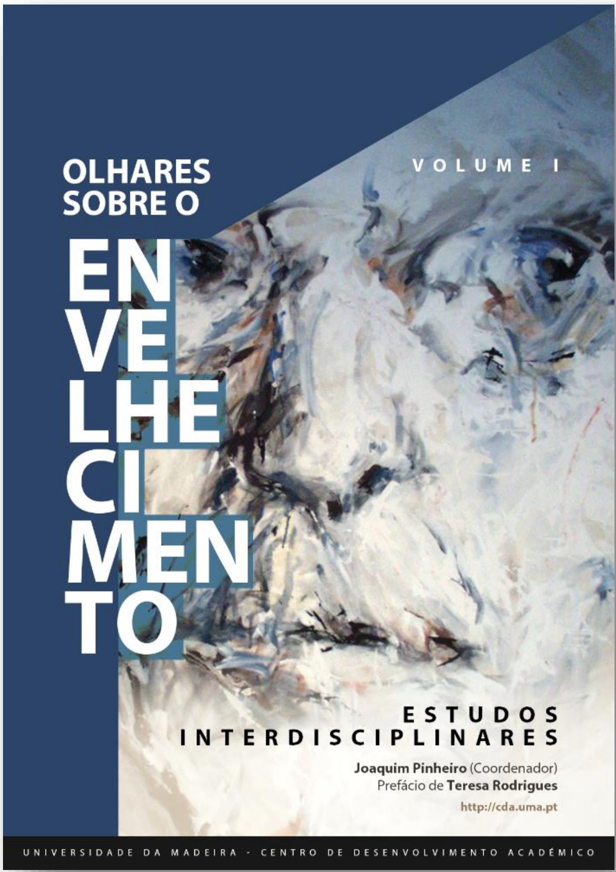

Mónica Spínola (2021). Cognitive function in healthy aging – A theoretical overview on the effects of cognitive training combined with Transcranial Direct Current Stimulation (tDCS). In Joaquim Pinheiro (coord.), *Olhares sobre o envelhecimento. Estudos interdisciplinares*, vol. I, pp. 287-296.

DOI: 10.34640/universidademadeira2021monicaspinola

ISBN: 978-989-8805-63-8

Nota de edição: Respeitou-se a norma ortográfica seguida pelos Autores.

doi: 10.34640/universidademadeira2021monicaspinola

Cognitive function in healthy aging – A theoretical overview on the effects of cognitive training combined with Transcranial Direct Current Stimulation (tDCS)

MÓNICA SPÍNOLA

NOVA LINCS

monica.spinola@m-iti.org

enviado a 18/03/2021 e aceite a 05/04/2021

Resumo

Nas últimas décadas, e como consequência do aumento progressivo da esperança de vida, diversos estudos se têm focado na população idosas e, em específico, no envelhecimento cerebral e respetivas consequências no funcionamento cognitivo. Mesmo no envelhecimento saudável, existe uma série de alterações cognitivas que se podem traduzir em perdas ao nível da funcionalidade. É urgente investigar formas de atenuar os efeitos do envelhecimento na função cognitiva e manter a autonomia da população idosa.

O treino cognitivo (TC) consiste numa técnica que visa a restauração, reorganização ou compensação das perdas cognitivas, promovendo a manutenção da funcionalidade e mitigando o declínio cognitivo. Por outro lado, a estimulação elétrica transcraniana (EET) emerge enquanto técnica não-invasiva de neuromodulação, que pode causar um impacto positivo no funcionamento cognitivo, através do envio de corrente elétrica de baixa intensidade para o crânio. Ainda que exista já evidência da eficácia destas técnicas, estão ainda pouco exploradas e aplicadas em Portugal. A presente revisão teórica visa explorar de que forma a aplicação combinada destas duas técnicas pode melhorar o funcionamento cognitivo no envelhecimento saudável.

Palavras-chave: Treino cognitivo; Estimulação elétrica transcraniana; EET; Envelhecimento saudável.

Abstract

In recent decades, and as a consequence of the progressive increase of lifespan, several studies have been focusing on the elderly population and specifically on brain ageing and its consequences on cognitive functioning. Even in healthy ageing, there is a series of cognitive changes, which may result in functional losses. It is urgent to investigate ways of attenuating the effects of ageing on cognitive function and maintain the autonomy of the elderly population.

Cognitive training (CT is a technique aimed at restoring, reorganizing or compensating cognitive losses, promoting the maintenance of functionality and delaying cognitive decline. On the other hand, Transcranial electrical stimulation (TES) emerges as a non-invasive neuromodulation technique that can have a positive impact on cognitive functioning, by sending a low-intensity electrical current to the skull. Although there is already evidence of the effectiveness of these techniques, they are still poorly explored and applied in Portugal. This theoretical overview aims to explore how the combined application of these two techniques can enhance cognitive function in healthy ageing.

Keywords: Cognitive training; Transcranial direct current stimulation; tDCS; Healthy ageing.

Background

a) Healthy aging

It is known that the world's elderly population is fast and uncontrollably growing and the lifespan is quickly increasing. Herewith, there comes the need to augment human cognitive span and to promote the preservation of cognitive function until more advanced ages so that the ability of making informed decisions and living independently is maintained (Chapman et al., 2013).

This way, the term “Successful aging” emerges. Successful aging is, according to Rowe and Kahn (1997), defined in three essential parts and the relationship among them: low probability of disease/disease-related disability; high cognitive and physical function capacity; and active engagement with life. Over the years, this definition has been studied and adapted, considering the several findings on this field (e.g., Baltes & Baltes, 1990; Depp & Jeste, 2006 as cited in Martin et al., 2014). Martin et al. (2014), through a review of literature, have found that the most recent and integrative one considers as main components to a “Successful aging” physical functioning, cognitive functioning, life satisfaction/well-being, social/productive engagement, presence/absence of illness, longevity, self-rated health, personality, environment/finances and self-rated successful aging. As cognitive function remains as a significant part of successful aging, being consistent over the several approaches, self-perception emerges on the most recent one as a significant factor to the subjects’ well-being. This suggests that the subjects’ perception of its condition may influence the condition itself.

The “Successful aging” theory is actually consistent with the different models of quality of life (QoL). For example, the “Global Model of Quality of Life” (Felce & Perry, 1993, 1995, as cited in Vilar et al., 2016), which serves as a foundation to the World Health Organization model (WHOQOL Group, 1995), enhances the role of the subjects’ self-perception of well-being, as this well-being evolves both objective and subjective dimensions such as the physical condition, social, material and emotional well-being, personal development and the involvement on significant activities. The similarity of these approaches suggests that a successful aging and quality of life have a direct influence on each other. Additionally, this subjective new dimension, that appears on the most recent definition of “Successful aging”, can be seen as a core point of interest when allied to objective measures. However, to consider the individual’s self-perception there comes the need to ensure its’ cognitive integrity in a way that allows the information obtained to be considered as valid (Vilar et al., 2016).

b) Cognitive changes in healthy aging

As we know, aging is a gradual and inevitable process that occurs differently in each person and is perceived by each person differently. Even in the absence of a diagnosed dementia, evidence shows continuous age- related cognitive declines (Cappell et al., 2010; Cepeda et al., 2001; Kennedy et al., 2009; Mahncke et al., 2006; Mattay et al., 2006, as cited in Chapman et al., 2013) and concomitant brain losses of white matter integrity and functional connectivity, more visible in frontal and temporal networks (Cappell et al. 2010; Hafkemeijer et al. 2012; Kennedy et al. 2009, as cited in Chapman et al., 2013).

Commonly, people over 60 years old report cognitive difficulties, especially in memory (Ávila & de Campos Bottino, 2006). However, brain modifications associated to the aging process are usually combined with vision and hearing changes and generate alterations on the other main mental/cognitive functions such as language, executive and visuospatial functions, even in the absence of neurological diseases. In fact, older adults need much more time to learn new information, to remember it and even to do everyday tasks (Yassuda et al., 2011).

This aging process and its consequent cognitive changes are highly influenced by different endogenous and exogenous factors. It is known that about 50% of cognitive variability in the elderly may be explained by genetic factors and about 30% of that variability can be explained by their educational level. Besides, healthy elder people who frequently perform mental stimulating activities show better performance in cognitive tests and less longitudinal decline. Additionally, factors as personality and humor do have an influence on cognitive changes. For example, depression is associated to self-perceived insufficiencies and performance deficits in memory tasks. Also, elder people with specialized knowledge about the aging process tend to develop compensatory strategies, that allows them to deal with their cognitive losses, maintaining a high-performance level. In addition, social and cultural environment, cognitive training practice, gender, racial and ethnic differences are also influence factors on cognitive changes due to aging (Cancela, 2007).

Once memory decline is one of the main and first complaints manifested by elder people, especially short-term memory (STM), it becomes extremely important referring that this type of memory is responsible for both maintenance and processing of information and it does suffer from changes caused by the aging process. As people get older, it becomes more difficult to execute mental calculation, problem resolution and the mental organization of the tasks that need to be accomplished (Yassuda et al., 2011).

Besides that, some classes of long-term memory (LTM) also reveal changes duo the aging process as it becomes more difficult to codify new information, mainly when it involves retaining details about the physical and temporal context (Yassuda et al., 2011). LTM is divided in two large classes: implicit (non-declarative) memory and explicit (declarative) memory, which includes semantic memory and episodic memory. Implicit memory refers to procedural memory and the Perceptual Representation System (supporting priming effects and classical and operant conditioning). Explicit memory refers to the conscious process of recalling information, whether it refers to general facts and knowledge (semantic memory) or information about personal experiences and their temporal and spatial contexts (episodic memory) (Tromp et al., 2015).

Studies show that episodic memory is the most sensitive to the aging process, being the first memory system to show decline both in normal and pathological aging. Once general knowledge and vocabulary are well preserved in normal aging, semantic memory seems to be immune to some of the effects of the aging process. In contrast, episodic memory, whose function is sustained by a vast cerebral network such as the frontal system, parietal cortex, cerebellum, thalamus and the cingulate gyrus, seems to be highly affected by aging (Tromp et al., 2015). Episodic memory performance progressively declines from middle age to old age (Nyberg et al., 2003). Older people experience losses in information processing, which becomes less efficient and both episodic encoding and retrieval processes are impaired. For example, elderly tend to suffer from difficulties in recalling the encoded context and stored information in a detailed way, sometimes exhibiting false recognitions (Tromp et al., 2015).

Regarding to language, elder healthy people tend to use various words in substitution of an adjective or a target noun; to describe the function of the object or its features instead of naming it; and to have difficulties in comprehension and production of complex sentences and organizing their speech. However, this kind of difficulties do not prevent the performance of daily, social and occupational activities (Yassuda et al., 2011).

It is also verified that up to approximately 60 years there is an increase of performance in skills related to the accumulation of past processing (e.g., vocabulary tasks, lexical knowledge, oral production and fluency, general knowledge about the world), associated with semantic memory concepts and crystallized intelligence. However, there is a decrease in performance on tasks that require attentional focus and transformation of information at the moment of the evaluation, associated with tasks of episodic memory and working memory (fluid intelligence) (e.g., general sequential reasoning, induction, quantitative reasoning, speed of reasoning) (Strauss et al., 2006; Yassuda et al., 2011). In fact, Manard and colleagues (2014) consider that these alterations on fluid intelligence (particularly on speed of reasoning) may be on the basis of the decline in proactive control abilities that older adults reveal.

In what concerns to executive function, it is associated to abilities as the formulation of a goal, the planning, and the execution of tasks efficiently and the ability to evaluate and correct these actions. For example, in daily tasks, it shows up in actions as estimating time, alternating between tasks, ordinate actions and to control impulses and inadequate actions. In general, healthy elderly do not present significant changes in the essential functions to daily activities and maintenance of autonomy, and only once again there is some slowness and possible use of external aids (such as lists, schedules, alarms) (Yassuda et al., 2011). However, studies have revealed a significant hippocampal shrinkage in people in their mid-50s and an estimated average decline of about 5% of the prefrontal cortex per decade after the age of 20, associated with the degradation of the executive function (Tromp et al., 2015).

As far as visuospatial functions are concerned, they are generally preserved in healthy elderly people who, in the absence of significant visual changes, usually have a good orientation of the physical space, both inside and outside the home (Yassuda et al., 2011).

In what concerns to attentional processes, Lezak and colleagues (2012) considered that attention span, similarly to short-term memory and working memory, is a limited capacity. According to McDowd and Birren (1990) older adult’s attentional resources are reduced and may influence the execution of cognitive processes. Craik and Byrd (1982) and Mather and Carstensen (2005) considered that age-related changes occurred mainly in situations where attention must be intensively focused, especially in presence of interferences and distractions or when needed a large amount of attentional resources, and due to the need of high degree cognitive control required on those situations. However, attentional processes can refer to several types of attention: 1. attention switching – ability of monitoring two or more stimuli alternately – can be slightly reduced due to generalized decrease of processing-speed (Hartley & Little, 1999); 2. sustained attention – ability of maintaining performance on a task for an extended period – seems to be relatively well preserved; 3. Selective attention – ability of filtering and focusing on the relevant information from all information given by environment – seems to be affected by aging, being this decline related to the efficiency of inhibitory processes (Zacks & Hasher, 1994).

In addition, the so-called "normal" aging of the brain may be accompanied by mental changes that are superimposable to those found in incipient dementia, leading to differential diagnosis problems (such as in Mild Cognitive Impairment and early stages of dementia, especially Alzheimer's disease). Although neuropsychological, pathological, and consensus neuroimaging criteria are currently established for the differentiation between normal and pathological, brain aging, and its alterations continue to raise diagnostic problems in cases of mild cognitive deficits (Damasceno, 1999).

The changes described as characteristic of aging appear as causes of cognitive deficits observed as natural, for example, forgetfulness of recent facts, difficulties of calculation and changes of attention. Many times, the loss itself can only be observed if the patient requires more of his memory than the ordinary, that is, individuals with an established routine, without great need of intellectual activity, tend to detect the loss later (Nordon et al., 2009).

However, cognitive loss may also be due to other causes, such as stroke, head trauma, metabolic encephalopathy, infection, acute confusion, dementia, alcoholism, hypothyroidism, cancer and even the use of medications (such as anxiolytics, antipsychotics, tricyclic antidepressants, hypnotics, antihistamines, among others) (Nordon et al., 2009).

For example, considering Alzheimer's Disease, it is known as the most common form of dementia and affects both cognitive (specially memory and executive functions) and behavioral domains (Cavallo et al., 2016). Initially it causes alterations mainly on memory domain, evolving to other cognitive functions such as language, visuospatial abilities, and executive functions, leading progressively to total dependency (Albuquerque et al., 2016). Even though patients with this pathology gradually lose their decision-making ability, World Health Organization's recommendations for cognitive interventions with these patients aims to promote an active role of the subject in decision-making as well as in participating and defining aims for that intervention (Clare, 2008, as cited in Silva, 2016a). Thus, even in the presence of pathology, cognitive interventions such as cognitive training have proven to have an important role on promoting the patient's wellbeing.

From a healthcare perspective, there is a major concern within the aging population and its higher prevalence of age-related impairment in cognitive function. This highlights the requirement of the development of strategies in attempt to maintain or enhance cognitive functions. There comes the need of a quick, effective and low-cost identification of solutions to delay cognitive decline caused by the aging process (Kueider et al., 2012).

c) Cognitive Training (CT)

The most that our brain is involved in intellectual activities, the more plasticity it will have and slower will be the process of presenting symptomatologic losses (Nordon et al., 2009). Actually, studies have shown that there is a significant potential to alter trajectories of cognitive decline on healthy aging. However, the definition of the intervention process may become difficult once older population is characterized as diversified and heterogeneous. The way that the aging process affects individuals is related to a group of complex biological, psychological and environmental variables and the interaction between them (Silva, 2016a).

Once cognitive losses are implemented, there comes the need to use a rehabilitative intervention. Rehabilitation is the process that aims to habilitate the patient to function in an adequately and appropriate way. It requires the evolvement of both professional and patient so that the second one achieves the optimum level of functioning (Wilson, 1999). Thus, Skeel and Edwards (2009) define three types of rehabilitation: restoration (restore lost abilities); reorganization (substitution of lost abilities for preserved abilities); and behavioral compensation (use of strategies to augment existent abilities). The type of rehabilitation technique applied must consider the deterioration level as well as the as the aims of that interventional process.

Therefore, CT, as a restoration psychological intervention, aims to improve cognition in subjects with cognitive impairment (Willis et al., 2006). Its programs focus on the process or functions that show impairment in the target population besides building up remaining capacities and strengths (Belleville et al., 2006). This way, rehabilitation process can involve the use of intern strategies (aiming the optimization of residual functions and/or replacement of impaired functions) and extern strategies (aiming the compensation of lost functions) (Silva, 2016b). It has been defined in four operationalized criteria: 1. repeated practice; 2. focus on tasks with an inherent problem; 3.use of standardized tasks; 4. target specific cognitive domains (Gates & Valenzuela, 2010). In what concerns to evaluating the efficiency of the rehabilitation process, Hampstead et al. (2014, as cited in Silva, 2016a), reached some parameters that can be considered: neuropsychological measures, self-report, external informant and ecological measures.

CT aims to cause cognitive improvement in specific domains, using a restorative or rehearsal-based approach. It has been shown that CT interventions have effective results concerning the enhancement of cognition and daily functions both in healthy and clinical patients (Willis et al., 2006).

Considering healthy adults samples, Willis et al. (2006) showed that cognitive training tasks can improve cognitive function up to 5 years from the beginning of the intervention, causing better performance on specifically trained abilities, when applied to independent, well-functioning subjects. Ball et al. (2002) confirm this conclusion once their results support the effectiveness and durability of cognitive training on target cognitive functions.

When considering a clinical sample, Belleville et al. (2006) showed that CT, including delayed list recall and face-name association tasks, can improve episodic memory tasks when applied to subjects with mild cognitive impairment. Also, referring to patients with “No Alzheimer’s Disease”, Kueider et al. (2012) found that classical CT tasks improve reaction time, processing speed, working memory, executive function, memory, visual special ability, and attention in subjects older than 55 years old. These authors differ two types of CT: computerized (including neuropsychological software programs and videogames) and classical CT, that consist in pen-and-paper exercises. Computerized CT had a positive impact on cognitive performance and visual spatial abilities when using neuropsychological software programs and enhanced reaction time, processing speed, executive function and global cognition when using videogames. These computerized CT tasks seem to be a good alternative to classical tasks, once they allow the realization of more specific intervention, considering the subject’s individual need. Its administration has lower costs and does not demand a face to face intervention. However, older subjects may not feel comfortable performing this type of tasks, once they may not be familiarized with this type of technology. However, as times are changing, in a near future our elder population will be comfortable using computerized techniques, once technology is being more and more used in our daily routine.

One example of a computerized cognitive training platform is COGWEB. COGWEB is an online platform, developed by Portuguese researchers, that allows the implementation of personalized cognitive training programs decided by a professional. Its aim is to address the major needs identified in memory clinic settings and its exercises involve training several cognitive functions. Even though only 66% of the participants had used a computer before, all of them made positive reviews about the platform (Cruz et al., 2013; Cruz et al., 2014).

Another example of computerized cognitive training is RehaCom®. RehaCom® is a computer-based program that includes several exercises of attention, concentration, memory, perception and daily living activities and different levels to each of them, being appropriate to different rehabilitation phases. It allows the patient to do an independent training as it provides all the instructions necessary and monitors the patient's performance giving feedback and selecting the following levels. Also, it is available in several languages and has been considered ecologically valid as its tasks are similar to real life context tasks (HASOMED, 2012).

Although both COGWEB and RehaCom® platforms are available in the Portuguese language, there were found no validation studies for this population.

d) Transcranial Direct Current Stimulation (tDCS)

Transcranial electrical stimulations, including tDCS, are non-invasive brain stimulation (NIBS) techniques that are mostly used for central nervous system excitability's modulation. The tDCS' main mechanism of action is a subthreshold modulation of neuronal membrane potentials, causing the alter of cortical excitability and activity dependent on the current flow direction through the target neurons (Woods et al., 2016). These techniques have been tested as approaches to improve or maintain cognitive performance both in healthy (Zimerman & Hummel, 2010) and clinical populations (Demirtas-Tatlidede et al., 2013). Over time, there have been evidences of favorable motor and cognitive behavioral effects, once these techniques have an influence on behavior by facilitating or inhibiting neural activity (Hummel & Cohen, 2006; Reis, Schambra, Cohen et al., 2009, as cited in Martins et al., 2017).

tDCS technique has been considered as having a promising capacity in the increasing of learning and cognition for the development of enhanced therapeutic interventions (Martin et al., 2014). There is strong evidence that NIBS techniques can be used to modulate cognitive functioning both in healthy and neurologic and psychiatric disorders (Martins et al., 2017). Literature shows that tDCS induces significant changes in cortical plasticity (Simis et al., 2013, as cited in Martins et al., 2017) and its results are quite favorable in what respects to cognitive function in healthy older adults (Martins et al., 2017).

In what concerns to memory processes, when comparing Sham stimulation and NIBS, literature supports positive results in increasing memory performance (Martins et al., 2017). Anodal tDCS is an active stimulation and Sham is an inactive form of stimulation used to control the placebo effect. However, there might be an influence of the education level on the effects of tDCS, has Berryhill and Jones (2012, cited in Martins et al., 2017) found that this technique was only beneficial in subjects with more education. Besides, the effects of tDCS may be influenced by the location of the stimulation. Although Ross et. al (2011, cited in Martins et al., 2017) found similar results in older and younger adults, the lateralization of the effect showed differences on those two groups, suggesting that the lateralization of processes such as encoding and retrieval may be associated with aging. These investigators found that only tDCS applied over the left regions increased the retrieval process in older adults.

e) Combined appliance of CT and tDCS

One hypothesized method for improving CT's results is its combination with tDCS. This technique enhances synaptic strength in neuronal pathways that are activated by CT, amplifying the effects of training. Behind the link between CT and tDCS is the principle that an "endogenous" activation (CT) and an "exogenous" neuromodulation (tDCS) will facilitate the activation of neuronal networks which sub serve cognitive functions (Elmasry, Loo, & Martin, 2015).

There is preliminary evidence that suggests that tDCS may transfer these effects to non-trained tasks in some domains as working memory, cognitive control, approximate number sense and arithmetic processing (Elmasry et al., 2015).When synaptic interconnections are strengthened by the interaction between cognitive activity (due do CT and tDCS) and training-based reinforcement, further enlargement of the cortical representation within the activated neuronal network will be allowed, therefore promoting generalization to non-trained tasks (Elmasry et al., 2015).

In fact, it has been proved that the simultaneous use tDCS and CT may augment the subjects' performance on cognitive trained tasks in different cognitive functions, both in healthy and clinical samples (Elmasry et al., 2015).

Stephens and Berryhill (2016) designed a study to evaluate if the combination of tDCS and working memory training improves performance on ecologically valid transfer measures administered in participants' homes. They verified that all the participants demonstrated improvement on trained tasks and that tDCS induced greater transfer gains after 1 month without contact. These gains were observed on standard far transfer tasks along with ecologically valid far transfer tasks. Their results highlight the translational value of the use of interventions based on tDCS in healthy older adults when attempting to maintain their cognitive function.

Also considering healthy older adults, Park and colleagues (2014) studied the long-term effects of tDCS of the bilateral prefrontal cortex combined with computer-assisted CT on working memory and cognitive function. In their study, there were two groups of participants: anodal and Sham. Both groups completed 10 sessions of computer-assisted CT combined with tDCS of the bilateral prefrontal cortex. The results demonstrated improvements on the accuracy of verbal working memory task and on the performance on the digit span forward test, having the effect last up to 4 weeks in verbal memory test. This way, the authors concluded that tDCS changes that altered the bilateral prefrontal excitability during computer-assisted CT may be a beneficial influence on age-related cognitive decrement.

When considering a clinical population, Penolazzi et al. (2015) carried out a case study of Alzheimer's disease with the aim of testing the cognitive effects of tDCS. The effects on cognitive performance were evaluated by the computerized tasks and by neuropsychological tests assessing global cognitive function. They found out that whereas the condition that combined transcranial direct current stimulation and cognitive training had little effects on computerized tasks, it induced stability on the patient's global cognitive functions, lasting approximately 3 months and these effects were not achieved with the Sham condition. They concluded that the synergetic use of transcranial direct current stimulation and computerized tasks of cognitive training appeared to slow down the cognitive decline of the patient.

f) Conclusion

The present study aimed to understand how the combined appliance of CT and tDCS can impact cognitive function in healthy aging. However, there is still a lack of studies reporting the combined use of these two techniques, especially with healthy older adults.

The results of the few studies analyzed are encouraging for the combined appliance of CT and tDCS, presenting tDCS as a way of enhancing the effects of CT and, therefore, potentiating its positive impact on cognitive functioning. Nevertheless, there is still a need for the creation of defined protocols, with stimulation parameters (such as strength, duration, and stimulation brain area), according to the goals of the intervention.

References

Albuquerque, E., Esteves, P. S., & Cerejeira, J. (2016). Doença de Alzheimer. In H. Firmino, M. R. Simões, & J. Cerejeira (Coord.), *Saúde mental das pessoas mais velhas* (pp. 309-320). Coimbra: Lidel.

Ávila, R., & de Campos Bottino, C. M. (2006). Atualização sobre alterações cognitivas em idosos com síndrome depressiva [Cognitive changes update among elderly with depressive syndrome]. *Revista Brasileira de Psiquiatria*, *28*(4), 316-320.

Belleville, S., Gilbert, B., Fontaine, F., Gagnon, L., Ménard, É., & Gauthier, S. (2006). Improvement of episodic memory in persons with mild cognitive impairment and healthy older adults: Evidence from a cognitive intervention program. *Dementia and Geriatric Cognitive Disorders*, *22*(5-6), 486-499. https://doi.org/10.1159/000096316

Cancela, D. (2007). *O processo de envelhecimento. Complemento ao diploma de Licenciatura*. Porto: Universidade Lusíada.

Cavallo, M., Zanalda, E., Johnston, H., Bonansea, A., & Angilletta, C. (2016). Cognitive training in a large group of patients affected by early- stage Alzheimer's disease can have long-lasting effects: A case-control study. *Brain Impairment*, *17*(2), 182-192. https://doi.org/10.1017/brimp.2016.2

Chapman, S. B., Aslan, S., Spence, J. S., Hart Jr, J. J., Bartz, E. K., Didehbani, N.,… Lu, H. (2013). Neural mechanisms of brain plasticity with complex cognitive training in healthy seniors. *Cerebral Cortex*, *25*(2), 396-405. https://doi.org/10.1093/cercor/bht234

Craik, F. I. M., & Byrd, M. (1982). Aging and cognitive deficits. The role of attentional resources. In F. I. M., Craik, & S. E. Trehub, *Aging and Cognitive Processes* (pp. 191-211). Plenum Press: New York.

Cruz, V. T., Pais, J., Alves, I., Ruano, L., Mateus, C., Barreto, R.,… Coutinho, P. (2014). Web-based cognitive training: Patient adherence and intensity of treatment in an outpatient memory clinic. *Journal of Medical Internet Research*, *16*(5). https://doi.org/10.2196/jmir.3377

Cruz, V. T., Pais, J., Bento, V., Mateus, C., Colunas, M., Alves, I.,… Rocha, N. P. (2013). A rehabilitation tool designed for intensive web-based cognitive training: Description and usability study. *Journal of Medical Internet Research*, *15*(12). https://doi.org/10.2196/resprot.2899

Damasceno, B. P. (1999). Envelhecimento cerebral. *Arquivos de Neuropsiquiatria*, *57*(1), 78-83.

Demirtas-Tatlidede, A., Vahabzadeh-Hagh, A. M., & Pascual-Leone, A. (2013). Can noninvasive brain stimulation enhance cognition in neuropsychiatric disorders?. *Neuropharmacology*, *64*, 566-578.

Elmasry, J., Loo, C., & Martin, D. (2015). A systematic review of transcranial electrical stimulation combined with cognitive training. *Restorative Neurology and Neuroscience*, *33*(3), 263-278.

Gates, N., & Valenzuela, M. (2010). Cognitive exercise and its role in cognitive function in older adults. *Current Psychiatry Reports, 12*(1), 20-27. https://doi.org/10.1007/s11920-009-0085-y

Hartley, A. A., & Little, D. M. (1999). Age-related differences and similarities in dual-task interference. *Journal of Experimental Psychology: General*, *128*(4), 416. https://doi.org/10.1037//0096-3445.128.4.416

HASOMED/Hardware and Software for Medicine (2012). RehaCom 2012. Cognitive Rehabilitation. Magdeburg, Germany: HASOMED.

Hummel, F., & Cohen, L. (2006). Non-invasive brain stimulation: a new strategy to improve neurorehabilitation after stroke?. *The Lancet Neurology*, *5*(8), 708-712. https://doi.org/10.1016/s1474-4422(06)70525-7

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*(7), e40588. https://doi.org/10.1371/journal.pone.0040588

Lemaire, P. (2016). *Cognitive aging: The role of strategies*. London: Psychology Press.

Lezak, M. D., Howieson, D. B., Bigler, E. D., & Tranel, D. (2012). *Neuropsychological assessment* (5th ed.) New York: Oxford University Press.

Manard, M., Carabin, D., Jaspar, M., & Collette, F. (2014). Age-related decline in cognitive control: The role of fluid intelligence and processing speed. *BMC Neuroscience*, *15*(1), 7. https://doi.org/10.1186/1471- 2202-15-7

Martin, D. M., Liu, R., Alonzo, A., Green, M., & Loo, C. K. (2014). Use of transcranial direct current stimulation (tDCS) to enhance cognitive training: Effect of timing of stimulation. *Experimental Brain Research*, *232*(10), 3345-3351.

Martin, P., Kelly, N., Kahana, B., Kahana, E., Willcox, B., Willcox, D., & Poon, L. (2014). Defining successful aging: A tangible or elusive Concept?. *The Gerontologist*, *55*(1), 14-25.

Martins, A. R., Fregni, F., Simis, M., & Almeida, J. (2017). Neuromodulation as a cognitive enhancement strategy in healthy older adults: Promises and pitfalls. *Aging, Neuropsychology, and Cognition*, *24*(2), 158-185. https://doi.org/10.1080/13825585.2016.1176986

Mather, M., & Carstensen, L. (2005). Aging and motivated cognition: The positivity effect in attention and memory. *Trends in Cognitive Sciences*, *9*(10), 496-502. https://doi.org/10.1016/j.tics.2005.08.005

McDowd, J. M., & Birren, J. E. (1990). Aging and attentional processes. *Handbook of the psychology of aging: Aging and attentional processes* (Cap.*3*, pp.222-233). United Kingdom: Academic Press Limited.

Nordon, D., Guimarães, R., Kozonoe, D., Mancilha, V., & Neto, V. (2009). Perda cognitiva em idosos. *Revista da Faculdade de Ciências Médicas de Sorocaba, 11*(3), 5-8.

Nyberg, L., Maitland, S., Rönnlund, M., Bäckman, L., Dixon, R., Wahlin, A., & Nilsson, L. (2003). Selective adult age differences in an age- invariant multifactor model of declarative memory. *Psychology and Aging*, *18*(1), 149-160. https://doi.org/10.1037/0882-7974.18.1.149

Park, S. H., Seo, J. H., Kim, Y. H., & Ko, M. H. (2014). Long-term effects of transcranial direct current stimulation combined with computer- assisted cognitive training in healthy older adults. *Neuroreport*, *25*(2), 122-126. https://doi.org/10.1097/wnr.0000000000000080

Penolazzi, B., Bergamaschi, S., Pastore, M., Villani, D., Sartori, G., & Mondini, S. (2015). Transcranial direct current stimulation and cognitive training in the rehabilitation of Alzheimer disease: A case study. *Neuropsychological Rehabilitation*, *25*(6), 799-817. https://doi.org/10.1080/09602011.2014.977301

Rowe, J. W., & Kahn, R. L. (1997). Successful aging. *The Gerontologist*, *37*(4), 433-440.

Silva, A. R. (2016a). Memory stimulation in mild Alzheimer disease: *The role of SenseCam to improve cognitive function and wellbeing*. Doctoral dissertation. Coimbra: Faculdade de Psicologia e de Ciências da Educaçãoda/UC.

Silva, A. R. (2016b). Reabilitação neuropsicológica. In H. Firmino, M. R. Simões, & J. Cerejeira (Coord.), *Saúde mental das pessoas mais velhas* (pp. 405-421). Coimbra: Lidel.

Simões, M. R. (2012). Instrumentos de avaliação psicológica de pessoas idosas: Investigação e estudos de validação em Portugal. *Revista Iberoamericana de Diagnóstico e Avaliação Psicológica, 34(1)*, 9-33.

Skeel, R. L., & Edwards, S. (2009). The assessment and rehabilitation of memory impairments. In B. Johnstone, & H. H. Stonnington (Eds.), *Rehabilitation of neuropsychological disorders: A practical guide for rehabilitation professionals* (2nd ed., pp. 47-73). Philadelphia, PA: Psychology Press.

Stephens, J. A., & Berryhill, M. E. (2016). Older adults improve on everyday tasks after working memory training and neurostimulation. *Brain Stimulation*, *9*(4), 553-559. https://doi.org/10.1016/j.brs.2016.04.001

Strauss, E., Sherman, E., & Spreen, O. (2006). *A compendium of neuropsychological tests: Administration, norms and commentary* (3rd ed.). New York: Oxford University Press.

Tromp, D., Dufour, A., Lithfous, S., Pebavle, T., & Després, O. (2015). Review: Episodic memory in normal aging and Alzheimer disease: Insights from imaging and behavioral studies. *Ageing Research Reviews, 24*(Part B), 232-262. https://doi.org/10.1016/j.arr.2015.08.006

Vilar, M., Sousa, L. B., Firmino, H., & Simões, M. R. (2016). Envelhecimento e qualidade de vida. In H. Firmino, M. R. Simões, & J. Cerejeira (Coord.), *Saúde mental das pessoas mais velhas* (pp. 19- 43). Coimbra: Lidel.

Willis, S. L., Tennstedt, S. L., Marsiske, M., Ball, K., Elias, J., Koepke, K. M.,... Wright, E. (2006). Long-term effects of cognitive training on everyday functional outcomes in older adults. *Journal of the American Medical Association*, *296*(23), 2805-2814. https://doi.org/10.1001/jama.296.23.2805

Wilson, B. A. (1999). *Case studies in neuropsychological rehabilitation*. New York: Oxford University Press.

Woods, A. J., Antal, A., Bikson, M., Boggio, P. S., Brunoni, A. R., Celnik, P.,... Knotkova, H. (2016). A technical guide to tDCS, and related non-invasive brain stimulationtools. *Clinical Neurophysiology*, *127*(2), 1031-1048. https://doi.org/10.1016/j.clinph.2015.11.012

Yassuda, M. S., Viel, T. A., Lima-Silva, T. B., & Albuquerque, M. S. (2011). Memória e envelhecimento: Aspectos cognitivos e biológicos. In E. V. Freitas, & L. Py (Eds.), *Tratado de Geriatria e Gerontologia* (pp. 1477-1485). Rio de Janeiro: Guanabara.

Zacks, R. T., & Hasher, L. (1994). Directed ignoring: Inhibitory regulation of working memory. In D. Dagenbach & T. H. Carr (Eds.), *Inhibitory processes in attention, memory, and language* (pp. 241-264). San Diego, CA, US: Academic Press.

Zimerman, M., & Hummel, F. C. (2010). Non-invasive brain stimulation: Enhancing motor and cognitive functions in healthy old subjects. *Frontiers in Aging Neuroscience*, *2*, 149. https://doi.org/10.3389/fnagi.2010.00149