



Cognitive Intervention and Brain Stimulation Therapies for Dementia

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The number of people with dementia is escalating globally. About 47 million people were living with dementia in 2015 worldwide.¹ Dementia is a chronic disease and patients need to live with cognitive impairment for a substantial period of time, which in turn causes a lot of distress and difficulties to patients, their families and society. However, the effectiveness of anti-dementia drugs, namely cholinesterase inhibitors and memantine, in preventing cognitive decline is limited. Some patients may not tolerate the side effects of anti-dementia drugs. Non-pharmacological approaches, such as cognitive intervention and brain stimulation methods, are used. This article would present an overview of these approaches.

COGNITIVE INTERVENTION

Cognitive interventions are widely employed in hostels, day centres and hospitals for patients suffering from mild to moderate dementia. They encompass a diverse range of cognitive activities. Clare and Woods (2004) broadly classified these cognitive interventions into three approaches, namely cognitive stimulation, cognitive training and cognitive rehabilitation.²

Cognitive Stimulation

Cognitive stimulation has the strongest evidence base among cognitive intervention approaches and is cost-effective in improving cognition.¹ It has been shown in meta-analysis that cognitive stimulation can benefit general cognition and self-reported quality of life.¹ It is usually a group-based intervention led by a coordinator or facilitator. Its emphasis is to involve multiple cognitive domains, instead of targeting on one specific domain.

Cognitive stimulation essentially comprises a range of activities, including reminiscence therapy, reality orientation, multisensory stimulation, and social activity. One example is 14 twice-weekly group sessions that take place over 7 weeks.³ These sessions cover different topics, such as childhood, faces/scenes, food, using money and current affairs. However, it was unclear which aspects of cognitive stimulation are the most effective and such cognitive stimulation might not be applicable in all settings.¹

Cognitive Training

Unlike cognitive stimulation, cognitive training is more focused on standardised training related to specific cognitive domain.⁴ The training format can be in a

group but can also be individualised. Its emphasis is to restore a specific function through practice. However, as there are various cognitive domains, there is marked variability in training strategies and outcome measures. While training may have observable effects on healthy elderly, evidence on its effectiveness in patients with dementia is limited and warrants further evaluation.¹

Interestingly, training in some specific cognitive functions may lead to an improvement in untrained general cognitive function. Chunking is a psychological process of recognising or enforcing patterns upon information gathering and of compressing information into a more recall-efficient pattern. The ability to use chunking is preserved in early Alzheimer's disease. Huntley et al. (2017) reported a randomised controlled trial providing, over the trial period of eight weeks, eighteen 30-minute sessions of either adaptive working memory training in verbal chunking strategies or a control intervention. Patients with Alzheimer's disease demonstrated significant improvement in trained verbal working memory task, and also on general cognitive function in comparison to control subjects.⁵

Cognitive Rehabilitation

The importance of rehabilitation for patients with dementia has long been recognized.⁴ For dementia, the aim of rehabilitation is to optimise everyday function by helping the patient set individual goals and devising strategies to achieve these goals. Such rehabilitation is individual-based and is mainly used for mild dementia. It involves multi-disciplinary input. Carers are regarded as team members but care for family carers is also an important goal of rehabilitation.

The evidence on its effectiveness is growing. Regan et al. (2017) reported a 2-year multicentre randomised controlled trial.⁶ Their intervention was four-weekly 1-hour sessions delivered to patients and their carers in the patients' homes with a focus on an individualised intervention addressing personally meaningful goals (such as to learn the names of people at church, to remember more about grandchildren's activities, or to take medication reliably). Patients and their carers were encouraged to help brainstorm and select the most appropriate strategies. They found that patients in the intervention group reported higher level of goal performance and satisfaction than those in the control group.

A large multicentre study of goal-orientated cognitive rehabilitation in mild dementia was recently published.⁷

In this study, participants were asked to identify areas in which they would see improvements and set goals. Their cognitive rehabilitation consisted of 10 weekly sessions with therapists over 3 months, followed by four sessions over the following 6 months. It was found that the 209 participants who received cognitive rehabilitation were doing significantly better than with those who received treatment as usual in relation to their goals, and these improvements were sustained 6 months later.

BRAIN STIMULATION

Empirical studies showed that two main brain stimulation therapies might be useful in improving one's cognitive performance. They are transcranial direct current stimulation (tDCS) and repetitive transcranial magnetic stimulation (rTMS).

Transcranial Direct Current Stimulation

tDCS is a simple, non-invasive brain stimulation technique that is capable of modulating cortical activity and inducing neuroplasticity mechanism.⁸ During the treatment, a weak electrical current is delivered through two scalp electrodes by a portable battery-powered stimulator. The current density, calculated on the basis of the power intensity divided by the area of the electrode, is used as a marker of dosage and influences the after-effects.⁹

Studies have demonstrated that tDCS enhances memory function in cognitive rehabilitation. Ferrucci et al. (2008) reported that tDCS delivered over the temporoparietal areas could specifically affect a recognition memory performance in patients with Alzheimer disease.¹⁰ It was postulated that tDCS could improve cognitive function of older adults with dementia by altering

- a) neuronal activity,¹¹
- b) cerebral blood flow,¹²
- c) synaptic and non-synaptic after-effects,¹³
- d) neurotransmitter polarity-dependency,¹⁴
- e) oscillatory brain activity^{15,16} and
- f) functional connectivity patterns in the brain.¹⁷

However, further large-scale clinical and mechanism-oriented studies are needed to establish its therapeutic efficacy in different types of dementia.^{18,19}

It is noteworthy that there has been a trend to develop a protocol in combining rehabilitation training with tDCS and cognitive training.²⁰ Andre et al. (2016) found that in patients with mild vascular dementia, anodal tDCS of the left dorsolateral prefrontal cortex (DLPFC) could produce additional effects to cognitive training on some tasks.²¹

Repetitive Transcranial Magnetic Stimulation

rTMS has been increasingly used in the management of various neurological and psychiatric disorders. For dementia, rTMS has been used to non-invasively modulate cortical excitability and induce lasting effects. Cotelli et al. (2011) applied daily high frequency (HF) rTMS over the left DLPFC of patients with Alzheimer's

disease, 25 minutes per day, five days a week for two weeks. In this study, real rTMS was found to improve performance in cognitive tests for up to 8 weeks following the end of treatment.²² A study by another group reported that five daily sessions of HF rTMS applied over the left then the right DLPFC could improve cognitive function in patients with mild to moderate Alzheimer's disease for up to 3 months after the stimulation period.²³

A randomised double-blind study reported that a 6-week cognitive training combining daily sessions of HF rTMS can improve cognitive function in Alzheimer's disease.²⁴ However, more large-scaled studies are needed to replicate the findings. Like tDCS, its clinical utility and protocols need further evaluation.

CONCLUSION

Cognitive intervention and brain stimulation therapies may benefit the cognitive function in patients with dementia non-invasively. These interventions may improve the quality of life of patients and their carers. These therapies can be used in combination with each other. However, more studies and evidence are needed to evaluate their clinical utilities and to enable formulation of clear clinical recommendations.

References

1. Livingston G, Sommerland A, Orgeta V et al. Dementia prevention, intervention, and care. *Lancet* 2017; 390: 2673-2734.
2. Clare L, Woods R. Cognitive training and cognitive rehabilitation for people with early-stage Alzheimer's disease: a review. *Neuropsychological Rehabilitation* 2004; 14: 385-401.
3. Rai H, Yates L, Orrell M. Cognitive stimulation therapy for dementia. *Clinical Geriatric Medicine* 2018; 34(14): 653-665.
4. Clare L. Cognitive training and cognitive rehabilitation for people with early-stage dementia. Review in *Clinical Gerontology* 2003; 13: 75-83.
5. Huntley JD, Hampshire A, Bor D, Owen A, Howard RJ. Adaptive working memory strategy training in early Alzheimer's disease: randomised controlled trial. *British Journal of Psychiatry* 2017; 210: 61-66.
6. Regan B, Wells Y, Farrow M, O'Halloran P, Workman B. MAXCOG – Maximizing cognition: a randomized controlled trial of the efficacy of goal-oriented cognitive rehabilitation for people with mild cognitive impairment and early Alzheimer disease. *American Journal of Geriatric Psychiatry* 2017; 25(13): 258-269.
7. Clare L, Kudlicka A, Oyeboed JR, et al. Goal-orientated cognitive rehabilitation for early-stage Alzheimer's and related dementias: the Great RCT. *Health Technology Assessment* 2019; 23(10): 1-242.
8. Boggio P, Ferrucci R, Mameli F., et al. Prolonged visual memory enhancement after direct current stimulation in Alzheimer's disease. *Brain Stimulation* 2012; 5(3): 223-230.
9. Stagg C, Nitsche N. Physiological basis of transcranial direct current stimulation. *Neuroscientist* 2011; 17(1): 37-53.
10. Ferrucci R, Mrakic-Spota S, Gardini S., et al. Behavioral and neurophysiological effects of transcranial direct current stimulation (tDCS) in fronto-temporal dementia. *Frontiers in Behavioral Neuroscience* 2018; 12: 235.
11. Ye H, Chen S, Huang D, Zheng H, Jia Y, & Luo J. Modulation of neural activity in the temporoparietal junction with transcranial direct current stimulation changes the role of beliefs in moral judgment. *Frontier Human Neuroscience*, 2015; 9: 659.
12. Shiozawa P, Santos M, Piovesan F., et al. Cerebral blood flow changes after transcranial direct current stimulation for a patient with schizophrenia: a case report. *The Journal of Neuropsychiatry and Clinical Neuroscience*, 2014; 26(2): E03-05.
13. Wu Y, Lin C, Yeh C. et al. Repeated transcranial direct current stimulation improves cognitive dysfunction and synaptic plasticity deficit in the prefrontal cortex of streptozotocin-induced diabetic rats. *Brain Stimulation*, 2017; 10(6): 1079-1087.
14. Naegel S, Biermann J, Theysohn N, et al. Polarity-specific modulation of pain processing by transcranial direct current stimulation - a blinded longitudinal fMRI study. *Journal of Headache Pain*. 2018 4;19(1): 99.
15. Rehmann R, Sczesny-Kaiser M, Lenz M. et al. Polarity-specific cortical effects of transcranial direct current stimulation in primary somatosensory cortex of healthy humans. *Frontiers in Human Neuroscience*. 2016; 10: 208



16. Holgado D, Zandonai T, Ciria LF, et al. Transcranial direct current stimulation (tDCS) over the left prefrontal cortex does not affect time-trial self-paced cycling performance: Evidence from oscillatory brain activity and power output. *PLoS ONE* 2019; 14(2): e0210873
17. Polania R, Nitsche M, Paulus W. Modulating functional connectivity patterns and topological functional organization of the human brain with transcranial direct current stimulation. *Human Brain Mapping* 2011; 32(8): 1236-1249.
18. Ferrucci R, Mameli F, Guidi I, et al. Transcranial direct current stimulation improves recognition memory in Alzheimer disease. *Neurology* 2008; 71(7):493-498.
19. Inagawa ., Narita Z, Sugawara N, Maruo K, Stickley A, Yokoi Y, Sumiyoshi, T. A meta-analysis of the effect of multisession transcranial direct current stimulation on cognition in dementia and mild cognitive impairment. *Clinical EEG and Neuroscience*. 2019;50(4): 273-282.
20. Manenti R, Cotelli MS, Cobelli C, et al. Transcranial direct current stimulation combined with cognitive training for the treatment of Parkinson Disease: A randomized, placebo-controlled study. *Brain Stimulation* 2018; 11(6): 1251-1262.
21. Andre S, Heinrich S, Kayser F, et al. At-home tDCS of the left dorsolateral prefrontal cortex improves visual short-term memory in mild vascular dementia. *Journal of the Neurological Sciences* 2016; 369: 185-190.
22. Cotelli M, Calabria M, Manenti R, et al. Improved language performance in Alzheimer's disease following brain stimulation. *Journal of Neurology, Neurosurgery and Psychiatry* 2011; 82(7): 794-797.
23. Ahmed M, Darwish E, Khedr E, et al. Effects of low versus high frequencies of repetitive transcranial magnetic stimulation on cognitive function and cortical excitability in Alzheimer's dementia. *Journal of Neurology* 2012; 259(1): 83-92.
24. Rabey J, Dobronevsky E, Aichenbaum S, et al. Repetitive transcranial magnetic stimulation combined with cognitive training is a safe and effective modality for the treatment of Alzheimer's disease: a randomized, double-blind study. *Journal of Neural Transmission* 2013; 120(5): 813-819.

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