경도인지장애와 치매환자를 위한 신경인지치료

한 현 정
명지병원 신경과, 치매진료센터

Neurocognitive Intervention Therapy for Patients with Cognitive Decline: MCI and Probable Alzheimer's Disease

Hyun Jeong Han, MD, PhD
Department of Neurology, Dementia and Neurocognitive Center, Myongji Hospital, Goyang, Korea

Brain aging and aging-related neurodegerative disorders are major health challenges faced by modern societies. Brain aging is associated with cognitive and functional decline and represents the favorable background for the onset and development of dementia. Indentifying protective factors or effective prevention strategies may lead to considerable benefits. A growing body of evidence supports the notion that cognitive training and rehabilitation can preserve and enhance operational skills in elderly individuals as well as reduce the incidence of dementia. Actively participating in cognitive activities during mid- or late life may be beneficial in preventing the risk of Alzheimer's disease and other dementia in the elderly. This review aims at providing a brief overview of the most recent data that support the support the efficacy of non-pharmacological interventions aimed at enhancing cognition and brain plasticity in healthy elderly individuals as well as delaying the cognition decline associated with dementia.

Key Words: Cognitive training; Rehabilitation; Alzheimer's disease

Introduction

Brain aging is associated with cognitive and functional decline and represents the favorable background for the onset and development of dementia. Cognitive impairments, particularly memory problems, are a defining feature of mild cognitive impairment (MCI) and the early stages of Alzheimer's disease (AD). AD is becoming a major socio-economical challenge for society and human health systems. It is therefore imperative to act during this extended pre-clinical phase and promote endogenous responses in brains that still have a large cognitive reserve and optimal levels of neural plasticity.[1] Beside pharmacological interventions, a great deal of interest resides on ways that allow modulation of brain plasticity in the elderly by acting on cognitive training and stimulations. Cognitive training and cognitive rehabilitation are specific interventional approach designed to address difficulties with memory and other aspects of cognitive functioning.[2]

Current data suggest that participation in cognitive activities may lower the risk of dementia by improving neuronal and cognitive reserves.[3] Cognitive activities may be defined as activities that individuals engage in for enjoyment or well-being that are independent of work or activities of daily living. This line of intervention can be also critical in delaying the cognitive decline associated with dementia or other widespread neurodegenerative diseases. This review will focus on the role of cognitive activities in prevention of cognitive decline in MCI and early AD and provided a brief overview of recent data.

Hyun Jeong Han, MD, PhD
Department of Neurology, Dementia and Neurocognitive center, Myongji Hospital, Hwajeong-dong 697-24, Deukyang-gu, Goyang 412-270, Korea
TEL: +82-31-810-5403 FAX: +82-31-969-0500
E-mail: neurohan5403@gmail.com

Cognitive and neural reserve

The central nervous system is highly dynamic structure that undergoes continuous functional remodeling. In this context, CNS plasticity is the ability to adopt functional or structural responses aimed at promoting successful adaptive behavior.[4] Plasticity requires a complex process of molecular, structural, and functional integrations that are carried out in neurons, glia, and subcellular compartments like dendrites, spines, and synapses. These biochemical and morphological changes go along with spatiotemporal synchronization of large neuronal populations across different brain regions. Cognitive reserve is the concept that has been proposed to explain the functional adaptation occurring in conditions that are associated brain damage, but where structural impairment dose not translate inpatient cognitive deficits. Brain reserve refers to the amount of preserved CNS "hardware", namely the intergrity of synapses, dentrites, neurons, glia, and pathways while cognitive reserve indicates the CNS "software", in short the brain capability to reorganize its activity by setting in motion compensatory cognitive mechanisms.[5] Thus, the cognitive reserve concept imposes to shift the attention from brain morphological integrity to functioning. Cognitive reserve is positively influenced by educational, environmental, nutritional as well as genetic factors.[6] The modulation of cognitive reserve has been indicated as a resource to be has tapped on in AD patients who despite the presence of large amount of Ad-related pathology show relative paucity of clinical symptoms and signs. The process is thought to require the formation of new synapses as well as the plastic remodeling and functioning of brain networks. The drawback is that these patients can go undetected for longtime and then, when exhaustion of the cognitive reserve occurs, eventually show a precipitous cognitive decline.[7] Cognitive activity is thought to provide some protection against dementia, but the mechanism and timing of these effects are unknown. Although the exact underlying biological mechanisms for why cognitive activities are beneficial are yet to be established, possible explanations include strengthening neuronal connections in vulnerable brain areas, reducing chronic stress or promoting a healthy lifestyle.

Cognitive activities have been proposed to have a preventive function that can retard the onset of dementia.[2] The repetition of cognitive skills may improve processing skills such as working memory and perceptual speed by possibly dendritic plasticity. Education and cognitive activities could lead to more neurons and synapses and therefore delay the onset of dementia despite the accumulation of disease pathology.[8] In experiments on rats, environmental enrichment has been shown to inhibit spontaneous apotosis, increased neurogenesis in dentate gyrus and spatial memory.[9] This may suggest a possible link between environment/social cognitive stimulation and regenerative brain processes.

Evidence from clinical trials of neurocognitive intervention

Cognitive exercise involving multiple cognitive domains appears to demonstrate greater efficacy than uni-modal memory strategy training. Multi-domain exercises provide a broader range of cognitive challenges to directly stimulate plasticity and in several studies has resulted in global cognitive function.[10,11] By contrast, little evidence was found for the efficacy of memory strategy training in MCI which was consistent with outcomes from a recent meta-analysis in healthy and MCI subjects that found training effects were equivalent to those seen in active controls.[12] High volume cognitive exercise appeared to result in greater benefit than lower volumes of training, although no dose-response studies were identified. Very frequent training for twelve weeks let to greater effect on memory than longer, less regular training.[10,13] Meta-analysis of cognitive training in healthy adults has suggested that two or three month training periods may have persistent protective benefit, however current findings in MCI suggest that frequency and total volume of sessions are also important. The current data show cognitive exercise also has promise for enhancing cognitive function in MCI[10,11,14,15] and may slow decline in at risk individuals. The effectiveness of cognitive exercise in those with established AD is likely to be modest,[16] although a recent trial of

computer-based exercises found delayed progression of disease by the end of training compared to controls.[17] Computer-delivered interventions are rapidly becoming popular. Computerized cognitive exercise has been successfully implemented across the age spectrum and research suggests that older adults are often the fastest growing users of computer and internet technology.

Conclusions

Further research is required in order to substantiate the efficacy of cognitive training as a therapeutic intervention in patient with cognitive decline. It is vital to clarly distinguish between various cognitive interventions and differentiate between training exercise and memory strategies. These data suggests cognitive interventions may be effective at enhancing cognitive outcomes, but several limitations have been identified which precludes firm conclusions.

References

1. Pieramico V, Esposito R, Cesinaro S, Frazzini V, Sensi SL. Effects of non-pharmacological or pharmacological interventions on cognition and brain plasticity of aging individuals. Front Sys Neurosci 2014;8:153 (1-10).
2. Purandare N, Ballard C, Burns A. Preventing dementia. Advances in psychiatric treatment. 2005;11:176-183.
3. Verumi P, Lesnick TG, Przybelski SA, Machulda M, Knopman DS, Meilke MM, et al. Association of lifetime intellectual enrichment with cognitive decline in the older population. JAMA Neurol 2014;71(8):1017-24.
4. Grangly K., Poo MM. Activity-dependent neural plasticity from bench to bedside. Neuron 2013;80:729-741.
5. Stern Y. Cognitive reserve. Neuropsychologia 2009;47:2015-2028.
6. Mora F. Successful brain aging: plasticity, environmental enrichment and lifestyle. Dialogue Clin Neurosci 2013;15:45-52.
7. Amieva H., Mokri H., Le Goff., Meilon C., Jacqmin-Gadda H., Foubert-Samier A, et al. Compensatory mechanism in higher-educated subjects with Alzheimer's disease: a study of 20 years of cognitive declin. Brain 2014;137:1167-1175.
8. Nisson M, Perfilieva E, Johansson U, Orwar O, Eriksson PS. Enriched environment increases neurogenesis in the adult rat dentate gyrus and improves spatial memory. J Neurobiol 1999;39:569-78.
9. Wilson RS, Bennett DA, Bienias JL, Aggarwal NT, Leon CF, Morris MC, et al. Cognitive activity and incident AD in a population-based sample of older persons. Neurology 2002; 59:1910-1914.
10. Rozzini L, Costal D, Chilovi V, Franzoni S, Trabucchi M, Padovani A. Efficacy of cognitive rehabilization in patients with mild cognitive impairement treated with cholinesterase inhibitors. Int J Geriatr Psychiatry 2007;22(4): 356-360.
11. Talassi E, Guerreschi M, Feriani M, Fedi V, Bianchetti A, Trabucchi M. Effectiveness of a cognitive rehabilitation program in mild dementia (MD) and mild cognitive impairment (MCI): A case control study. Arch Gerontol Geriatr 2007, suppl(1):391-399.
12. Valenzuela MJ, Breakspear M, Sachdev P: Complex mental activity and the aging brain: Molecular, cellular and cortical network mechanisms. Brain Res Rev 2007, 56(1):198-213.
13. Olazaran J, Muniz R, Reisberg B, Pena-Casanova J, Del Ser T, Cruz-Jentoft AJ, et al. Benefits of cognitive-motor intervention in MCI and mild to moderate Alzheimer disease. Neurology 2004, 2(63):2348-2353.
14. Barnes D, Yaffe K, Belfor N, Jagust W, DeCarli C, Reed B, et al. Computer-based cognitive training for mild cognitive impairment. Results from a pilot randomised, controlled trial. Alzheimer Dis Assoc Disord 2009, 23(3):205-210.
15. Troyer A, Murphy K, Anderson N, Moscovitch M, Craik FI. Changing everyday memory behaviour in amnestic mild cognitive impairment: A randomised controlled trial. Neuropsychol Rehabil 2008; 18(1):65-88.
16. Sitzer DI, Twamley EW, Jeste DV. Cognitive training in Alzheimer's disease: A meta-analysis of the literature. Acta Psychiatrica Scandinavica 2006;114(2):75-90.
17. Wagner N, Hassanein K, Head M: Computer-use by older adults: a multidisciplinary review. Computers in human behaviour 2010, 26(5):870-882.