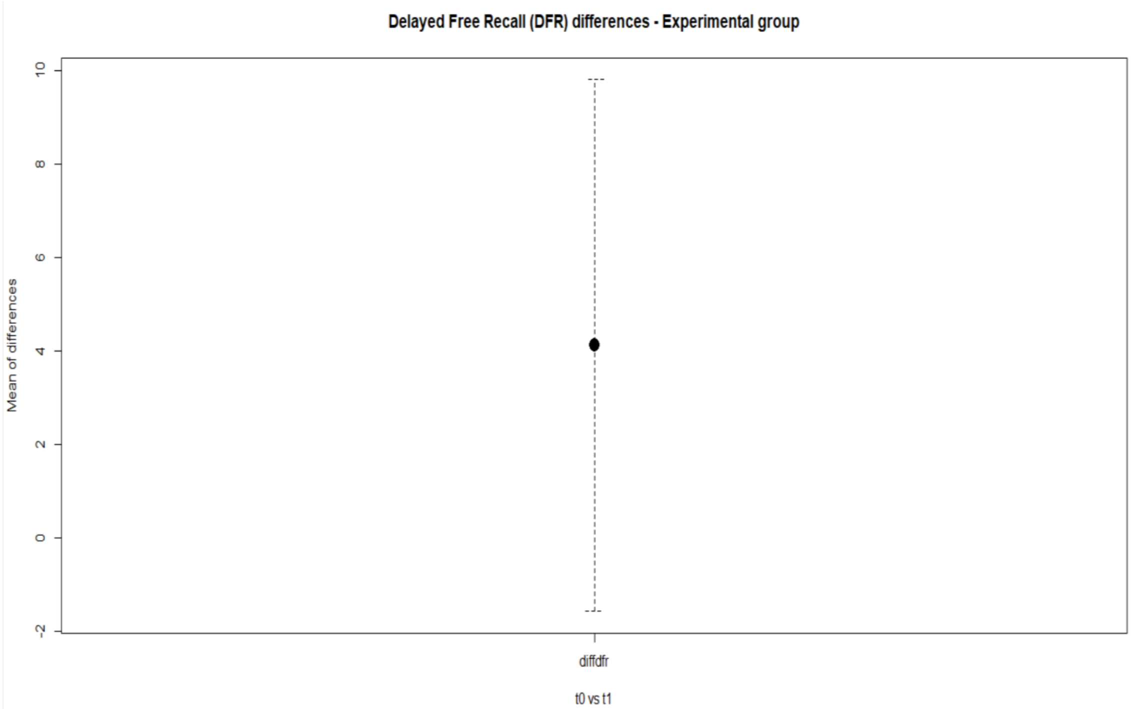
Graphic 2. Mini-Mental State Examination (t0 vs t1) [mean: 0.91; lwr.ci: 0.21; upr.ci: 1.61; wd = 0.70].



Graphic 3. Addenbrooke's Cognitive Examination Revised (t0 vs t1) [mean: 71.17; lwr.ci: 32.34; upr.ci: 109.99; wd = 38.83].



Graphic 4. ACE-R’s memory subtest [mean: 1; lwr.ci: 0.00(3); upr.ci: 1.10; wd: 0.91].



Graphic 5. FCSRT’s delayed free recall task differences [mean: 4.12; lwr.ci: -1.58; upr.ci: 9.81; wd: 5.70].

Correlations were calculated using test significance with the Pearson's method to verify the hypothesis of a relation between WHOQOL-BREF and ACE-R scores (always with the corresponding subtests) and GDS and ACE-R scores. No one of them resulted significative. Results of Pearson's correlations in the experimental group showed:

- ➔ A positive relationship between memory performance and fluency performance post-intervention (p = 0.01; cor = 0.71), with a large confidence interval (0.20<CI<0.92).
- ➔ A positive relationship with borderline significance between general cognitive performance (ACE-R) and general QoL (p = 0.07; cor = 0.55), with a large confidence interval (-0.06<CI<0.87).

Other correlations between cognitive, QoL, and physical variables did not result significative. General linear models were used to detect the possible prediction role of single variables at both t0 and t1. Table 3 reports only the significative models with one or more predicted variables (Y). No one resulted to be significative both for the control and the experimental one, except for the QoL level, which resulted to be predictive of higher scores at MMSE (p = 0.03, R2 = 1.67), and ACE-R ones (p = 0.04, R2 = 0.31) in the experimental group post-intervention.

	MODEL 1	MODEL 2	MODEL 3	MODEL 4	MODEL 5	MODEL 6	MODEL 7	MODEL 8	MODEL 9	MODEL 10	MODEL 11	MODEL 12
Group	S	S	S	S	C	S	C	C	C	S	S	S
X	ACE-R (t1)	Memory subtest	Tinetti	MMSE	ACE-R (t1)	CRI-q	CRI-q	CRI-q	CRI-q	MAC2-AF	MAC2-AF	MAC2-AF
Y	WHOQOL (t1)	MMSE (t1)	WHOQOL	Tinetti	GDS (t1)	ACE-R (t1)	ACE-R (t1)	GDS (t0)	GDS (t1)	Tinetti (t1)	Rounds (t1)	WHOQOL (t1)
Y2	-	-	GDS	-	-	-	-	-	-	-	-	ACE-R (t1)
ESTIMATE	0.96	1.53	2.15	3.01e-13	-0.14598	1.00	-0.42	0.19	0.20	-1.23	6.49	79.04
ESTIMATE 2	-	-	1.30	-	-	-	-	-	-	-	-	0.33
ST. ERROR	0.47	1.65	1.78	6.90e-13	0.07	5.47e-1	0.07	0.04	0.04	0.08812	0.47	62.93
p-value	0.07*	0.03*	0.04*	0.02*	0.06*	< 2.2e-16*	0.02*	0.02*	0.88e-4*	0.20e-6*	0.24e-6*	0.02*
R2	0.31	0.17	0.32	0.48	0.33	1	0.79	0.66	0.72	0.96	0.95	0.49
R2 adjusted	0.23	0.12	0.20	0.42	0.26	1	0.77	0.62	0.69	0.95	0.94	0.43
F	4.07	1.80	2.55	8.27	4.54	3.35	34.61	17.62	23.83	196.50	189.70	8.60

Table 3. Significative linear models considered in the study. For each one was reported: estimated value, standard error, p-value, coefficient of determination (R2), and the F-test for evaluating of the overall significance of each model.

In the control group ACE-R scores were predictive of better GDS evaluations ($p = 0.06$; $R2 = 33$). In the experimental group CRI-q scores predicted a higher ACE-R performance post-intervention, while in the control one it resulted to be predictive of a better ACE-R performance post-intervention, and of higher GDS' scores pre-and post-intervention. A borderline significance revealed that only in the experimental group ACE-R scores could predict the grade of QoL ($p = 0.07$; $R2 = 0.31$), while the control group reported a borderline level of significance in the linear model which considered the ACE-R scores as predictive of GDS' scores ($p = 0.06$; $R2 = 1$), with higher levels of ACE-R that explain lower levels of depressive symptoms. Tinetti scale resulted to be predictive of both WHOQOL and GDS scores ($p = 0.04$; $R2 = 0.32$) and predicted by MMSE scores post-intervention ($p = 0.02$; $R2 = 0.48$). The last three models (10, 11, 12) represent results on MAC2-AF variable, which was not considered for t-test significance evaluations. Answers resulted to be predictive of a better Tinetti performance ($p = 0.20e-6$; $R2 = 0.96$), number of total rounds ($p = 0.24e-6$; $R2 = 0.95$), and of both WHOQOL and ACE-R performance taken together post-intervention ($p = 0.02$; $R2 = 0.49$).

3.4. **Discussion and limitations.**

The present pilot study was the first attempt to unify cognitive stimulation and Nordic Walking activity in a preventive protocol that promotes behavioral change and an active attitude towards well-being in healthy elderly individuals. The strength of the trial was its originality and the promising impact of its results, obtained by the combination of physical and cognitive intervention, which was supported as promising technique from previous research (Lauenroth et al., 2016). The main limitation that must be underlined is the number of subjects, which could have influenced the power of tests and their efficacy to reveal significative effects between time 0 and time 1. Nevertheless, it must be considered that the commitment required to each subject for participating to the study was notable, because they had to follow as much as possible the program to better assess its efficacy. Similar previous studies in which the sample size was formally determined by statistical power analysis involved about 15-20 participants per experimental group, which can be considered a good reference for future studies (Gomeñuka et al., 2019; Muollo et al., 2019). Moreover, in the present study both samples of experimental and control group are composed by more women than men, so that the groups cannot be considered fully balanced. The sample size also weighted on the quality of correlations, which showed extremely large confidence intervals: this means that within the population the effect of relations is real but not easily identifiable, taking shape as rare. The focus on environmental and social factors resulted to be fundamental because, as said in chapter two, social engagement could be a strong proxy to improve the quality of aging. In the present study QoL was evaluated with the WHOQOL-BREF scores, which resulted to predict cognitive performance, demonstrating that quality of life can be an important outcome that have influence on cognitive performance and can be confirmed as an important aspect to preserve in elderly people, as already demonstrated from literature (Jin et al., 2016; Şahin et al., 2019). In a combined cognitive and physical stimulation protocol, similar to this one, on 16 participants (Tanaka et al., 2020) consisting in an 8-week intervention program (2 per week, 45 minutes each) of group exercise and cognitive stimulation, it was shown the positive impact of cognitive activity on social relationship, social engagement, and autonomy. Brain Walking Green, albeit on a small sample, has shown that quality of life is an important element to promote cognitive performance and encouraging self-improvement. In both control and experimental groups scores in ACE-R's memory subtest resulted to be significant, and memory subtest itself was a good predictor of total MMSE performance: this could be useful for future studies to consider memory as a variable with strong influence on cognitive performance, especially in combined protocols that require the presence of physical activity.

These results demonstrate the strong impact of working on memory capacity within the training session, to promote awareness toward its modification during age and hinder worries about it within participants. Only in the experimental group it was observed a significant reduction in blood pressure after the post-intervention walking test, confirming the beneficial effects of NW on cardiovascular and circulatory systems, as previously reported by literature (Tschentscher et al., 2013). Nature exposure was another element that could mediate stress responses and amplify the effects of walking, but also of cognitive exercise, as it allows to use all the senses and experience them in synergy. Berman and colleagues (2008) proved nature as an efficient vehicle for the improvement of cognitive performance, especially in attentional tasks, and has a role in decreasing anxiety and rumination behavior (Bratman et al., 2015). The choice of NW as a "brain friendly" activity derives from previous studies (see par. 3.1.4.) that, as said before, demonstrated its efficacy in chronic conditions like Parkinson's disease, diabetes, obesity, and so on. The present study was the first one to formally include this type of activity in a combined and preventive protocol addressed to elderly people. Conclusive self-reports evaluations demonstrated that participants really appreciated the bodily stimulation purposed by NW activity and showed evident improving session by session. Even if significance was not demonstrated, GDS scores resulted to be reduced for both experimental and control group at time 1, and the perceived wellness of participants is confirmed by self-reported answers collected at the end of the protocol, which revealed a general improvement in self-efficacy towards cognitive, psychological, and physical status. A good cognitive performance was predictive of lower GDS' scores, in line with evidence that report a significative relationship between cognitive performance and depressive or anxiety symptoms in elderly (Shimada et al., 2014). Participants affirmed to feel generally more confident and reassured by the intervention, suggesting to re-purpose it soon. Besides, the SF-12 questionnaire, which was considered as a quality evaluation questionnaire in this study, reported higher scores of PCS and MCS, a result in line with WHOQOL-BREF mean scores. In each session, most of participants communicated with others in a verbally or nonverbally way and, through these interactions, they seemed to raise their motivation and purpose to challenge themselves with each task. The cognitive reserve level (CR), which was assessed at the beginning of the intervention, resulted predictive of GDS' scores in the control group (t0 and t1) and in the experimental group (time 1), enhancing the importance of *(p)reserve* the quality of social environment, education, and occupation during lifetime. CR level had influence also on general cognitive performance: in fact, especially in old people it represents an important variable that can actively prevent decline and mood-related critical conditions (Farina et al., 2018). From a qualitative point of view, participants resulted to be generally motivated and involved in the protocol activities and purpose. Engagement and motivation are dimensions that actively emerged from participants' feedback at the end of the protocol, since they affirmed to be more propositional about changing their habits and strongly oriented to better take care of their general health.

4. Conclusion and future directions.

The strongest point of the study is the fact of being the first attempt to verify and test the complex interplay between biological, physical, psychological, social, and environmental aspects of prevention, which can contribute to contrast cognitive decline. Even if detected in a very small sample, results can serve as a guide for future protocols to synergistically evaluate the role of physical activity and cognitive stimulation in healthy elderly people. Besides, they encourage to include quality of life, considered as the sum of social interactions, self-awareness, feelings and mood, enjoyment of activities, and response to surroundings, as a variable that could influence both physical and cognitive functioning in late life. Since the protocol resulted to have relevant effects on cognition, memory capacity and cardiovascular functioning, future research that could: a) increase the number of samples ensuring a better distribution by gender; b) evaluate the role of gender, civil status and schooling on cognitive outcomes; c) enlarge the total number of session, but maintaining the same time length; d) analyze the effect of this intervention in MCI patients and understand its role in slowing down the progression of decline; e) improve the evaluation of motivation and general quality of life; f) enlarge the follow-up evaluation timing; g) considering brain and cognitive reserve a key point for aging well through awareness raising projects that can actively involve the citizenship.

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