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Highlights:

- Cognition in ageing is influenced by PA, cognitive training and other factors
- Social networks have a role in cognitive maintenance in ageing.
- Interventional studies aim to prevent and/or delay age-related cognitive decline.
- Multi-domain interventions may have synergistic effects in enhancing neuroplasticity.
- RCTs will profit from integrating activities embedded into a social engagement framework.
- There is a need for new multi-domain synergistic interventions in healthy ageing.

Maintaining Older Brain Functionality: A Targeted Review

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ABSTRACT

The unprecedented growth in the number of older adults in our society is accompanied by the exponential increase in the number of elderly people who will suffer cognitive decline and dementia in the next decades. This will create an enormous cost for governments, families and individuals. Brain plasticity and its role in brain adaptation to the process of aging is influenced by other changes as a result of co-morbidities, environmental factors, personality traits (psychosocial variables) and genetic and epigenetic factors. This review summarizes recent findings obtained mostly from interventional studies that aim to prevent and/or delay age-related cognitive decline in healthy adults. There are a multitude of such studies. In this paper, we focused our review on physical activity, computerized cognitive training and social enhancement interventions on improving cognition, physical health, independent living and wellbeing of older adults. The methodological limitations of some of these studies, and the need for new multi-domain synergistic interventions, based on current advances in neuroscience and social-brain theories, are discussed.

Keywords: aging, neuroplasticity, social-brain, cognitive training, physical exercise, physical activity, social networks, video games, Tai Chi, dance, Information and Communication Technology (Doja et al.)

1. Introduction

Modern societies are experiencing an extraordinary growth in the percentage of older adults in relation to the total population, primarily due to increasing longevity and falling birth rates. The percentage of older adults in Europe is expected to reach 30% in 2060 (FUTURAGE European project, 2011; UN, 2011). By 2060, it is estimated that the number of Europeans aged 65 and over will be larger than the number of children less than 16 years of age (Oeppen and Vaupel, 2002). This demographic shift has increased the interest in research on aging. The rapid growth of the percentage of older adults is accompanied by the exponential increase in the number of older adults who will suffer cognitive decline and dementia in the coming decades. Costs of caring for older adults with cognitive impairment and dementia are expected to double within the next four decades (Hurd et al., 2013). The rate of Alzheimer´s disease (AD), the most common form of dementia, is expected to increase two- to three-fold in the next few decades adding significant costs to governments, families and individuals (Brookmeyer et al., 2011).

Although normal ageing is associated with cognitive and brain changes, many older adults continue to function adequately until they are very old (Jacobs et al., 2009). The older human brain still has the capacity to adapt to physical, cognitive and social environment challenges, while facing a decline in sensory-motor and cognitive abilities (Goh, 2011; Goh and Park, 2009). The brain response to decreasing physical and cognitive abilities in aging is understood as neuroplasticity (Kraft, 2012; Zolyniak et al., 2014), meaning the ability of the brain to adapt to an environmental change by modifying neural connectivity and brain function in response to changing demands and environments throughout the lifespan (Bavelier et al., 2012; Knaepen et al., 2010). Neuroplasticity changes do not always imply an improvement in behavioral performance, rather these changes are usually associated with function preservation or a reduction in the rate of decline (Dinse, 2005). Experience-related changes induced by the modification of social environments, physical activity, and cognitive training affect brain structure and function. Research on brain plasticity in aging and its relationship to experiential changes has increased dramatically and attracts significant public interest (Erickson et al., 2014; Raz and Lindenberger, 2013).

Neuroscience and cognitive aging research has revealed a promising set of complex and synergic processes and networks that support a variety of theories and related interventions, with the hopeful potential for healthier brain aging. Most notably, the scaffolding theory, cognitive reserve, compensation and dedifferentiation theories of the adapting brain are a giant step forward for cognitive aging research (Ewing, 2012; Goh and Park, 2009; Park and Reuter-Lorenz, 2009; Reuter-Lorenz and Lustig, 2005; Reuter-Lorenz and Park, 2014). In addition, the ecological model of aging (Satariano, 2006) suggests that cognitive aging is influenced also by other factors including social networks, personality traits and genetic and epigenetic factors (Nielsen and Mather, 2011; Pickersgill et al., 2013; Satariano, 2006; Zammit et al., 2014); (Bennett et al., 2014; Cole, 2014; Zheng et al., 2015). These factors, when viewed in conjunction with the antecedents of chronic disease, such as diabetes, cardiovascular diseases, obesity and metabolic syndrome, point to possibilities for optimism for a healthier aging brain. Health effects associated with these chronic diseases may be modifiable through changes aiming at increasing physical activity/decreasing sedentary lifestyles, better stress management and participation in meaningful social networks, leading to a decrease in comorbidities and thus a healthier aging brain (Berchicci et al., 2014; Bodde et al., 2013; Daffner, 2010; Dunton et al., 2009; Holman and de Villers-Sidani, 2014;

Pinazo-Duran et al., 2014; Piniewski et al., 2011; Puska, 2009; Spiro and Brady, 2011; Topiwala and Ebmeier, 2012; Voss et al., 2013).

This review summarizes recent theoretical and basic research on neuroplasticity, scaffolding, and social brain theories. At the core of this review are seminal interventional and cohort studies that aim to prevent and/or delay age-related cognitive declines as well as seminal cohort studies where wellbeing and cognitive function are reported. Although there are a multitude of such studies, we focused on randomized controlled studies on physical activity, cognitive training and social (connectivity) enhancement interventions on maintaining cognition, physical health, independent living and wellbeing of cognitively healthy older adults. When available, we also considered results of meta-analytic studies on these topics conducted to clarify inconsistencies among published results. The methodological limitations of some of these studies, and the large epidemiological evidence of the single domain interventions, when combined with the new advances in neuroscience, support the need for innovative multi-domain blended synergistic interventions, as supported by advances in neuroscience and social-brain theories discussed in this targeted review paper. The rational for combined multi-domain interventions is discussed as the most hopeful and practical approach for maintaining older brain functionality, while generating testable hypothesis to push forward basic research on the specific bio-psychological pathways and mechanisms that influence healthy brain aging.

2. Theories of cognitive aging-based on neuroplasticity

Aging is considered a dynamic set of gains and losses rather than a declining process that leads inevitably to cognitive deficits (Baltes et al., 2005; Lovden et al., 2010). Cognitive studies have shown that even in advanced age, the brain displays certain plasticity (Berry et al., 2010; Cheng et al., 2012; Edwards et al., 2002; Edwards et al., 2005; Jones et al., 2006; Smith et al., 2009). Structural imaging has shown substantial age-related grey and white matter shrinkage, especially in anterior brain regions (lateral prefrontal cortex), the hippocampus, and basal ganglia while neural loss is minimal in the occipital brain areas (Raz et al., 2005). On the other hand, a compensatory process appears to occur with a shift from posterior-anterior areas and a reduction in brain asymmetry in older adults (Dennis and Cabeza, 2008), suggesting a compensatory frontal recruitment for deficits that occur with age (Park and Reuter-Lorenz, 2009). The prolonged mismatch between functional organic supplies and environmental demands produces cognitive plasticity and demonstrates the capacity of the brain to exhibit behavioral flexibility (Bavelier et al., 2012; Lovden et al., 2010).

For example, a recent event-related fMRI study (Ballesteros et al., 2013a) investigated age-related differences in brain activity in young and older adults performing a conceptual timed living/non-living classification task with three repetitions of pictures of familiar objects. Although both groups demonstrated similar significant repetition priming effects (better performance with repeated items compared to non-repeated ones), the imaging results showed altered neural priming in older adults, suggesting that age-preserved behavioral priming is the result of more sustained neural processing of stimuli in older adults. Electrophysiological studies have also shown additional frontal recruitment in older adults compared to young adults when performing a verbal cued-recall task (Osorio et al., 2009) and a word-stem completion task to assess implicit memory (Osorio et al., 2010). Both young and older adults exhibited robust behavioral priming and similar ERP repetition effects at posterior sites but only the older group showed additional frontal activity, suggesting that older adults compensate for their lower level of parieto-occipital functioning reflected by smaller

P300 amplitude at posterior sites. The frontal recruitment suggests a mode of adaptation to cope with the memory task demand. Similarly, other implicit (Sebastian and Ballesteros, 2012) and memory recognition studies for objects explored by touch (Sebastian et al., 2011) reported similar behavioral performance in young and older adults but induced brain oscillations showed age-related differences in amplitude in the theta, alpha and beta bands (4-30 Hz). Older adults required greater effort to maintain attention and recruited more brain resources than young adults. Moreover, N2pc and P3b amplitudes increased after training, reflecting brain allocation of attention that leads to capacity enhancement (O'Brien et al., 2013). These imaging findings suggest that the older human brain uses different types of compensation as a form of adaptation. Below, we comment briefly two theoretical accounts on cognitive and brain aging.

2.1. The cognitive reserve hypothesis

The cognitive reserve hypothesis was proposed to explain why individuals who engaged in higher levels of mental and physical activity were at a lower risk for developing dementia in later life (Nithianantharajah and Hannan, 2009; Stern, 2002, 2009; Valenzuela et al., 2008). The terms cognitive reserve and brain reserve are used to explain a shifting of task processing, recruiting additional parts of the brain not customarily used for the specified task. Cognitive reserve may also include other structural changes such as neurogenesis, synaptogenesis, angiogenesis, and the formation of dendritic branching (Valenzuela et al., 2007).

2.2. The scaffolding theory of aging and cognition (STAC and STAC-r)

‘Scaffolding’ is a normal process present across the lifespan that involves development of complementary, alternative neural circuits to achieve a particular cognitive goal (Park and Reuter-Lorenz, 2009). The scaffolding theory of aging and cognition (STAC) proposed that the increased frontal activation with age is an indicator of brain adaptation, promoting compensatory scaffolding. The adaptive brain responds to the declines occurring in the neural structures and functional processes. STAC suggests that cognitive engagement, mental training, and exercise promote and strengthen scaffolding. Recently, the more elaborated STAC-r (revisited) theory (Reuter-Lorenz and Park, 2014) incorporated lifestyle factors that serve to enhance or deplete neural resources, thereby influencing the developmental course of brain structure and function, as well as cognition throughout the lifespan. These processes are engaged to meet cognitive challenges and to ameliorate the adverse effects of structural and functional decline. STAC-r introduced two new constructs, *neural resource enrichment* and *neural resource depletion*. The first construct takes into account influences that enhance brain structure or function. Numerous correlational data suggest that individuals engaged in intellectual and social activities during adulthood suffer less age-related cognitive decline as they age (e.g., Amieva et al., 2010; Stern, 2009; Wilson et al., 2013). Similarly, individuals with a high level of education and physical fitness as well as those engaged in leisure activities and bilinguals appear to have healthier brain aging (Amieva et al., 2014; Amieva et al., 2010; Bialystok et al., 2012; Christensen et al., 2009; Erickson et al., 2013; Landau et al., 2012). The second construct - neural resource depletion - refers to negative influences on brain structure, neural function and cognition. The presence of the APOE-4 gene, vascular risk factors such as smoking, diabetes and obesity, all have negative effects on the brain and cognition.

In summary, there are similarities between certain aspects of the cognitive and brain reserve theory (Barulli and Stern, 2013; Stern, 2002, 2009, 2012) and the STAC-r theory. Enriching variables as well as depleting variables cited in STAC-r can enhance or diminish cognitive and brain reserve.

2.3. Theories of the impact of social engagement on healthy aging

Social engagement is defined as participation in social activities which maintain and create social ties in real life activities and reinforce meaningful social roles (Berkman et al., 2000). This definition is slightly different from "social networks" (Wrzus et al., 2013) defined as "the set of people with whom an individual is directly involved", included the cultural context of social networks (Litwin, 2010). Four major aspects of social networks have particular relevance for the older population, namely network structure and interaction, social exchange, social engagement, and subjective network perceptions which must be placed within the cultural context of the person. The nature of these domains is culture dependent. The construct of perceived emotional support is associated with self-reported individual wellbeing, and is linked to the concept of social engagement (Benyamini, 2008). Thus, emotions are an important variable of social enhancement efforts (see, Carstensen et al., 2003; Carstensen et al., 2011; Charles and Carstensen, 2010; Fiori and Jager, 2012). In broad terms, social engagement is understood as the individual making social and emotional connections with people and the community. A theoretical model includes "upstream factors" such as culture, socioeconomic and political factors, and the structure of the social network ties, their density and direction. The "downstream factors" comprise social support, access to resources, social influence as well health behaviors, psychological and physiological pathways (Berkman et al., 2000).

To summarize, social networks act at the behavioral level, providing social support, social influence, social engagement, and access to resources. This holistic model also brings into question the possible negative effects of the downstream factors that may link networks to undesirable health outcomes (Sneed and Cohen, 2014).

The term social networks is most often defined by the sociological principle of homophily, “birds of a feather stick together” (McPherson et al., 2001) . This broad principle includes ties of every type: marriage, friendship, work, advice, support, information transfer, exchange, co-membership, and other types of relationships not necessarily emotional or interpersonal in the psychosocial sense. Furthermore, at the core of homophily lies the assumption that cultural, behavioral, genetic, or material information that flows through networks will tend to be localized. Therefore, people's personal networks are homogeneous with regard to many socio-demographic, behavioral, and intrapersonal characteristics and health (Smith and Christakis, 2008).

The theory of homophily is supported by the concept of sociological aging (Charles and Carstensen, 2010). This review highlights the contrast between findings that clearly demonstrate decreased biological, physiological and cognitive capacity, with other findings suggesting that people are generally satisfied in old age and experience relatively high levels of emotional wellbeing. Thus, there appears to be a “paradox” of aging. This could be explained by the fact that that for each individual, his or her aging is heavily influenced by the nature of experiences within his/her social networks, and this plays a significant role in maintaining cognitive function, sense of wellbeing and positive attitude despite biological aging (Carstensen, 1992; Carstensen and Cone, 1983; Carstensen et al., 2011)

Although we may associate social networks with the socioeconomic factors of aging, there is significant research suggesting that belonging and social networking, are some of the most primitive and fundamental evolutionary brain developments (Dunbar, 1998; Gurven, 2012). As Dunbar suggests in his Social Brain hypothesis, the mesolimbic dopamine activity is a key brain system for triggering emotions. This function modulates lifelong learning as part of the emotional experiences in human learning and behavior (Dunbar, 1998). Furthermore, the need to belong, from an evolutionary brain development perspective, gives rise to a set of neuronal networks that are genetically transmitted as a specific phenotype of social cognition (Lesch, 2007). Social cognition is the capacity to generate representations of internal somatic states, interpersonal knowledge and motivations, and procedures used to decode and encode one's self in relation to other people and the environment. These distinct circuits are orchestrated via a complex set of processes in order to enable social functioning and communication, which is so essential for survival.

The individual's social cognition capacity is the product of the interaction between genes and environmental factors (Fowler et al., 2009; Lesch, 2007; Shanahan, 2013; Slavich and Cole, 2013). Although social cognition is also affected by physiologic aging, it is preserved through both scaffolding and compensatory enhancement within the context of social networks. The lack of or decrease in social enhancements/networks, as human epidemiological studies have shown, may result in pre-symptomatic dementia, although they are not the cause of dementia (Dodge et al., 2014). Social enhancement theories therefore, do not stand-alone but interconnect with all the above theories related to cognitive reserve, scaffolding and neuroplasticity, to improve our understanding of human genomic potential.

In summary, social enhancement is deeply embedded in human genomics, brain development and functionality through complex and newly explored physiological pathways rapidly shaping the field of social genomics (Cole, 2014). Social genomics studies suggest that the central nervous systems is both influenced and influences, how social enhancement stimuli are translated into specific cellular mechanisms, that impact on health and cognition throughout the lifespan.

Based on the above theoretical biosocial underpinnings, in the following section we will review intervention and cohort studies where various factors contributing to a healthy aging brain were evaluated. We will focus on studies that examine physical activity, cognitive training, and social enhancement. These interventions may have a significant impact on brain health functionality and can be implemented in public health policies and practices.

3. Intervention studies: Improving cognition and brain health

A wealth of data supports the view that there is a potential for positive changes in older adults (Hertzog et al., 2008; Park and Bischof, 2013; Valenzuela and Sachdev, 2009). Currently, researchers are investigating different types of interventions to improve and/or to maintain cognitive functions in the aging brain (see Figure 1).

[Insert Figure 1 about here]

Many studies have shown that interventions targeting physical activity, cognitive training, and social engagement in older adults are effective for improving performance in the trained tasks immediately after training. However, two major questions need to be answered: (Stigsdotter) whether the improvements observed in the trained individuals are transferable to other untrained functions (Buitenweg et al., 2012; Lustig et al., 2009; Williams et al., 2014); and (2) whether these effects remain over time, after the intervention ends (Dahlin et al., 2008b; Zelinski et al., 2011).

3.1. Physical activity training in ageing

Physical activity (PA) is an umbrella term describing a multitude of activities associated with purposeful body movements. Recent reviews have nicely summarized the crucial relationship of PA and cognitive function (Prakash et al., 2015) and intended to untangle the respective distinctions between different forms of PA (Bamidis et al., 2014). For the purpose of this review, we will subdivide PA activity into 3 main categories: first, PA as exercise training (aerobic and non-aerobic); second, complex activities in which PA is one component such as dancing; and third, PA in a sportive environment, for example martial arts or meditative movements such as Tai Chi or Qigong. Some forms of PA are difficult to classify into a particular category. For instance, Tai Chi includes elements of dance, meditation and sport.

3.1.1. Aerobic, resistance, and coordination training

Ever since the seminal study by Kramer and associates, exercise has been considered an important activity to improve cognitive function in old age (Kramer et al., 1999). Subsequent work has further developed some of the original observations and extended the concepts expressed there. Much of the work performed recently indicates some degree of improvement in cognitive function as a result of aerobic exercise (Bamidis et al., 2014).

An important distinction has to be made between aerobic and non-aerobic exercise. The latter can be further subdivided into coordination, stretching, and resistance training. Whereas aerobic exercise can be quantified by amount of energy expenditure expressed in metabolic equivalents, coordination training is difficult to quantify. Research to date concludes that all forms of exercise have shown to have effects on cognitive function of older adults (Hötting and Roder, 2013).

In addition to behavioral effects on cognition, non-aerobic exercise generated a different response in brain circuits in comparison to aerobic exercise. Voelcker-Rehage and colleagues studied three groups with aerobic, coordination and stretching (as a control condition) exercise and found three patterns of activity-related responses in an executive control task (Flanker task): increased task-related activity over frontal and anterior cingulate gyrus for the control condition, decreased activity for superior, middle and medial frontal areas (corresponding to Brodmann Areas 6,9) in the aerobic and coordination group. The findings for the aerobic and coordination group could be interpreted as a more efficient activity for the older subjects after aerobic and coordination training compared to the control condition (Voelcker-Rehage et al., 2011).

A 1-year intervention study showed similar results: that aerobic exercise improved the aging brains' functional efficiency in cognitive networks. One year of walking increased functional connectivity between aspects of the frontal, posterior, and temporal cortices within the Default Mode Network and a Frontal Executive Network. Effects were observed only after twelve months of training, compared to non-significant trends after six months (Voss et al., 2010). The changes in connectivity were behaviorally relevant, since increased functional connectivity was associated with a greater improvement in executive function, as measured with the Wisconsin Card Sorting Test (WCST) and a task-switching paradigm. Interestingly, the control group assigned to non-aerobic fitness training (stretching and toning) also showed increased functional connectivity.

Erickson and colleagues showed the beneficial effects of exercise on crucial brain structures involved in memory processing such as the hippocampus (Erickson et al., 2011). A 2% increase of hippocampal volume was associated with greater serum levels of BDNF, a mediator of neurogenesis in the dentate gyrus of the hippocampus. Unfortunately, it is very difficult to establish what the structural and physiologic correlate for the volume increase really is. Given the experimental data on animals and the concomitant increase of BDNF, it is tempting to speculate that these findings reflect adult neuroneogenesis, though previous work using different fMRI methodology would also suggest perfusion or synaptic density as the cause for this volume increase (Ilg et al., 2008). Unfortunately, these authors did not test whether these improvements in the spatial memory transferred to other cognitive domains such as improvements in executive function.

A cross-sectional study has shown that a long-lasting physically active lifestyle improves executive control, controlled processing (choice reaction time), and processing speed (simple reaction time) compared to sedentary older adults (Ballesteros et al., 2013b). A three-month practice of an aerobic fitness training program demonstrated that the trained group improved in processing speed (Renaud et al., 2010). The authors of the Cochrane review on the effects of PA on cognition in elderly individuals (Angevaren et al., 2008) concluded that there are beneficial effects of regular physical exercise on cognitive function. The authors identified eleven randomized controlled trials fulfilling appropriate quality standards. Eight of the eleven trials showed beneficial effects of regular physical exercise.

3.1.2. Effects of dance and movement interventions

There is an increasing amount of research regarding the potential benefits of (amateur) dancing. One of the first systematic studies (Kattenstroth et al., 2010) compared a group of elderly participants with a history of multi-year amateur dancing to an age-, education-, and sex- matched control sample. Compared to the control group, individuals of the amateur dancing group showed higher cognitive performance as well as better posture and balance parameters. Individual analysis of the data revealed that the amateur dancing population lacked individuals showing poor performance instead of showing individuals with better results than average. This implies that maintaining a regular schedule of dancing into old age can preserve cognitive, motor and perceptual abilities. This study points towards other important co-variables implied in successful aging including diet and social interaction. Since dance is highly interactive socially, this might be as important as the aerobic exercise component of ballroom (or amateur) dancing.

A subsequent study was carried out in order to rule out if the effects observed were due to a pre-selection of particularly trained subjects (Kattenstroth et al., 2013). In this follow-up study, they conducted a prospective, six months dance intervention in 35 elderly subjects comparing 1 h/week dancing activity with the Agilando ™ programme with no intervention. The study showed that besides having impressive effects on improved posture and balance, dancing also had major effects in a whole range of cognitive skills, including reaction time and working memory. Interestingly, dancing did not change the cardiorespiratory function, again indicating that aerobic exercise is not the only physical activity with beneficial effects to cognition. Compared to other activities such as physical exercise or playing an instrument, dancing offers a unique combination of activities potentially useful for maintaining a multitude of functions in advanced age. Brown et al. (2006) have documented that cortical, subcortical and cerebellar regions were active at the systems level, providing neurophysiological support regarding why dancing in a social context may ameliorate not only cognitive function but also other age-related declines including balance and motor strength.

The postulated mechanisms for dance movement training, as suggested recently (Kattenstroth et al., 2010), is that dance movement combines a physical activity with a rich sensorimotor and cognitive engagement, as well as other social and emotional stimuli. There are multiple studies that have shed a positive light on the impact of dance related interventions and healthy aging for both the cognition and physical capacity domains. The type of dance did not seem to make any difference; a broad range of different types of dance, ranging from folklore dance, through tango to salsa and jazz, showed beneficial effects (Alpert et al., 2009; Coubard et al., 2011; Currie et al., 2012; Dechamps et al., 2010; Fosshage, 2004; Granacher et al., 2012; Gray, 2008; Heiberger et al., 2011; Keogh et al., 2009; Kim et al., 2011; Koch and Bräuninger, 2005; Sevdalis and Keller, 2011).

3.1.3. Sport, Tai Chi and martial arts as interventions

A considerable amount of literature is available on specific forms of PA, such as sportive activities like Tai Chi and martial arts. In particular, studies using Tai Chi have generated a substantial body of evidence (Lelard et al., 2010; Rogers et al., 2009; Wei et al., 2014). A detailed appreciation of all this work is beyond the scope of this review. A meta-analysis by Rogers and colleagues of 36 studies including a total population of 3799 participants older than 55 years concluded that significant improvement could be achieved in physical function, reduced risk of falls, depression and anxiety (Rogers et al., 2009). In addition, there is a major ongoing trial that will focus on biological and behavioral effects of practicing Tai Chi (Wayne et al., 2013).

Martial arts such as Kung Fu, Judo, Karate or Taekwondo have also been shown to improve cognitive domains in older adults including postural control (Krampe et al., 2014), visual-spatial attention (Muinos and Ballesteros, 2014), dynamic visual acuity (Muiños and Ballesteros, 2015) as well as working memory and information processing speed (Pons van Dijk et al., 2013).

A recent meta-analysis (Kelly et al., 2014b) that included 25 RCTs revealed significant improvements for resistance training compared to stretching on measures of reasoning; and for Tai Chi compared to controls (no exercise) on attention and processing speed. The results of the meta-analytic study, combined with results from other meta-analyses (Colcombe and Kramer, 2003; Wayne et al., 2014) suggest that the combination of aerobic fitness with resistance training (such as Tai Chi) may produce larger benefits for promoting healthy cognitive function in older adults.

3.2. Cognitive training approaches

Cognitive training is an intervention that provides structured practice on tasks relevant to different aspects of cognition, such as attention, memory, or executive functions. Theoretically, these studies suggest that the older human brain maintains some level of neural plasticity at several levels of the neural substrate (Bialystok and Craik, 2006; Li et al., 2006; Li et al., 2008). Furthermore, the behavior of the aging individual can influence this plasticity (Cacciopo et al., 2006).

Despite the intent to introduce an order into the terminology of cognitive interventions (Clare and Woods, 2004), the debate is still alive (Gates and Valenzuela, 2010). A recent review (Bamidis et al., 2014) outlined the main characteristics of cognitive rehabilitation versus cognitive training. Other researchers refer to this set of interventions based on mental stimulation as brain training (Buitenweg et al., 2012), cognitive exercise (Gates and Valenzuela, 2010) or cognitive rehabilitation (Hampstead et al., 2008; Hampstead et al., 2012; Stuss et al., 2007; Winocur et al., 2007). In our technological society, computer-based training programs and video games have attracted researchers' attention as possible tools for improving and/or maintaining perceptual and cognitive functions in older adults. However, scientific evidence of the potential of these interventions is mixed at best.

Most cognitive training studies have used cross-sectional designs to compare the performance of two or more groups of participants in a number of tasks (e.g., young adults versus older adults; comparison of individuals with different levels of expertise as video game players versus non players). A smaller number of studies examined training effects using longitudinal designs with trained (experienced) and control groups. The latter studies have the advantage of controlling for cohort effects (the comparison of participants with different levels of education, nutrition, social and economic conditions) and allow the investigation of training effects over time (pre-training/post-training/follow-up) performance comparisons in a series of variables. These longitudinal studies have several shortcomings, including the relative small number of participants, attrition, practice effects, the use of inadequate control groups or, in some cases, the lack of a control group. For a detailed discussion, see (Kramer and Morrow, in press).

Past experience as well as living in an enriched and complex environment can modify brain and cognition (Hertzog et al., 2008; Stern, 2002, 2009; Valenzuela et al., 2007). Some training programs have been effective in improving older adults' cognitive performance in memory tasks (e.g., Craik et al., 2007; Hampstead et al., 2012; Smith et al., 2009) and other cognitive functions such as attention, working memory, reasoning, processing speed, cognitive control and dual-task switching (Anguera et al., 2013; Berry et al., 2010; Bherer et al., 2006; Edwards et al., 2005; Erickson et al., 2007; Mozolic et al., 2011b).

In this section, we mainly focus on cognitive training intervention studies that provide structured practice on one or several aspects of cognition, using standardized tasks. The aim of these controlled interventions is to use a set of clearly specified exercises to improve cognition in older adults. These exercises are usually practiced on a computer and the difficulty is adjusted to the trainee's performance. We reviewed the current evidence on cognitive interventions (with trained and control groups) specifically designed to train one or more cognitive processes using structured, mostly computerized programs based on experimental designs and, where available, randomized controlled trials (e.g., Dahlin et al., 2008b; Valenzuela and Sachdev, 2009; Wolinsky et al., 2013). The increased interest in investigating the effectiveness of computerized cognitive training in enhancing cognition of cognitively healthy older adults is shown by the recent publication of systematic reviews and meta-analyses that investigated this issue (Kelly et al., 2014a; Lampit et al., 2014). In the second part of this section, we focus on longitudinal training studies that have used video games to improve older minds and brains. This type of intervention has also been the subject of a recent systematic review (Kueider et al., 2012) and a meta-analysis (Toril et al., 2014).

3.2.1. Computerized brain training in aging

Cognitive training interventions based on repetitive practice on cognitive processes have been effective in improving the trained process but not so much for other untrained cognitive functions (Ball et al., 2002; Ball et al., 2007; Hampstead et al., 2012; Mozolic et al., 2011b). Some clinical trials, however, have shown transfer to other domains different than that of the trained exercises (Cheng et al., 2012; Mahncke et al., 2006; Oswald et al., 2006; Richmond et al., 2011; Willis et al., 2006).

Computerized training is the preferred option in most of the intervention studies as the program can automatically adapt to the trainee’s daily performance. The intervention could be useful depending on the extent of the improvement to abilities not directly trained during the intervention. The degree to which a learned skill is shown in proximal (near transfer) or more distant (far transfer) tasks and contexts is central regarding cognitive training interventions. Near transfer effects are found after training in tasks close to the trained task (e.g., improvements on a verbal WM task after training on a spatial WM task). Far transfer effects are shown in tasks very different from those of trained tasks (e.g., improvements on intelligence tests scores, attention, arithmetic, language abilities, or everyday activities). Unfortunately, evidence for the effective transfer of cognitive training to untrained tasks is mixed (Tidwell et al., 2014) with some studies suggesting positive results, while others showing none or only a limited improvement (Buitenweg et al., 2012; Dahlin et al., 2008b; Lustig et al., 2009; Noack et al., 2009; Paap et al., 2009; Sandberg et al., 2014). Table 1 summarizes the characteristics and main results of recent cognitive training studies conducted to counteract age-related cognitive declines.

[Insert Table 1 about here]

Two previous meta-analyses have investigated the effects of cognitive training interventions in healthy older adults (Paap et al., 2009; Valenzuela and Sachdev, 2009). The first included 10 RCT studies and only half of them showed improvement immediately after cognitive training on the trained task and there was no evidence of a transfer of training to other untrained tasks (Paap et al., 2009). The weighted mean effect size (Cohen's *d*) of cognitive intervention across all outcome measures after training was very modest [0.16 (95% confidence interval (CI) 0.138 to 0.186)].

The other meta-analysis (Valenzuela and Sachdev, 2009) included just 7 RCT studies that met inclusion criteria with a cumulative sample of 3194 participants -2832 of whom were from the Advance Cognitive Training for Independent and Vital Elderly (ACTIVE) study. The authors examined the effect of cognitive training to investigate transfer of training to untrained domains and persistence over a follow-up period after training. The results showed a moderate mean effect size of 0.6. Cognitive training of healthy older adults improved performance on the trained task immediately after the end of the intervention (see also, Rebok et al., 2007). The meta-analysis also showed that 2-3 months of training has long-lasting effects on cognition in healthy older adults (between 1.2 and 2.6 points in the MMSE). Although promising, these results must be interpreted with caution because only the primary outcome variable per clinical trial was included in the meta-analysis while secondary outcomes, which are usually less robust, were not included. Moreover, not all studies followed the CONSORT clinical trials guidelines rigorously. Limitations of the literature may account for the discrepancies of the results. The heterogeneity of the studies included in the meta-analyses relates to the number of participants, the inclusion or not of a matched active control group, the lack of follow-up assessments in some studies, inadequate outcome measures that should include measures of everyday functioning and a wide variety of cognitive skills.

The first RCT and the largest cognitive training study conducted so far has been the single-domain ACTIVE study (Ball et al., 2002). ACTIVE was a multicenter cognitive training study with 2832 older adults from 65 to 94 years old who were randomly assigned to three cognitive interventions (memory, speed of processing, and reasoning) or to a no-contact control group. Each training regime consisted of 10 sessions distributed over 5-6 weeks. Several outcome measures (including problem solving and tests) were used as composite measures to assess overall abilities in each trained cognitive domain). Furthermore, a percentage of the participants (60%) received 4 booster-training sessions almost a year after end of the training programs. The study showed that when memory, processing speed, and problem solving were trained independently, trainees in each one of these conditions improved in the skill trained, but there was no transfer to other untrained skills and these improvements lasted over a period of 2 years after training. There was no evidence of transfer to every-day activities and the benefits did not transfer to other untrained functions (Buitenweg et al., 2012; Lustig et al., 2009). The results of a 10-years follow-up study (Rebok et al., 2014) of the

ACTIVE data (mean age at baseline: 73.6 years) suggest that the three treatments resulted in less decline in self-reported Instrumental Activities of Daily Living (IADLs). At 82 years of age, 60% of the trainees versus 50% of control participants were above their baseline of IADL score. Interestingly, the groups trained in reasoning and speed, but not the group trained on memory, had preserved the improved trained cognitive ability ten-years after the intervention.

A recent meta-analysis (Lampit et al., 2014) on the effectiveness of computerized cognitive training in cognitively healthy older adults from the inception of databases to July 2014 included 52 RCT studies. The global overall effect was small but significant (Hedges' g random effect model = 0.22; 95% CI 0.15 to 0.29). The authors concluded that computerized cognitive training is moderately effective at improving cognitive performance. However, effectiveness varies across cognitive domains. Unsupervised at-home training and very intensive training regimes of three or more times per week were shown to be ineffective. Another meta-analysis (Kelly et al., 2014b) showed that transfer effects occurred more often when training was adaptive, with at least 10 training sessions and by training in groups compared to individual training at home. Interestingly, both meta-analytic studies suggest that training at home ("do-it-yourself") does not produce any improvements. The supervision by a trainer in a center or laboratory as well as performing 1-3 sessions per week is necessary to create moderate improvements.

Is working memory training in older adults effective? WM is a key component of cognition that deteriorates greatly with age. It is a flexible, capacity limited workspace that stores and processes information needed for ongoing cognition (Baddeley, 2000; Baddeley and Hitch, 1974). Intervention studies aimed at improving WM addressed near and far transfer effects after training executive and WM functions related to the control of goal-directed actions and use of immediate memory, the maintenance and manipulation of recently attended information, switching and task priorities in multitasking. These functions depend on prefrontal cortex and basal ganglia, brain structures that suffer great shrinkage (Raz et al., 2005; West, 1996), reduced structural connectivity (Madden et al., 2009) and ongoing dopamine depletion (Backman et al., 2006) with age.

Many recent training studies have been designed to improve WM, assuming that its capacity could be enhanced through training and that, in turn, other mental abilities would also improve (Klingberg, 2010). However, several recent reviews have been rather skeptical (Buitenweg et al., 2012; Melby-Lervag and Hulme, 2013; Shipstead et al., 2012b; Tidwell et al., 2014). Similarly, a meta-analytic study (Melby-Lervag and Hulme, 2013) conducted with 23 randomized controlled trials or quasi-experiments (with 30 groups comparisons) that had a treatment group and a control group and included children and adults showed that training produced short-term improvements in WM skills, but the results did not transfer to other cognitive skills.

The main assumption of the training studies conducted to improve WM is that some aspect of executive control would be enhanced and that this would transfer to other cognitive functions and to daily life performance. However, executive control is not a single function but includes several cognitive abilities such as memory updating, task shifting and inhibition (Miyake et al., 2000). The idea behind these training studies is that a general improvement in WM performance should improve those functions and tasks that rely on WM processes (Buschkuehl et al., 2008).

Dahlin and colleagues (Dahlin et al., 2008a; Dahlin et al., 2008b) investigated the plasticity of executive functioning in young and older adults to explore transfer effects to untrained tasks and maintenance of gains 18 months after finalizing a 5-weeks computerized training program consisting of updating information in working memory. The results showed that young and older trained participants improved more than controls on the trained task. Those improvements were still significant 18 months later. Learning was long-lasting in older adults but there was no transfer to other tasks and this was attributed to the large changes occurring in the striatum with age, as this region plays an important role in transfer of an updated skill (Dahlin et al., 2008a).

Other studies trained participants to perform two tasks simultaneously. Older adults have more difficulties (Verhaeghen et al., 2003) than young adults when performing two tasks (dual-tasking costs). Bherer and colleagues trained young and older adults for 5-60 min sessions over 3 weeks to perform an auditory and a visual discrimination task, either concurrently or separately (Bherer et al., 2006). The findings showed substantial and age-equivalent training and transfer benefits on both the ability to maintain multiple task sets and to perform multiple tasks concurrently. The positive results might be due to the continuous, individualized adaptive feedback and priority instructions provided to the participants in an effort to improved dual-task performance.

An important often not addressed question is whether training in dual tasks is transferable to daily life tasks. Hahn and colleagues trained 14 young and 14 older adults in a driving simulation environment with a visual-motor tracking task (primary task) and a visual attention task (secondary task) under dual-task conditions for a relatively long duration (Hahn et al., 2011). The situation tried to simulate driving under task demands and to provoke fatigue. The results showed that older adults reduced the number of errors and response time more than young adults after training, suggesting that older adults benefit from training in complex environments. A further study showed that tracking performance was specially affected after target presentation which was more pronounced in the older than in the younger participants. Electrophysiological results suggested that the older adults invested more resources than the younger group in dual tasking during the cue-stimulus interval. The increased motor interference, a deficient context processing together with the investment of more processing resources suggest that vehicle information systems for older drivers should support cue maintenance instead of requiring simultaneous motor demands (Wild-Wall et al., 2011).

Interestingly, Berry and colleagues showed direct transfer after training perceptual discrimination tasks to untrained WM performance. The adaptive training program consisted of the discrimination of the contraction or expansion of Gabor patterns. Electroencephalographic recordings showed posterior occipital N1 decrease after training that correlated with performance in a WM task, and no change in the control group. This change in N1 was interpreted as a neural marker of the perceptual gains after training, which produced improvements in WM task performance (Berry et al., 2010).

Tasks directed to training cognitive flexibility, targeting several mechanisms of executive control simultaneously might be more efficient (Buitenweg et al., 2012; Karbach and Kray, 2009; Stigsdotter, 2015). However, two recent intervention studies (McAvinue et al., 2013; Sandberg et al., 2014) failed to show evidence of improvement in WM capacity. A 5-week online randomized adaptive training study based on the Baddeley model (Baddeley, 2000) to train auditory and visual-spatial short-term WM (McAvinue et al., 2013) showed improvement in short-term memory but not in WM despite the extensive training on updating and n-back tasks. The expansion of auditory short-term memory up to 6 months, and the transfer to long-term episodic memory (although not maintained at follow-up) is interesting. An intriguing result that deserves further investigation is the negative correlation between time spent on training and proportional improvement on the auditory short-term memory task, indicating that more time spent on training produced less improvement. Another recent study (Sandberg et al., 2014) demonstrated that training multiple executive functions (updating, shifting and inhibition) was not enough to produce transfer beyond the very near tasks in older adults. Even the younger group did not show far transfer after training. Intermediate transfer was found, but only in the younger group. These results suggest important age-related constraints in the transfer of the trained executive skills.

A recent brain imaging study (Heinzel et al., 2014) has investigated whether the WM load-dependent pattern of blood oxygen level-dependent (BOLD) response and functional connectivity in WM regions of interest (ROIs) are associated with training-related performance gains and other cognitive functions in young and older adults. The assessment battery to investigate transfer pre-test to post-test training effects included short-term memory tasks (Digit Span forward and backward), processing speed (Digit Symbol, D2 test), executive functions (Verbal Fluency, Stroop interference), and reasoning (Raven SPM and Figural relations). They used a computerized version of the n-back adaptive procedure (from 0-, 1- 2- and 3-back conditions) to train older adults over 4 weeks (12 sessions each lasting for approximately 45 minutes). Only older adults were trained. The results showed, as expected, that young adults' WM was superior in the n-back task and neuropsychological tests at pre-test. Young adults showed lower BOLD activations in the WM network at 1-back and higher at 3-back conditions compared to older adults at pre-test. The most important finding was that the neural efficiency and capacity of the WM load-dependent brain response in the WM network can predict for WM plasticity in older adults. It is like that of those older adults who show a youth-like WM load-dependent brain response, which responds better to WM intervention programs. However, only older adults received WM training and the design did not include a control group. A replication of these results in a RCT with pre-post and follow-up design and larger sample size will be necessary to corroborate these interesting findings.

In summary, present data reveal inconsistent results. While it seems that training studies have consistently shown improved performance in the trained task, and sometimes near transfer, far transfer effects to untrained cognitive functions are weak or non-existent. More research is clearly needed before we can conclude that WM training in older adults is effective and that its capacity can be enhanced with training. Future studies should include a proper control group and several measures to assess the domain of interest and to test near transfer effects with WM tasks different from those used in the training protocol. Until there are more conclusive results, WM training remains an important line of research in progress that deserves close attention (Melby-Lervag and Hulme, 2013; Shipstead et al., 2012a; Shipstead et al., 2012b; Tidwell et al., 2014).

Memory training studies. Numerous training programs have been developed to improve and/or maintain long-term episodic memory among older adults because this type of memory is vital for independent living. Most of them teach participants to use different memory strategies that help to encode and retrieve information (Craik et al., 2007; Gross and Rebok, 2011). Several reviews and meta-analyses have been conducted on the effects of long-term memory training programs with healthy participants (Gross et al., 2012; Verhaeghen et al., 1992; Zehnder et al., 2009) as well as in elderly with MCI (Belleville, 2008). In general, studies support the idea that memory training is effective. A meta-analysis of almost five decades of memory training studies with healthy older adults has shown that. The overall effect size estimate (pre-post change between memory trained and control groups) was 0.31. Training on more than one strategy was associated with memory improvement but was not significant after adjustment for multiple comparisons (Gross et al., 2012).

Cheng et al. (2012) conducted a randomized cognitive training study including control waiting-list group, single domain and multi-domain cognitive trained groups, The multi-domain cognitive intervention trained memory, reasoning, problem solving, visual-spatial map reading, handcraft making and health lessons. The single-domain group was trained in reasoning. The results showed that both trained groups obtained training-related effects. Multi-domain cognitive training improved memory while single-domain training improved visuospatial ability and attention. The group also improved on the RBANS total score, delayed memory, visuospatial ability, language, and word interference score. While both types of cognitive training produced positive results improving memory, visual reasoning, and visuospatial abilities, the multi-domain approach had longer training effect maintenance while single-domain training improved attention and visuospatial skills.

To summarize, memory-training interventions have the potential to improve long-term episodic memory in healthy elders. However, as in the case of WM and executive control training studies, the transfer to other cognitive functions and daily living activities needs further research using well designed studies with pre-post assessments in a wider variety of cognitive measures and daily life performance, and longer follow-up periods.

3.2.2. Training older brains with video games

A video (digital) game is a game that requires human interaction with a computer. There are different genres, including serious games (Gopher et al., 1994) primarily designed to provide a learning experience to the gamer and educational games as Brain

Age and Brain Training (McDougall and House, 2012). Most video games, however, are action games that were not developed considering the interests or needs of the older adults. Accumulated evidence suggests that playing action video games improves aspects of cognition in young adults, including visual-spatial attention, executive control, and peripheral vision (e.g., Boot et al., 2008; Chisholm and Kingstone, 2012; Green and Bavelier, 2003, 2006, 2008; Green et al., 2010). Video game training also enhances visual short-term memory, task switching, object mental rotation and executive control in young and older individuals (Basak et al., 2008; Boot et al., 2008; Cain et al., 2012; Colzato et al., 2010; Lee et al., 2012); for reviews, see (Bavelier et al., 2012). However, some studies did not find transfer to cognitive functioning (Boot et al., 2013a; Owen et al., 2010) or improvements were very small (Ackerman et al., 2010). For instance, Owen et al. (2010) trained 11430 participants online for 6 weeks on cognitive tasks designed to improve planning, memory, reasoning, visual-spatial abilities, and attention but they found no evidence that training improved cognitive functioning beyond the trained tasks.

In summary, evidence of transfer from video game training to untrained tasks is at best mixed with positive and negative results. However, it is worth noting that video game training is a very active area of research.

Most action video games are fast, emphasize peripheral processing, require selection between different action plans, and are sometimes violent, and therefore not appropriate or interesting for older participants (Chisholm and Kingstone, 2012; Feng et al., 2007; Green and Bavelier, 2003; Green et al., 2010). When older adults were asked to judge the games, action games were rated as less enjoyable than non-action games (Boot et al., 2013a; McKay and Maki, 2010; Nap et al., 2009). Moreover, these types of games led to the lowest intervention compliance compared to non-action games. In addition, studies with older adults (Ackerman et al., 2010; Anguera et al., 2013; Ballesteros et al., 2014b; Cassavaugh and Kramer, 2009; McDougall and House, 2012; Nouchi et al., 2012) suggest that non-action video games can improve aspects of cognition. Despite the increasing interest in using video games as intervention tools, the evidence on their efficiency is mixed.

The use of video games to boost cognitive functioning of older adults have advantages over other more traditional cognitive training programs because these games are inexpensive, and can be gratifying and fun (Zelinski and Reyes, 2009). Interestingly, a recent study (Allaire et al., 2013) has showed that both regular and occasional video game players reported significantly higher levels of well-being and suffer less depression than non-video game players. For these reasons, researchers consider video games as good tools for cognitive enrichment (Achtman et al., 2008; Green and Bavelier, 2008). Early studies with older adults revealed improvements in several cognitive functions after video game training, including processing speed (Clark et al., 1987; Dustman et al., 1992; Goldstein et al., 1997), intelligence, visual-motor coordination (Drew and Waters, 1986), attention (Belchior, 2008) and global cognitive function (Torres, 2008). In contrast, other studies did not find a significant transfer of training to cognitive and perceptual functioning (e.g., Ackerman et al., 2010; Boot et al., 2013b; Owen et al., 2010). If the transfer of video game training to untrained cognitive functions could be demonstrated, this would be a very important finding.

One of the main difficulties in obtaining a clear picture of the effects of video game training is the great variability of several key features of the intervention studies, including the type of video game used, the type of cognitive process assessed, the way in which these cognitive processes were evaluated, and the different personal characteristics of the trainees. This variability seems to be the main cause of the mixed results reported in the literature. While several studies reported positive results after training (Anguera et al., 2013; Ballesteros et al., 2014b; Goldstein et al., 1997; Torres, 2008), others did not find cognitive improvement (Ackerman et al., 2010; Boot et al., 2013a; Owen et al., 2010). A recent meta-analysis (Toril et al., 2014) re-analyzed the 20 individual video game training studies published on this topic between 1986 and 2013. The studies involved 474 trained and 439 healthy older controls. All studies have pre- and post-training measures and all except two with trained and control groups. Table 2 (adapted from Toril et al., 2014) displays the main characteristics of the studies, including number of participants, their mean age, type of control group, video game(s) trained, duration of training and summary of the main findings of each study.

[Insert Table 2 about here]

The mean effect size (Cohen's *d*) was moderate (0.37). The results suggest that training older adults with non-action video games improves speed of processing, attention, memory and global cognition. These main findings were moderated by several methodological and personal factors. The effects were larger under short training programs (1-6 weeks) rather than under longer training regimes (7-12 weeks). The age of the trainees was also a significant variable in the analysis as the benefits increase in the older more than in the younger participants.

A recent RCT study (Ballesteros et al., 2014a; Mayas et al., 2014) investigated the effects of training healthy older adults with non-action video games to determine whether the benefits transfer to a broad number of cognitive functions and wellbeing. The trained healthy older adults went through 20 one-hour sessions over the course of 10 to 12 weeks. In each session, the trainees practiced 10 non-action video games twice. The pre- and post-test results in a series of psychological tests and computerized tasks of the trained group were compared with those of a control group to examine possible transfer of training to untrained tasks. The trained group improved in processing speed, attention (reduction of distraction by irrelevant sounds and increase of alertness), immediate and delayed memory for pictures, and in two dimensions of subjective wellbeing (affection and assertiveness) compared to the control group. However, the trained group showed neither transfer to executive control (assessed with the WCST) nor to spatial WM. Results of a 3-month follow-up (Ballesteros et al., 2015) showed improvements from baseline to follow-up only in affection and assertiveness, two dimensions of subjective wellbeing in the trained group, and no change in the control group. Significant improvements after training in processing speed, attention and memory became non-significant after 3-months. These findings are in agreement with other results (Buschkuehl et al., 2008; Stern et al., 2011). Modest transfers after training disappeared at the follow-up. The results suggest that to maintain the benefits some boosting sessions would be necessary.

The ineffectiveness of training, despite the fact that several of the practiced non-action video games mimic WM tasks, is also found in two recent reviews (Melby-Lervag and Hulme, 2013; Shipstead et al., 2012b). More importantly, a recent randomized, placebo-controlled study with young adults who received 20 sessions of practice on an adaptive computerized n-back training program found no evidence of improvement in multiple measures of verbal and spatial fluid intelligence, multitasking, or WM capacity (Redick et al., 2013). Boot and colleagues reported similar results (Boot et al., 2013a).

The lack of benefits of training on executive functions was found in meta-analytic studies (Lampit et al., 2014; Toril et al., 2014) and in a systematic review (Kueider et al., 2012). Overall, results suggest that older participants have more limited neural plasticity, reducing their ability to transfer an executive skill (information updating). As reviewed above, even when the program trained several components (updating, shifting and inhibition) far transfer to other WM tasks was not found. Furthermore, a meta-analysis conducted with published studies with children, young adults, adults, and older adults also yielded negligible effects for executive functions (Powers et al., 2013).

The reviewed studies indicate that video game training improves some aspects of cognition but not others. These results have important practical implications as exploring new ways of helping older adults to maintain cognitive health may reduce the risk of dependency. It will be important for future studies to demonstrate these positive effects, considering the limitations of the studies currently available. These limitations include: (a) the relative small sample sizes of longitudinal intervention studies (Ballesteros et al., 2014b; Cassavaugh and Kramer, 2009; Clark et al., 1987; Drew and Waters, 1986; Goldstein et al., 1997; Maillot et al., 2012; Nouchi et al., 2012), (b) individual motivational factors, and (c) more sophisticated statistical designs to address the placebo effect resulting from familiarity with the investigators. For example, most studies included just a passive, non-contact (or limited contact) control group (e.g., Ballesteros et al., 2014a; Basak et al., 2008; Goldstein et al., 1997; Maillot et al., 2012; McDougall and House, 2012), or do not even have a control group (Ackerman et al., 2010; Cassavaugh and Kramer, 2009) to compare performance with that of the trained group. However, a meta-analytic study (Toril et al., 2014) calculated the effect sizes of those published studies that used both an active and a passive control group (5 out of the 20 published studies included in the meta-analysis). The mean effect size (Cohen's *d*) for the active control was 0.36 and for the passive control 0.37. The difference was not statistically significant.

In summary, computerized cognitive training has shown small to moderate improvements in certain cognitive domains with no significant effects in executive functions. Unsupervised training at home was not effective compared to group-based supervised training at a center or laboratory. Moreover, training regimes of more than 3-sessions per week seem ineffective. Working memory and executive functions do not improve after training and may require perhaps multi-modal interventions. Further studies are needed to investigate maintenance after training and transfer to daily life activities. Video game developers need to work together with aging psychologists and neuroscientists to create attractive and useful games specifically designed for aging people because the produced video games need to be interesting enough to older people to motivate them to play the games. The video games that older adults might find engaging are not necessarily those that young adults and adolescents enjoy.

3.3. Social engagement approaches

There is no standardized definition of what is the exact meaning or measure of social engagement. The epidemiological and interventional studies reviewed here show a wide spectrum of definitions where the common denominator is individual human interaction with other humans. The seminal study on social engagement (Berkman and Syme, 1979) describes a longitudinal study of 5-year duration of older adults in Alameda, California. This study identifies four types of social engagement, including marriage, network size (number of relatives and friends seen frequently), church membership, and participation in formal or informal groups. A summary measure of these four ties was called the "Social Network Index". The higher index was associated with better host resistance and reduced mortality. Similar findings were reported by several cohort studies over the years, however not all used the same social network index. Numerous studies show that increased social engagement in older adults is associated with greater quality of life (Levasseur et al., 2004), lower rates of dementia and of overall mortality (Wrzus et al., 2013). In this section, we review longitudinal cohort studies, as well as the few intervention studies, where the impact of social networks across several domains of healthy aging has been examined, such as decreased risk of adverse health outcomes including depression, cognitive decline, dementia, motor decline, and all-cause mortality.

3.3.1. Longitudinal cohort studies

There are a large number of articles based on longitudinal cohort studies on social networks and cognitive aging. However, few studies have examined specifically the cognitive impact of social enhancement. We focus on studies that have measured cognitive function outcomes and/or wellbeing (see Table 3).

[Insert Table 3 about here]

In a cohort study of the Rush Memory and Aging Project (James et al., 2011), 1138 older adults without dementia at baseline and with a mean age of 79.6 (SD = 7.5) were followed for up to 12 years. The analysis of this cohort used a mixed model adjusted for age, sex, education, race, social network size, depression, chronic conditions, disability, neuroticism, extraversion, cognitive activity, and physical activity. Social activity was measured in terms of frequency of the following six common types of activities that involve social interaction such as (Stigsdotter and Nyberg, 2015) go to restaurants, sporting events or off-track betting, or play bingo; (2) go on day trips or overnight trips; (3) do unpaid community or volunteer work; (4) visit relatives' or friends' houses; (5) participate in groups, such as senior center, Knights of Columbus, Rosary Society, or something similar; and (6) attend church or religious services. Higher level of social activity was associated with less cognitive decline during average follow-up of 5.2 years. Furthermore, a one-point increase in the social activity score (range = 1-4.2; mean = 2.6; SD = 0.6) was associated with a 47% decrease in the rate of decline in global cognitive function ($p < .001$). Conversely, the rate of global cognitive decline was reduced by an average of 70% in persons who were frequently socially active (score = 3.33, 90th percentile) as compared to persons who were infrequently socially active (score = 1.83, 10th percentile). This association was similar across five domains of cognitive function. Nineteen tests were used to create summary indices of global cognitive function and 5 specific cognitive domains: episodic memory, semantic memory, working memory, perceptual speed and visuospatial ability. Using a fully adjusted model, on average, a one-point increase in social activity score was associated with a 0.034 unit reduction in rate of cognitive decline per year, or a 47% decrease in the annual rate of decline in global cognitive function. In a person who is socially active (score = 3.33; 90th percentile), the rate of global cognitive decline was reduced by an average of 70%, as compared to a person who is infrequently socially active (score = 1.83; 10th percentile). The effect of level of social activity on preventing cognitive decline remained even after adjusting for income status. Furthermore, a level of social activity was consistently associated with a reduced cognitive decline in all five cognitive abilities.

Another cohort study (Wang et al., 2002) of almost 1300 participants followed over 6.5 years showed that the adjusted relative risk for dementia according to social participation was 0.67 (95% CI 0.34 to 1.33), slightly higher than for physical activity 0.61 (95% CI 0.40 to 0.93), but slightly less than for cognitive activities 0.70 (95% CI 0.49 to 1.01). A seminal study of social activities (Berkman and Syme, 1979) with 6900 participants and a nine year follow-up demonstrated that the association between social ties and mortality was independent of self-reported physical health status at the time of the 1965 survey, socioeconomic status, and health-related practices such as smoking, alcohol consumption, obesity, physical activity and utilization of preventive health services, as well as a cumulative index of health practices.

A cohort (Zunzunegui et al., 2003) with over 1500 enrolled individuals showed a slightly more nuisance definition of social network. The probability of cognitive decline was lower for both men and women with a high frequency of visual contact with relatives and community social integration. However, interestingly enough, engagement with friends was protective for cognitive decline in women but not in men.

An important different set of results were reported in a cohort study (Jacobs et al., 2011) of 1861 adults 70-85 years old over the past 15 years. This study of Jerusalemites showed that the 70 olds were overall well in terms of general cognition and activities of daily living. Moreover, the overall health profile was favorable, prevalence of geriatric syndromes was low, cognitive and functional status was preserved, and health service utilization was low. However, there was a progressive deterioration after age 78 and more profoundly so, after age 85. The authors suggest that given the good status of this cohort, the cut-off point beyond age 70 may better serve to define entry into old age instead of the customary 65. Unfortunately, this study did not measure social networks specifically. Yet another publication of the same cohort (Stessman et al., 2005) reported that social factors had the highest correlation with a longer life.

It is interesting to compare the findings of the (Jacobs et al., 2011) study to those found in the study reported by (Eisele et al., 2012), where the average age is 82.5 years. The latter is the only cohort study that showed a negative association between social support, understood as the emotional component of social enhancement and cognitive function. The results of this longitudinal cohort study, drawn from a national primary care practice sample of 1800 elder with mean age of 75, did not show any effect on cognitive function or mortality, over an 18-month follow-up time frame. The authors concluded that the follow-up period was too short to show any significant impact. This study was drawn from primary medical practices as opposed to a national random sample and it is also possible that this kind of population represents a more complex medical sample having a higher degree of morbidity.

Social integration, frequent contact with family and friends, and playing an important role with significant others have beneficial effects in maintaining cognitive function in later life (Zunzunegui et al., 2003). These positive effects of social networks however are contextually bound, as showed by reports using SHARE data (Litwin, 2010) comparing wellbeing and social networks of 5 Mediterranean and 7 non-Mediterranean cultures. Although the association remains positive, this study demonstrated the contextual difference among cultures, the Mediterranean cultures putting more emphasis on the face-to-face family relations. The impact of social networks on cognitive function has been documented even when the social networks increase only at later stages in life (see for example (Buchman et al., 2009). Studies looking at ethnic minority populations (Park et al., 2013) and also longitudinal studies from Korea (Youn et al., 2011) report similar positive associations between wellbeing/longevity/mortality/ and social networks as the above cited western-based longitudinal studies. However, a cohort study demonstrated specific gender/culture effects, with men benefiting more from social networks with key role involvement, specifically in rural areas (Takagi et al., 2013). Interestingly, this gender related social network/depressive symptoms protection was not found in a comparable population in the USA, highlighting the cultural/gender domains as they related to social network impact and mental wellbeing (Tiedt, 2013). In addition to gender issues, outdoor activities as part of the embedded social enhancement appear to be factors in need of further research (Sjogren and Stjernberg, 2010). However, the relationship of social engagement and cognitive function is complex and (Small et al., 2012) the cohort studies appear to support a dual hypothesis that: (a) lifestyle engagement may buffer some of the cognitive changes observed in late life, and (b) persons who are exhibiting poorer cognitive performance may also relinquish some social enhancements activities.

There is solid evidence that decreased mortality is associated with increased social engagement, as shown by a large meta-analysis of 148 studies, involving 308 849 participants (Holt-Lunstad et al., 2010). The Caerphilly Cohort Study of 3500 adults over 35 years (Elwood et al., 2013) demonstrated a significant protective effect on cognition for those adopting healthier lifestyles (healthier diet, higher physical activity, decrease smoking and alcohol). This cohort study (personal communication) also examined the social enhancement factors, but did not report results on this topic (Elwood et al., 2013). The association between social networks and socioeconomic status still remains a difficult challenge, since recent studies indicate that the two variables also affect the “built environment” of poorer older adults, including clutter and disorder, as well as riskier living conditions (Cornwell, 2014).

A recent report on SHARE data (N= 38777) examined social network activity and cognitive function, using word recall and self-rated cognitive wellbeing (Litwin and Stoeckel, 2015). Multivariate analyses demonstrated that social activity participation yielded stronger positive associations with word recall and self-rated memory than social networks alone. Thus, it appears that it is the activity of social networks that is contributing to both objective and subjective cognitive wellbeing later in life. Interestingly, the extent of the positive benefit of the activity count on cognition decreases when greater social network resources are available. This decreased benefit as more social networks are available may be related to the aging brain's capacity to deal with an increasing processing load, consistent with the cognitive reserve theory. However, it may also be related to the physiologic changes observed in white matter twining that occur with physiological aging as discussed in a recent study (Molesworth et al., 2015). The study showed that there is a large variation in white matter integrity with aging however, and thus other pathways and networks may be involved in translating social network activity into brain health protective mechanisms (see for example, (Gianaros et al., 2013; Kempermann, 2015; Verstynen et al., 2013).

Similar beneficial effect of social networks on subjective wellbeing from the ELSA study (N=4116) were found over a 6 year observational period (Rafnsson et al., 2015). The authors concluded that social network size and network contact frequency were positively and independently associated with satisfaction and quality of life, after controlling for confounding factors, including demographic characteristics, socioeconomic factors, and long-standing illness. However, unlike the Litwin study, there are no cognitive specific self-reported measurements.

3.3.2. Intervention studies

Table 4 summarizes the few intervention studies that have measured social enhancement and cognitive function. These studies can be broadly divided into the following categories: interventional studies focusing on tradition/cultural community interventions, technology based interventions and blended studies of ICT and community of practice interventions. All the studies in Table 4 are small in size and yet informative. All, except one, have showed that social enhancement positively impacts the sense of wellbeing and cognition. The positive effect of social enhancement interventions is also supported by (Verhaeghen et al., 2012), in the comparison of cognitive tests in the lab with real life where emotions and motivational factors enter as compensatory mechanisms, most of which are of social/motivational variety.

[Insert Table 4 about here]

The traditional/cultural interventions include exercise programs, dance and other community-based activities focusing on volunteering. For example, exercising with others to whom one has an emotionally meaningful connection could enhance aspects of exercise that are important to continued participation, such as interest, affect, and motivation (Christensen et al., 2006). Among the activities that can be considered as involving social networks are the culturally oriented dance groups that have sprung up worldwide in community-based programs for aging populations (see, for example, Horowitz and Chang, 2004; Osgood et al., 1990).

As shown in Table 4, Alpert et al. (2009) did not find any positive association between cognitive function and jazz group classes in older people living in communities. However, the study included only 13 participants and no controls. Another type of creative activity that involves social encounters is music. The impact of music on healthy aging is remarkable. An illustrative example is a randomized controlled study with over 1000 community dwelling 65+ elders, who participated in a chorale program (Cohen et al., 2006). This study involved a creative art activity conducted by trained professionals within a social enhancement group environment. Although cognition was not directly measured, social activity increased in the intervention group, as well as overall health, with a decrease in falls and hospitalizations.

Lifelong learning programs may also be considered within the social enrichment domains. These type of programs designed specifically for older adults show positive effects on sense of wellbeing and social engagement (Ballesteros et al., 2014b; Pao, 2014). Technology-based studies such as teleconferencing was the channel used by trained volunteers with urban elders recruited from primary care practices (Mountain et al., 2014). This pilot RCT study aimed to recruit individuals aged 74 + with a good cognitive function and living independently in order to establish whether a home-based intervention set up on telephone communication delivered through trained volunteers could improve or successfully maintain mental wellbeing of older people who were vulnerable and hard to reach. The study did not continue past 6 months post intervention, mainly due to attrition of volunteers, as well as participants who were uninterested in continuing to participate in the RCT. The methodological and operational difficulties identified in this English study appear to be the key finding also of a meta-analysis aimed at reducing self-reported social isolation, either by in person or by technology-assisted interventions (Medical Advisory Secretariat, 2008). The authors suggest that no specific conclusions can be drawn since the number of recruited participants was small and the interventions variable and the instruments measuring outcome were different. However, the simple technological means of reaching lonely older adults and having an impact on their degree of loneliness and perhaps cognitive function seems like an achievable goal.

Nistor et al. (2013) used a pilot technology-based virtual university community (vCoP) with a total of 133 participants, mostly female, ranging in age from 24 to 75+ with a high educational level. There were no cognitive enhancement measurements but the study measured two variables that are relevant to our review: technology anxiety and the time spent by the participants in the virtual community of practice, which may be considered a measure of social connectivity. The study showed low diversity in social connectivity among the participants in relation to age or educational level. For our purposes here, those of 65+, more than 50% of total participants, demonstrated equal level of social connectivity in vCoP.

In summary, all studies reviewed here, except one, demonstrated that social enhancement does contribute to healthier brain aging. Although none of the intervention studies were dedicated to exploring the mechanisms of social enhancement on cognitive brain aging, it appears that this effect is modulated through specific gene regulation expression involving the CNS and its interaction with neuroendocrine and sympathetic systems, more specifically the immune system (Cacioppo et al., 2015; Gianaros et al., 2013; Goossens et al., 2015; Molesworth et al., 2015; Slavich and Cole, 2013; Zhu et al., 2014). We are therefore, at the early staging of bridging the gap from observations and associations of social enhancement to specific neuro-psychosocial pathways that lead to healthy brain aging. However, from a public health perspective, we should be asking the question if this evidence is sufficient to guide public health policy regarding interventions involving social enhancement in our efforts to impact on healthy brain aging. Some researchers suggest that this degree of evidence is sufficient (Glasgow et al., 2012; Green and Glasgow, 2006; Kessler and Glasgow, 2011; Russell E. Glasgow, 2007).

4. Single-domain versus multi-domain training interventions: Rationale for combined interventions

Most of the intervention studies conducted so far focus on a single domain of training. There are few studies where the effects RCT interventions focus on combined multiple training domains (multi-domain). We now present the potential rationale for multi-domain cognitive training interventions and the key multi-domain interventions found in the literature.

From the previous sections, it appears evident that future RCT would profit from integrating different types and scope of activities designed to enhance cognition, while being embedded into a social engagement framework. Social engagement has, like aging itself, an individual trajectory that we have the capacity to influence through behavioral modification (Yokoyama et al., 2014).

In order to achieve social enhancement there is a need for building the appropriate societal infrastructures to allow aging individuals to participate in the meaningful activities so critical to cognitively healthy aging. This infrastructure would include establishing volunteering networks for older adults, environmentally-related activities and peer support groups among disabled/able older adults (Carlson, 2011; Geller and Zenick, 2005; Hofer and Busch, 2013; Steinerman et al., 2010; Styles, 2005; Wagenet and Pfeffer, 2007; Wright et al., 2003).

There are examples in the literature of how such social engagement supports healthy aging and cognition, for example, by encouraging volunteering in old age in elder-helping-elder programs (Butler and Eckart, 2007) or programs aiming at increasing informal social interactions, such as cultural programs (Cohen et al., 2006) or occupational therapy programs (Hay et al., 2002). These kinds of initiatives are not new to social networks, having a long tradition as Communities of Practice (CoP). These communities are defined as groups of people sharing goals, activities and experiences in the frame of a given practice over lengthy periods of time (Wenger, 1998; Wenger et al., 2011). Social relationship-based interventions represent a major opportunity to enhance not only quality of life but also overall survival (Holt-Lunstad et al., 2010).

Cognitive training, physical activity, social networking and healthy lifestyles may turn out to be the epigenetic modifiers of the psychosocial genetic aging of the human brain. If these lifestyle changes are implemented in a synchronous intervention in a practical feasible clinical trial (Ferrara et al., 2014; Tunis et al., 2003), there exists a potential of yielding a synergistic impact on the brain cognition maintenance that resembles the complex synergistic networks the aging brain naturally employs through neuroplasticity and scaffolding to maintain lifelong learning and health (Fissler et al., 2013). Creating a social climate of supportiveness for older individuals to have culturally appropriate and meaningful social networks could emerge as an optimal framework for preserving a healthy brain and body, complementing and supporting strategies to improve knowledge and behaviors on nutrition and physical exercise. The hypothesized combined impact of practical trials incorporating multi-domain interventions that resembles the complex synergistic networks the aging brain naturally employs may be the promising road for maintaining healthy brains and bodies (Hanleybrown and Mark Kramer, 2012).

Mental health promotion in older adults would require public policy initiatives supporting older adults in building and maintaining friend-based social networks, for example, by creating the infrastructure needed to initiate and encourage volunteering in old age in elder-helping-elder programs (Butler and Eckart, 2007). Evidence support the notion that participation in volunteer activities is associated with the satisfaction of accomplishing something, doing something meaningful, and of belonging (Miles et al., 1998). Government efforts to encourage volunteering in ecological connected projects (Wagenet and Pfeffer, 2007) are the kind of social enrichment networks for an aging population that appear to be supported by already existing research discussed in this paper. These potential community-based interventions can be studied utilizing the synergistic model of channeling change among older persons toward more socially enriched and active lifestyles (Hanleybrown et al., 2012; Piniewski et al., 2011).

A few multi-domain intervention studies have been published. Table 5 summarizes the main results. An early study investigated long-term effects of cognitive training or physical training on everyday activities in adults over 75 years of age (Oswald et al., 2006). There were three training conditions, cognitive training, psycho-educational training and physical training. Each training approach was carried out as a single-domain training protocol or as a combination of cognitive and physical training or psycho-educational and physical training. The best results were obtained in the combined cognitive training and physical training compared to the control group. Enhanced cognitive performance was maintained over 5 years after training with large effect sizes. The success might be in part due to the fact that some of the participants continued performing some of the exercises on their own. Participants also showed better every day functioning when assessed by a composite measure formed by self-rating and interviewer rating of independence, care services, and nursing services at home.

The MAX trial (Barnes et al., 2013) was set to examine the combined effects of physical plus mental activity on cognitive function in older adults. A total of 126 inactive, community residing older adults with cognitive complaints were included in the study. All participants engaged in home-based mental activity (1 hour/day, 3 days/week) plus class-based physical activity (1 h/day, 3 days/week) for 12 weeks and were randomized, to either mental activity intervention (intensive computer) or mental activity control (educational DVDs) plus exercise intervention (aerobic) or exercise control (stretching and toning). Global cognitive change was assessed by means of a comprehensive neuropsychological test battery. Results show that there were significant improvements in global cognition with no evidence of differences between intervention and active control groups. This may reflect practice effects or suggest that the amount of activity is more important than the type of activity in this type of population.

A randomized controlled four-group design (Shatil, 2013) - computer-based cognitive intervention, physical activity intervention, combined cognitive-physical activity intervention, and book reading and discussion control group - was set to evaluate the efficacy of cognitive training, physical activity training, and both combined to improve cognitive function in healthy seniors (mean age = 76.8 years). The study found that the two groups of older persons who engaged in cognitive training (separately or combined) significantly improved their memory, processing speed, eye-hand coordination, naming, and visuospatial processing ability scores. No such improvements were observed in the groups that did not engage in cognitive training, with the differences and improvements holding true not only between groups but also within groups. While the effects for speed of visuospatial information processing, visual scanning, and global visual memory were of medium size, those for naming and hand-eye coordination were large.

A study evaluating morphofunctional changes occurring in the brain of healthy elderly people who were stimulated for six months with a set of structured multimodal activities, including cognitive training/stimulation and aerobic training, found that such combination can be an effective strategy to counteract aging-related cognitive decline (Pieramico et al.).

Results from the Mayo Clinic Study of Aging (Geda et al., 2012), a population-based observational study of aging and MCI examined the impact of physical exercise and computer use during the study period, after adjusting for a third lifestyle factor (caloric intake), age, sex, education, medical comorbidity and depression. Results show that participants who engaged in both moderate physical exercise and computer use had significantly decreased odds of having MCI (odds ratio [95% confidence interval], 0.36 [0.20 to 0.68]) compared with the reference group. In the interaction analyses, there was an additive interaction ($p = .012$) but not multiplicative interaction ($p = .780$).

The results of a multimodal intervention (Li et al., 2014) set to investigate the functional plasticity in resting-state connectivity of the prefrontal cortex and the medial temporal lobe in older adults suggest that multi-domain intervention composed of cognitive training, Tai Chi exercise, and group counseling could postpone the effects of aging and improve the function of the regions that are most heavily influenced by aging, as well as help to preserve the brain and cognition during old age.

The simultaneous training of both cognitive and physical domains offers a greater potential on daily life functioning, which usually involves the recruitment of multiple abilities and resources rather than a single one. A recent study (Theill et al., 2013) involved 73 participants (age range 65 to 84) who either performed the simultaneous training, a single working memory training, or attended no training at all. Cognitive transfer tasks (selective attention, paired-associated learning, executive control, reasoning, memory span, and information processing speed) and verbal working memory training (computer-based n-back training and serial position training) were done on a computer platform. During the motor-cognitive dual task, researchers investigated gait performance under single- and dual- task conditions while performing a working memory task. Participants walked at their normal, self-selected speed over a distance of 20 meters, with a turning point at a cone after 10 meters. Under dual task condition, participants performed a working memory task at the same time, by counting backwards in steps of seven, beginning alternately with 501, 502, or 503. The results show similar training progress and larger improvements in the executive control task for both training groups when compared to the passive control group. However, the simultaneous training resulted in larger improvements compared to the single cognitive training in the paired-associates task and was able to reduce the step-to-step variability during the motor-cognitive dual task when compared to the single cognitive training and the passive control group.

A recent longitudinal study tested the hypothesis that learning new skills that activate working memory, episodic memory and reasoning would improve cognitive function in older adults (Park et al., 2014). Three groups were tested in the productive training engagement conditions (the quilting training group, the digital photograph training group and the dual or the multi-modal condition that learn both photo and quilt). In all conditions, older participants were involved for 3-months in learning these new skills. A fourth social control group was engaged in social activities (as cooking, watching movies, going on regular weekly field-trips) for the same amount of time as the other groups but did not learn new skills. There were also a placebo condition and a no-treatment condition. The results suggest that sustained engagement in cognitively demanding, novel activities enhances memory function in older adulthood compared with social and placebo conditions. Participants in the placebo (baseline) group had limited social contact as they worked alone on tasks that they believed improve cognition. Importantly, the three productive-engagement groups showed better episodic memory than the social group. The result suggests that the acquisition of a demanding new skill improved memory while socializing did not. More detailed comparisons showed that the digital photo training group and the dual condition group (photo and quilting) improved memory significantly whereas the effect was not significant in the quilting group. The dual training condition did not produce better results than the photography group alone. These findings are worth further investigation as they suggest the importance of engagement in novel and challenging learning activities to improve memory in older adults. Interestingly, the study showed no memory improvement of social engagement, which might have been a confusing variable in other previous studies. At this point, it is not clear why multi-domain training did not produce better results than quilting training alone. More studies on multi-domain training (photo and quilting) and on social engagement are needed before these results could be accepted as conclusive.

The results of a recent study (Rahe et al., 2015) suggest that combined cognitive and physical training might lead to stronger long-term effects on attention. Yet, the difference between the group offered cognitive training and the group engaged in the combined training was only evident at follow-up, suggesting that effects cannot be interpreted as a direct consequence of combined training. Indeed, the authors suggest that they may have been related to sustained physical activity after the end of the intervention, opening new avenues for research and intervention.

Exceptionally powerful mobile technology has opened a new landscape of possibilities. This has been reflected by major funding initiatives, for instance from the European Union (EU). Within the Ambient Assisted Living Joint Program (http://www.aal-europe.eu/about/), several EU funding calls have led to a substantial number of different consortia, in which ICT topics were addressed. Most of these consortia have not provided original publications of the results yet.

Long Lasting Memories (LLM) (http://www.longlastingmemories.eu/), an EU funded project with 5 pilots in 4 European countries and languages (Greek, Spanish, German and French) has addressed the three areas (Frantzidis et al., 2014) and has been presented as a unified solution for cognitive and physical health for senior citizens (http://www.longlastingmemories.eu/). The cognitive program was designed to train processing of auditory sensory information, memory, attention and learning. Physical training was performed through the FitForAll (FFA) platform, a gaming environment-based on the Nintendo Wii Remote and Balance Board, with exercises aimed to enhance body flexibility and strength but also physical endurance through aerobic training. The project also provides means to connect to family and friends, care and medical services and alarm and rescue center. Using quantitative electroencephalography, results published (Frantzidis et al., 2014) from the Greek pilot with 103 participants (53 in the training group and 50 in the active group) showed that the LLM intervention was effective in increasing synchronization across the two hemispheres at rest when compared to an active control group, a result that might have clinical relevance, since disturbance of long-range connections among distant brain regions (anterior-posterior) is one of the main characteristics of pathological aging. In Spain, results from the study with 267 healthy and MCI participants (Franco et al., 2013) showed an improvement after the LLM training in global cognitive function, in verbal memory, processing speed, episodic memory and depressive symptoms. The increase of age was associated with a decreased in the improvement of cognitive performance.

The AGNES project (User-sensitive home-based system for successful Ageing in a Networked Society) was one of this ICT European initiatives conducted to investigate the potential of technological mediated social networks for improving quality of life of older adults living at home (Ballesteros et al., 2014b; Peter et al., 2013). In AGNES, a home-based system allows older adults to connect with their family and friends over the Internet. The system used ambient displays, tangible interfaces and wearable devices for interaction with the network, and other sensors for generating information on the older adult for the significant persons. The use of the AGNES system had some positive effects on the mental state of the users' group compared to the control group. The study suggests the potential of the system to improve older adults' perceived wellbeing. However, more research is needed to determine the effects of AGNES as a tool to maintain mental health and independent living in aging. A greater variety of psychological tests and larger samples of older adults randomly assigned to experimental and active control groups would be important to validate the preliminary results.

[Insert Table 5 about here]

In summary, the studies reviewed above revealed that the multi-domain or combined training seems a promising way to promote cognitive maintenance and independent living among older adults. However, it is premature to draw solid conclusions from the available data, leading us to conclude that there is a strong need to move toward multi-domain robust studies specifically designed to measure cognitive aging within socially embedded enhancement infrastructures. In addition, multi-domain studies may allow us an opportunity to decipher the "paradox" between the documented levels of neuropathology on the one hand and the level of generally lower than expected cognitive impairment observed clinically (Bennett et al., 2014; Carstensen et al., 2011)

5. Conclusions and future directions

The studies reviewed above suggest that there are protective, although moderate positive effects of physical activity, cognitive training and social engagement on reducing cognitive decline in older adults. Some of the reviewed interventions reflect real life activities, which already qualify as exemplary scenarios for a multi-domain approach.

Amateur dance (Kattenstroth et al., 2013) as well as Tai Chi combined physical exercise, cognitive practice and social engagement. These activities provide paradigmatic models for future interventions. Dance movement combines physical activity with sensorimotor and cognitive engagement, as well as other social and emotional aspects, which creates synergies protecting older adults from physical and cognitive decline. Similarly, Tai Chi has shown a significant capacity to improve physical function and reduce the risk of falls, depression and anxiety (Rogers et al., 2009), as well as to ameliorate cognitive functions and to increase brain volume (Mortimer et al., 2012). Future studies need to control for the selection of participants more closely and to determine the specific contributions of physical activity in a multi-domain setting.

More structured randomized controlled multi-domain intervention studies would be useful to evaluate the currently unresolved questions of the relative contribution and the possible synergist effect of concomitant stimulation of cognitive capacity through diverse neural networks. These studies need to use larger samples and to include two control groups, an active group and a non-contact control group to account for the issues of retest effects, as well as issues related to expectations (motivation/placebo effects) and the effect of social contact with the experimenters (for an interesting discussion, see (Boot et al., 2013b). The inclusion in the same study of these two types of control groups would allow for the comparison of the performance on the outcomes of the trained group (or groups) with active and passive controls as well as the performance of each type of control group in the study outcomes.

In addition to methodological and study design considerations, our review suggests that researchers, health practitioners, community action groups and policy makers should consider the use of synergistic multi-domain practical interventions in real life scenarios, in order to be able to study the influence of meaningful social engagements as a separate factor in cognitive healthy aging. One additional lesson learned from the clinical trials is that the non-intervention control group is susceptible to very high attrition rates and given the body of knowledge on the usefulness of social interventions on maintenance of cognition, it may not be entirely ethical at this point, as we have learned from cancer treatment trials. On the other hand, the use of blended social enhancement activities that involve technological and social channels does not seem to affect the recruitment or retention of older persons, despite concerns to that effect. Information and communication technologies provide great opportunities and challenges to improve or facilitate the implementation of multi-domain interventions in aging. Technology based approaches offer a large array of possibilities such as the acquisition and recording of the user's data with or without their direct participation, delivering a specific training component online such as in video games for cognitive training, coaching the user, evaluating the results or any combination of these functionalities.

Multi-domain blended interventions that are embedded in social enhancement networks, cognitive and physical stimulation seem to show promise for supporting a higher cognitive and daily activity function, despite the physiological aging of the brain. Our review suggests that there are challenges inherent in the design and implementation of multi-domain synergistic trials, which may be classified in the following three categories: 1) the design and application of complex statistical tools for tackling multi-domain synchronous interventions with large number of outcome variables; 2) the definition of outcome measures that have functional significance in the life of older adults; and 3) the development of translational research methodologies based on results from controlled laboratory studies to scenarios of practical community-based interventions.

Therefore, further research would benefit from embracing the complex and promising basic neuroscience findings, and consider the structuring of synergistic multi-domain interventions that can be embedded in the within the activities of daily living of a fast growing aging population. Today there is a need for well-designed large-scale longitudinal studies, designed to investigate the potential superior enhancements and daily life performance of older adults with combined cognitive training, physical activity and social interaction.

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Figure Captions

Figure 1. Overview of individual components of multi-domain interventions for healthy brain aging: A selection of possible elements for cognitive training and physical activity embedded in a social environment, depending on specific biological factors.

References

Achtman, R.L., Green, C.S., D., B., 2008. Video games as a tool to train visual skills Restorative Neurology and Neuroscience, 435-446.

Ackerman, P.L., Kanfer, R., Calderwood, C., 2010. Use it or lose it? Wii brain exercise practice and reading for domain knowledge. Psychol Aging 25, 753-766.

Allaire, J.C., McLaughin, A.C., Trujillo, A., Whitlock, L.A., LaPorte, L., Gandy, M., 2013. Successful aging through digital games: Socioemotional differences between older adult gamers and non-gamers. Computers in Behavior 29, 1302-1306.

Alpert, P.T., Miller, S.K., Wallmann, H., Havey, R., Cross, C., Chevalia, T., Gillis, C.B., Kodandapari, K., 2009. The effect of modified jazz dance on balance, cognition, and mood in older adults. J Am Acad Nurse Pract 21, 108-115.

Amieva, H., Mokri, H., Le Goff, M., Meillon, C., Jacqmin-Gadda, H., Foubert-Samier, A., Orgogozo, J.M., Stern, Y., Dartigues, J.F., 2014. Compensatory mechanisms in higher-educated subjects with Alzheimer's disease: a study of 20 years of cognitive decline. Brain 137, 1167-1175.

Amieva, H., Stoykova, R., Matharan, F., Helmer, C., Antonucci, T.C., Dartigues, J.F., 2010. What aspects of social network are protective for dementia? Not the quantity but the quality of social interactions is protective up to 15 years later. Psychosom Med 72, 905-911.

Angevaren, M., Aufdemkampe, G., Verhaar, H.J., Aleman, A., Vanhees, L., 2008. Physical activity and enhanced fitness to improve cognitive function in older people without known cognitive impairment. Cochrane Database Syst Rev, CD005381.

Anguera, J.A., Boccanfuso, J., Rintoul, J.L., Al-Hashimi, O., Faraji, F., Janowich, J., Kong, E., Larraburo, Y., Rolle, C., Johnston, E., Gazzaley, A., 2013. Video game training enhances cognitive control in older adults. Nature 501, 97-101.

Backman, L., Nyberg, L., Lindenberger, U., Li, S.C., Farde, L., 2006. The correlative triad among aging, dopamine, and cognition: current status and future prospects. Neurosci Biobehav Rev 30, 791-807.

Baddeley, A., 2000. The episodic buffer: a new component of working memory? Trends Cogn Sci 4, 417-423.

Baddeley, A., Hitch, G., 1974. Working memory, in: Bower, G.H. (Ed.), The psychology of learning and motivation: Advances in research and theory. New York: Academic Press, pp. 47-89.

Ball, K., Berch, D.B., Helmers, K.F., Jobe, J.B., Leveck, M.D., Marsiske, M., Morris, J.N., Rebok, G.W., Smith, D.M., Tennstedt, S.L., Unverzagt, F.W., Willis, S.L., 2002. Effects of cognitive training interventions with older adults: a randomized controlled trial. JAMA 288, 2271-2281.

Ball, K., Edwards, J.D., Ross, L.A., 2007. The impact of speed of processing training on cognitive and everyday functions. J Gerontol B Psychol Sci Soc Sci 62 Spec No 1, 19-31.

Ballesteros, S., Bischof, G.N., Goh, J.O., Park, D.C., 2013a. Neural correlates of conceptual object priming in young and older adults: an event-related functional magnetic resonance imaging study. Neurobiol Aging 34, 1254-1264.

Ballesteros, S., Mayas, J., Prieto, A., Toril, P., Pita, C., Laura Pde, L., Reales, J.M., Waterworth, J.A., 2015. A randomized controlled trial of brain training with non-action video games in older adults: results of the 3-month follow-up. Front Aging Neurosci 7, 45.

Ballesteros, S., Mayas, J., Reales, J.M., 2013b. Does a physically active lifestyle attenuate decline in all cognitive functions in old age? Curr Aging Sci 6, 189-198.

Ballesteros, S., Prieto, A., Mayas, J., Toril, P., Pita, C., Ponce de Leon, L., Reales, J.M., Waterworth, J., 2014a. Brain training with non-action video games enhances aspects of cognition in older adults: a randomized controlled trial. Front Aging Neurosci 6, 277.

Ballesteros, S., Toril, P., Mayas, J., Reales, J.M., Waterworth, J., 2014b. An ICT-mediated social network in support of successful ageing. Gerontechnology 13, 39-48.

Baltes, P.B., Freund, A.M., Li., S.-C., 2005. The psychological science of human ageing, in: Johnson, M.L. (Ed.), The Cambridge Handbook of Age and Ageing. Cambridge University Press, Cambridge, UK, pp. 47-71.

Bamidis, P.D., Vivas, A.B., Styliadis, C., Frantzidis, C., Klados, M., Schlee, W., Siountas, A., Papageorgiou, S.G., 2014. A review of physical and cognitive interventions in aging. Neurosci Biobehav Rev 44, 206-220.

Barnes, D.E., Santos-Modesitt, W., Poelke, G., Kramer, A.F., Castro, C., Middleton, L.E., Yaffe, K., 2013. The Mental Activity and eXercise (MAX) trial: a randomized controlled trial to enhance cognitive function in older adults. JAMA Intern Med 173, 797-804.

Barulli, D., Stern, Y., 2013. Efficiency, capacity, compensation, maintenance, plasticity: emerging concepts in cognitive reserve. Trends Cogn Sci 17, 502-509.

Basak, C., Boot, W.R., Voss, M.W., Kramer, A.F., 2008. Can training in a real-time strategy video game attenuate cognitive decline in older adults? Psychol Aging 23, 765-777.

Bavelier, D., Green, C.S., Pouget, A., Schrater, P., 2012. Brain plasticity through the life span: learning to learn and action video games. Annu Rev Neurosci 35, 391-416.

Belchior, P.D.C., 2008. Cognitive training with video games to improve driving skills and driving safety among older adults [dissertation]. Dissertation Abstract International: The Sciences and Engineering, pp. 68(69 –B).

Belleville, S., 2008. Cognitive training for persons with mild cognitive impairment. Int Psychogeriatr 20, 57-66.

Bennett, D.A., Arnold, S.E., Valenzuela, M.J., Brayne, C., Schneider, J.A., 2014. Cognitive and social lifestyle: links with neuropathology and cognition in late life. Acta Neuropathol 127, 137-150.

Benyamini, Y., 2008. Self-ratings of health and longevity: A health psychologist's viewpoint on epidemiological findings. The European Journal Of Health Psychologist 10.

Berchicci, M., Lucci, G., Perri, R.L., Spinelli, D., Di Russo, F., 2014. Benefits of physical exercise on basic visuo-motor functions across age. Front Aging Neurosci 6, 48.

Berkman, L.F., Glass, T., Brissette, I., Seeman, T.E., 2000. From social integration to health: Durkheim in the new millennium. Soc Sci Med 51, 843-857.

Berkman, L.F., Syme, S.L., 1979. Social networks, host resistance, and mortality: a nine-year follow-up study of Alameda County residents. Am J Epidemiol 109, 186-204.

Berry, A.S., Zanto, T.P., Clapp, W.C., Hardy, J.L., Delahunt, P.B., Mahncke, H.W., Gazzaley, A., 2010. The influence of perceptual training on working memory in older adults. PLoS One 5, e11537.

Bherer, L., Kramer, A.F., Peterson, M.S., Colcombe, S., Erickson, K., Becic, E., 2005. Training effects on dual-task performance: are there age-related differences in plasticity of attentional control? Psychol Aging 20, 695-709.

Bherer, L., Kramer, A.F., Peterson, M.S., Colcombe, S., Erickson, K., Becic, E., 2006. Testing the limits of cognitive plasticity in older adults: application to attentional control. Acta Psychol (Amst) 123, 261-278.

Bialystok, E., Craik, F.I., Luk, G., 2012. Bilingualism: consequences for mind and brain. Trends Cogn Sci 16, 240-250.

Bialystok, E., Craik, F.I.M., 2006. Lifespan cognition: Mechanisms of change. Oxford University Press.

Bodde, A.E., Shippee, N.D., May, C.R., Mair, F.S., Erwin, P.J., Murad, M.H., Montori, V.M., 2013. Examining health promotion interventions for patients with chronic conditions using a novel patient-centered complexity model: protocol for a systematic review and meta-analysis. Syst Rev 2, 29.

Boot, W.R., Champion, M., Blakely, D.P., Wright, T., Souders, D.J., Charness, N., 2013a. Video games as a means to reduce age-related cognitive decline: attitudes, compliance, and effectiveness. Front Psychol 4, 31.

Boot, W.R., Kramer, A.F., Simons, D.J., Fabiani, M., Gratton, G., 2008. The effects of video game playing on attention, memory, and executive control. Acta Psychol (Amst) 129, 387-398.

Boot, W.R., Simmons, D.J., Stothart, C., Stutts, C., 2013b. The pervasive problem with placebos in psychology. Why active control groups are not sufficient to rule out placebo effects. Perspect. Psychol. Sci. 8, 445-454.

Bozoki, A., Radovanovic, M., Winn, B., Heeter, C., Anthony, J.C., 2013. Effects of a computer-based cognitive exercise program on age-related cognitive decline. Arch Gerontol Geriatr 57, 1-7.

Brookmeyer, R., Evans, D.A., Hebert, L., Langa, K.M., Heeringa, S.G., Plassman, B.L., Kukull, W.A., 2011. National estimates of the prevalence of Alzheimer's disease in the United States. Alzheimers Dement 7, 61-73.

Buchman, A.S., Boyle, P.A., Wilson, R.S., Fleischman, D.A., Leurgans, S., Bennett, D.A., 2009. Association between late-life social activity and motor decline in older adults. Arch Intern Med 169, 1139-1146.

Buitenweg, J.I.V., Murre, J.M.J., Ridderinkhof, K.R., 2012. Brain training in progress: a review of trainability in healthy seniors. Frontiers in Human Neuroscience 6.

Buschkuehl, M., Jaeggi, S.M., Hutchison, S., Perrig-Chiello, P., Dapp, C., Muller, M., Breil, F., Hoppeler, H., Perrig, W.J., 2008. Impact of working memory training on memory performance in old-old adults. Psychol Aging 23, 743-753.

Butler, S.S., 2006. Evaluating the Senior Companion Program: a mixed-method approach. J Gerontol Soc Work 47, 45-70.

Butler, S.S., Eckart, D., 2007. Civic engagement among older adults in a rural community: A case study of the senior companion program. Journal of Community Practice 15, 77–98.

Cacciopo, J.T., Hughes, M.E., Waite, L.J., Hawkley, L.C., Thisted, R.A., 2006. Loneliness as a specific risk factor for depressive symptoms: Cross-sectional and longitudinal analyses. Psychol. Aging 21, 140-151.

Cacioppo, S., Grippo, A.J., London, S., Goossens, L., Cacioppo, J.T., 2015. Loneliness: clinical import and interventions. Perspectives on psychological science : a journal of the Association for Psychological Science 10, 238-249.

Cain, M.S., Landau, A.N., Shimamura, A.P., 2012. Action video game experience reduces the cost of switching tasks. Attention Perception & Psychophysics 74, 641-647.

Carlson, M.C., 2011. Promoting Healthy, Meaningful Aging Through Social Involvement: Building an Experience Corps, Cerebrum: the Dana Forum on Brain Science 2011.

Carlson, M.C., Parisi, J.M., Xia, J., Xue, Q.L., Rebok, G.W., Bandeen-Roche, K., Fried, L.P., 2012. Lifestyle activities and memory: variety may be the spice of life. The women's health and aging study II. J Int Neuropsychol Soc 18, 286-294.

Carstensen, L.L., 1992. Motivation for social contact across the life span: a theory of socioemotional selectivity. Nebr Symp Motiv 40, 209-254.

Carstensen, L.L., Cone, J.D., 1983. Social desirability and the measurement of psychological well-being in elderly persons. Journals of Gerontology 38, 713-715.

Carstensen, L.L., Fung, H.H., Charles, S.T., 2003. Socioemotional selectivity theory and the regulation of emotion in the second half of life. Motivation and Emotion 27, 103-123.

Carstensen, L.L., Turan, B., Scheibe, S., Ram, N., Ersner-Hershfield, H., Samanez-Larkin, G.R., Brooks, K.P., Nesselroade, J.R., 2011. Emotional experience improves with age: evidence based on over 10 years of experience sampling. Psychol Aging 26, 21-33.

Cassavaugh, N.D., Kramer, A.F., 2009. Transfer of computer-based training to simulated driving in older adults. Applied Ergonomics 40, 943-952.

Charles, S.T., Carstensen, L.L., 2010. Social and emotional aging. Annual Review of Psychology 61, 383-409.

Cheng, Y., Wu, W., Feng, W., Wang, J., Chen, Y., Shen, Y., Li, Q., Zhang, X., Li, C., 2012. The effects of multi-domain versus single-domain cognitive training in non-demented older people: a randomized controlled trial. BMC Med 10, 30.

Chisholm, J.D., Kingstone, A., 2012. Improved top-down control reduces oculomotor capture: The case of action video game players (vol 74, pg 257, 2012). Attention Perception & Psychophysics 74, 1074-1074.

Christensen, H., Batterham, P.J., Mackinnon, A.J., Anstey, K.J., Wen, W., Sachdev, P.S., 2009. Education, atrophy, and cognitive change in an epidemiological sample in early old age. Am J Geriatr Psychiatry 17, 218-226.

Christensen, U., Schmidt, L., Budtz-Jorgensen, E., Avlund, K., 2006. Group cohesion and social support in exercise classes: results from a danish intervention study. Health Educ Behav 33, 677-689.

Clare, L., Woods, R.T., 2004. Cognitive training and cognitive rehabilitation for people with early-stage Alzheimer's disease: A review. Neuropsychological Rehabilitation 14, 385-401.

Clark, J.E., Lanphear, A.K., Riddick, C.C., 1987. The Effects of Videogame Playing on the Response Selection Processing of Elderly Adults. Journals of Gerontology 42, 82-85.

Cohen, G.D., Perlstein, S., Chapline, J., Kelly, J., Firth, K.M., Simmens, S., 2006. The impact of professionally conducted cultural programs on the physical health, mental health, and social functioning of older adults. Gerontologist 46, 726-734.

Colcombe, S., Kramer, A.F., 2003. Fitness effects on the cognitive function of older adults: a meta-analytic study. Psychol Sci 14, 125-130.

Cole, S.W., 2014. Human social genomics. PLoS Genet 10, e1004601.

Colzato, L.S., van Leeuwen, P.J., van den Wildenberg, W.P., Hommel, B., 2010. DOOM'd to switch: superior cognitive flexibility in players of first person shooter games. Front Psychol 1, 8.

Cornwell, E.Y., 2014. Social resources and disordered living conditions: Evidence from a national sample of community-residing older adults. Research on Aging 36, 399-430.

Coubard, O.A., Duretz, S., Lefebvre, V., Lapalus, P., Ferrufino, L., 2011. Practice of contemporary dance improves cognitive flexibility in aging. Front Aging Neurosci 3, 13.

Craik, F.I.M., Winocur, G., Palmer, H., Binns, M.A., Edwards, M., Bridges, K., Glazer, P., Chavannes, R., Stuss, D.T., 2007. Cognitive rehabilitation in the elderly: Effects on memory. Journal of the International Neuropsychological Society 13, 132-142.

Currie, G., Dingwall, R., Kitchener, M., Waring, J., 2012. Let's dance: Organization studies, medical sociology and health policy. Soc Sci Med 74, 273-280.

Daffner, K.R., 2010. Promoting successful cognitive aging: a comprehensive review. J Alzheimers Dis 19, 1101-1122.

Dahlin, E., Neely, A.S., Larsson, A., Backman, L., Nyberg, L., 2008a. Transfer of learning after updating training mediated by the striatum. Science 320, 1510-1512.

Dahlin, E., Nyberg, L., Backman, L., Neely, A.S., 2008b. Plasticity of executive functioning in young and older adults: Immediate training gains, transfer, and long-term maintenance. Psychology and Aging 23, 720-730.

Dechamps, A., Alban, R., Jen, J., Decamps, A., Traissac, T., Dehail, P., 2010. Individualized cognition-action intervention to prevent behavioral disturbances and functional decline in institutionalized older adults: a randomized pilot trial. Int J Geriatr Psychiatry 25, 850-860.

Dennis, N.A., Cabeza, R., 2008. Neuroimageing of healthy cognitive ageing, in: Craik, F.I.M., Salthouse, T.A. (Eds.), The handbook of ageing and cognition. Psychology Press, New York, pp. 1-54.

DiNapoli, E.A., Wu, B., Scogin, F., 2014. Social isolation and cognitive function in Appalachian older adults. Research on Aging 36, 161-179.

Dinse, H.R., 2005. Treating the aging brain: cortical reorganization and behavior. Re-engineering of the Damaged Brain and Spinal Cord: Evidence-Based Neurorehabilitation 93, 79-84.

Dodge, H.H., Ybarra, O., Kaye, J.A., 2014. Tools for advancing research into social networks and cognitive function in older adults. Int Psychogeriatr 26, 533-539.

Doja, A., Eady, K., Horsley, T., Bould, M., Victor, J., Sampson, M., 2014. The h- index in medical education: an analysis of medical education journal editorial boards. BMC Med Educ 14, 251.

Drew, D., Waters, J., 1986. Video games: Utilization of a novel strategy to improve perceptual motors skills and cognitive functioning in the no institutionalized elderly. Cognit. Rehabil. 4, 26-31.

Dunbar, R., 1998. The Social Brain Hypothesis. Evolutionary Anthropology, 178-190.

Dunton, G.F., Atienza, A.A., Castro, C.M., King, A.C., 2009. Using ecological momentary assessment to examine antecedents and correlates of physical activity bouts in adults age 50+ years: a pilot study. Ann Behav Med 38, 249-255.

Dustman, R.E., Emmerson, R.Y., Steinhaus, L.A., Shearer, D.E., Dustman, T.J., 1992. The effects of videogame playing on neuropsychological performance of elderly individuals. J Gerontol 47, P168-171.

Edwards, J.D., Wadley, V.G., Myers, R.S., Roenker, D.L., Cissell, G.M., Ball, K.K., 2002. Transfer of a speed of processing intervention to near and far cognitive functions. Gerontology 48, 329-340.

Edwards, J.D., Wadley, V.G., Vance, D.E., Wood, K., Roenker, D.L., Ball, K.K., 2005. The impact of speed of processing training on cognitive and everyday performance. Aging & Mental Health 9, 262-271.

Eisele, M., Zimmermann, T., Kohler, M., Wiese, B., Heser, K., Tebarth, F., Weeg, D., Olbrich, J., Pentzek, M., Fuchs, A., Weyerer, S., Werle, J., Leicht, H., Konig, H.H., Luppa, M., Riedel-Heller, S., Maier, W., Scherer, M., 2012. Influence of social support on cognitive change and mortality in old age: results from the prospective multicentre cohort study AgeCoDe. BMC Geriatr 12, 9.

Elwood, P., Galante, J., Pickering, J., Palmer, S., Bayer, A., Ben-Shlomo, Y., Longley, M., Gallacher, J., 2013. Healthy lifestyles reduce the incidence of chronic diseases and dementia: evidence from the Caerphilly cohort study. PLoS One 8, e81877.

Erickson, K.I., Colcombe, S.J., Wadhwa, R., Bherer, L., Peterson, M.S., Scalf, P.E., Kim, J.S., Alvarado, M., Kramer, A.F., 2007. Training-induced plasticity in older adults: Effects of training on hemispheric asymmetry. Neurobiol Aging 28, 272-283.

Erickson, K.I., Creswell, J.D., Verstynen, T.D., Gianaros, P.J., 2014. Health Neuroscience: Defining a New Field. Curr Dir Psychol Sci 23, 446-453.

Erickson, K.I., Gildengers, A.G., Butters, M.A., 2013. Physical activity and brain plasticity in late adulthood. Dialogues Clin Neurosci 15, 99-108.

Erickson, K.I., Voss, M.W., Prakash, R.S., Basak, C., Szabo, A., Chaddock, L., Kim, J.S., Heo, S., Alves, H., White, S.M., Wojcicki, T.R., Mailey, E., Vieira, V.J., Martin, S.A., Pence, B.D., Woods, J.A., McAuley, E., Kramer, A.F., 2011. Exercise training increases size of hippocampus and improves memory. Proceedings of the National Academy of Sciences of the United States of America 108, 3017-3022.

Ewing, G., 2012. From Neuroplasticity to Scaffolding: A Giant Step for Cognitive Aging Research? International Journal of User-Driven Healthcare 2, 24-43.

Feng, J., Spence, I., Pratt, J., 2007. Playing an action video game reduces gender differences in spatial cognition. Psychol Sci 18, 850-855.

Fernández-Ballesteros, R., Molina, M.Á., Schettini, R., del Rey, Á.L., 2012. Promoting active aging through university programs for older adults: An evaluation study GeroPsych: The Journal of Gerontopsychology and Geriatric Psychiatry 25, 145.

Ferrara, A., Hedderson, M.M., Albright, C.L., Brown, S.D., Ehrlich, S.F., Caan, B.J., Sternfeld, B., Gordon, N.P., Schmittdiel, J.A., Gunderson, E.P., Mevi, A.A., Tsai, A.L., Ching, J., Crites, Y., Quesenberry, C.P., Jr., 2014. A pragmatic cluster randomized clinical trial of diabetes prevention strategies for women with gestational diabetes: design and rationale of the Gestational Diabetes' Effects on Moms (GEM) study. BMC Pregnancy Childbirth 14, 21.

Fiori, K.L., Jager, J., 2012. The impact of social support networks on mental and physical health in the transition to older adulthood. International Journal of ehavioral Development 36, 117-129.

Fissler, P., Küster, O., Schlee, W., Kolassa, I.-T., 2013. Novelty Interventions to Enhance Broad Cognitive Abilities and Prevent Dementia: Synergistic Approaches for the Facilitation of Positive Plastic Change, in: Michael, M.N., Merzenich, M., Thomas, M.V.V.T. (Eds.), Progress in Brain Research. Elsevier, pp. 403-434.

Fosshage, J.L., 2004. The explicit and implicit dance in psychoanalytic change. J Anal Psychol 49, 49-65.

Franco, M., Palau, F.G., Jiménez, F., Parra, E., Losada, R., Cid, T., Canejo, P.G., Bernate, M., Toribio, J.M., Ruiz, Y., Solis, A., Bueno, Y., 2013. Examining the effectiveness of a new software technology platform for cognitive and physical training in mild cognitive impairment and healthy older adults. Converging Clinical and Engineering Research on Neurorehabilitation Biosystems & Biorobotics 1, 917-921.

Frantzidis, C.A., Ladas, A.K., Vivas, A.B., Tsolaki, M., Bamidis, P.D., 2014. Cognitive and physical training for the elderly: evaluating outcome efficacy by means of neurophysiological synchronization. Int J Psychophysiol 93, 1-11.

Fratiglioni, L., Wang, H.X., Ericsson, K., Maytan, M., Winblad, B., 2000. Influence of social network on occurrence of dementia: a community-based longitudinal study. Lancet 355, 1315-1319.

FUTURAGE European project, 2011. The FUTURAGE Road Map for European Aging Research.

Gates, N., Valenzuela, M., 2010. Cognitive Exercise and Its Role in Cognitive Function in Older Adults. Current Psychiatry Reports 12, 20-27.

Geda, Y.E., Silber, T.C., Roberts, R.O., Knopman, D.S., Christianson, T.J., Pankratz, V.S., Boeve, B.F., Tangalos, E.G., Petersen, R.C., 2012. Computer activities, physical exercise, aging, and mild cognitive impairment: a population-based study. Mayo Clin Proc 87, 437-442.

Geller, A.M., Zenick, H., 2005. Aging and the environment: a research framework. Environ Health Perspect 113, 1257-1262.

Gianaros, P.J., Marsland, A.L., Sheu, L.K., Erickson, K.I., Verstynen, T.D., 2013. Inflammatory pathways link socioeconomic inequalities to white matter architecture. Cerebral Cortex 23, 2058-2071.

Glasgow, R.E., Vinson, C., Chambers, D., Khoury, M.J., Kaplan, R.M., Hunter, C., 2012. National Institutes of Health approaches to dissemination and implementation science: current and future directions. Am J Public Health 102, 1274-1281.

Goh, J.O., 2011. Functional Dedifferentiation and Altered Connectivity in Older Adults: Neural Accounts of Cognitive Aging. Aging Dis 2, 30-48.

Goh, J.O., Park, D.C., 2009. Neuroplasticity and cognitive aging: the scaffolding theory of aging and cognition. Restor Neurol Neurosci 27, 391-403.

Goldstein, J., Cajko, L., Oosterbroek, M., Michielsen, M., Van Houten, O., Saavedra, F., 1997. Videogame and elderly. Social Behavior and Personality 25, 345-352.

Goossens, L., van Roekel, E., Verhagen, M., Cacioppo, J.T., Cacioppo, S., Maes, M., Boomsma, D.I., 2015. The genetics of loneliness: linking evolutionary theory to genome-wide genetics, epigenetics, and social science. Perspectives on psychological science : a journal of the Association for Psychological Science 10, 213-226.

Gopher, D., Weil, M., Bareket, T., 1994. Transfer of skill from a computer game trainer to flight. Human Factors 36, 387 - 405.

Granacher, U., Muehlbauer, T., Bridenbaugh, S.A., Wolf, M., Roth, R., Gschwind, Y., Wolf, I., Mata, R., Kressig, R.W., 2012. Effects of a salsa dance training on balance and strength performance in older adults. Gerontology 58, 305-312.

Gray, W.D., 2008. Cognitive architectures: choreographing the dance of mental operations with the task environment. Hum Factors 50, 497-505.

Green, C.S., Bavelier, D., 2003. Action video game modifies visual selective attention. Nature 423, 534-537.

Green, C.S., Bavelier, D., 2006. Effect of action video games on the spatial distribution of visuospatial attention. J Exp Psychol Hum Percept Perform 32, 1465-1478.

Green, C.S., Bavelier, D., 2008. Exercising your brain: a review of human brain plasticity and training-induced learning. Psychol Aging 23, 692-701.

Green, C.S., Li, R.J., Bavelier, D., 2010. Perceptual Learning During Action Video Game Playing. Topics in Cognitive Science 2, 202-216.

Green, L.W., Glasgow, R.E., 2006. Evaluating the relevance, generalization, and applicability of research: issues in external validation and translation methodology. Evaluation & the health professions 29, 126-153.

Gross, A.L., Parisi, J.M., Spira, A.P., Kueider, A.M., Ko, J.Y., Saczynski, J.S., Samus, Q.M., Rebok, G.W., 2012. Memory training interventions for older adults: a meta-analysis. Aging Ment Health 16, 722-734.

Gross, A.L., Rebok, G.W., 2011. Memory training and strategy use in older adults: results from the ACTIVE study. Psychol Aging 26, 503-517.

Gurven, M.S., pp 2012. Human Survival and Life History in Evolutionary Perspective, in: Mitani, J.C.J.C., Kappeler, P.M., Palombit, R.A., Silk, J.B. (Eds.), The Evolution of Primate Societies., pp. 293-315.

Hahn, M., Wild-Wall, N., Falkenstein, M., 2011. Age-related differences in performance and stimulus processing in dual task situation. Brain Res 1414, 66-76.

Hampstead, B.M., Sathian, K., Moore, A.B., Nalisnick, C., Stringer, A.Y., 2008. Explicit memory training leads to improved memory for face-name pairs in patients with mild cognitive impairment: results of a pilot investigation. J Int Neuropsychol Soc 14, 883-889.

Hampstead, B.M., Sathian, K., Phillips, P.A., Amaraneni, A., Delaune, W.R., Stringer, A.Y., 2012. Mnemonic strategy training improves memory for object location associations in both healthy elderly and patients with amnestic mild cognitive impairment: A randomized, single-blind study. Neuropsychology 26, 385-399.

Hanleybrown, F., Kania, J., Kramer, M., 2012. Channeling change: Making collective impact work. Stanford Social Innovation Review.

Hanleybrown, F., Mark Kramer, J.K., 2012. Channeling Change:Making Collective Impact Work. Stanford Social Innovation Review, 1-8.

Hay, J., LaBree, L., Luo, R., Clark, F., Carlson, M., Mandel, D., Zemke, R., Jackson, J., Azen, S.P., 2002. Cost-effectiveness of preventive occupational therapy for independent-living older adults. J Am Geriatr Soc 50, 1381-1388.

Heiberger, L., Maurer, C., Amtage, F., Mendez-Balbuena, I., Schulte-Monting, J., Hepp-Reymond, M.C., Kristeva, R., 2011. Impact of a weekly dance class on the functional mobility and on the quality of life of individuals with Parkinson's disease. Front Aging Neurosci 3, 14.

Heinzel, S., Lorenz, R.C., Brockhaus, W.R., Wustenberg, T., Kathmann, N., Heinz, A., Rapp, M.A., 2014. Working memory load-dependent brain response predicts behavioral training gains in older adults. J Neurosci 34, 1224-1233.

Hertzog, C., Kramer, A.F., Wilson, R.S., Lindenberger, U., 2008. Enrichment effects on adult cognitive development. Psychol. Sci. Public Interest 9, 1-65.

Hofer, J., Busch, H., 2013. Living in accordance with one's implicit motives: Cross-cultural evidence for beneficial effects of motive-goal congruence and motive satisfaction, in: Efklides, A., Moraitou, D. (Eds.), A Positive Psychology Perspective on Quality of Life. Springer, Netherlands, pp. 51-66.

Holman, C., de Villers-Sidani, E., 2014. Indestructible plastic: the neuroscience of the new aging brain. Front Hum Neurosci 8, 219.

Holt-Lunstad, J., Smith, T.B., Layton, J.B., 2010. Social relationships and mortality risk: a meta-analytic review. PLoS Med 7, e1000316.

Horowitz, B.P., Chang, P.-F.J., 2004. Promoting well-being and engagement in life through occupational therapy lifestyle redesign: A pilot study within adult day programs. Topics in Geriatric Rehabilitation 20, 46-58.

Hötting, K., Roder, B., 2013. Beneficial effects of physical exercise on neuroplasticity and cognition. Neurosci Biobehav Rev 37, 2243-2257.

Hurd, M.D., Martorell, P., Langa, K.M., 2013. Monetary costs of dementia in the United States. N Engl J Med 369, 489-490.

Huxhold, O., Miche, M., Schuz, B., 2014. Benefits of having friends in older ages: differential effects of informal social activities on well-being in middle-aged and older adults. J Gerontol B Psychol Sci Soc Sci 69, 366-375.

Ilg, R., Wohlschlager, A.M., Gaser, C., Liebau, Y., Dauner, R., Woller, A., Zimmer, C., Zihl, J., Muhlau, M., 2008. Gray matter increase induced by practice correlates with task-specific activation: a combined functional and morphometric magnetic resonance imaging study. J Neurosci 28, 4210-4215.

Jacobs, J.M., Cohen, A., Bursztyn, M., Azoulay, D., Ein-Mor, E., Stessman, J., 2009. Cohort profile: the Jerusalem longitudinal cohort study. Int J Epidemiol 38, 1464-1469.

Jacobs, J.M., Cohen, A., Ein-Mor, E., Maaravi, Y., Stessman, J., 2011. Frailty, cognitive impairment and mortality among the oldest old. Nutrition, Health & Aging 15, 678-682.

James, B.D., Boyle, P.A., Buchman, A.S., Bennett, D.A., 2011. Relation of late-life social activity with incident disability among community-dwelling older adults. J Gerontol A Biol Sci Med Sci 66, 467-473.

Jones, S., Nyberg, L., Sandblom, J., Stigsdotter Neely, A., Ingvar, M., Magnus Petersson, K., Backman, L., 2006. Cognitive and neural plasticity in aging: general and task-specific limitations. Neurosci Biobehav Rev 30, 864-871.

Karbach, J., Kray, J., 2009. How useful is executive control training? Age differences in near and far transfer of task-switching training. Dev Sci 12, 978-990.

Kattenstroth, J.C., Kalisch, T., Holt, S., Tegenthoff, M., Dinse, H.R., 2013. Six months of dance intervention enhances postural, sensorimotor, and cognitive performance in elderly without affecting cardio-respiratory functions. Front Aging Neurosci 5, 5.

Kattenstroth, J.C., Kolankowska, I., Kalisch, T., Dinse, H.R., 2010. Superior sensory, motor, and cognitive performance in elderly individuals with multi-year dancing activities. Front Aging Neurosci 2.

Kelly, M.E., Loughrey, D., Lawlor, B.A., Robertson, I.H., Walsh, C., Brennan, S., 2014a. The impact of cognitive training and mental stimulation on cognitive and everyday functioning of healthy older adults: a systematic review and meta-analysis. Ageing Res Rev 15, 28-43.

Kelly, M.E., Loughrey, D., Lawlor, B.A., Robertson, I.H., Walsh, C., Brennan, S., 2014b. The impact of exercise on the cognitive functioning of healthy older adults: a systematic review and meta-analysis. Ageing Res Rev 16, 12-31.

Kempermann, G., 2015. Activity-Based Maintenance of Adult Hippocampal Neurogenesis: Maintaining a Potential for Lifelong Plasticity, in: H. Georg Kuhn, A.J.E. (Ed.), Neural Stem Cells in Development, Adulthood and Disease. Springer, pp. 119-123.

Keogh, J.W., Kilding, A., Pidgeon, P., Ashley, L., Gillis, D., 2009. Physical benefits of dancing for healthy older adults: a review. J Aging Phys Act 17, 479-500.

Kessler, R., Glasgow, R.E., 2011. A proposal to speed translation of healthcare research into practice: dramatic change is needed. American journal of preventive medicine 40, 637-644.

Kim, S.H., Kim, M., Ahn, Y.B., Lim, H.K., Kang, S.G., Cho, J.H., Park, S.J., Song, S.W., 2011. Effect of dance exercise on cognitive function in elderly patients with metabolic syndrome: a pilot study. J Sports Sci Med 10, 671-678.

Klingberg, T., 2010. Training and plasticity of working memory. Trends Cogn Sci 14, 317-324.

Knaepen, K., Goekint, M., Heyman, E.M., Meeusen, R., 2010. Neuroplasticity - exercise-induced response of peripheral brain-derived neurotrophic factor: a systematic review of experimental studies in human subjects. Sports Med 40, 765-801.

Koch, S.C., Bräuninger, I., 2005. International dance/movement therapy research: Theory, methods, and empirical findings. American Journal of Dance Therapy 27, 37-46.

Kraft, E., 2012. Cognitive function, physical activity, and aging: possible biological links and implications for multimodal interventions. Neuropsychol Dev Cogn B Aging Neuropsychol Cogn 19, 248-263.

Kramer, A.F., Hahn, S., Cohen, N.J., Banich, M.T., McAuley, E., Harrison, C.R., Chason, J., Vakil, E., Bardell, L., Boileau, R.A., Colcombe, A., 1999. Ageing, fitness and neurocognitive function. Nature 400, 418-419.

Kramer, A.F., Morrow, D.G., in press. Cognitive training and expertise, in: Park, D.C., Schwarz, N. (Eds.), Cognitive aging: A Premier, Second Edition ed. Psychology Press.

Krampe, R.T., Smolders, C., Doumas, M., 2014. Leisure sports and postural control: can a black belt protect your balance from aging? Psychol Aging 29, 95-102.

Kueider, A.M., Parisi, J.M., Gross, A.L., Rebok, G.W., 2012. Computerized cognitive training with older adults: a systematic review. PLoS One 7, e40588.

Lampit, A., Hallock, H., Valenzuela, M., 2014. Computerized cognitive training in cognitively healthy older adults: a systematic review and meta-analysis of effect modifiers. PLoS Med 11, e1001756.

Landau, S.M., Marks, S.M., Mormino, E.C., Rabinovici, G.D., Oh, H., O'Neil, J.P., Wilson, R.S., Jagust, W.J., 2012. Association of lifetime cognitive engagement and low beta-amyloid deposition. Arch Neurol 69, 623-629.

Lee, H., Boot, W.R., Basak, C., Voss, M.W., Prakash, R.S., Neider, M., Erickson, K.I., Simons, D.J., Fabiani, M., Gratton, G., Low, K.A., Kramer, A.F., 2012. Performance gains from directed training do not transfer to untrained tasks. Acta Psychol (Amst) 139, 146-158.

Lelard, T., Doutrellot, P.L., David, P., Ahmaidi, S., 2010. Effects of a 12-week Tai Chi Chuan program versus a balance training program on postural control and walking ability in older people. Arch Phys Med Rehabil 91, 9-14.

Lesch, K.P., 2007. Linking emotion to the social brain. The role of the serotonin transporter in human social behaviour. EMBO Rep 8 Spec No, S24-29.

Levasseur, M., Desrosiers, J., Noreau, L., 2004. Is social participation associated with quality of life of older adults with physical disabilities? Disabil Rehabil 26, 1206-1213.

Li, R., Zhu, X., Yin, S., Niu, Y., Zheng, Z., Huang, X., Wang, B., Li, J., 2014. Multimodal intervention in older adults improves resting-state functional connectivity between the medial prefrontal cortex and medial temporal lobe. Front Aging Neurosci 6.

Li, S.C., Brehmer, Y., Shing, Y.L., Werkle-Bergner, M., Lindenberger, U., 2006. Neuromodulation of associative and organizational plasticity across the life span: empirical evidence and neurocomputational modeling. Neurosci Biobehav Rev 30, 775-790.

Li, S.C., Schmiedek, F., Huxhold, O., Rocke, C., Smith, J., Lindenberger, U., 2008. Working memory plasticity in old age: practice gain, transfer, and maintenance. Psychol Aging 23, 731-742.

Litwin, H., 2010. Social networks and well-being: a comparison of older people in Mediterranean and non-Mediterranean countries. J Gerontol B Psychol Sci Soc Sci 65, 599-608.

Litwin, H., Stoeckel, K.J., 2015. Social Network, Activity Participation, and Cognition: A Complex Relationship. Res Aging.

Lovden, M., Backman, L., Lindenberger, U., Schaefer, S., Schmiedek, F., 2010. A theoretical framework for the study of adult cognitive plasticity. Psychol Bull 136, 659-676.

Lussier, M., Gagnon, C., Bherer, L., 2012. An investigation of response and stimulus modality transfer effects after dual-task training in younger and older. Front Hum Neurosci 6, 129.

Lustig, C., Shah, P., Seidler, R., Reuter-Lorenz, P.A., 2009. Aging, training, and the brain: a review and future directions. Neuropsychol Rev 19, 504-522.

Madden, D.J., Bennett, I.J., Song, A.W., 2009. Cerebral white matter integrity and cognitive aging: contributions from diffusion tensor imaging. Neuropsychol Rev 19, 415-435.

Mahncke, H.W., Connor, B.B., Appelman, J., Ahsanuddin, O.N., Hardy, J.L., Wood, R.A., Joyce, N.M., Boniske, T., Atkins, S.M., Merzenich, M.M., 2006. Memory enhancement in healthy older adults using a brain plasticity-based training program: a randomized, controlled study. Proc Natl Acad Sci U S A 103, 12523-12528.

Maillot, P., Perrot, A., Hartley, A., 2012. Effects of interactive physical-activity video-game training on physical and cognitive function in older adults. Psychol Aging 27, 589-600.

Mayas, J., Parmentier, F.B., Andres, P., Ballesteros, S., 2014. Plasticity of attentional functions in older adults after non-action video game training: a randomized controlled trial. PLoS One 9, e92269.

McAvinue, L.P., Golemme, M., Castorina, M., Tatti, E., Pigni, F.M., Salomone, S., Brennan, S., Robertson, I.H., 2013. An evaluation of a working memory training scheme in older adults. Front Aging Neurosci 5, 20.

McDougall, S., House, B., 2012. Brain training in older adults: evidence of transfer to memory span performance and pseudo-Matthew effects. Neuropsychol Dev Cogn B Aging Neuropsychol Cogn 19, 195-221.

McKay, S.M., Maki, B.E., 2010. Attitudes of older adults toward shooter video games: An initial study to select an acceptable game for training visual processing. Gerontechnology 9, 5-17.

McPherson, M., Smith-Lovin, L., Cook, J., 2001. Birds of a feather: Homophily in social networks. Annual Review of Sociology, 415-444.

Medical Advisory Secretariat, 2008. Social isolation in community-dwelling seniors: an evidence-based analysis. Ontario Health Technology Assessment Series 8.

Melby-Lervag, M., Hulme, C., 2013. Is working memory training effective? A meta-analytic review. Develop Psychol 49, 270-291.

Miles, I., Sullivan, W.C., Kuo, F.E., 1998. Ecological restoration volunteers: the benefits of participation. Urban Ecosystems 2, 27-41.

Miyake, A., Friedman, N.P., Emerson, M.J., Witzki, A.H., Howerter, A., Wager, T.D., 2000. The unity and diversity of executive functions and their contributions to complex "frontal lobe" tasks: A latent variable analysis. Cognitive Psychology 41, 49-100.

Molesworth, T., Sheu, L.K., Cohen, S., Gianaros, P.J., Verstynen, T.D., 2015. Social network diversity and white matter microstructural integrity in humans. Soc Cogn Affect Neurosci.

Mortimer, J.A., Ding, D., Borenstein, A.R., DeCarli, C., Guo, Q., Wu, Y., Zhao, Q., Chu, S., 2012. Changes in brain volume and cognition in a randomized trial of exercise and social interaction in a community-based sample of non-demented Chinese elders. J Alzheimers Dis 30, 757-766.

Mountain, G.A., Hind, D., Gossage-Worrall, R., Walters, S.J., Duncan, R., Newbould, L., Rex, S., Jones, C., Bowling, A., Cattan, M., Cairns, A., Cooper, C., Edwards, R.T., Goyder, E.C., 2014. 'Putting Life in Years' (PLINY) telephone friendship groups research study: pilot randomised controlled trial. Trials 15, 141.

Mozolic, J.L., Long, A.B., Morgan, A.R., Rawley-Payne, M., Laurienti, P.J., 2011a. A cognitive training intervention improves modality-specific attention in a randomized controlled trial of healthy older adults. Neurobiol of Aging 32, 655-668.

Mozolic, J.L., Long, A.B., Morgan, A.R., Rawley-Payne, M., Laurienti, P.J., 2011b. A cognitive training intervention improves modality-specific attention in a randomized controlled trial of healthy older adults. Neurobiol Aging 32, 655-668.

Muinos, M., Ballesteros, S., 2014. Peripheral vision and perceptual asymmetries in young and older martial arts athletes and nonathletes. Atten Percept Psychophys 76, 2465-2476.

Muiños, M., Ballesteros, S., 2015. Sports can protect dynamic visual acuity from aging: A study with young and older judo and karate martial arts athletes. Atten Percept Psychophys, 1-13.

Nap, H.H., de Kort, Y.A.W., Ijselsteijn, W.A., 2009. Senior gamers: Preferences, motivations and needs. Gerontechnology 8, 247-262.

Nielsen, L., Mather, M., 2011. Emerging perspectives in social neuroscience and neuroeconomics of aging. Soc Cogn Affect Neurosci 6, 149-164.

Nistor, N., Dascalu, M., Trausan-Matu, S., Mihaila, D., Baltes, B., Smeaton, G., 2013. Virtual Communities of Practice in Academia: Automated Analysis of Collaboration Based on the Social Knowledge-Building Model, Scaling up Learning for Sustained Impact. Springer, pp. 623-624.

Nithianantharajah, J., Hannan, A.J., 2009. The neurobiology of brain and cognitive reserve: mental and physical activity as modulators of brain disorders. Progress in Neurobiology 89, 369-382.

Noack, H., Lovden, M., Schmiedek, F., Lindenberger, U., 2009. Cognitive plasticity in adulthood and old age: gauging the generality of cognitive intervention effects. Restor Neurol Neurosci 27, 435-453.

Nouchi, R., Taki, Y., Takeuchi, H., Hashizume, H., Akitsuki, Y., Shigemune, Y., Sekiguchi, A., Kotozaki, Y., Tsukiura, T., Yomogida, Y., Kawashima, R., 2012. Brain training game improves executive functions and processing speed in the elderly: a randomized controlled trial. PLoS One 7, e29676.

O'Brien, J.L., Edwards, J.D., Maxfield, N.D., Peronto, C.L., Williams, V.A., Lister, J.J., 2013. Cognitive training and selective attention in the aging brain: an electrophysiological study. Clin Neurophysiol 124, 2198-2208.

Oeppen, J., Vaupel, J.W., 2002. Demography. Broken limits to life expectancy. Science 296, 1029-1031.

Osgood, N.J., Meyers, B.S., Orchowsky, S., 1990. The impact of creative dance and movement training on the life satisfaction of older adults: An exploratory study. Journal of Applied Gerontology 9, 255-265.

Osorio, A., Ballesteros, S., Fay, S., Pouthas, V., 2009. The effect of age on word-stem cued recall: a behavioral and electrophysiological study. Brain Res 1289, 56-68.

Osorio, A., Fay, S., Pouthas, V., Ballesteros, S., 2010. Ageing affects brain activity in highly educated older adults: An ERP study using a word-stem priming task. Cortex 46, 522-534.

Oswald, W., Gunzelmann, T., Rupprecht, R., Hagen, B., 2006. Differential effect of single versus combined cognitive and physical training with older adults: The SimA study in a 5-years perspective. Eur. J. Ageing 3, 179-192.

Owen, A.M., Hampshire, A., Grahn, J.A., Stenton, R., Dajani, S., Burns, A.S., Howard, R.J., Ballard, C.G., 2010. Putting brain training to the test. Nature 465, 775-U776.

Paap, K.V., Walsh, S.J., Snyder, P.J., 2009. Immediate and delayed effects of cognitive interventions in healthy elderly: A review of current literature and future directions. Alzheimers Dementia 5, 50-60.

Pao, C.-L., 2014. Using the Internet to Increase The Elderly's Quality of Life. National San-Yan Sen University , China.

Park, D.C., Bischof, G.N., 2013. The aging mind: neuroplasticity in response to cognitive training. Dialogues Clin Neurosci 15, 109-119.

Park, D.C., Lodi-Smith, J., Drew, L., Haber, S., Hebrank, A., Bischof, G.N., Aamodt, W., 2014. The impact of sustained engagement on cognitive function in older adults: the Synapse Project. Psychol Sci 25, 103-112.

Park, D.C., Reuter-Lorenz, P., 2009. The adaptive brain: aging and neurocognitive scaffolding. Annu Rev Psychol 60, 173-196.

Park, N.S., Jang, Y., Lee, B.S., Ko, J.E., Haley, W.E., Chiriboga, D.A., 2013. An Empirical Typology of Social Networks and Its Association With Physical and Mental Health: A Study With Older Korean Immigrants. The Journals of Gerontology Series B: Psychological Sciences and Social Sciences.

Peretz, C., Korczyn, A.D., Shatil, E., Aharonson, V., Birnboim, S., Giladi, N., 2011. Computer-based, personalized cognitive training versus classical computer games: a randomized double-blind prospective trial of cognitive stimulation. Neuroepidemiology 36, 91-99.

Peter, C., Kreiner, A., Schroter, M., Kim, H., Bieber, G., Ohberg, F., Hoshi, K., Waterworth, E.L., Waterworth, J., Ballesteros, S., 2013. AGNES: Connecting people in a multimodal way. Journal on Multimodal User Interfaces 7, 229-245.

Pickersgill, M., Niewohner, J., Muller, R., Martin, P., Cunningham-Burley, S., 2013. Mapping the new molecular landscape: social dimensions of epigenetics. New Genet Soc 32, 429-447.

Pieramico, V., Esposito, R., Sensi, F., Cilli, F., Mantini, D., Mattei, P.A., Frazzini, V., Ciavardelli, D., Gatta, V., Ferretti, A., Romani, G.L., Sensi, S.L., 2012. Combination training in aging individuals modifies functional connectivity and cognition, and is potentially affected by dopamine-related genes. PLoS One 7, e43901.

Pinazo-Duran, M.D., Gallego-Pinazo, R., Garcia-Medina, J.J., Zanon-Moreno, V., Nucci, C., Dolz-Marco, R., Martinez-Castillo, S., Galbis-Estrada, C., Marco-Ramirez, C., Lopez-Galvez, M.I., Galarreta, D.J., Diaz-Llopis, M., 2014. Oxidative stress and its downstream signaling in aging eyes. Clin Interv Aging 9, 637-652.

Piniewski, Codagnone, C., Osimo, 2011. Nudging lifestyles for better health outcomes: crowdsourced data and persuasive technologies for behavioural change, in: Commission, J.-I.E. (Ed.).

Pons van Dijk, G., Huijts, M., Lodder, J., 2013. Cognition Improvement in Taekwondo novices over 40. Results from the SEKWONDO Study. Front Aging Neurosci 5, 74.

Powers, K.L., Brooks, P.J., Aldrich, N.J., Palladino, M.A., Alfieri, L., 2013. Effects of video-game play on information processing: A meta-analytic investigation. Psychonomic Bulletin & Review 20, 1055-1079.

Prakash, R.S., Voss, M.W., Erickson, K.I., Kramer, A.F., 2015. Physical activity and cognitive vitality. Annu Rev Psychol 66, 769-797.

Puska, P., 2009. Fat and heart disease: yes we can make a change--the case of North Karelia (Finland). Ann Nutr Metab 54 Suppl 1, 33-38.

Rafnsson, S.B., Shankar, A., Steptoe, A., 2015. Longitudinal Influences of Social Network Characteristics on Subjective Well-Being of Older Adults: Findings From the ELSA Study. J Aging Health.

Rahe, J., Petrelli, A., Kaesberg, S., Fink, G.R., Kessler, J., Kalbe, E., 2015. Effects of cognitive training with additional physical activity compared to pure cognitive training in healthy older adults. Clin Interv Aging 10, 297-310.

Raz, N., Lindenberger, U., 2013. Life-span plasticity of the brain and cognition: from questions to evidence and back. Neurosci Biobehav Rev 37, 2195-2200.

Raz, N., Lindenberger, U., Rodrigue, K.M., Kennedy, K.M., Head, D., Williamson, A., Dahle, C., Gerstorf, D., Acker, J.D., 2005. Regional brain changes in aging healthy adults: general trends, individual differences and modifiers. Cerebral Cortex 15, 1676-1689.

Rebok, G.W., Ball, K., Guey, L.T., Jones, R.N., Kim, H.Y., King, J.W., Marsiske, M., Morris, J.N., Tennstedt, S.L., Unverzagt, F.W., Willis, S.L., 2014. Ten-year effects of the advanced cognitive training for independent and vital elderly cognitive training trial on cognition and everyday functioning in older adults. J Am Geriatr Soc 62, 16-24.

Rebok, G.W., Carlson, M.C., Langbaurn, J.B.S., 2007. Training and maintaining memory abilities in healthy older adults: Traditional and novel approaches. Journals of Gerontology Series B-Psychological Sciences and Social Sciences 62, 53-61.

Redick, T.S., Shipstead, Z., Harrison, T.L., Hicks, K.L., Fried, D.E., Hambrick, D.Z., Kane, M.J., Engle, R.W., 2013. No evidence of intelligence improvement after working memory training: A randomized, placebo-controlled study. Journal of Experimental Psychology-General 142, 359-379.

Renaud, M., Bherer, L., Maquestiaux, F., 2010. A High Level of Physical Fitness Is Associated With More Efficient Response Preparation in Older Adults. Journals of Gerontology Series B-Psychological Sciences and Social Sciences 65, 317-322.

Reuter-Lorenz, P.A., Lustig, C., 2005. Brain aging: reorganizing discoveries about the aging mind. Curr Opin Neurobiol 15, 245-251.

Reuter-Lorenz, P.A., Park, D.C., 2014. How does it STAC up? Revisiting the scaffolding theory of aging and cognition. Neuropsychology review 24, 355-370.

Richmond, L.L., Morrison, A.B., Chein, J.M., Olson, I.R., 2011. Working memory training and transfer in older adults. Psychol Aging 26, 813-822.

Rogers, C.E., Larkey, L.K., Keller, C., 2009. A review of clinical trials of tai chi and qigong in older adults. West J Nurs Res 31, 245-279.

Russell E. Glasgow, K.M.E., 2007. How Can We Increase Translation of Research into Practice? Types of Evidence Needed. Annu Rev Public Health 28, 413-433.

Sandberg, P., Ronnlund, M., Nyberg, L., Stigsdotter Neely, A., 2014. Executive process training in young and old adults. Neuropsychol Dev Cogn B Aging Neuropsychol Cogn 21, 577-605.

Satariano, W., 2006. Epidemiology of aging: An ecological approach. Jones & Bartlett Learning.

Sebastian, M., Ballesteros, S., 2012. Effects of normal aging on event-related potentials and oscillatory brain activity during a haptic repetition priming task. Neuroimage 60, 7-20.

Sebastian, M., Reales, J.M., Ballesteros, S., 2011. Ageing affects event-related potentials and brain oscillations: a behavioral and electrophysiological study using a haptic recognition memory task. Neuropsychologia 49, 3967-3980.

Sevdalis, V., Keller, P.E., 2011. Captured by motion: dance, action understanding, and social cognition. Brain Cogn 77, 231-236.

Shanahan, M.J., 2013. Social Genomics and the Life Course: Opportunities and Challenges for Multilevel Population Research, in: Waite, L.J., Plewes, T.J. (Eds.), New Directions in the Sociology of Aging, Washington (DC).

Shatil, E., 2013. Does combined cognitive training and physical activity training enhance cognitive abilities more than either alone? A four-condition randomized controlled trial among healthy older adults. Front Aging Neurosci 5, 8.

Shipstead, Z., Hicks, K.L., Engle, R.W., 2012a. Cogmed working memory training: Does the evidence support the claims? Journal of Applied Research in Memory and Cognition 1, 185-193.

Shipstead, Z., Redick, T.S., Engle, R.W., 2012b. Is working memory training effective? Psychol Bulletin 138, 628-654.

Sjogren, K., Stjernberg, L., 2010. A gender perspective on factors that influence outdoor recreational physical activity among the elderly. BMC Geriatr 10, 34.

Slavich, G.M., Cole, S.W., 2013. The Emerging Field of Human Social Genomics. Clin Psychol Sci 1, 331-348.

Small, B.J., Dixon, R.A., McArdle, J.J., Grimm, K.J., 2012. Do changes in lifestyle engagement moderate cognitive decline in normal aging? Evidence from the Victoria Longitudinal Study. Neuropsychology 26, 144-155.

Smith, G.E., Housen, P., Yaffe, K., Ruff, R., Kennison, R.F., Mahncke, H.W., Zelinski, E.M., 2009. A cognitive training program based on principles of brain plasticity: results from the Improvement in Memory with Plasticity-based Adaptive Cognitive Training (IMPACT) study. J Am Geriatr Soc 57, 594-603.

Smith, K.P., Christakis, N.A., 2008. Social networks and health. Annu. Rev. Sociol 34, 405-429.

Sneed, R.S., Cohen, S., 2014. Negative social interactions and incident hypertension among older adults. Health Psychol 33, 554-565.

Sosa, G., 2011. The impact of video game intervention in the cognitive functioning, self- efficacy, self-esteem and video games attitude of older adults. A final project. CUG Theses and Dissertations.

Spiro, A., Brady, C.B., 2011. Integrating health into cognitive aging: Toward a preventive cognitive neuroscience of aging. The Journals of Gerontology Series B: Psychologcal Sciences and Social Sciences 66B, 17-25.

Steinerman, J.R., Hall, C.B., Sliwinski, M.J., Lipton, R.B., 2010. Modeling cognitive trajectories within longitudinal studies: a focus on older adults. J Am Geriatr Soc 58 Suppl 2, S313-318.

Stepankova, H., Lukavsky, J., Buschkuehl, M., Kopecek, M., Ripova, D., Jaeggi, S.M., 2014. The malleability of working memory and visuospatial skills: a randomized controlled study in older adults. Dev Psychol 50, 1049-1059.

Stern, Y., 2002. What is cognitive reserve? Theory and research application of the reserve concept. Journal of the International Neuropsychological Society 8, 448-460.

Stern, Y., 2009. Cognitive reserve. Neuropsychologia 47, 2015-2028.

Stern, Y., 2012. Cognitive reserve in ageing and Alzheimer's disease. Lancet Neurol 11, 1006-1012.

Stern, Y., Blumen, H.M., Rich, L.W., Richards, A., Herzberg, G., Gopher, D., 2011. Space Fortress game training and executive control in older adults: a pilot intervention. Neuropsychol Dev Cogn B Aging Neuropsychol Cogn 18, 653-677.

Stessman, J., Hammerman-Rozenberg, R., Maaravi, Y., Azoulai, D., Cohen, A., 2005. Strategies to enhance longevity and independent function: the Jerusalem Longitudinal Study. Mech Ageing Dev 126, 327-331.

Stigsdotter, N.A., Nyberg, L. (2015 in press). Working memory training in late adulthood, 2015. Working memory training in late adulthood, in: Logie, R.H., Morris, R.G. (Eds.), Working memory and aging. Psychology Press.

Stuss, D.T., Robertson, I.H., Craik, F.I., Levine, B., Alexander, M.P., Black, S., Dawson, D., Binns, M.A., Palmer, H., Downey-Lamb, M., Winocur, G., 2007. Cognitive rehabilitation in the elderly: a randomized trial to evaluate a new protocol. J Int Neuropsychol Soc 13, 120-131.

Styles, K., 2005. A healthy environment for older adults: The Aging Initiative of the Environmental Protection Agency. Generations 29, 65-69.

Takagi, D., Kondo, K., Kawachi, I., 2013. Social participation and mental health: moderating effects of gender, social role and rurality. BMC Public Health 13, 701.

Theill, N., Schumacher, V., Adelsberger, R., Martin, M., Jancke, L., 2013. Effects of simultaneously performed cognitive and physical training in older adults. BMC Neurosci 14, 103.

Thomas, G.N., Macfarlane, D.J., Guo, B., Cheung, B.M., McGhee, S.M., Chou, K.L., Deeks, J.J., Lam, T.H., Tomlinson, B., 2012. Health promotion in older Chinese: a 12-month cluster randomized controlled trial of pedometry and "peer support". Med Sci Sports Exerc 44, 1157-1166.

Tidwell, J.W., Dougherty, M.R., Chrabaszcz, J.R., Thomas, R.P., Mendoza, J.L., 2014. What counts as evidence for working memory training? Problems with correlated gains and dichotomization. Psychon Bull Rev 21, 620-628.

Tiedt, A.D., 2013. Cross-National Comparisons of Gender Differences in Late-Life Depressive Symptoms in Japan and the United States. The Journals of Gerontology Series B: Psychological Sciences and Social Sciences 68, 443-454.

Topiwala, A., Ebmeier, K.P., 2012. Vascular changes and brain plasticity: a new approach to neurodegenerative diseases. Am J Neurodegener Dis 1, 152-159.

Toril, P., Reales, J.M., Ballesteros, S., 2014. Video game training enhances cognition of older adults: a meta-analytic study. Psychol Aging 29, 706-716.

Torres, A., 2008. Cognitive effects of video games on older people. ICDVRAT 19, 191-198.

Tunis, S.R., Stryer, D.B., Clancy, C.M., 2003. Practical clinical trials: increasing the value of clinical research for decision making in clinical and health policy. JAMA 290, 1624-1632.

UN, 2011. World Population Ageing – profiles of ageing 2011. Department of Economic and Social Affairs Population Division.

Valenzuela, M., Sachdev, P., 2009. Can Cognitive Exercise Prevent the Onset of Dementia? Systematic Review of Randomized Clinical Trials with Longitudinal Follow-up. American Journal of Geriatric Psychiatry 17, 179-187.

Valenzuela, M.J., Breakspear, M., Sachdev, P., 2007. Complex mental activity and the aging brain: Molecular, cellular and cortical network mechanisms. Brain Research Reviews 56, 198-213.

Valenzuela, M.J., Sachdev, P., Wen, W., Chen, X., Brodaty, H., 2008. Lifespan mental activity predicts diminished rate of hippocampal atrophy. PLoS One 3, e2598.

van Muijden, J., Band, G.P., Hommel, B., 2012. Online games training aging brains: limited transfer to cognitive control functions. Front Hum Neurosci 6, 221.

Verhaeghen, P., Marcoen, A., Goossens, L., 1992. Improving memory performance in the aged through mnemonic training: a meta-analytic study. Psychol Aging 7, 242-251.

Verhaeghen, P., Martin, M., Sedek, G., 2012. Reconnecting cognition in the lab and cognition in real life: The role of compensatory social and motivational factors in explaining how cognition ages in the wild. Neuropsychol Dev Cogn B Aging Neuropsychol Cogn 19, 1-12.

Verhaeghen, P., Steitz, D.W., Sliwinski, M.J., Cerella, J., 2003. Aging and dual-task performance: a meta-analysis. Psychol Aging 18, 443-460.

Verstynen, T.D., Weinstein, A., Erickson, K.I., Sheu, L.K., Marsland, A.L., Gianaros, P.J., 2013. Competing physiological pathways link individual differences in weight and abdominal adiposity to white matter microstructure. Neuroimage 79, 129-137.

Voss, M.W., Erickson, K.I., Prakash, R.S., Chaddock, L., Kim, J.S., Alves, H., Szabo, A., Phillips, S.M., Wojcicki, T.R., Mailey, E.L., Olson, E.A., Gothe, N., Vieira-Potter, V.J., Martin, S.A., Pence, B.D., Cook, M.D., Woods, J.A., McAuley, E., Kramer, A.F., 2013. Neurobiological markers of exercise-related brain plasticity in older adults. Brain Behav Immun 28, 90-99.

Voss, M.W., Prakash, R.S., Erickson, K.I., Basak, C., Chaddock, L., Kim, J.S., Alves, H., Heo, S., Szabo, A.N., White, S.M., Wojcicki, T.R., Mailey, E.L., Gothe, N., Olson, E.A., McAuley, E., Kramer, A.F., 2010. Plasticity of brain networks in a randomized intervention trial of exercise training in older adults. Front Aging Neurosci 2.

Wagenet, L.P., Pfeffer, M.J., 2007. Organizing Stakeholder Engagement for Democratic Environmental Planning. Journal of Society and Natural Resources 20, 801-813.

Wang, H.X., Karp, A., Winblad, B., Fratiglioni, L., 2002. Late-life engagement in social and leisure activities is associated with a decreased risk of dementia: a longitudinal study from the Kungsholmen project. Am J Epidemiol 155, 1081-1087.

Wayne, P.M., Manor, B., Novak, V., Costa, M.D., Hausdorff, J.M., Goldberger, A.L., Ahn, A.C., Yeh, G.Y., Peng, C.K., Lough, M., Davis, R.B., Quilty, M.T., Lipsitz, L.A., 2013. A systems biology approach to studying Tai Chi, physiological complexity and healthy aging: design and rationale of a pragmatic randomized controlled trial. Contemp Clin Trials 34, 21-34.

Wayne, P.M., Walsh, J.N., Taylor-Piliae, R.E., Wells, R.E., Papp, K.V., Donovan, N.J., Yeh, G.Y., 2014. Effect of tai chi on cognitive performance in older adults: systematic review and meta-analysis. J Am Geriatr Soc 62, 25-39.

Wei, G.X., Dong, H.M., Yang, Z., Luo, J., Zuo, X.N., 2014. Tai Chi Chuan optimizes the functional organization of the intrinsic human brain architecture in older adults. Front Aging Neurosci 6, 74.

Wenger, E., 1998. Communities of practice, learning, meaning, and identity. Cambridge University Press, Cambridge.

Wenger, E., Trayner, B., de Laat, M., 2011. Promoting and assessing value creation in communities and networks: A conceptual framework, in: Open University of the Netherlands, R.d.M.C. (Ed.), Rapport 18, Herleen, NL.

West, R.L., 1996. An application of prefrontal cortex function theory to cognitive aging. Psychol Bull 120, 272-292.

Wild-Wall, N., Hahn, M., Falkenstein, M., 2011. Preparatory processes and compensatory effort in older and younger participants in a driving-like dual task. Hum Factors 53, 91-102.

Williams, K., Herman, R., Bontempo, D., 2014. Reasoning exercise in assisted living: A cluster randomized trial to improve reasoning and everyday problem solving. Clin. Interv. Aging 9, 981-996.

Willis, S.L., Tennstedt, S.L., Marsiske, M., Ball, K., Elias, J., Koepke, K.M., Morris, J.N., Rebok, G.W., Unverzagt, F.W., Stoddard, A.M., Wright, E., 2006. Long-term effects of cognitive training on everyday functional outcomes in older adults. JAMA 296, 2805-2814.

Wilson, R.S., Boyle, P.A., Yu, L., Barnes, L.L., Schneider, J.A., Bennett, D.A., 2013. Life-span cognitive activity, neuropathologic burden, and cognitive aging. Neurology 81, 314-321.

Winocur, G., Craik, F.I.M., Levine, B., Robertson, I.H., Binns, M.A., Alexander, M., Black, S., Dawson, D., Palmer, H., McHugh, T., Stuss, D.T., 2007. Cognitive rehabilitation in the elderly: Overview and future directions. Journal of the International Neuropsychological Society 13, 166-171.

Wolinsky, F.D., Vander Weg, M.W., Howren, M.B., Jones, M.P., Dotson, M.M., 2013. A randomized controlled trial of cognitive training using a visual speed of processing intervention in middle aged and older adults. PLoS One 8, e61624.

Wright, S.D., Caserta, M., Lund, D.A., 2003. Older adults' attitudes, concerns, and support for environmental issues in the "New West". Int J Aging Hum Dev 57, 151-179.

Wrzus, C., Hanel, M., Wagner, J., Neyer, F.J., 2013. Social network changes and life events across the life span: a meta-analysis. Psychol Bull 139, 53-80.

Yokoyama, J.S., Evans, D.S., Coppola, G., Kramer, J.H., Tranah, G.J., Yaffe, K., 2014. Genetic modifiers of cognitive maintenance among older adults. Hum Brain Mapp.

Youn, J.H., Lee, J.Y., Kim, S., Ryu, S.H., 2011. Multistrategic memory training with the metamemory concept in healthy older adults. Psychiatry Investig 8, 354-361.

Zammit, A.R., Starr, J.M., Johnson, W., Deary, I.J., 2014. Patterns and associates of cognitive function, psychosocial wellbeing and health in the Lothian Birth Cohort 1936. BMC Geriatr 14, 53.

Zehnder, F., Martin, M., Altgassen, M., Clare, L., 2009. Memory training effects in old age as markers of plasticity: a meta-analysis. Restor Neurol Neurosci 27, 507-520.

Zelinski, E.M., Reyes, R., 2009. Cognitive benefits of computer games for older adults. Gerontechnology 8, 220-235.

Zelinski, E.M., Spina, L.M., Yaffe, K., Ruff, R., Kennison, R.F., Mahncke, H.W., Smith, G.E., 2011. Improvement in memory with plasticity-based adaptive cognitive training: results of the 3-month follow-up. J Am Geriatr Soc 59, 258-265.

Zheng, Z., Zhu, X., Yin, S., Wang, B., Niu, Y., Huang, X., Li, R., Li, J., 2015. Combined cognitive-psychological-physical intervention induces reorganization of intrinsic functional brain architecture in older adults. Neural plasticity 2015, 713104.

Zhu, Z., Hakun, J.G., Johnson, N.F., Gold, B.T., 2014. Age-related increases in right frontal activation during task switching are mediated by reaction time and white matter microstructure. Neuroscience 278, 51-61.

Zolyniak, N., Schulte-Gocking, H., Kraft, E., 2014. Neuroplasticity in Aging Implications for Behavioral and Lifestyle Combined Interventions. Topics in Geriatric Rehabilitation 30, 15-17.

Zunzunegui, M.V., Alvarado, B.E., Del Ser, T., Otero, A., 2003. Social networks, social integration, and social engagement determine cognitive decline in community-dwelling Spanish older adults. J Gerontol B Psychol Sci Soc Sci 58, S93-S100.

Highlights:

- Cognition in aging is influenced by PA, cognitive training and other factors
- Social networks have a role in cognitive maintenance in aging.
- Interventional studies aim to prevent and/or delay age-related cognitive decline.
- Multi-domain interventions may have synergistic effects in enhancing neuroplasticity.
- RCTs will profit from integrating activities embedded into a social engagement framework.
- There is a need for new multi-domain synergistic interventions in healthy aging.

Table 1
Characteristics of the cognitive training studies and main findings of core studies of older adults.

STUDY	AGE	CONTROL	N	TRAINING PROGRAMME	DURATION OF TRAINING	SIGNIFICANT FINDINGS
(Ball et al., 2002) (RCT)	65-85	NC	2832 O	Speed of processing, memory, problem solving training	10 sessions of 60 min over 5 weeks	Proximal training effects on the trained skill that continued at lower level 2 years later. Absence transfer to real world outcomes.
(Berry et al., 2010)	60-89	NC	30 O	Perceptual discrimination Sweep Seeker, InSight, Pos Sci	10 hours over 3-5 weeks	TG showed transfer to WM N1 amplitude (a new neural marker) decrease correlated with WM performance.
(Bherer et al., 2005)	M=20 M=70	NC	36 O 36 O	Computer-based adaptive training: auditory discriminant and visual identification independently or concurrently	5 training sessions of 60 min over 3 weeks	Reduced latency in Y and O. Substantial and age-equivalent training and transfer benefits for maintaining multiple task sets and to perform multiple tasks concurrently.
(Buschkuehl et al., 2008)	M=80	AC	32 O	Computer-based adaptive training: 3 variant of a spatial WM task and 2 verbal choice RT tasks	2 training sessions of 45 min over 12 weeks	Improvements in all the trained tasks. Near transfer to a block span task and some evidence in a visual free recall task. Gains were lost 12 months later.

(Cheng et al., 2012) (RCT)	60-75	NC	193 O	Cognitive training (CogTr): Single-domain and multi-domain training compared to a waiting list control group	24 session, 60 min each over 12 weeks	Multi-domain CogTr improved FBANS, visual reasoning, and memory. Effects remained 12 months later on delayed memory and visual reasoning; Single-domain training effects on FBANS, visual reasoning, word interference, and visual-spatial score. After 12 months only effects on word interference.
(Dahlin et al., 2008b)	M=24 M=68	NC NC	26 Y 29 O	WM updating computer-based training program with numbers, letters, spatial locations and colors	15 sessions, 45 min each over 5 weeks	TGs similar training improvement in Y and O updating in WM. Practice gains maintained 18 months later. Transfer to an untrained (3-back) updating task in Y not in O.
(Karbach and Kray, 2009)	M=9 M=22 M=69	-------	56 C 56 Y 56 O	Computer training: Single task; task-switching	4 training sessions over 8 weeks, 60-70 min each	Near transfer of task-switching training in all groups. Far transfer to other executive tasks and fluid intelligence in all groups. TG improved RT.
(Li et al., 2008)	M=25 M=74.5	NC	19 Y 21 O	Computer-based training with a spatial WM with two demand levels	45 days intervention, 15 min per day	TGs similar improvements in the trained tasks in Y and O Near transfer to a spatial 3-back task and to numerical 2 and 3-back tasks. No evidence of far transfer to complex span tasks. Near transfer gains maintained 3 months later in Y and O.

(Lussier et al., 2012)	72-85	NC NC	23 Y 23 O	Computerized dual-task Computerized dual-task	5 training sessions of 1 hour over 2-3 weeks	Y and O TGs enhanced performance on the 3 transfer dual-tasks; training did not reduce task-set costs in the transfer conditions.
(Mahncke et al., 2006)	65-75	AC NC	182182	Computer-based training with Posit Science, San Francisco (CA)	8-10 weeks; 60 min/5 days a week	TG improved in trained tasks. Transfer over unrelated memory tasks. Memory enhancement after 3-month of no contact. No change /no difference between AC and NC suggesting no placebo effect.
(McAvinue et al., 2013)	64-79	AC	36	Computerized online adaptive training; education on WM and practice of 9 WM tasks (span: numbers & colors; focus: faces & names; running span tasks; n-back (faces, spaces, names), dual tasking (space + names); auditory serial attention task	5 weeks; at least 30 min/5 days a week	TG improved in short-term memory maintained at 3- and 6 months follow-up; in episodic memory but not maintained at follow-up; no improvement on auditory WM or episodic memory tasks. TG and AC did not change in self-reported memory and attention slips; both showed higher satisfaction ratings during post-training assessments.
(Mozolic et al., 2011b) (RCT)	69.4	AC	62 O	Training program to suppress irrelevant stimuli	8 weeks; 1 h per week	TG improved ability to ignore irrelevant cross-modal stimuli but not within modality distraction. Training generalized to untrained domains (processing speed and dual-task performance).
(Richmond et al., 2011) (RCT)	60-80 M=66	AC (Trivial learning)	40 O	Complex adaptive spatial and verbal WM tasks	20 sessions; 30 min over 4-5 weeks	TG improved Reading Span and number of repetitions on the CVLT. TG more likely to self-report improvements in everyday attention.

(Sandberg et al., 2014)		NC	29 Y 30 O	Computerized training of multiple executive tasks	15 sessions; 45 min over 5 weeks	TGs pronounced gains in trained tasks. Near transfer to non-trained tasks. Y only intermediate transfer to 2 complex WM tasks and no far transfer for either age group.
(Stepankova et al., 2014) (RCT)	M=68	NC	65	N-Back training task	5 weeks; 9 or 20 sessions	TGs improved in an n-back task and showed reliable transfer to composites measures of WM and visuospatial skills.
(Wolinsky et al., 2013) (RCT)	50-64 65 plus	AC (Computerized crosswords puzzles)	620	Computerized Visual Speed Training (*Active Tour*, Posit Science Corporation)	10 -14 hours	Training on site or at home resulted in improvement on the primary outcome (UFOV) and stabilization or improvement in several executive function tests that translate to 3 to 4.1 years of protection against age-related declines.

***Abbreviations*:** M = Mean Age; TG = Trained Group; AC = Active Control Group; NC = No Contact Control Group; HC = Healthy control group; WM = Working Memory; RT= Reaction Time; MCI = Mild Cognitive Impaired older adult; RCT = Randomized Controlled Trial; Y = young adults; O = older adults; UFOV = Useful Field of View; CVLT = California Verbal Learning Test; FBANS = The Repeatable Battery for the Assessment of Neuropsychological Status.

Table 2

Characteristics and main findings of the video game training studies included in the Toril et al. (Toril et al.) meta-analysis and the study from Ballesteros (Ballesteros et al., 2014a).

STUDY	AGE	CONTROL	N	VIDEO GAMES	DURATION OF TRAINING	SIGNIFICANT FINDINGS
(Ackerman et al., 2010)	50-71	------	78	Wii Big Brain Academy	4 weeks: 5x/weeks	No significant transfer of training from Wii practice or reading tasks to measures of cognitive and perceptual speed.
(Anguera et al., 2013)	M=67	AC/NC	46	Neuroracer	4 weeks	Training enhanced cognitive control. These benefits were extended to untrained abilities.
(Ballesteros et al., 2015; Ballesteros et al., 2014b) RCT	57-80	NC	40	Lumosity	10-12 weeks; 20 1-h sessions	TG improved processing speed, attention, visual recognition, affection and affectivity but not VSWM and executive control. Except Affection and Assertiveness, the other benefits disappeared at 3-month follow-up.
(Belchior, 2008)	63-75	NC	39	Rise of Nations	4-5 weeks: 3x/weeks	TG improved memory, executive function and visuospatial abilities.
(Belchior, 2008)	67-84	AC (Tetris) NC	58	UFOV or Medal of Honor	2 weeks: 2-3/week	TG improved processing speed more than NC.
(Boot et al., 2013a)	M=74	NC	40	Brain Age	12 weeks	Cognitive abilities did not improve.
(Boot et al., 2013a)	M=74	NC	34	Mario Kart	12 weeks	Cognitive abilities did not improve.
(Bozoki et al., 2013)	60-80	AC (Online activities)	60	Online video games	6 weeks	No transfer effects. The effect sizes were relatively small.

(Cassavaugh and Kramer, 2009)	M=71.7	------	21	Computer training program	2-3 weeks: 8 sessions	TG improved RT.
(Clark et al., 1987)	57-83	NC	14	Pac Man or Donkey Kong	7 weeks: 120 min/week	TG improved RT.
(Drew and Waters, 1986)	61-78	AC	13	Atari Crystal Castle	8 weeks: 12x/week	TG improved psychomotor speed and global cognition.
(Dustman et al., 1992)	62-71	NC AC (Movies)	60	Breakout, Galaxian Frogger Kaboom, PacMan, …	11 weeks: 3x/week	TG improved RT.
(Goldstein et al., 1997)	72-85	NC	22	SuperTetris	5 weeks: 300 min/week	TG improved RT; TG and control group also improved executive functions with no differences between groups.
(Maillot et al., 2012)	65-75	NC	32	Nintendo Wii	12 weeks	TG improved more than NC physical function, executive control and processing speed but not on visuospatial measures.
(McDougall and House, 2012)	M=74	NC	41	Nintendo Brain Training	6 weeks	TG improved in Digit Span Test and other tests.
	M=69	AC (Tetris)	28	Brain Age	4 weeks	TG improved executive functions and processing speed.
(Peretz et al., 2011)	60-77	AC (Computer games)	121	C. Personal Coach	12 weeks: 3x/week	TG and AC improved focused and saturated attention, memory recognition and mental flexibility.
(Sosa, 2011)	M=74	NC	31	Brain Age	5 weeks: 1/week	TG improved syllable, arithmetic and Stroop.

(Stern et al., 2011)	M=66	NC AC	60	Space Fortress	12 weeks: 36 hours	One measure of executive control improved in TG.
(Torres, 2008)	60-86	NC AC (Muscle relaxation)	43	Super Granny, Zoo Keeper, Penguin Push, Bricks, Memory Games	8 weeks: 1/week	TG showed less cognitive decline than NC and AC.
(van Muijden et al., 2012)	60-77	AC (Documentary group)	72	Anagram, Falling bricks	7 weeks/ 24.5 hours	TG modest support for the potential of video game training to improve cognitive functions.

Note: Main characteristics of the studies published between 1986 and 2013 included in their meta-analytic study conducted to investigate whether video game training interventions produce positive effects in cognition. Adapted from Toril et al. (2014), *Psychology and Aging*, 29, 706-716. (p. 710). Abbreviations: M = Mean Age; TG = Experimental Group; AC = Active control group; NC = No contact control group; UFOV = Useful Field of View; RT = Reaction time; VSWM= visualspatial working memory.

Table 3
Intervention studies including social enhancement activities.

STUDY	AGE	N	SOCIAL ACTIVITY	DURATION	METODOLOGY	SIGNIFICANT FINDINGS
(Alpert et al., 2009)	60+	13	Jazz dancing	15 sessions	Pre/post	No impact on cognition or mood control, improvement in balance.
(Butler, 2006)	60+	33 pairs	Peer companionship	12 months	Mixed methodology Interviews	Increased independence, reduced anxiety.
(Cohen et al., 2006)	60+	166	Chorale music	12 months	Intervention/usual activity	TG showed better health, less doctor visits, medication use, falls, loneliness, improved morale, and trend toward more social activities. The NC showed decrease in social activities.
(Fernández-Ballesteros et al., 2012)	65	82	Life Long Learning University	3 years curriculum	Quasi experimental, pre/post	Enrollees maintained their cognitive performance, their self-reported health status, level of information-seeking and social activities.
(Hay et al., 2002)	60+	Not clear	OT/social group activities/no intervention.	9 months	3-arm RTC	A 4.5% OT-differential between OT versa/combined groups, also a significant decrease in costs of health care.
(Mountain et al., 2014)	>74	56	Telephone social interaction	6 months	RTC with trained volunteers delivering intervention	The study terminated 6 months post randomization due to volunteer drop out...
(Nistor et al., 2013)	24-85+	86	Active cognitive training, memory, speed processing, with booster sessions.	Over a 10-year period	RTC single blind	60% of TG, versus 50% of controls ($p < .05$) were at or above their baseline level of self-reported IADL. The reasoning and speed-of-processing were also maintained

(Thomas et al., 2012)	65+	207	Exercise in groups vCoP	12 months	RTC	There were no cognitive enhancement measurements. The participants accepted the vCoP technology to a high degree regardless of age or gender. There was higher level of social connectivity and exercise adherence in TG.

Abbreviations: Age- year at recruitment M = Mean Age; TG = Experimental Group; AC = Active control group; NC = No contact control group; vCoP = virtual Community of Practice; IADL-Intellectual Activities of Daily life, RTC= Randomized Clinical Trial, OT= Occupational Therapy; QALY= quality-adjusted life years.

Table 4
Cohort studies including social enhancement in older adults.

STUDY	AGE AT ENROLLMENT	N	MEASUREMENTS	LENGTH OF OBSERVATION	SIGNIFICANT FINDINGS
(Berkman and Syme, 1979)	30-69	6928	Mortality, social index.	9 years	People who lacked social and community ties were more likely to die in the follow-up period than those with more extensive contacts. This association remained even after adjusting for cumulative index of healthy practices.
(Buchman et al., 2009)	65+	906	Index score of social activities/global motor function.	9 years	Each 1-point decrease in social activity was associated with about a 33% more rapid rate of decline in motor function.
(Carlson et al., 2012)	70-79	436	Enriched lifestyles/cognition.	9.5 years	Only female community dwellers were included. Participation in variety of lifestyle activities was more predictive of risk of dementia and cognitive decline than frequency or level of cognitive challenge.
(DiNapoli et al., 2014)	70–94	267	Index social activities/cognition.	2 years	Appalachian older adults with social activity decrease and perceived social isolation had significantly lower global cognitive scores.
(Eisele et al., 2012)	80+	1869	Perceived social support/cognition.	18 months	Perceived social support did not influence cognition and mortality over an 18 months period.
(Fratiglioni et al., 2000)	>75	1203	Social index/mortality.	3 years	Decrease social index increased the risk of dementia by 60%.
(Huxhold et al., 2014)	40-85	2830	Social wellbeing.	6 years	Middle-aged adults performed more social activities than older adults. Informal social activities are beneficial for all three aspects of social wellbeing in older adults.

(James et al., 2011)	65+	11138	Index score of social activities/ADL/ cognition/morbidity.	5.1 years	The rate of global cognitive decline was reduced by an average of 70% in socially active people, compared to infrequently socially active. The risk of ADL related disability decreased by 43% for each unit of increase in social activity.
(Litwin, 2010)	60+	9054	Index of social activities/wellbeing.	2 years	Non-Mediterranean respondents participated in more social activities, Mediterranean respondents reported feeling lonelier, with more depressive symptoms and a greater difficulty in making ends meet. Social networks are contextually bound.
Litwin et al, 2015	60+	38,777	Social networks and social activity, word recall, and subjective measure of self-perceived memory., and quality of life.	2 years	Social network connectedness and the extent of activity participation were independently related to better word recall. and quality of life.
Rafninsson et al., 2015	50+	4,116	Social network size and frequency.	6 years	Social network size and network contact frequency, were positively and independently associated with life satisfaction and quality of life.
(Small et al., 2012)	65-79	459	Physical, social, cognitive activities.	9 years	Participation in everyday leisure activities and cognitive performance decline preceded declines in social activities.
(Takagi et al., 2013)	65+	2728	Social activities/cognition/ epression.	3 years	Social participation was positively associated with less depressive symptoms.

(Wang et al., 2002)	>75	1375	Social index and cognitive function.	6.5 years	The adjusted relative risk for dementia according to participation was: for mental activity, 0.70 (95% CI 0.49 to 1.01) for social activity, 0.67 (95% CI 0.34 to 1.33) for physical activity, 0.61 (95% CI 0.40 to 0.93).
(Zunzunegui et al., 2003)	65+	1540	Social networks, social integration, and social engagement, cognitive function.	4 years	Visual contact with relatives and social integration were associated with lower degree of cognitive decline. This association was stronger in women than men.

Abbreviations; TG = Experimental Group; AC = Active control group; NC = No contact control group; CI = Confidence Interval.

Table 5

Characteristics of the multi-modal/multicomponent interventions on older adults and main findings of published studies.

STUDY	AGE	CONTROL	N	TRAINING PROGRAMME	DURATION OF TRAINING	SIGNIFICANT FINDINGS
(Barnes et al., 2013)	M=73.4	AC	126	Cognitive training; Exercise training. MA-I group: (Posit Science). MA-C group: DVDs of educational lectures. The EX-I class: 10 min warm-up, 30 min aerobic exercise, 5 min cool down, 10 min strength training, and 5 min stretching & relaxation. The EX-C class: 10 min warm-up, 30 min stretching & toning, 10 min strength training, and 10 min relaxation.	All groups attended study-specific group exercise classes for 60 min/day, 3 day/week, 12 weeks.	Significant improvements in global cognition with no evidence of differences between TG and AC.
(Franco et al., 2013)	M=75.9		267 healthy and MCI	CT used the Gradior European software. PA implemented by the FitForAll software.	156 participants received 1 hour of physical training (FFA) and 35 minutes of cognitive training (Gradior), 3 times a week during 11 weeks.	Improvement in global cognition, verbal memory, processing speed, episodic memory and depressive symptoms. Increasing aging was associated with decreased in cognitive improvement.

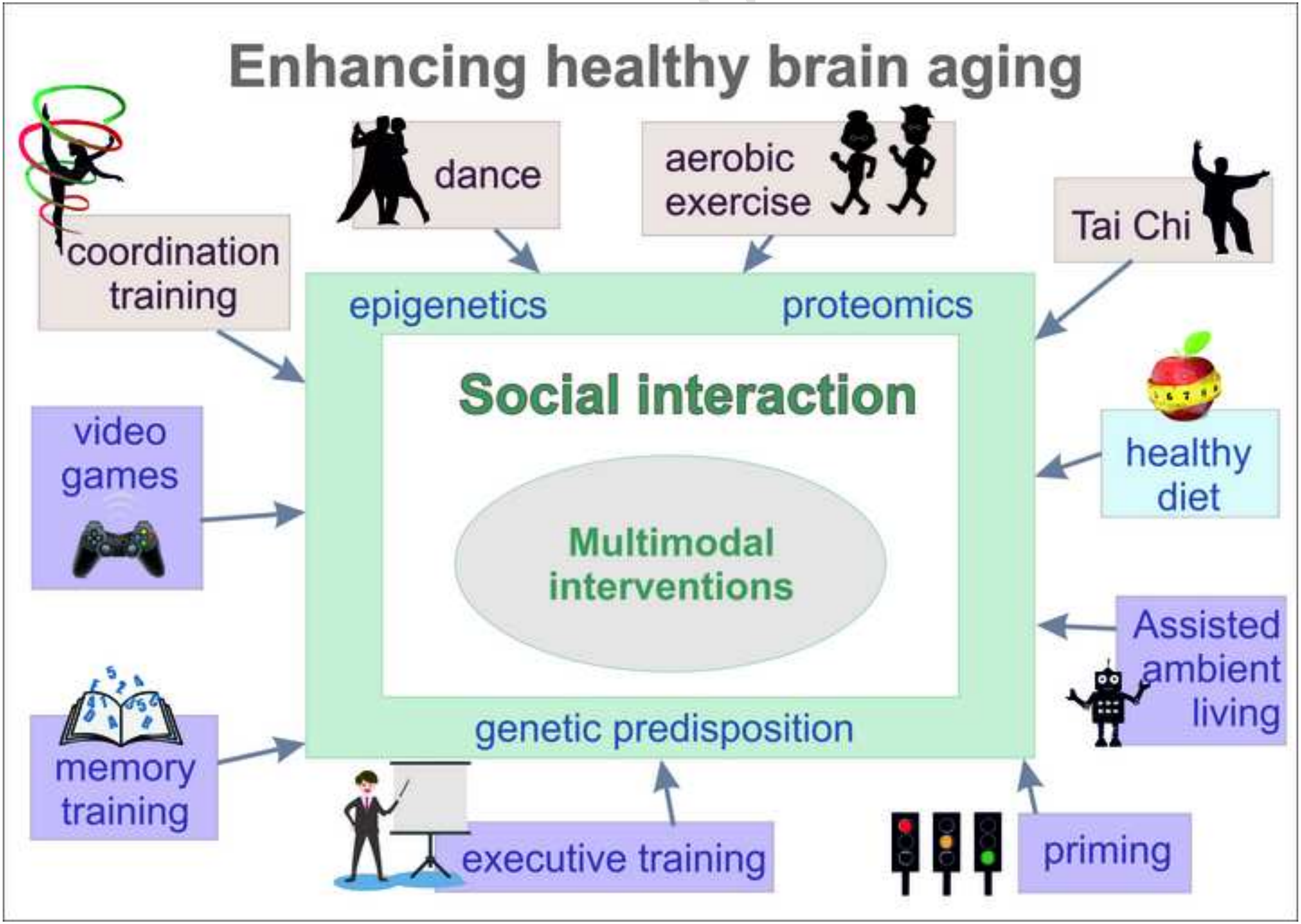
(Frantzidis et al., 2014)	M_{study}=70.5	AC	103	CT trained auditory sensory information, memory, attention and learning. CT with Brain Fitness software (© PositScience, USA). PT with FitForAll (FFA), an exergaming environment based on the Nintendo Wii Remote and Balance Board, with exercises to enhance body flexibility and strength, physical endurance through aerobic training Means to connect to outside community, including family and friends.	The cognitive programme consisted of 6 auditory exercises 15 min. each. 1h of Cognitive training 1h 3-5 days per week during 8 weeks.	TG Increased synchronisation across the two hemispheres at rest when compared to AC
(Geda et al., 2012)	70-93	------	926	Moderate physical exercise and computer training.	Participants completed self-reported questionnaires on physical exercise, computer use, and caloric intake within 1 year of the date of interview.	Significantly decreased odds of having MCI.
(Li et al., 2014)	60+	AC	45 (26 TG, 19 AC).	Multimodal activities including cognitive intervention, Tai Chi exercise, and group counselling.	CT consisted of 18 1-h sessions over 6 weeks, alternating between MT and EFT. Tai Chi consisted of 1-h sessions 3 times per week for 6 weeks. Counselling sessions of 90-min were held weekly for 6 weeks, focusing on three different topics: career, family, and health.	Multimodal intervention postponed the effects of aging and improved the function of the regions that are most heavily influenced by aging.

(Oswald et al., 2006)	75-93	NTC	375	CT plus PT, with a cognitive demanding, everyday-oriented psycho-educational training as alternative approach to the CT.	In the combined training, each session consisted of 90 min of cognitive or psycho-educational training plus 45 min of physical training. The training took place every week over 30 sessions.	Physical and cognitive status in CT were preserved at a higher level compared to baseline, and fewer depressive symptoms than the NTC. Training effects lasted 5 years after baseline.
(Pieramico et al., 2012)	60-75	NC	30, 15 study and 15 control	Combination of cognitive training, aerobic training and sensorial stimuli.	6 months program with daily cognitive training (rest on Sunday) and aerobic training and sensorial stimuli 3 times a week.	CT improved cognitive/occupational performances and reorganized functional connectivity and showed specific dopamine-related genotypes.
(Rahe et al., 2015)	50-85	Data from a database of 31 subjects who had already been trained with CT.	24, 15 available for the 1-year follow-up	CPT	90-minute sessions twice weekly for 6.5 weeks	Interaction effect on attention, with comparable gains from CPT and CT from pre- to post-test, but stronger effects of CPT at follow-up. Significant effects in terms of cognitive state, letter verbal fluency and immediate and delayed verbal memory.

(Shatil, 2013)	M=76.8	AC	180	Four-group design - CT, PA, CbT, and book reading and discussion control group.	CT with CogniFit; first 20 min spent training on combinations of three of the 21 tasks available; remaining 20 min used on any three tasks of their own choice among the 21 tasks. PA with Fitness Forever™ Senior Exercise Video; 3 weekly 45 min sessions, during 16 weeks. Participants in the CbT undergo both the CT and the PA training.	CT (separately or combined) improved memory, processing speed, eye-hand coordination, naming, and visuospatial processing. No improvements in the groups that did not engage in CT, with the differences and improvements holding true between groups and within groups.
(Theill et al., 2013)	65-84 M=71.8	NC	63	Three-group design: ST, WM training, no training. Simultaneous training of CT and PT: the participants walked at their normal, self-selected speed over a distance of 20 meters, with a turning point at a cone after 10 meters; under dual task condition, the participants performed a WM task at the same time, by counting backwards in steps of seven, beginning alternately with either 501, 502, or 503.	The trained groups attended to 20 training sessions	Larger improvements in executive control for both training groups. ST resulted in larger improvements compared to the single cognitive training in the paired-associates task and reduce the step-to-step variability in the motor-cognitive dual task when compared to the single CT and NC control groups.

***Abbreviations*:** M = Mean Age; TG = Trained Group; AC = Active Control Group; NTC = No-Treatment Control Group; NC = No contact control; WM = Working Memory; MCI = Mild Cognitive Impaired older adult; RCT = Randomised Controlled Trial; ST = Simultaneous Training; MT = Working Memory Training; EFT = Executive Function Training; PA = Physical Activity; CT = Cognitive Training; MA-I = Mental Activity - Intervention; MA – C = Mental Activity – Control; CbT = Combined Cognitive-Physical Activity Intervention; CPT = Cognitive Training with additional Physical activity.

Figure



Enhancing healthy brain aging
coordination training
dance
aerobic exercise
Tai Chi
epigenetics
proteomics
Social interaction
Multimodal interventions
video games
healthy diet
Assisted ambient living
genetic predisposition
memory training
executive training
priming