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Hong Kong Psychogeriatric Association Newsletter
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MESSAGE FROM THE NEWSLETTER COMMITTEE

This issue of HKPGA newsletter records a new milestone for HKPGA after its 25th anniversary. You will read a summary of the presentations by Associate Professor Allen LEE of the Chinese University of Hong Kong and Assistant Professor Calvin CHENG of the University of Hong Kong at our annual scientific meeting cum tripartite Chinese psychogeriatric meeting. The presentation by representatives of the mainland and Taiwan will be published in the next issue. Meanwhile, please see the snapshot photos of the anniversary meeting and visit *www.hkpga.org* for archives of the HKPGA newsletters.

Application of Non-Invasive Brain Stimulation (NIBS) in mental health of older adults

Dr. Calvin P.W. CHENG,
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Pharmacological treatment and psychotherapy are the two main streams of treatment modalities in modern Psychiatry. However, there are limitations to each kind of treatment modality in older adults, including side effects of the medications, the labour intensity and cost-ineffectiveness of psychotherapy, and the non-responsiveness or inadequate response of both modalities. Therefore, new options for treatment modality have become a pressing issue in the field of Psychiatry.

In recent decades, non-invasive brain stimulation (NIBS) has been under the spotlight in mental health research. The most common forms of NIBS are transcranial magnetic stimulation (TMS) and transcranial direct current stimulation (tDCS). With the advancement of neuroscience, mental illness nowadays is viewed as a kind of brain disorder. Specific brain areas or networks are believed to contribute to the pathophysiology of those disorders. Therefore, if we could target specific brain abnormalities, it would be possible

to cure or alleviate the symptoms without causing generalised side effects by using non-specific approaches. The recent development of neurostimulation and neuro-navigation techniques has allowed us to target specific brain areas or networks with direct electric current, induced electric current or ultrasound shock wave, to modulate activities at cellular level and change the neuroplasticity. Another advantage of this treatment modality (NIBS) is that it is usually well-tolerated without the need for generalised anaesthesia. Some patients might experience mild and transient physical discomfort such as headache, itchiness and redness of scalp, but only a few people have experienced a seizure in TMS.

TMS and its application

Transcranial magnetic stimulation uses an electromagnetic field to induce an electrical current within the brain. Repetitive TMS (rTMS) delivers a train of pulses at the same intensity over time at a particular region of the brain. It either stimulates or suppresses neuronal activity, depending on the frequency and the inter-train interval between pulses. The effect of rTMS is mediated by modulating the neuronal activities of the targeted dysfunctional area. Distributed modulation of brain activities via a specific brain network may also be achieved. The clinical effects of rTMS may be affected by many factors, including the number of sessions, the intensity level of pulses, the interval between sessions, and the position and shape of the coil.

TMS has been most studied in the treatment of depression. For adults with depression and on whom antidepressants have failed, application of high frequency rTMS over the dorsolateral prefrontal cortex (DLPFC) for 4-6 weeks daily, usually five times per week, is a standard treatment protocol approved by the U.S. Food and Drug Administration (FDA) in 2008. In recent years, the FDA has approved a newer treatment parameter of TMS using theta-burst stimulation, which has the advantage of shorter treatment time. The recent systemic review and meta-analysis supported the efficacy of rTMS in older adults with depression. The effect size of rTMS in older adults was comparable with in general adults despite the concern of brain atrophy.

Repetitive transcranial magnetic stimulation has also been applied to patients with cognitive impairment. There is growing evidence suggested rTMS could enhance the general cognition and specific cognitive domains such as memory, attention and working memory, despite the results are conflicting sometimes.

Transcranial direct current stimulation and its application

Transcranial DCS is a neurostimulation technique where a mild direct current (1-2 mA) is induced through the cerebral cortex via electrodes placed on the scalp, which in turn modifies cortical excitability, depending on the polarity directions. It is easier and cheaper to administer compared to TMS, and it can also be delivered at home. Its effects are possibly exerted through modulating cortical excitability. Long-term plasticity is enhanced, with modulations in the rate of neurotransmitter release.

The application of tDCS in clinical use is less supported by evidence. To date, there is not yet any FDA approval for tDCS for the treatment of any mental illness. Transcranial direct current stimulation studies are most commonly done on depression. In a recent meta-analysis of six randomised controlled trials (RCTs) with 289 adult patients, tDCS was shown to be significantly superior to sham-control treatment in response, remission and improvement in depression. In most studies, the left DLPFC was stimulated, and the effect size was comparable with those reported for antidepressant drug treatment and rTMS. However, a recent large international RCT of adult patients with depression showed no difference in reducing depressive symptoms between active and sham stimulation in patients with unipolar or bipolar depression. The conflicting results warrant further high-quality RCTs to determine the efficacy of tDCS. Our team has conducted an open-label pilot study in alleviating depressive symptoms and cognitive deficits in late-life depression which showed promising results. Therefore, our team is now conducting a randomized controlled trial in this area.

Emerging NIBS technique

Besides the aforementioned most commonly investigated NIBS, there is a new NIBS which uses transcranial shockwave to modulate brain activity. Compared with TMS and tDCS, this technique has a higher spatial resolution and can reach deeper structures. Its safety profile is comparable to that of the other NIBS techniques.

The underlying mechanism of this technique is mechanotransduction. It is a biological pathway through which the cells convert the mechanical TPS stimulus into biochemical responses. It could affect neurons and induce neuroplastic effects through several pathways, including increasing cell permeability; stimulation of mechanosensitive ion channels; release of nitric oxide resulting in vasodilation; increased metabolic activity and angiogenesis; stimulation of vascular growth factors (VEGF); and stimulation of brain-derived neurotrophic factor (BDNF).

Most of the existing studies have been done on healthy volunteers to test the neuromodulation effect in different parts of the brain, including the thalamus and basal ganglia. With the adjustment of stimulation parameters, it can cause the suppression or facilitation of neural activity. Such a technique has also been applied to five patients with unresponsive wakefulness syndrome, resulting in significant improvement in their vigilance and oropharyngeal motor functions.

Another application is on Alzheimer's disease (AD). TPS was obtained with CE marking in 2018 for the treatment of the central nervous system (CNS) in patients with mild to moderate Alzheimer's disease (AD). In a recent study, TPS was applied to elderly patients with AD in three sessions (6000 pulses each) per week for 2-4 weeks, either over classical AD affected sites such as the dorsolateral prefrontal cortex, areas of the memory and language network, or over all accessible brain areas (global brain stimulation). Significant improvement in the CERAD (Consortium to Establish a Registry for Alzheimer's Disease) score was demonstrated (immediately as well as 1 and 3 months after stimulation). fMRI also showed significantly increased connectivity within the memory network. Our team also has conducted TPS study in older adults with mild cognitive impairment. The patients showed significant improvement in cognition both immediate post and 3 months after intervention. Since this NIBS technique is still relatively new, further studies should be done with various disease groups before it can be applied in a clinical setting.

Conclusion

NIBS is a group of non-invasive neuromodulation techniques which are potentially useful to treat various mental illnesses in elderly such as depression, OCD, schizophrenia and dementia. Their administration is easier, and their safety profile is better than traditional psychosurgery or deep brain stimulation. Their efficacy in some conditions such as depression and OCD has been proven to be comparable to pharmacological treatment. Further effort in researching this area will provide more evidence of the effect of these NIBS techniques in clinical use.

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Abbreviated Prescribing Information

[Ebixa®]/[Memantine hydrochloride] Presentation: Film-coated tablets 10 and 20mg. Indication: Treatment of patients with moderate to severe Alzheimer's disease. Dosage: Maintenance dose is 20 mg. Once-daily, taken with or without food. Treatment starts with half a 10mg tablet per day in the 1st week; the 2nd week one 10mg tablet per day; the 3rd week one and a half 10 mg tablet per day; and from the 4th week 20mg once daily. In patients with moderate renal impairment, the daily dose should be 10mg per day, and it could be increased to 20mg/day according to standard titration scheme if the patients tolerated well. In patients with severe renal impairment daily dose should be 10 mg per day. Not recommended in patients with severe hepatic impairment. Route of administration: oral use Contraindications: Hypersensitivity to active substance or any of the excipients. Special precautions: Caution is recommended with patients suffering from epilepsy. Concomitant use of amantadine, ketamine or dextromethorphan should be avoided. Clinical data are limited on patients with myocardial infarction, uncompensated congestive heart failure or uncontrolled hypertension and patients with these conditions should be closely supervised. Urinary pH increase may elevate plasma levels of memantine. Interactions: Effects of L-dopa, dopaminergic agonists and anticholinergics may be enhanced. Effects of barbiturates, neuroleptics and hydrochlorothiazide may be reduced. Effects of dantrolene and baclofen may be modified. Plasma levels of cimetidine, ranitidine, procainamide, quinidine, quinine and nicotine may be increased. Undesirable effects: Common (1-10%): Dizziness, headache, constipation, hypertension, dyspnoea, somnolence, drug hypersensitivity, balance disorders, elevated liver function test. Uncommon (0.1-1%): Fatigue, confusion, hallucinations (mainly in severe AD), vomiting, gait abnormal, fungal infections, venous thrombosis/ thromboembolism, cardiac failure. Very rare (<0.1%): Seizures. Not known: Psychotic reactions and pancreatitis (cases reported in postmarketing experience), hepatitis. Overdose: Symptomatic treatment. Legal category: POM.
Marketing Authorisation Holder: H. Lundbeck A/S, Ottiliavej 9, DK-2500 Valby, Denmark. Revision Date: May 2012. Full prescribing information is available upon request. REG_00116239

HK-LU-2023.08-AD01

Benefits of Cognitive Interventions on Brain Health in Older Adults

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Dementia poses a significant public health challenge in Hong Kong, especially given our rapidly ageing population. While monoclonal antibodies that target beta-amyloid plaques have been approved by the Food and Drug Administration (FDA) in the USA for the treatment of Alzheimer's disease, their long-term cost-effectiveness and safety profile remain uncertain. To address the growing problem of dementia, prevention strategies are crucial.

Increasing evidence suggests that staying cognitively active in late life is essential for maintaining cognitive function. Our longitudinal collaborative study with the Department of Health of the Government of Hong Kong found that regular engagement in cognitive activities was associated with a lower risk of dementia among local Chinese older adults.

With the support of the Research Grants Council, our team conducted a randomized controlled trial and demonstrated that increasing Chinese calligraphy handwriting practice, one of the traditional "Four Arts" in China, improves working memory and, more importantly, strengthens the functional connectivity of the default mode network in older adults who were free of mild cognitive impairment (MCI) or dementia.

Our findings highlight the importance of participating more in cognitive activities in late life. Compared to other lifestyle interventions, calligraphy practice offers several unique advantages: it is safe and can be practised indoors, alone, and at little cost. Hence, healthcare professionals should encourage older adults to stay cognitively active for better brain health.

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Abbreviations: ADT: Antidepressant treatment; IDS-SR$_{10}$: Inventory of Depressive Symptomatology Self-Report (10 items); MDD: Major depressive disorder; MADRS: Montgomery-Asberg Depression Rating Scale.
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* Refers to 76.5% and 52.9% MADRS response and remission rates respectively. MADRS response is defined as a ≥ 50% reduction in MADRS total score from baseline. MADRS remission is defined as ≥ 50% reduction in MADRS total score from baseline and MADRS total score ≤ 10.[2]

^ This study investigated the effects of REXULTI® (2 - 3mg/day) adjunct to ADT on patient life engagement over the short and long term, using the 10-item Inventory of Depressive Symptomatology Self-Report (IDS-SR$_{10}$) Life Engagement subscale. Over 6 weeks, ADT + REXULTI® (n = 579) showed greater improvement in IDS-SR$_{10}$ Life Engagement subscale score than ADT + placebo (n = 583), with a least squares mean difference of -1.19 (95% confidence limits: -1.78, -0.59; p = 0.0001; Cohen's d effect size: 0.23). The 10 items are categorized into the following domains of IDS-SR$_{10}$ subscale; physical (feeling slowed down and energy level); cognitive (concentration/ decision making); emotion (view of my future, view of myself, response to the mood to good or desired events and capacity for pleasure or enjoyment); social (general interest, interpersonal sensitivity and interest in sex). These are some of the examples of each domain of IDS-SR$_{10}$ improvement in short-term efficacy and the improvement in particular domains (concentration/ decision making and feeling slowed down) is not statistically significant.[1,3]

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COUNCIL NEWS

The Tripartite Chinese Psychogeriatric Meeting 2023

The Tripartite Chinese Psychogeriatric Meeting 2023 was held on 24th to 25th November.

On 24th November 2023, delegates from the mainland China and Taiwan joined a visit to Castle Peak Hospital in the morning and the Hong Kong Alzheimer's Disease Association Gene Hwa Lee Centre in the afternoon. In the evening, a business meeting was held at the Sheraton Hotel to discuss the recent development of the psychogeriatric services in the three regions, and the potential collaborations among the Chinese Society of Geriatric Psychiatry, Taiwanese Society of Geriatric Psychiatry and HKPGA.

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On 25th November, the Tripartite Psychogeriatric Meeting was held in the ballroom of the Langham Hotel. We celebrated the HKPGA's 25th anniversary with a video slide show, a cake-cutting and wine-toasting ceremony, and insightful messages from our international advisors Prof. Edmond Chiu and Prof. George Grossberg. Dr. Calvin Cheng and Dr. Allen Lee from Hong Kong, Dr. Tzung-Jeng Hwang and Dr. Kun-Po Chen from Taiwan, and Prof. Huali Wang and Dr. Bingyu Li from mainland China shared with us their latest research and recent advances in the psychogeriatric field. We had over 100 on-site participants and over 750 online participants attending the event.


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The HKPGA would like to thank the following sponsors for their contribution and support to our Tripartite Psychogeriatric Meeting:

The HKPGA 25th Annual General Meeting was also held on 25th November 2023. The new council was elected as below:

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