Neuroscience and Biobehavioral Reviews 37 (2013) 2689–2698

Contents lists available at ScienceDirect

Neuroscience and Biobehavioral Reviews

journal homepage: www.elsevier.com/locate/neubiorev

Review

Foreign language training as cognitive therapy for age-related cognitive decline: A hypothesis for future research

Mark Antoniou[a], Geshri M. Gunasekera[b], Patrick C.M. Wong[a,*]

[a] Department of Linguistics and Modern Languages, The Chinese University of Hong Kong, Hong Kong Special Administrative Region, China
[b] The Roxelyn and Richard Pepper Department of Communication Sciences and Disorders, Northwestern University, Evanston, IL, United States

ARTICLE INFO

Article history:
Received 27 March 2013
Received in revised form 22 August 2013
Accepted 9 September 2013

Keywords:
Aging
Language learning
Cognitive decline
Cognitive reserve
Training

ABSTRACT

Over the next fifty years, the number of older adults is set to reach record levels. Protecting older adults from the age-related effects of cognitive decline is one of the greatest challenges of the next few decades as it places increasing pressure on families, health systems, and economies on a global scale. The disease-state of age-related cognitive decline—Alzheimer's disease and other dementias—hijacks our consciousness and intellectual autonomy. However, there is evidence that cognitively stimulating activities protect against the adverse effects of cognitive decline. Similarly, bilingualism is also considered to be a safeguard. We propose that foreign language learning programs aimed at older populations are an optimal solution for building cognitive reserve because language learning engages an extensive brain network that is known to overlap with the regions negatively affected by the aging process. It is recommended that future research should test this potentially fruitful hypothesis.

Contents

1. The far-reaching effects of age-related cognitive decline

Successfully managing the adverse health effects linked with an aging population is one of the great challenges facing humankind in the twenty-first century. Individuals aged over 60 are the fastest growing age group on earth. There are currently 700 million over-60-year-olds in the world, with that number set to increase to 2 billion by 2050 (Department of Economic and Social Affairs Population Division, 2007). As the number of older adults increases, age-related health issues, both physical and cognitive, and their associated costs, are also set to increase. With increasing age, the prevalence of neurodegenerative diseases, such as Alzheimer's disease, is also expected to increase. Conservative estimates of the prevalence of Alzheimer's disease are approximately 5% for those aged above 60 (Plassman et al., 2007), meaning that by 2050 there will be at least 100 million older adults diagnosed with Alzheimer's disease worldwide (Ferri et al., 2005). Moreover, the effects of age-related cognitive decline and disease are not limited to the affected individual but also place emotional and financial stress on family members and loved ones. Caring for older individuals who are unable to function independently has become a major health issue. As such, promoting optimal cognitive aging is of profound importance to both individuals and the field of public health, and protecting older adults from the age-related cognitive decline is one of the greatest challenges to be overcome in the next few decades. In this review, we will outline the aging-related benefits of two seemingly unconnected lines of research: cognitive training programs and multilingualism, and make the case that by synthesizing

* Corresponding author at: Department of Linguistics and Modern Languages, The Chinese University of Hong Kong, Leung Kau Kui Building, Shatin, N.T., Hong Kong Special Administrative Region. Tel.: +852 3943 7009.
E-mail address: p.wong@cuhk.edu.hk (P.C.M. Wong).

0149-7634/$ – see front matter © 2013 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.neubiorev.2013.09.004

the two, foreign language learning could be an especially beneficial safeguard for ensuring healthy cognitive function in older adults.

Decline in cognitive abilities due to aging has been extensively documented (for a review see Craik and Salthouse, 2008). The aging process typically involves cognitive decline related to brain atrophy (particularly in frontal regions and areas that subserve declarative memory), loss of neuronal synaptic connections, and signs of neuropathology associated with dementia (Drachman, 2006; Greenwood, 2007; Whalley et al., 2004). The effects of aging are somewhat greater on cognitive processes supported by the prefrontal cortex than on processes that depend on posterior regions. Although procedural memory functions well in older adults (Mitchell and Bruss, 2003; Schacter, 1992), the interaction between declarative and procedural memory, and the processing of implicit information is impaired (Harrington and Haaland, 1992; Nelson et al., 1992). Increasing age is associated with decline across different domains of cognitive function (Cullum et al., 2000), memory decline (Grady and Craik, 2000; Park et al., 1996; Prull et al., 2000), poorer working memory (Park et al., 2002), reduced verbal span (Bopp and Verhaeghen, 2005), delayed verbal recall (Chodosh et al., 2002), reduced information processing speed (Cerella, 1985; Eckert et al., 2010; Salthouse, 1996), and increased variability (Morse, 1993). Language and communication is also affected, including speech perception in real word environments (Wong et al., 2009), speech production (Burke and Shafto, 2004), comprehension of meaning (semantics) and vocabulary (Peelle et al., 2010; Wingfield et al., 2003), grammar (syntax) (Smith, 2010), and discourse (Federmeier et al., 2003).

The effects of age-related cognitive declines largely result from age-related neuroanatomical (e.g., Gunning-Dixon and Raz, 2003) and neurophysiological changes (e.g., Cabeza, 2002; Cabeza et al., 2004; Greicius et al., 2004), including changes in functional connectivity among brain regions (e.g., Rogers et al., 2007). The brain network involved is extensive, including the prefrontal cortex and areas that subserve working memory and attentional processes (e.g., Gunning-Dixon and Raz, 2003; Raz et al., 1998), the striatal dopaminergic system and measures of episodic and procedural memories, perceptual speed and executive functioning more broadly (Bäckman et al., 2010), and the medial temporal lobe and structures associated with declarative memory (Jack et al., 1997). Some researchers emphasize the role of neurobiological processes in age-related decline (Hedden and Gabrieli, 2005), whereas others emphasize the importance of psychosocial factors (Pushkar et al., 1999). Although distinct, these two sets of factors need not be incompatible. Reductions of gray matter in the elderly (e.g., due to neurodegenerative disease processes) have been linked to functional impairments (Raz et al., 2004). Specifically, anatomical brain-imaging studies have demonstrated that reduction in gray matter volume in prefrontal cortex is associated with cognitive impairments in executive function tasks such as the Wisconsin Card Sorting Test and Tower of Hanoi (Gunning-Dixon and Raz, 2003; Raz et al., 1998). In addition, studies of neurochemical markers have demonstrated that dopamine receptor binding accounts for the majority of age-related variance in tasks such as self-ordered pointing and trail making (Bäckman and Farde, 2005). Older adults also show a decline in white matter, attributable to the gradual process of demyelinization (Raz, 2000), and less efficient blood oxygen level dependent activations have been observed in older adults associated with nonselective recruitment of task-irrelevant brain regions (Logan et al., 2002). The consequences of these degenerative neural processes are that older adults may ultimately lose their independence and come to rely on others in order to live their lives safely. The disease-state of such a decline—Alzheimer's disease and other cognitive disorders—not only hijacks our consciousness and intellectual autonomy, but also burdens families and health care systems.

Subtle cognitive deficits attributable to the very early stages of Alzheimer's disease may precede the actual onset of the disorder by more than a decade (La Rue and Jarvik, 1987), making it difficult to distinguish cognitive declines that are due to Alzheimer's disease from those due to 'normal' age-related processes. The initial cognitive deficit in the majority of patients with Alzheimer's disease is a gradually progressive difficulty with learning and retention of new information, generally referred to as a deficit in episodic memory. This is consistent with the fact that the earliest pathological changes of the disease are the presence of amyloid plaques and neurofibrillary tangles in medial temporal lobe regions essential for normal memory (Braak and Braak, 1995; Drachman, 2006; Giannakopoulos et al., 1997), such as the entorhinal cortex and hippocampus (Braak and Braak, 1998; Gallagher and Koh, 2011). The transitive state between normal aging and Alzheimer's disease is termed mild cognitive impairment (MCI) (Petersen, 2011), although the exact definition of MCI remains controversial (Albert et al., 2011). There is increasing evidence that the pathology of Alzheimer's disease can take many years, if not decades, to evolve. This suggests that some individuals who appear normal (i.e., functionally asymptomatic) have gradually accumulating pathology. Indeed, the timing and rate of decline vary markedly across individuals (Salthouse and Ferrer-Caja, 2003).

Geneticists, molecular neurobiologists, and pharmacologists have made fundamental advances to explain the pathogenesis of Alzheimer's disease, and treatments have been developed which are administered as soon as symptoms begin. However, recent clinical trials, the majority of which have focused on the use of pharmacological agents, have not been successful in delaying the onset or halting the progression of Alzheimer's disease (Selkoe, 2012). Consequently, there are increasing calls to treat the disease, possibly in the form of preventive regiments, even before it has progressed to its mild to moderate stages (e.g., Bartus, 2000; Daffner, 2010; Hughes, 2010; Middleton and Yaffe, 2010; Selkoe, 2012; Thal, 2006).

2. Boosting cognitive reserve may offset cognitive decline

While cognitive decline is prevalent among older adults, there exists variability in the timeline of the onset of cognitive difficulty, even when biological evidence seemingly suggests otherwise. In a study on anatomical and physiological changes associated with dementia and Alzheimer's disease, some participants, despite showing the physical markers of dementia (e.g., neocortical plaques), maintained a healthy and age-typical cognitive status (Katzman et al., 1988). One possible explanation for this discrepancy between biology and behavior is that individual differences in *cognitive reserve* are responsible. Cognitive reserve is defined as resilience to neuropathological damage of the brain, and is thought to be the result of experience-based neural changes that are a consequence of a physically and mentally stimulating lifestyle (Whalley et al., 2004). These studies are based on an extensive research literature on animal models which has demonstrated that interacting with a complex environment influences neurogenesis and dendritic complexity, and promotes cognitive abilities and the capacity to compensate for injury (Albert, 2007; Billings et al., 2007; Connor et al., 1981; Fan et al., 2007; Gould et al., 1999; Greenough et al., 1985; Kempermann et al., 1997; Van Praag et al., 2000; Volkmar and Greenough, 1972). For example, physical activity has been found to regulate brain plasticity and, consequently, learning (Van Praag et al., 1999). Environmental enrichment may re-establish access to long term memories even after significant brain atrophy and neuronal loss have occurred (Fischer et al., 2007).

Although the mechanisms responsible are not fully understood (i.e., they may include synaptogenesis), the effectiveness of environmental enrichment is not disputed (Meshi et al., 2006). Importantly, the global cognitive benefits of environmental enrichment have been observed in animal models of Alzheimer's disease (Arendash et al., 2004). Similarly, spatial training in middle-aged mice has been demonstrated to delay the onset of neuropathology (Billings et al., 2007). Increased cognitive reserve is thought to be responsible for such effects of environmental enrichment (Nithianantharajah and Hannan, 2006).

Findings from the literature on environmental enrichment in animal models stand in parallel with research suggesting that lifestyle variables, such as cognitive leisure activities can moderate the risk of Alzheimer's disease, even later in life (e.g., Sattler et al., 2012; Verghese et al., 2003). Higher levels of cognitive functioning have been associated with higher occupational status, continuing involvement in education, stimulating leisure activities, and physical fitness (Brayne et al., 2010; Foubert-Samier et al., 2012; Kramer et al., 2004; McDowell et al., 2007; Staff et al., 2004; Valenzuela and Sachdev, 2006).

Two central proposals have been offered to explain the mechanism by which cognitive reserve benefits the individual (Valenzuela and Sachdev, 2006). The first possibility is that certain hardwired anatomical and physiological properties of an individual's brain may act as a protective mechanism by creating a higher threshold to sustain brain injury (Satz, 1993). For example, cognitively intact individuals with neuropathology also had increased brain size and a greater amount of large neurons in the frontal, parietal, and temporal cortices (Katzman et al., 1988). Structural brain differences have also been reported in MCI patients and these were linked to preserved cognitive abilities (Solé-Padullés et al., 2009). An alternative possibility is that cognitive reserve may reflect the brain's efficacious use of available resources and processing strategies. This view is supported by research suggesting that a lifetime of mental and physical enrichment may actively benefit the brain and subsequent cognitive processing of the individual, such that a brain with more cognitive reserve is able to use more efficient or alternative neural networks in the event of gradual brain decline (Stern, 2002). Certain lifestyle variables can explain differences in cognitive status among older adults. There is converging evidence that physical exercise is one such lifestyle variable that leads to improved physical and mental health (Colcombe et al., 2003; Hillman et al., 2008; Kramer et al., 1999; Kramer and Erickson, 2007; Wingfield and Grossman, 2006), and reduced risk of Alzheimer's disease even when initiated in later life (Scarmeas et al., 2009). Similar positive effects of physical exercise have been observed in individuals diagnosed with MCI (Lautenschlager et al., 2010) and Alzheimer's disease (Heyn et al., 2004).

Numerous studies have assessed mentally-stimulating lifestyle activities by incidentally evaluating a range of cognitive activities in which the participant might engage (e.g., reading books, going to lectures, playing board games, etc.) and developing a measure of the total hours spent doing these activities, adjusted for potentially confounding factors (Wilson et al., 2003, 2002). A common finding has been that older adults who regularly engage in intellectually stimulating exercises, such as reading newspapers and magazines, playing puzzle games, and going to museums, may delay or even reduce the occurrence of cognitive problems, including those related to dementia and Alzheimer's disease (Fratiglioni et al., 2004; Friedland et al., 2001; Scarmeas et al., 2001; Stern and Munn, 2010; Wang et al., 2002). Such intellectually stimulating activities have also been shown to reduce hippocampal atrophy (Valenzuela et al., 2008). In a study of 469 older adults (over 75 years), those who completed crossword puzzles four days per week had a 47% lower risk of developing dementia than those who completed puzzles only one day per week (Verghese et al., 2003), and a similar finding has been reported for individuals with the amnestic form of MCI, a precursor of Alzheimer's disease (Verghese et al., 2006). In a longitudinal investigation of 488 adults of which 101 developed dementia, it was found that each additional self-reported day of cognitive activity at baseline delayed the onset of accelerated memory decline by 0.18 years (Hall et al., 2009). A meta-analysis of over 29,000 individuals showed that those with high cognitive reserve were 46% less likely to develop dementia than those with low cognitive reserve, and this held over a 7.1 year follow-up period (Valenzuela and Sachdev, 2006).

Overall, it seems that a cognitively stimulating lifestyle yields positive cognitive outcomes, and this conclusion is consistent with prevalence studies that show that people with more years of education are at lower risk of developing Alzheimer's disease and other dementias. Hall et al. (2007) investigated the protective effect of education in 117 individuals with dementia as measured by the Buschke Selective Reminding Test, and found that each year of education delayed cognitive decline by 0.21 years. Snowdon et al. (2000) quantified linguistic ability in 74 older adults (aged 78–92 years) by examining biographies written in young adulthood (between the ages of 19 and 37). A negative correlation was found between linguistic ability in young adulthood and incidence of Alzheimer's disease in old age.

Incidental retrospective studies such as those reviewed above have raised the question of whether cognitively stimulating activities can be proactively administered to older adults in the form of cognitive training regiments (Stuss et al., 2007). Improvements brought about by training are attributed to *brain plasticity*, defined as functional changes in neural processing, caused by alterations at the cellular and synaptic levels, based on environmental demands (Buonomano and Merzenich, 1998; Greenwood, 2007). Cognitive training improvements have been demonstrated in younger adults for fluid intelligence (Jaeggi et al., 2008), and structural brain alterations have been observed following relatively short term (5-day) training interventions (May et al., 2007). Similarly, short-term working memory training has been associated with changes in the density of cortical dopamine D1 receptors in young adults (McNab et al., 2009). Importantly, training-related changes are not restricted to younger adults, and even when training occurs later in life, it can still yield positive cognitive outcomes due to brain plasticity in older adulthood.

Oswald et al. (1996) compared cognitive and psychomotor training in 375 older adults (aged 75 and over) for 2–3 h, 1 day per week, for 30 weeks. Combined psychomotor and memory training yielded improvements in psychomotor performance and led to reduced symptoms of dementia. Such findings that plasticity occurs at all ages has led to the development of computerized cognitive training regiments aimed at older populations that promote optimal cognitive health (Carlson et al., 2009; Dahlin et al., 2008; Günther et al., 2003; Simpson et al., 2012; Wolinsky et al., 2006) including in individuals with MCI (Barnes et al., 2009) and Alzheimer's disease (Tárraga et al., 2006). One such commercial program is LACE (Neurotone, 2011), a four-week computer-based auditory training protocol which improves older subjects' ability to listen to speech in noise (Henderson Sabes and Sweetow, 2007). Smith et al. (2009) compared over-65-year-olds who used the Brain Fitness Program (Posit Science, 2009) cognitive training software with a control group that viewed educational videos on history, art, and literature, and were quizzed on the content. Training occurred for 1 h per day, 5 days per week, over 8 weeks. The primary outcome measure was derived from the auditory subtests of the Repeatable Battery for the Assessment of Neuropsychological Status, and as expected, adults who trained using the Brain Fitness Program showed greater improvement. Performance improvements also generalized to untrained measures of memory and attention, and participants in the experimental group also reported improvements in cognitive functioning.

The positive effects of cognitive training techniques have also been shown to persist over time. Cognitive training studies with adults have shown that improvements in mental function last for months (or even years) post-training, when followed up with booster or 'refresher' sessions. Adults aged 65–94 who were trained to improve their memory, inductive reasoning, or speed of processing experienced enhancement, and those improvements were maintained for two years (Ball et al., 2002). Similarly, adults over the age of 65 who received 10-day training sessions lasting 60–75 min, over 5 weeks in either memory, reasoning, or speed of processing experienced improvement which continued for a subsequent five years when followed up by a yearly booster session (Willis et al., 2006). Adults aged 60 and over were tested on a series of auditory learning and memory tasks ranging from simple exercises dealing with acoustic building blocks to more complex auditory perception and speech comprehension training (Mahncke et al., 2006). Training was adaptive to each individual's ability and consisted of a 1 h session, 5 days per week, for 10 weeks. Individuals who had experienced the active training program showed immediate improvements in not only the trained tasks, but also generalized improvement in global auditory memory, and importantly, at the 3-month follow-up, improvements had been sustained. Similarly, adults at a retirement residence were given a 14-week computer-based cognitive training program (Günther et al., 2003). Despite the average age of the participants (mid-80s), the researchers observed improvements on all cognitive measures, and a marked improvement in learning verbal material and a reduction in interference tendency (a cause of memory loss) five months following the cessation of training.

These findings are evidence that cognitive training programs lead to unique cognitive enhancements that are not tapped by other activities. Encouragingly, those older adults who are at risk of neural dysfunction have shown sizeable positive responses to training (Valenzuela et al., 2003). Positive effects of training interventions have also been found in individuals with MCI (Belleville et al., 2011; Clare et al., 2000; Greenaway et al., 2008; Hampstead et al., 2011, 2008; Kinsella et al., 2009; Kurz et al., 2009; Troyer et al., 2008) and Alzheimer's disease (Bottino et al., 2005; Breuil et al., 1994; Clare et al., 2010). Older adults with Alzheimer's disease who completed mental exercises such as arithmetic calculations and reading aloud showed improved scores on the Frontal Assessment Battery, a neuropsychological measure of executive functioning, as well as improvements in communication and independence relative to a control group (Kawashima et al., 2005).

Despite converging evidence of the efficacy of cognitive training, some remain skeptical of its generalizability to improvements in cognitive ability in older adults or Alzheimer's patients (for a discussion see Fuyuno, 2007). For instance, Owen et al. (2010) found no evidence of transfer effects after 11,430 adults (aged 18–60) completed an online training program for a minimum of 10 min per day, 3 days per week, over 6 weeks. The training was designed to improve reasoning, memory, visuospatial skills, and attention, but generalization to other cognitive domains did not occur. However, an important limitation of the Owen et al. study is that the training may not have been of sufficient intensity or length to yield transfer effects. Thus, although not all researchers agree on the generalizability of cognitive training, there is sufficient evidence to recommend cognitive training to older adults given its relatively low cost and risk and potentially large benefit. Two recent reviews of cognitive interventions in individuals with MCI concluded that cognitive interventions with a social component yield tangible and long-lasting benefits, and thus participation in cognitive and social activities is recommended (Petersen, 2011; Simon et al., 2012).

3. Foreign language training as a cognitively stimulating exercise

We have reviewed findings that older adults who participate in cognitively stimulating activities, including proactively administered cognitive training, benefit from improved cognitive function, build cognitive reserve, and can delay the onset of more severe functional decline. The types of cognitive training that have been administered range from arithmetic and logic puzzles to social activities and board games. However, no study to date has examined foreign language learning as a type of cognitive training activity for older adults. We will make the case that foreign language learning in particular is likely to make a sizeable contribution to cognitive reserve, and in turn, healthy cognitive function. Our argument is based on evidence that has shown multilingualism to be a better predictor of cognitive ability than age, age at immigration, education, or gender (Kavé et al., 2008; Mohamed Zied et al., 2004), and its effects can be seen across the lifespan (Green, 1998). Older adults who speak two or more languages also tend to perform better on a variety of cognitive tasks. This advantage in cognitive ability is thought to depend on experience with two languages, which requires a somewhat different set of attention and control procedures in bilinguals compared to monolinguals (Green, 1998). Consequently, bilingual older adults show a less steep decline in the slowing down of cognitive functions with age (see Bialystok, 2009), they outperform age-matched monolinguals on measures of executive functioning, such as the Simon task (Bialystok et al., 2004), and these cognitive advantages have neurological correlates, such as maintained white matter integrity (Luk et al., 2011). There is even evidence that bilingualism delays the onset of dementia by 4 years as compared to monolingual controls (Bialystok et al., 2007; Craik et al., 2010). Bilingual patients diagnosed with probable Alzheimer's disease showed substantially more atrophy in temporal regions than did their monolingual counterparts, but were still able to function at the same cognitive level (Schweizer et al., 2012). Thus, bilingualism, like engagement in cognitively stimulating lifestyle activities, may yield positive age-related cognitive outcomes. It is conceivable that benefits may also be observed in older adults who receive intensive training in a foreign language. We acknowledge that foreign language training initiated in later life may not lead to bilingualism per se, however, there is a great deal of evidence to suggest that the older adult brain retains plasticity (Boyke et al., 2008), and thus, language training should yield tangible results.

Language learning engages an extensive network of the brain (Rodríguez-Fornells et al., 2009) that overlaps with the network of decline due to aging (e.g., Raz, 2000). A number of cognitive processes are involved, such as working memory, inductive reasoning, sound discrimination, speech segmentation, task switching, rule learning, and semantic memory. The brain network involved in language learning in adulthood can be characterized into multiple major streams. The learning of new speech sounds (phonological contrasts) is associated with the dorsal audio-motor interface covering the posterior temporal region and the dorsal frontal lobe regions such as the ventral premotor cortex and posterior inferior frontal gyrus (IFG) (Hickok and Poeppel, 2007; Wong et al., 2007). The acquisition of meaning involves the ventral stream, including medial, inferior, and anterior temporal regions (Saur et al., 2008; Wong et al., 2010), as well as regions in the IFG for semantic retrieval and additional complex processing (Thompson-Schill, 2003). Word learning also often involves a fast mapping process between sound and meaning which is associated with the medial temporal lobe (Davis and Gaskell, 2009; Markson and Bloom, 1997; Ullman, 2001). The learning of grammatical rules (syntax) is linked to the frontostriatal system (Tyler et al., 2005; Ullman, 2001). Furthermore, additional attentional resources are needed especially during the initial phases of learning which might result in the engagement of the prefrontal cortex (Ellis, 2008; Ullman, 2001). The exact functional roles of these streams are not always uncontroversial, however, few would deny that the acquisition of a new language involves a large brain network with regions similar to those described above.

Second language learning largely involves the same neural structures as the native language, although this is modulated by age of acquisition and second language proficiency (Abutalebi, 2008). It is also important to distinguish between the brain regions involved in second language processing (such as syntax and grammar networks), and those structures responsible for controlling the first and second language networks themselves (Abutalebi et al., 2012; Green, 1998). In terms of grammar processing, both high and low proficiency bilinguals engage the same neural structures for the native and second languages, but those who acquire the second language later in life typically show additional activity in left prefrontal areas (Abutalebi, 2008). In terms of syntax, learners have been shown to recruit brain areas related to native language processing (such as the left IFG) following only 6 months of foreign language learning (Indefrey et al., 2005). Structural changes have been observed in the parietal lobes as a result of foreign speech sound learning (Golestani et al., 2007). In general, lexical tasks result in more left prefrontal activity when the learner has not achieved native-like competence, but as proficiency increases the brain activity of the first and second languages converges (Green, 2003). Indeed, increasing proficiency has been linked to functional changes in language-related brain regions, such as the left prefrontal and parietal areas (Chee et al., 2001; Mechelli et al., 2004; Perani and Abutalebi, 2005; Yetkin et al., 1996).

It is important to note that the positive bilingual outcomes in older adults reviewed above (e.g., Bialystok et al., 2007) concerned those individuals who spoke two or more languages over the course of a lifetime, and the studies were performed retrospectively (with regard to the subjects' language learning). Whether or not bilingualism initiated later in life (through foreign language training) could improve cognitive functions remains to be investigated prospectively. Evidence from young adult learners suggests that foreign language training initiated in adulthood induces structural brain changes. Stein et al. (2012) examined learning-related structural changes in English native speakers (aged 18 years) following five months of foreign language learning and found a correlation between proficiency in Swiss German and gray matter density in the left IFG and the left anterior temporal lobe (ATL). The left IFG has been linked with increasing second language proficiency in semantic (Perani et al., 1998) and syntactic tasks (Sakai, 2005), and the left ATL has been linked with integrating semantic information (Vigneau et al., 2006) and holding information in memory before consolidation processing (Miyashita, 2004). Mårtensson et al. (2012) examined Swedish native speakers (aged 21 years) after three months of intensive training in an unfamiliar language (Dari, Russian or Arabic). They observed significant changes in cortical thickness in the fronto-temporal cortex of the left hemisphere, indicating that adult foreign language learning is accompanied by increases of gray matter volume in language-related areas. Plasticity was also observed in the hippocampus and left superior temporal gyrus (STG), consistent with findings in the bilingual literature that neural changes resulting from foreign language learning may constitute the mechanism behind the delaying effect of bilingualism on the onset of dementia (e.g., Craik et al., 2010). A tantalizing possibility is whether proactively administered foreign language learning in older adults may result in brain changes that can ultimately lead to a cognitive protective effect. We believe that such training can be effective not only because various cognitive training activities initiated later in life have been shown to result in cognitive improvement, but also because language learning targets a widespread neural network that overlaps with the neurocognitive network that has been found to decline, extending beyond the network of executive control. Through mechanisms of microanatomical plasticity, training would result in better cognitive outcomes.

As a starting point, we put forth the following hypothesis concerning how foreign language learning might modulate neural plasticity for optimal cognitive gain in older adults. Aging is associated with various symptoms of decline, ranging from the general (e.g., reduced working memory availability and attention) to the language-specific (e.g., slower lexical retrieval). Language learning is a form of behavioral stimulation that engages an extensive network and naturally incorporates social aspects that have been shown to be effective in inducing positive cognitive outcomes (e.g., Pushkar et al., 1999). The language learning network overlaps substantially with the network of decline seen in cognitive aging, including structures on the lateral surface of the brain (prefrontal cortex, IFG, and temporal lobe) as well as medial and subcortical structures. Language learning may promote positive neurophysiological changes within the network, via synaptic processes that are commonly associated with neuronal plasticity and repair (e.g., Merzenich et al., 1984; Recanzone et al., 1992). Structural plasticity is subserved by cellular mechanisms including synapse formation (Knott et al., 2002), growth and retraction of dendritic spines (Hofer et al., 2009), axonal remodeling (Holtmaat and Svoboda, 2009), astrocyte modifications (Theodosis et al., 2008), and potentially neurogenesis (Ming and Song, 2005). It has been suggested that the dendritic spines of pyramidal neurons (which are important for long distance neural connections) in the cerebral cortex may be the sites of synapses that are selectively modified by learning (Yuste and Bonhoeffer, 2001). This position is consistent with research on animal models that has documented experience-dependent changes in the adult brain following short-term training (Black et al., 1990; Lerch et al., 2011; Quallo et al., 2009), including differences in long term potentiation (Matsuzaki et al., 2004). Work on humans has corroborated that training-related changes in tissue microstructure are likely to lead to recruitment of more efficient brain networks, and are linked to physiological and cognitive outcomes (Hofstetter et al., 2013; Sagi et al., 2012). These brain changes are unlikely to occur in isolation because plasticity of regional brain volume likely reflects a cascade of changes in dendritic branching, synapses, cell numbers, cell sizes, and capillaries (Lövdén et al., 2013). Increases in brain volume and connectivity between regions involved in the foreign language learning process are likely to reflect synaptogenesis and changes in dendritic morphology, and may result in a transfer of cognitive benefits to other non-language related domains. Foreign language training may engage a larger brain network than other forms of cognitive training that have been investigated (e.g., math and crossword puzzles), and it is likely to require long distance neural connections. The end result of foreign language learning may be that language function is promoted, the integrity of the brain structures involved is maintained, and a greater number of potential neural circuits could be available that allow for compensation of age-related cognitive declines. The neural hypothesis here is obviously preliminary, but provides an exciting starting point for language-related research in older adult learners.

4. Special considerations for older learners

Taken together, a large body of research studies point to the fact that cognitive decline and the accompanied brain network are extensive. Some older adults show less of a cognitive decline profile, including those who engage in active cognitively stimulating activities and those who speak more than one language. Because even the older adult brain is plastic, it is possible that initiating language learning will not only improve language-related functions but also improve cognitive functions in older adults. Given the need to develop preventive treatment for Alzheimer's disease and other cognitive disorders, training older adults who have age-typical cognitive abilities might lead to improved clinical outcomes. In order to test this possibility it will be necessary to compare healthy older adults with those who have neurodegenerative diseases (e.g., Alzheimer's disease) or suffer from other conditions that may hinder learning (e.g., depression). Despite the cognitive and practical benefits of second language learning, no studies have examined both second language learning and cognitive ability in older adults along the same timeline. Indeed very little research has been conducted on older language learners (above age 65) at all. The adult learning literature equates older learners (e.g., 65-year-olds) with young adults (e.g., 25-year-olds), and in doing so conflates the known learning differences between younger and older learners (for a review see Krashen et al., 1979; Marinova-Todd et al., 2000). Adult learners differ from child learners in four key ways (Knowles, 1973): they are self-directed and do not depend on the teacher to guide their learning, they benefit from experiential learning, they have already acquired the basic skills needed to succeed in life and absorb information on a 'need to know' basis, and adults are more performance-centered in their learning (e.g., speed, in-depth analysis, vocabulary).

Older adults also face biological and physical challenges to learning. Recent advances in functional brain imaging have made it possible to examine whether older adults show the same types of brain–behavior relationships observed in younger adults. It appears that they may not. Older adults instead demonstrate patterns of activation that may reflect compensation for a reduced ability to meet the demands of cognitively challenging tasks, or an age-related shift in cognitive strategy (Reuter-Lorenz and Sylvester, 2005; Rypma and D'Esposito, 2000). For example, some functions represented unilaterally in the brains of young adults are bilaterally represented in the brains of older adults (Cabeza et al., 2002). More generally, factors such as cognitive decline, auditory and visual problems, and other health issues (including cardiovascular risks, genetics and lifestyle) may prevent older adults from fully benefiting from traditional learning situations originally designed for young learners (Knowles, 1973). Mixed classroom settings (including both young and older learners) may not be the optimal environment for the older learners because they may feel that their abilities are deficient, which in turn lowers confidence and motivation (Marinova-Todd et al., 2000). Similarly, older learners may not fare as well on memorization and rote learning tasks, and competitive exercises involving speed (Schleppegrell, 1987).

Another important consideration is the prior level of education of the subjects. The protective effect of bilingualism on age-related cognitive decline appears to be greatest for low education individuals (Gollan et al., 2011). Encouragingly, structural brain changes have been found in highly educated young adults following foreign language training (Mårtensson et al., 2012; Stein et al., 2012). Taken together, these findings suggest that effects could potentially be observed in older adults of varying education levels who learn a foreign language. In order to maximize foreign language outcomes and the associated benefits, it may be necessary to customize the training to suit individual learning profiles (Wong et al., 2012).

In the past, it was thought that adult learners were incapable of acquiring a foreign language (Lenneberg, 1967; Penfield and Roberts, 1959), although researchers now acknowledge that the language learning apparatus remain intact across the lifespan, and that adult language learners benefit from their experience-based linguistic knowledge, increased higher-order brain development, and more complex cognitive processing (Schleppegrell, 1987; Singleton and Lengyel, 1995). Motivation also plays a larger role in determining language learning success in older adults (Marinova-Todd et al., 2000). Therefore, it is crucial to identify the optimal learning method for older learners, namely by ensuring that older learners are motivated, that the material has immediate practical value and is personally rewarding (Grognet, 1997; Hamil-Luker and Uhlenberg, 2002; Homstad, 1987). Bearing this in mind, language learning is an ideal training activity for older learners because it has the associated benefits of being meaningful (an advantage over other cognitive training approaches) and it may expand post-retirement activities (e.g., improve travel, business interactions, and communication with speakers of other languages).

The method of delivery could be customized to meet the needs of individual learners. Computer-based language training has the advantages that it may be administered in a location and at times convenient to the learner, items may be repeated, volume may be adjusted to an optimum level for each learner, and it brings with it other benefits. For example, simply training older adults to use computers and the internet twice a week over four months has been found to contribute to well-being and sense of empowerment (Shapira et al., 2007). In addition to computer-based learning, regular social meetings guided by a native-speaking instructor are an essential component of any foreign language training regiment, and permit learners to practice and develop their language skills with other learners. Our review has established the importance of psychosocial factors on neurobiological decline. The social and communicative aspects of language training may provide a further boost to the expected linguistic effects, ultimately generating a larger effect than other cognitive activities, such as completing crossword and math puzzles.

5. Future directions

Given the gaps in the literature concerning language learning as a cognitive-reserve-building activity, and the paucity of studies involving older adult language learners, a useful line of future research would be to determine whether cognitive improvements can result from language learning in older adults (aged 65 and over). The proposed research has two overarching aims. The first is to determine whether foreign language learning initiated in later adulthood can result in improvements in cognitive functions (working memory, attention, and inhibitory control) measured objectively and by self-report, and the second is to compare the magnitude of the observed improvements with other cognitively stimulating activities (e.g., crossword puzzles/math problems), as well as a passive control baseline in which no training is provided.

It would be necessary to investigate learning success and also the longevity of the cognitive benefits of language training on working memory, processing speed, task switching, and inhibitory control using standardized cognitive tests at baseline, after training, and at several time points beyond the cessation of training. Successful foreign language learning requires that training be high intensity so as to drive proficiency. This means that in order for language learning to contribute to cognitive reserve, language training sessions will need to be of sufficient length and frequency (see discussion of Owen et al., 2010). Structural changes in the brains of adult learners have been reported well within the first year of foreign language learning, after only three (Mårtensson et al., 2012) and five months (Stein et al., 2012). We would expect to see effects in older adults within a comparable timeframe. In reference to older language learners, in an unpublished doctoral dissertation, Linhart-Wegschaider (2010) asked older adults to learn Mandarin via audio tapes for 30 min per day, 30 days per month, over 3 months. Based on these studies, learning-related changes in older adults should be expected within six months of commencing language training, with training occurring for 1 h per day, 5 days per week. Importantly, although such a language training schedule may not be sufficient for learners to attain native-like proficiency or improve executive functioning to the same extent as lifelong bilingualism, it is expected to yield statistically reliable cognitive improvements in measures of working memory and executive function.

If, as we hypothesize, foreign language training is shown to be effective in boosting cognitive reserve, the findings would lay the foundations for future investigations over a longer time-frame, allowing for detection of the incidence of dementia. We would predict that fewer subjects receiving foreign language training would develop dementia than those completing alternative cognitive training, such as crossword/math puzzles. Additionally, follow-up neural investigations would uncover the underlying brain mechanisms of cognitive resilience. Specifically, magnetic resonance imaging could be used to document training-related changes in gray matter in the dorsolateral prefrontal cortex, hippocampus, STG, and other areas of interest, which may be indicative of microanatomical changes such as synaptogenesis. Further, diffusion tensor imaging could be used to check white matter integrity and functional connectivity prior to and following language training. Changes may suggest modification in pyramidal cell projections. Traditionally, studies on the protection of individuals at risk for dementia have focused on mean level performance. Measuring subjects' cognitive profiles would allow researchers to ascertain which profiles benefit most, and it may be possible to use such predictors to customize language training protocols to maximize beneficial outcomes.

The risks of behavioral and psychosocial interventions such as that proposed are much smaller than those of pharmacological treatments. However, when recommending any intervention, it is necessary to consider any potential risks to subjects. One possible drawback is that foreign lexical items may compete with those of the native language during word retrieval (Ivanova and Costa, 2008) and this has been observed even after short-term foreign language immersion programs (Baus et al., 2013). Bearing this in mind, we do not hesitate to recommend foreign language training as an intervention because the potential benefits far outweigh any risks. More effortful lexical retrieval is not likely to impact on the everyday lives of treatment subjects in any meaningful or noticeable way, whereas the resulting cognitive improvements certainly will.

6. Conclusion

In this review, we have outlined the cognitive benefits of stimulating lifestyle activities and proactively administered cognitive training programs, and also of multilingualism. The review led us to propose that foreign language learning is likely to be particularly beneficial in promoting healthy cognitive function and protecting against decline because it combines elements from these separate, but beneficial, research literatures. Specifically, a line of research investigating language training as a type of cognitive-reserve-building activity in older adult learners is needed to quantify the benefits of language training on age-related cognitive decline as measured by standardized tests and self-report. Such a line of scientific inquiry would reveal if foreign language learning contributes to cognitive reserve and promotes healthy cognitive aging. The knowledge gained may inform second language teaching practice, potentially benefiting older adult students. The findings would add to the current literature on the learning potential of the elderly community, fill a societal need for language-learning opportunities specific to older learners, and also contribute to ensuring healthy cognitive function in older adults.

Acknowledgements

We would like to acknowledge the financial support of the National Science Foundation (BCS-1125144), the National Institutes of Health (R01DC008333 and K02AG035382) and Northwestern University.

References

Abutalebi, J., 2008. Neural aspects of second language representation and language control. Acta Psychol. 128, 466–478.
Abutalebi, J., Rosa, P.A.D., Green, D.W., Hernandez, M., Scifo, P., Keim, R., Cappa, S.F., Costa, A., 2012. Bilingualism tunes the anterior cingulate cortex for conflict monitoring. Cereb. Cortex 22, 2076–2086.
Albert, M.S., 2007. Changing the trajectory of cognitive decline? N. Engl. J. Med. 357, 502–503.
Albert, M.S., DeKosky, S.T., Dickson, D., Dubois, B., Feldman, H.H., Fox, N.C., Gamst, A., Holtzman, D.M., Jagust, W.J., Petersen, R.C., Snyder, P.J., Carrillo, M.C., Thies, B., Phelps, C.H., 2011. The diagnosis of mild cognitive impairment due to Alzheimer's disease: recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. Alzheimers Dement. 7, 270–279.
Arendash, G.W., Garcia, M.F., Costa, D.A., Cracchiolo, J.R., Wefes, I.M., Potter, H., 2004. Environmental enrichment improves cognition in aged Alzheimer's transgenic mice despite stable [beta]-amyloid deposition. Neuroreport 15, 1751–1754.
Bäckman, L., Farde, L., 2005. The role of dopamine systems in cognitive aging. In: Cabeza, R., Nyberg, L., Park, D. (Eds.), Cognitive Neuroscience of Aging: Linking Cognitive and Cerebral Aging. Oxford University Press, New York, pp. 58–84.
Bäckman, L., Lindenberger, U., Li, S.-C., Nyberg, L., 2010. Linking cognitive aging to alterations in dopamine neurotransmitter functioning: recent data and future avenues. Neurosci. Biobehav. Rev. 34, 670–677.
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. JAMA 288, 2271–2281.
Barnes, D.E., Yaffe, K., Belfor, N., Jagust, W.J., DeCarli, C., Reed, B.R., Kramer, J.H., 2009. Computer-based cognitive training for mild cognitive impairment. Alzheimer Dis. Assoc. Disord. 23, 205–210.
Bartus, R.T., 2000. On neurodegenerative diseases, models, and treatment strategies: lessons learned and lessons forgotten a generation following the cholinergic hypothesis. Exp. Neurol. 163, 495–529.
Baus, C., Costa, A., Carreiras, M., 2013. On the effects of second language immersion on first language production. Acta Psychol. 142, 402–409.
Belleville, S., Clément, F., Mellah, S., Gilbert, B., Fontaine, F., Gauthier, S., 2011. Training-related brain plasticity in subjects at risk of developing Alzheimer's disease. Brain 134, 1623–1634.
Bialystok, E., 2009. Bilingualism: the good, the bad, and the indifferent. Biling. Lang. Cogn. 12, 3–11.
Bialystok, E., Craik, F.I.M., Freedman, M., 2007. Bilingualism as a protection against the onset of symptoms of dementia. Neuropsychologia 45, 459–464.
Bialystok, E., Craik, F.I.M., Klein, R., Viswanathan, M., 2004. Bilingualism, aging, and cognitive control: evidence from the Simon task. Psychol. Aging 19, 290–303.
Billings, L.M., Green, K.N., McGaugh, J.L., LaFerla, F.M., 2007. Learning decreases Aβ*56 and Tau pathology and ameliorates behavioral decline in 3xTg-AD mice. J. Neurosci. 27, 751–761.
Black, J.E., Isaacs, K.R., Anderson, B.J., Alcantara, A.A., Greenough, W.T., 1990. Learning causes synaptogenesis, whereas motor activity causes angiogenesis, in cerebellar cortex of adult rats. Proc. Natl. Acad. Sci. U.S.A. 87, 5568–5572.
Bopp, K.L., Verhaeghen, P., 2005. Aging and verbal memory span: a meta-analysis. J. Gerontol. B: Psychol. Sci. Soc. Sci. 60, P223–P233.
Bottino, C.M.C., Carvalho, I.A.M., Alvarez, A.M.M.A., Avila, R., Zukauskas, P.R., Bustamante, S.E.Z., Andrade, F.C., Hototian, S.R., Saffi, F., Camargo, C.H.P., 2005. Cognitive rehabilitation combined with drug treatment in Alzheimer's disease patients: a pilot study. Clin. Rehabil. 19, 861–869.
Boyke, J., Driemeyer, J., Gaser, C., Büchel, C., May, A., 2008. Training-induced brain structure changes in the elderly. J. Neurosci. 28, 7031–7035.
Braak, H., Braak, E., 1995. Staging of Alzheimer's disease-related neurofibrillary changes. Neurobiol. Aging 16, 271–278.
Braak, H., Braak, E., 1998. Evolution of neuronal changes in the course of Alzheimer's disease. J. Neural. Transm. Suppl. 53, 127–140.
Brayne, C., Ince, P.G., Keage, H.A.D., McKeith, I.G., Matthews, F.E., Polvikoski, T., Sulkava, R., 2010. Education, the brain and dementia: neuroprotection or compensation? Brain 133, 2210–2216.
Breuil, V., de Rotrou, J., Forette, F., Tortratl, D., Ganansia-Ganem, A., Frambourt, A., Moulin, F., Boller, F., 1994. Cognitive stimulation of patients with dementia: preliminary results. Int. J. Geriatr. Psychiatry 9, 211–217.
Buonomano, D.V., Merzenich, M.M., 1998. Cortical plasticity: from synapses to maps. Annu. Rev. Neurosci. 21, 149–186.
Burke, D.M., Shafto, M.A., 2004. Aging and language production. Curr. Dir. Psychol. Sci. 13, 21–24.
Cabeza, R., 2002. Hemispheric asymmetry reduction in older adults: the HAROLD model. Psychol. Aging 17, 85–100.

Cabeza, R., Anderson, N.D., Locantore, J.K., McIntosh, A.R., 2002. Aging gracefully: compensatory brain activity in high-performing older adults. NeuroImage 17, 1394–1402.
Cabeza, R., Daselaar, S.M., Dolcos, F., Prince, S.E., Budde, M., Nyberg, L., 2004. Task-independent and task-specific age effects on brain activity during working memory, visual attention and episodic retrieval. Cereb. Cortex 14, 364–375.
Carlson, M.C., Erickson, K.I., Kramer, A.F., Voss, M.W., Bolea, N., Mielke, M., McGill, S., Rebok, G.W., Seeman, T., Fried, L.P., 2009. Evidence for neurocognitive plasticity in at-risk older adults: the Experience Corps Program. J. Gerontol. A: Biol. Sci. Med. Sci. 64, 1275–1282.
Cerella, J., 1985. Information processing rates in the elderly. Psychol. Bull. 98, 67–83.
Chee, M.W.L., Hon, N., Lee, H.L., Soon, C.S., 2001. Relative language proficiency modulates BOLD signal change when bilinguals perform semantic judgments. NeuroImage 13, 1155–1163.
Chodosh, J., Reuben, D.B., Albert, M.S., Seeman, T.E., 2002. Predicting cognitive impairment in high-functioning community-dwelling older persons: Macarthur Studies of Successful Aging. J. Am. Geriatr. Soc. 50, 1051–1060.
Clare, L., Linden, D.E.J., Woods, R.T., Whitaker, R., Evans, S.J., Parkinson, C.H., van Paasschen, J., Nelis, S.M., Hoare, Z., Yuen, K.S.L., Rugg, M.D., 2010. Goal-oriented cognitive rehabilitation for people with early-stage Alzheimer Disease: a single-blind randomized controlled trial of clinical efficacy. Am. J. Geriatr. Psychiatry 18, 928–939.
Clare, L., Wilson, B.A., Carter, G., Breen, K., Gosses, A., Hodges, J.R., 2000. Intervening with everyday memory problems in dementia of Alzheimer type: an errorless learning approach. J. Clin. Exp. Neuropsychol. 22, 132.
Colcombe, S.J., Erickson, K.I., Raz, N., Webb, A.G., Cohen, N.J., McAuley, E., Kramer, A.F., 2003. Aerobic fitness reduces brain tissue loss in aging humans. J. Gerontol. A: Biol. Sci. Med. Sci. 58, M176–M180.
Connor, J.R., Melone, J.H., Yuen, A.R., Diamond, M.C., 1981. Dendritic length in aged rats' occipital cortex: an environmentally induced response. Exp. Neurol. 73, 827–830.
Craik, F.I.M., Bialystok, E., Freedman, M., 2010. Delaying the onset of Alzheimer disease: bilingualism as a form of cognitive reserve. Neurology 75, 1726–1729.
Craik, F.I.M., Salthouse, T.A. (Eds.), 2008. The Handbook of Aging and Cognition. , 3rd ed. Psychology Press, New York.
Cullum, S., Huppert, F.A., McGee, M., Dening, T., Ahmed, A., Paykel, E.S., Brayne, C., 2000. Decline across different domains of cognitive function in normal ageing: results of a longitudinal population-based study using CAMCOG. Int. J. Geriatr. Psychiatry 15, 853–862.
Daffner, K.R., 2010. Promoting successful cognitive aging: a comprehensive review. J. Alzheimers Dis. 19, 1101–1122.
Dahlin, E., Neely, A.S., Larsson, A., Bäckman, L., Nyberg, L., 2008. Transfer of learning after updating training mediated by the striatum. Science 320, 1510–1512.
Davis, M.H., Gaskell, M.G., 2009. A complementary systems account of word learning: neural and behavioural evidence. Philos. Trans. R. Soc. B 364, 3773–3800.
Department of Economic and Social Affairs Population Division, 2007. World Population Ageing. United Nations Publications, New York.
Drachman, D.A., 2006. Aging of the brain, entropy, and Alzheimer disease. Neurology 67, 1340–1352.
Eckert, M.A., Keren, N.I., Roberts, D.R., Calhoun, V.D., Harris, K.C., 2010. Age-related changes in processing speed: unique contributions of cerebellar and prefrontal cortex. Front. Hum. Neurosci. 4, Article 10.
Ellis, N.C., 2008. Usage-based and form-focused language acquisition: the associative learning of constructions, learned attention, and the limited L2 endstate. In: Robinson, P., Ellis, N.C. (Eds.), Handbook of Cognitive Linguistics and Second Language Acquisition. Routledge, New York, pp. 372–405.
Fan, Y., Liu, Z., Weinstein, P.R., Fike, J.R., Liu, J., 2007. Environmental enrichment enhances neurogenesis and improves functional outcome after cranial irradiation. Eur. J. Neurosci. 25, 38–46.
Federmeier, K.D., van Petten, C., Schwartz, T.J., Kutas, M., 2003. Sounds, words, sentences: age-related changes across levels of language processing. Psychol. Aging 18, 858–872.
Ferri, C.P., Prince, M., Brayne, C., Brodaty, H., Fratiglioni, L., Ganguli, M., Hall, K., Hasegawa, K., Hendrie, H., Huang, Y., Jorm, A., Mathers, C., Menezes, P.R., Rimmer, E., Scazufca, M., 2005. Global prevalence of dementia: a Delphi consensus study. Lancet 366, 2112–2117.
Fischer, A., Sananbenesi, F., Wang, X., Dobbin, M., Tsai, L.-H., 2007. Recovery of learning and memory is associated with chromatin remodelling. Nature 447, 178–182.
Foubert-Samier, A., Catheline, G., Amieva, H., Dilharreguy, B., Helmer, C., Allard, M., Dartigues, J.-F., 2012. Education, occupation, leisure activities, and brain reserve: a population-based study. Neurobiol. Aging 33, 423.e15–423.e25.
Fratiglioni, L., Paillard-Borg, S., Winblad, B., 2004. An active and socially integrated lifestyle in late life might protect against dementia. Lancet Neurol. 3, 343–353.
Friedland, R.P., Fritsch, T., Smyth, K.A., Koss, E., Lerner, A.J., Chen, C.H., Petot, G.J., Debanne, S.M., 2001. Patients with Alzheimer's disease have reduced activities in midlife compared with healthy control-group members. Proc. Natl. Acad. Sci. U.S.A. 98, 3440–3445.
Fuyuno, I., 2007. Brain craze. Nature 447, 18–20.
Gallagher, M., Koh, M.T., 2011. Episodic memory on the path to Alzheimer's disease. Curr. Opin. Neurobiol. 21, 929–934.
Giannakopoulos, P., Hof, P.R., Michel, J.-P., Guimon, J., Bouras, C., 1997. Cerebral cortex pathology in aging and Alzheimer's disease: a quantitative survey of large hospital-based geriatric and psychiatric cohorts. Brain Res. Rev. 25, 217–245.
Golestani, N., Molko, N., Dehaene, S., LeBihan, D., Pallier, C., 2007. Brain structure predicts the learning of foreign speech sounds. Cereb. Cortex 17, 575–582.
Gollan, T.H., Salmon, D.P., Montoya, R.I., Galasko, D.R., 2011. Degree of bilingualism predicts age of diagnosis of Alzheimer's disease in low-education but not in highly educated Hispanics. Neuropsychologia 49, 3826–3830.
Gould, E., Beylin, A., Tanapat, P., Reeves, A., Shors, T.J., 1999. Learning enhances adult neurogenesis in the hippocampal formation. Nat. Neurosci. 2, 260.
Grady, C.L., Craik, F.I.M., 2000. Changes in memory processing with age. Curr. Opin. Neurobiol. 10, 224–231.
Green, D.W., 1998. Mental control of the bilingual lexico-semantic system. Biling. Lang. Cogn. 1, 67–81.
Green, D.W., 2003. The neural basis of the lexicon and the grammar in L2 acquisition. In: van Hout, R., Hulk, A., Kuiken, F., Towell, R. (Eds.), The Interface Between Syntax and the Lexicon in Second Language Acquisition. John Benjamins, Amsterdam, pp. 197–218.
Greenaway, M.C., Hanna, S.M., Lepore, S.W., Smith, G.E., 2008. A behavioral rehabilitation intervention for amnestic mild cognitive impairment. Am. J. Alzheimers Dis. Other Demen. 23, 451–461.
Greenough, W.T., Hwang, H.M., Gorman, C., 1985. Evidence for active synapse formation or altered postsynaptic metabolism in visual cortex of rats reared in complex environments. Proc. Natl. Acad. Sci. U.S.A. 82, 4549–4552.
Greenwood, P.M., 2007. Functional plasticity in cognitive aging: review and hypothesis. Neuropsychology 21, 657–673.
Greicius, M.D., Srivastava, G., Reiss, A.L., Menon, V., 2004. Default-mode network activity distinguishes Alzheimer's disease from healthy aging: evidence from functional MRI. Proc. Natl. Acad. Sci. U.S.A. 101, 4637–4642.
Grognet, A.G., 1997. Elderly Refugees and Language Learning. Center for Applied Linguistics, Washington, DC.
Gunning-Dixon, F., Raz, N., 2003. Neuroanatomical correlates of selected executive functions in middle-aged and older adults: a prospective MRI study. Neuropsychologia 41, 1929–1941.
Günther, V.K., Schäfer, P., Holzner, B.J., Kemmler, G.W., 2003. Long-term improvements in cognitive performance through computer-assisted cognitive training: a pilot study in a residential home for older people. Aging Ment. Health 7, 200–206.
Hall, C.B., Derby, C., LeValley, A., Katz, M.J., Verghese, J., Lipton, R.B., 2007. Education delays accelerated decline on a memory test in persons who develop dementia. Neurology 69, 1657–1664.
Hall, C.B., Lipton, R.B., Sliwinski, M., Katz, M.J., Derby, C.A., Verghese, J., 2009. Cognitive activities delay onset of memory decline in persons who develop dementia. Neurology 73, 356–361.
Hamil-Luker, J., Uhlenberg, P., 2002. Later life education in the 1990. J. Gerontol. B: Psychol. Sci. Soc. Sci. 57, S324–S331.
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., Stringer, A.Y., Stilla, R.F., Deshpande, G., Hu, X., Moore, A.B., Sathian, K., 2011. Activation and effective connectivity changes following explicit-memory training for face–name pairs in patients with mild cognitive impairment a pilot study. Neurorehabil. Neural Repair 25, 210–222.
Harrington, D.L., Haaland, K.Y., 1992. Skill learning in the elderly: diminished implicit and explicit memory for a motor sequence. Psychol. Aging 7, 425–434.
Hedden, T., Gabrieli, J.D.E., 2005. Healthy and pathological processes in adult development: new evidence from neuroimaging of the aging brain. Curr. Opin. Neurobiol. 18, 740.
Henderson Sabes, J., Sweetow, R.W., 2007. Variables predicting outcomes on listening and communication enhancement (LACE) training. Int. J. Audiol. 46, 374–383.
Heyn, P., Abreu, B.C., Ottenbacher, K.J., 2004. The effects of exercise training on elderly persons with cognitive impairment and dementia: a meta-analysis. Arch. Phys. Med. Rehabil. 85, 1694–1704.
Hickok, G., Poeppel, D., 2007. The cortical organization of speech processing. Nat. Rev. Neurosci. 8, 393–402.
Hillman, C.H., Erickson, K.I., Kramer, A.F., 2008. Be smart, exercise your heart: exercise effects on brain and cognition. Nat. Rev. Neurosci. 9, 58–65.
Hofer, S.B., Mrsic-Flogel, T.D., Bonhoeffer, T., Hübener, M., 2009. Experience leaves a lasting structural trace in cortical circuits. Nature 457, 313–317.
Hofstetter, S., Tavor, I., Moryosef, S.T., Assaf, Y., 2013. Short-term learning induces white matter plasticity in the fornix. J. Neurosci. 33, 12844–12850.
Holtmaat, A., Svoboda, K., 2009. Experience-dependent structural synaptic plasticity in the mammalian brain. Nat. Rev. Neurosci. 10, 647–658.
Homstad, A., 1987. Neurolinguistic and psycholinguistic research on learning modes of older language learners: classroom implications. Hispania 70, 374–380.
Hughes, T.F., 2010. Promotion of cognitive health through cognitive activity in the aging population. Aging Health 6, 111–121.
Indefrey, P., Hellwig, F., Davidson, D., Gullberg, M., 2005. Native-like hemodynamic responses during sentence comprehension after six months of learning a new language. In: Presented at the 11th Annual Meeting of the Organization for Human Brain Mapping, Toronto, Canada.
Ivanova, I., Costa, A., 2008. Does bilingualism hamper lexical access in speech production? Acta Psychol. 127, 277–288.
Jack, C.R., Petersen, R.C., Xu, Y.C., Waring, S.C., O'Brien, P.C., Tangalos, E.G., Smith, G.E., Ivnik, R.J., Kokmen, E., 1997. Medial temporal atrophy on MRI in normal aging and very mild Alzheimer's disease. Neurology 49, 786–794.
Jaeggi, S.M., Buschkuehl, M., Jonides, J., Perrig, W.J., 2008. Improving fluid intelligence with training on working memory. Proc. Natl. Acad. Sci. U.S.A. 105, 6829–6833.
Katzman, R., Terry, R., DeTeresa, R., Brown, T., Davies, P., Fuld, P., Renbing, X., Peck, A., 1988. Clinical, pathological, and neurochemical changes in dementia: a

subgroup with preserved mental status and numerous neocortical plaques. Ann. Neurol. 23, 138–144.
Kavé, G., Eyal, N., Shorek, A., Cohen-Mansfield, J., 2008. Multilingualism and cognitive state in the oldest old. Psychol. Aging 23, 70–78.
Kawashima, R., Okita, K., Yamazaki, R., Tajima, N., Yoshida, H., Taira, M., Iwata, K., Sasaki, T., Maeyama, K., Usui, N., Sugimoto, K., 2005. Reading aloud and arithmetic calculation improve frontal function of people with dementia. J. Gerontol. A: Biol. Sci. Med. Sci. 60, 380–384.
Kempermann, G., Kuhn, H.G., Gage, F.H., 1997. More hippocampal neurons in adult mice living in an enriched environment. Nature 386, 493–495.
Kinsella, G.J., Mullaly, E., Rand, E., Ong, B., Burton, C., Price, S., Phillips, M., Storey, E., 2009. Early intervention for mild cognitive impairment: a randomised controlled trial. J. Neurol. Neurosurg. Psychiatry 80, 730–736.
Knott, G.W., Quairiaux, C., Genoud, C., Welker, E., 2002. Formation of dendritic spines with GABAergic synapses induced by whisker stimulation in adult mice. Neuron 34, 265–273.
Knowles, M.S., 1973. The Modern Practice of Adult Education: From Pedagogy to Andragogy. Follett, Chicago.
Kramer, A., Hahn, S., Cohen, N., Banich, M., McAuley, E., Harrison, C., Chason, J., Vakil, E., Bardell, L., Boileau, R., Colcombe, A., 1999. Ageing, fitness and neurocognitive function. Nature 400, 418–419.
Kramer, A.F., Bherer, L., Colcombe, S.J., Dong, W., Greenough, W.T., 2004. Environmental influences on cognitive and brain plasticity during aging. J. Gerontol. A: Biol. Sci. Med. Sci. 59, M940–M957.
Kramer, A.F., Erickson, K.I., 2007. Capitalizing on cortical plasticity: influence of physical activity on cognition and brain function. Trends Cogn. Sci. 11, 342–348.
Krashen, S.D., Long, M.A., Scarcella, R.C., 1979. Age, rate and eventual attainment in second language acquisition. TESOL Q. 13, 573–582.
Kurz, A., Pohl, C., Ramsenthaler, M., Sorg, C., 2009. Cognitive rehabilitation in patients with mild cognitive impairment. Int. J. Geriatr. Psychiatry 24, 163–168.
La Rue, A., Jarvik, L.F., 1987. Cognitive function and prediction of dementia in old age. Int. J. Aging Hum. Dev. 25, 79–89.
Lautenschlager, N., Cox, K., Kurz, A., 2010. Physical activity and mild cognitive impairment and Alzheimer's disease. Curr. Neurol. Neurosci. Rep. 10, 352–358.
Lenneberg, E.H., 1967. Biological Foundations of Language. John Wiley and Sons, Oxford.
Lerch, J.P., Yiu, A.P., Martinez-Canabal, A., Pekar, T., Bohbot, V.D., Frankland, P.W., Henkelman, R.M., Josselyn, S.A., Sled, J.G., 2011. Maze training in mice induces MRI-detectable brain shape changes specific to the type of learning. NeuroImage 54, 2086–2095.
Linhart-Wegschaider, H., 2010. Foreign language learning and advanced age. Universitat Wien (Doctoral Dissertation).
Logan, J.M., Sanders, A.L., Snyder, A.Z., Morris, J.C., Buckner, R.L., 2002. Under-recruitment and nonselective recruitment: dissociable neural mechanisms associated with aging. Neuron 33, 827–840.
Lövdén, M., Wenger, E., Mårtensson, J., Lindenberger, U., Bäckman, L., 2013. Structural brain plasticity in adult learning and development. Neurosci. Biobehav. Rev. (in press).
Luk, G., Bialystok, E., Craik, F.I.M., Grady, C.L., 2011. Lifelong bilingualism maintains white matter integrity in older adults. J. Neurosci. 31, 16808–16813.
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.
Marinova-Todd, S.H., Marshall, D.B., Snow, C.E., 2000. Three misconceptions about age and L2 learning. TESOL Q. 34, 9–34.
Markson, L., Bloom, P., 1997. Evidence against a dedicated system for word learning in children. Nature 385, 813–815.
Mårtensson, J., Eriksson, J., Bodammer, N.C., Lindgren, M., Johansson, M., Nyberg, L., Lövdén, M., 2012. Growth of language-related brain areas after foreign language learning. NeuroImage 63, 240–244.
Matsuzaki, M., Honkura, N., Ellis-Davies, G.C.R., Kasai, H., 2004. Structural basis of long-term potentiation in single dendritic spines. Nature 429, 761–766.
May, A., Hajak, G., Gänßbauer, S., Steffens, T., Langguth, B., Kleinjung, T., Eichhammer, P., 2007. Structural brain alterations following 5 days of intervention: dynamic aspects of neuroplasticity. Cereb. Cortex 17, 205–210.
McDowell, I., Xi, G., Lindsay, J., Tierney, M., 2007. Mapping the connections between education and dementia. J. Clin. Exp. Neuropsychol. 29, 127–141.
McNab, F., Varrone, A., Farde, L., Jucaite, A., Bystritsky, P., Forssberg, H., Klingberg, T., 2009. Changes in cortical dopamine D1 receptor binding associated with cognitive training. Science 323, 800–802.
Mechelli, A., Crinion, J.T., Noppeney, U., O'Doherty, J., Ashburner, J., Frackowiak, R.S., Price, C.J., 2004. Neurolinguistics: structural plasticity in the bilingual brain. Nature 431, 757.
Merzenich, M.M., Nelson, R.J., Stryker, M.P., Cynader, M.S., Schoppmann, A., Zook, J.M., 1984. Somatosensory cortical map changes following digit amputation in adult monkeys. J. Comp. Neurol. 224, 591–605.
Meshi, D., Drew, M.R., Saxe, M., Ansorge, M.S., David, D., Santarelli, L., Malapani, C., Moore, H., Hen, R., 2006. Hippocampal neurogenesis is not required for behavioral effects of environmental enrichment. Nat. Neurosci. 9, 729–731.
Middleton, L.E., Yaffe, K., 2010. Targets for the prevention of dementia. J. Alzheimers Dis. 20, 915–924.
Ming, G., Song, H., 2005. Adult neurogenesis in the mammalian central nervous system. Annu. Rev. Neurosci. 28, 223–250.
Mitchell, D.B., Bruss, P.J., 2003. Age differences in implicit memory: conceptual, perceptual, or methodological? Psychol. Aging 18, 807–822.
Miyashita, Y., 2004. Cognitive memory: cellular and network machineries and their top-down control. Science 306, 435–440.
Mohamed Zied, K., Phillipe, A., Karine, P., Valerie, H.-T., Ghislaine, A., Arnaud, R., Gall Didier, L., 2004. Bilingualism and adult differences in inhibitory mechanisms: evidence from a bilingual stroop task. Brain Cogn. 54, 254–256.
Morse, C.K., 1993. Does variability increase with age? An archival study of cognitive measures. Psychol. Aging 8, 156–164.
Nelson, D.L., Schreiber, T.A., McEvoy, C.L., 1992. Processing implicit and explicit representations. Psychol. Rev. 99, 322–348.
Neurotone, 2011. LACE.
Nithianantharajah, J., Hannan, A.J., 2006. Enriched environments, experience-dependent plasticity and disorders of the nervous system. Nat. Rev. Neurosci. 7, 697–709.
Oswald, W.D., Rupprecht, R., Gunzelmann, T., Tritt, K., 1996. The SIMA-project: effects of 1 year cognitive and psychomotor training on cognitive abilities of the elderly. Behav. Brain Res. 78, 67–72.
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, 775–778.
Park, D.C., Lautenschlager, G., Hedden, T., Davidson, N.S., Smith, A.D., Smith, P.K., 2002. Models of visuospatial and verbal memory across the adult life span. Psychol. Aging 17, 299–320.
Park, D.C., Smith, A.D., Lautenschlager, G., Earles, J.L., Frieske, D., Zwahr, M., Gaines, C.L., 1996. Mediators of long-term memory performance across the life span. Psychol. Aging 11, 621–637.
Peelle, J.E., Troiani, V., Wingfield, A., Grossman, M., 2010. Neural processing during older adults' comprehension of spoken sentences: age differences in resource allocation and connectivity. Cereb. Cortex 20, 773–782.
Penfield, W., Roberts, L., 1959. Speech and Brain Mechanisms. Princeton University Press, Princeton.
Perani, D., Abutalebi, J., 2005. The neural basis of first and second language processing. Curr. Opin. Neurobiol. 15, 202–206.
Perani, D., Paulesu, E., Sebastián-Gallés, N., Dupoux, E., Dehaene, S., Bettinardi, V., Cappa, S.F., Fazio, F., Mehler, J., 1998. The bilingual brain. Proficiency and age of acquisition of the second language. Brain 121, 1841–1852.
Petersen, R.C., 2011. Clinical practice: mild cognitive impairment. N. Engl. J. Med. 364, 2227–2234.
Plassman, B.L., Langa, K.M., Fisher, G.G., Heeringa, S.G., Weir, D.R., Ofstedal, M.B., Burke, J.R., Hurd, M.D., Potter, G.G., Rodgers, W.L., Steffens, D.C., Willis, R.J., Wallace, R.B., 2007. Prevalence of dementia in the United States: the aging, demographics, and memory study. Neuroepidemiology 29, 125–132.
Posit Science, 2009. Brain Fitness Program. Posit Science, San Francisco, CA.
Prull, M.W., Gabrieli, J.D.E., Bunge, S.A., 2000. Age-related changes in memory: a cognitive neuroscience perspective. In: Craik, F.I.M., Salthouse, T.A. (Eds.), The Handbook of Aging and Cognition. Erlbaum, Mahwah, NJ, pp. 91–153.
Pushkar, D., Etezadi, J., Andres, D., Arbuckle, T., Schwartzman, A.E., Chaikelson, J., 1999. Models of intelligence in late life: comment on Hultsch et al. (1999). Psychol. Aging 14, 520–527.
Quallo, M.M., Price, C.J., Ueno, K., Asamizuya, T., Cheng, K., Lemon, R.N., Iriki, A., 2009. Gray and white matter changes associated with tool-use learning in macaque monkeys. Proc. Natl. Acad. Sci. U.S.A. 106, 18379–18384.
Raz, N., 2000. Aging of the brain and its impact on cognitive performance: integration of structural and functional findings. In: Craik, F.I.M., Salthouse, T.A. (Eds.), The Handbook of Aging and Cognition. Erlbaum, Mahwah, NJ, pp. 1–90.
Raz, N., Gunning-Dixon, F.M., Head, D., Dupuis, J.H., Acker, J.D., 1998. Neuroanatomical correlates of cognitive aging: evidence from structural magnetic resonance imaging. Neuropsychology 12, 95–114.
Raz, N., Gunning-Dixon, F.M., Head, D., Rodrigue, K.M., Williamson, A., Acker, J.D., 2004. Aging, sexual dimorphism, and hemispheric asymmetry of the cerebral cortex: replicability of regional differences in volume. Neurobiol. Aging 25, 377–396.
Recanzone, G.H., Merzenich, M.M., Jenkins, W.M., Grajski, K.A., Dinse, H.R., 1992. Topographic reorganization of the hand representation in cortical area 3b owl monkeys trained in a frequency-discrimination task. J. Neurophysiol. 67, 1031–1056.
Reuter-Lorenz, P.A., Sylvester, C.-Y.C., 2005. The cognitive neuroscience of working memory and aging. In: Cabeza, R., Nyberg, L., Park, D. (Eds.), Cognitive Neuroscience of Aging: Linking Cognitive and Cerebral Aging. Oxford University Press, New York, pp. 186–217.
Rodríguez-Fornells, A., Cunillera, T., Mestres-Missé, A., Diego-Balaguer, R.de., 2009. Neurophysiological mechanisms involved in language learning in adults. Philos. Trans. R. Soc. B 364, 3711–3735.
Rogers, B.P., Morgan, V.L., Newton, A.T., Gore, J.C., 2007. Assessing functional connectivity in the human brain by fMRI. Magn. Reson. Imaging 25, 1347–1357.
Rypma, B., D'Esposito, M., 2000. Isolating the neural mechanisms of age-related changes in human working memory. Nat. Neurosci. 3, 509–515.
Sagi, Y., Tavor, I., Hofstetter, S., Tzur-Moryosef, S., Blumenfeld-Katzir, T., Assaf, Y., 2012. Learning in the fast lane: new insights into neuroplasticity. Neuron 73, 1195–1203.
Sakai, K.L., 2005. Language acquisition and brain development. Science 310, 815–819.
Salthouse, T.A., 1996. The processing-speed theory of adult age differences in cognition. Psychol. Rev. 103, 403–428.
Salthouse, T.A., Ferrer-Caja, E., 2003. What needs to be explained to account for age-related effects on multiple cognitive variables? Psychol. Aging 18, 91–110.

Sattler, C., Toro, P., Schönknecht, P., Schröder, J., 2012. Cognitive activity, education and socioeconomic status as preventive factors for mild cognitive impairment and Alzheimer's disease. Psychiatry Res. 196, 90–95.
Satz, P., 1993. Brain reserve capacity on symptom onset after brain injury: a formulation and review of evidence for threshold theory. Neuropsychology 7, 273–295.
Saur, D., Kreher, B.W., Schnell, S., Kümmerer, D., Kellmeyer, P., Vry, M.-S., Umarova, R., Musso, M., Glauche, V., Abel, S., Huber, W., Rijntjes, M., Hennig, J., Weiller, C., 2008. Ventral and dorsal pathways for language. Proc. Natl. Acad. Sci. U.S.A. 105, 18035–18040.
Scarmeas, N., Levy, G., Tang, M.-X., Manly, J., Stern, Y., 2001. Influence of leisure activity on the incidence of Alzheimer's disease. Neurology 57, 2236–2242.
Scarmeas, N., Luchsinger, J.A., Schupf, N., Brickman, A.M., Cosentino, S., Tang, M.X., Stern, Y., 2009. Physical activity, diet, and risk of Alzheimer disease. JAMA 302, 627–637.
Schacter, D.L., 1992. Priming and multiple memory systems: perceptual mechanisms of implicit memory. J. Cogn. Neurosci. 4, 244–256.
Schleppegrell, M., 1987. The Older Language Learner. ERIC Clearinghouse on Languages and Linguistics, Washington, DC.
Schweizer, T.A., Ware, J., Fischer, C.E., Craik, F.I.M., Bialystok, E., 2012. Bilingualism as a contributor to cognitive reserve: evidence from brain atrophy in Alzheimer's disease. Cortex 48, 991–996.
Selkoe, D.J., 2012. Preventing Alzheimer's disease. Science 337, 1488–1492.
Shapira, N., Barak, A., Gal, I., 2007. Promoting older adults' well-being through Internet training and use. Aging Ment. Health 11, 477–484.
Simon, S.S., Yokomizo, J.E., Bottino, C.M.C., 2012. Cognitive intervention in amnestic Mild Cognitive Impairment: a systematic review. Neurosci. Biobehav. Rev. 36, 1163–1178.
Simpson, T., Camfield, D., Pipingas, A., Macpherson, H., Stough, C., 2012. Improved processing speed: online computer-based cognitive training in older adults. Educ. Gerontol. 38, 445–458.
Singleton, D.M., Lengyel, Z., 1995. The Age Factor in Second Language Acquisition: A Critical Look at the Critical Period Hypothesis. Multilingual Matters, Clevedon.
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, P.A., 2010. Ageing, auditory distraction, and grammaticality judgement. Aphasiology 24, 1342–1353.
Snowdon, D.A., Greiner, L.H., Markesbery, W.R., 2000. Linguistic ability in early life and the neuropathology of Alzheimer's disease and cerebrovascular disease: findings from the Nun Study. Ann. N.Y. Acad. Sci. 903, 34–38.
Solé-Padullés, C., Bartrés-Faz, D., Junqué, C., Vendrell, P., Rami, L., Clemente, I.C., Bosch, B., Villar, A., Bargalló, N., Jurado, M.A., Barrios, M., Molinuevo, J.L., 2009. Brain structure and function related to cognitive reserve variables in normal aging, mild cognitive impairment and Alzheimer's disease. Neurobiol. Aging 30, 1114–1124.
Staff, R.T., Murray, A.D., Deary, I.J., Whalley, L.J., 2004. What provides cerebral reserve? Brain 127, 1191–1199.
Stein, M., Federspiel, A., Koenig, T., Wirth, M., Strik, W., Wiest, R., Brandeis, D., Dierks, T., 2012. Structural plasticity in the language system related to increased second language proficiency. Cortex 48, 458–465.
Stern, C., Munn, Z., 2010. Cognitive leisure activities and their role in preventing dementia: a systematic review. Int. J. Evid. Based Healthc. 8, 2–17.
Stern, Y., 2002. What is cognitive reserve? Theory and research application of the reserve concept. J. Int. Neuropsychol. Soc. 8, 448–460.
Stuss, D.T., Robertson, I.H., Craik, F.I.m., 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.
Tárraga, L., Boada, M., Modinos, G., Espinosa, A., Diego, S., Morera, A., Guitart, M., Balcells, J., López, O.L., Becker, J.T., 2006. A randomised pilot study to assess the efficacy of an interactive, multimedia tool of cognitive stimulation in Alzheimer's disease. J. Neurol. Neurosurg. Psychiatry 77, 1116–1121.
Thal, L.J., 2006. Prevention of Alzheimer disease. Alzheimer Dis. Assoc. Disord. 20, S97–S99.
Theodosis, D.T., Poulain, D.A., Oliet, S.H.R., 2008. Activity-dependent structural and functional plasticity of astrocyte–neuron interactions. Physiol. Rev. 88, 983–1008.
Thompson-Schill, S.L., 2003. Neuroimaging studies of semantic memory: inferring how from where. Neuropsychologia 41, 280–292.
Troyer, A.K., Murphy, K.J., Anderson, N.D., Moscovitch, M., Craik, F.I.M., 2008. Changing everyday memory behaviour in amnestic mild cognitive impairment: a randomised controlled trial. Neuropsychol. Rehabil. 18, 65–88.
Tyler, L.K., Marslen-Wilson, W.D., Stamatakis, E.A., 2005. Differentiating lexical form, meaning, and structure in the neural language system. Proc. Natl. Acad. Sci. U.S.A. 102, 8375–8380.
Ullman, M.T., 2001. A neurocognitive perspective on language: the declarative/procedural model. Nat. Rev. Neurosci. 2, 717–726.
Valenzuela, M.J., Jones, M., Caroline Rae, W.W., Graham, S., Shnier, R., Sachdev, P., 2003. Memory training alters hippocampal neurochemistry in healthy elderly. Neuroreport 14, 1333–1337.
Valenzuela, M.J., Sachdev, P., 2006. Brain reserve and dementia: a systematic review. Psychol. Med. 36, 441–454.
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 Praag, H., Kempermann, G., Gage, F.H., 1999. Running increases cell proliferation and neurogenesis in the adult mouse dentate gyrus. Nat. Neurosci. 2, 266–270.
Van Praag, H., Kempermann, G., Gage, F.H., 2000. Neural consequences of environmental enrichment. Nat. Rev. Neurosci. 1, 191–198.
Verghese, J., LeValley, A., Derby, C., Kuslansky, G., Katz, M., Hall, C.B., Buschke, H., Lipton, R.B., 2006. Leisure activities and the risk of amnestic mild cognitive impairment in the elderly. Neurology 66, 821–827.
Verghese, J., Lipton, R.B., Katz, M.J., Hall, C.B., Derby, C.A., Kuslansky, G., Ambrose, A.F., Sliwinski, M., Buschke, H., 2003. Leisure activities and the risk of dementia in the elderly. N. Engl. J. Med. 348, 2508–2516.
Vigneau, M., Beaucousin, V., Hervé, P.Y., Duffau, H., Crivello, F., Houdé, O., Mazoyer, B., Tzourio-Mazoyer, N., 2006. Meta-analyzing left hemisphere language areas: phonology, semantics, and sentence processing. NeuroImage 30, 1414–1432.
Volkmar, F.R., Greenough, W.T., 1972. Rearing complexity affects branching of dendrites in the visual cortex of the rat. Science 176, 1445–1447.
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.
Whalley, L.J., Deary, I.J., Appleton, C.L., Starr, J.M., 2004. Cognitive reserve and the neurobiology of cognitive aging. Ageing Res. Rev. 3, 369–382.
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., Bennett, D.A., Bienias, J.L., Aggarwal, N.T., Mendes de Leon, C.F., Morris, M.C., Schneider, J.A., Evans, D.A., 2002. Cognitive activity and incident AD in a population-based sample of older persons. Neurology 59, 1910–1914.
Wilson, R.S., Bennett, D.A., Bienias, J.L., Mendes de Leon, C.F., Morris, M.C., Evans, D.A., 2003. Cognitive activity and cognitive decline in a biracial community population. Neurology 61, 812–816.
Wingfield, A., Grossman, M., 2006. Language and the aging brain: patterns of neural compensation revealed by functional brain imaging. J. Neurophysiol. 96, 2830–2839.
Wingfield, A., Peelle, J.E., Grossman, M., 2003. Speech rate and syntactic complexity as multiplicative factors in speech comprehension by young and older adults. Aging Neuropsychol. Cogn. 10, 310–322.
Wolinsky, F.D., Unverzagt, F.W., Smith, D.M., Jones, R., Stoddard, A., Tennstedt, S.L., 2006. The ACTIVE cognitive training trial and health-related quality of life: protection that lasts for 5 years. J. Gerontol. A: Biol. Sci. Med. Sci. 61, 1324–1329.
Wong, P.C.M., Ettlinger, M., Sheppard, J.P., Gunasekera, G.M., Dhar, S., 2010. Neuroanatomical characteristics and speech perception in noise in older adults. Ear Hear. 31, 471–479.
Wong, P.C.M., Jin, J.X., Gunasekera, G.M., Abel, R., Lee, E.R., Dhar, S., 2009. Aging and cortical mechanisms of speech perception in noise. Neuropsychologia 47, 693–703.
Wong, P.C.M., Morgan-Short, K., Ettlinger, M., Zheng, J., 2012. Linking neurogenetics and individual differences in language learning: the dopamine hypothesis. Cortex 48, 1091–1102.
Wong, P.C.M., Perrachione, T.K., Parrish, T.B., 2007. Neural characteristics of successful and less successful speech and word learning in adults. Hum. Brain Mapp. 28, 995–1006.
Yetkin, O., Zerrin Yetkin, F., Haughton, V.M., Cox, R.W., 1996. Use of functional MR to map language in multilingual volunteers. Am. J. Neuroradiol. 17, 473–477.
Yuste, R., Bonhoeffer, T., 2001. Morphological changes in dendritic spines associated with long-term synaptic plasticity. Annu. Rev. Neurosci. 24, 1071–1089.