

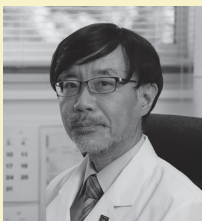
Impact Objectives

- Investigate the potential for transcranial direct current stimulation (tDCS) as a non-invasive neurostimulation tool
- Verify preliminary findings and perform randomised controlled studies to evaluate the effect of tDCS on functional capacity in patients with schizophrenia



An innovative approach to schizophrenia research

Psychiatry expert Dr Tomiki Sumiyoshi discusses the need to improve social needs of patients suffering from schizophrenia and unravels the significant role that transcranial direct current stimulation (tDCS) can play in facilitating this



Can you introduce your research into schizophrenia and how it will benefit patients?

Schizophrenia is a chronic mental disorder that changes the way we feel, think and behave. Patients suffering from this serious disease exhibit various psychotic symptoms, such as hallucinations and delusions. However, they also experience profound levels of cognitive impairment, such as disorganised and incoherent speech, confused thoughts, movement disorders, trouble concentrating, etc. These are symptoms that are strongly associated with negative social outcomes for these patients. Therefore, research has now shifted focus to identifying and implementing the means that can facilitate cognitive enhancement. In fact, research studies have recently reported that a very promising tool that can indeed instigate a higher level of functional outcomes for schizophrenic patients is transcranial direct current stimulation (tDCS).

Essentially, tDCS is a non-invasive type of neurostimulation that delivers a low electric current to the patient's scalp and it works by changing the electrical gradient between the inside and the outside of a neural cell, thus stimulating (strengthening or weakening) the respective synaptic transmissions

between neurons. If the benefits of tDCS for social function are confirmed, this will increase the chance of functional recovery for patients receiving conventional treatments. Hence, it is important to verify these preliminary findings and perform randomised controlled studies to evaluate the effect of tDCS on functional capacity in patients with schizophrenia.

What are some of the current barriers in our understanding of the neurobiological substrates responsible for cognitive impairment?

The most prominent obstacle that prevents scientists from understanding or even identifying the aetiology and pathophysiology of most psychiatric diseases is the fact that the initial diagnosis is based almost exclusively on clinical interviews. In fact, researchers employ this approach because of the distinct difficulties when examining the neurobiological derangements in the brain of living patients. Therefore, it comes as no surprise that not only are we still unaware of the causes triggering the manifestation of various psychiatric diseases, but this also explains the limited therapeutic approaches that can efficiently assist psychiatric patients. These facts are the fundamental elements that give great value to our research efforts because our research intends to investigate the efficiency of tDCS to treat cognitive impairment of psychiatric illnesses, and hence help these patients to live a normal life.

Can you talk about your randomised controlled trial and the preliminary results?

First of all, our study intends to conduct randomised controlled studies to evaluate the effect of tDCS on functional capacity in patients with schizophrenia. Patients included in this study will either receive active or sham stimulation, thus creating a baseline for the subsequent comparison between these two population samples. The functional capacity of these patients will be measured with the UCSD Performance-based Skills Assessment (UPSA), a method that is very effective at assessing skills related to community tasks. Furthermore, the Brief Assessment of Cognition in Schizophrenia will also quantify cognition, whereas the Positive and Negative Syndrome Scale will measure psychotic symptoms.

This study is primarily based on the success of previous clinical experiments in which tDCS was found to be extremely effective in treating impairment of daily-living skills in schizophrenic patients. In fact, these studies reveal that tDCS managed to improve both financial and communication skills in schizophrenic patients. Hence, our primary target is to verify these findings and to outline the efficiency of tDCS in terms of improving cognitive function in patients with schizophrenia. ▶

Addressing cognitive impairment in schizophrenia patients

Researchers at Japan's National Centre of Neurology and Psychiatry are creating a step change in the way cognitive functions of psychiatric patients can be improved through using innovative tools

Psychiatrist Dr Tomiki Sumiyoshi is the Director of Preventive Intervention for Psychiatric Disorders at National Centre of Neurology and Psychiatry, with extensive experience in clinical and basic research on schizophrenia and mood disorders. His deep interest in schizophrenia is driven by his background investigating neurobiological substrates responsible for cognitive impairment, but also in discovering effective therapeutics to facilitate social outcomes in patients with psychiatric conditions.

Sumiyoshi explains that the connection between psychiatric disorders and cognitive impairment is well-established. Yet, limited efforts have been made towards implementing novel approaches that can truly help psychiatric patients to overcome this impairment, and hence live a normal life. He believes it is critical that current research needs to shift its focus towards investigating innovative methods such as transcranial direct current stimulation (tDCS) that can facilitate cognitive enhancement in patients with schizophrenia. The application of tDCS to treat cognitive impairment of psychiatric

illnesses is an emerging field, and much remains to be explored,' Sumiyoshi explains. 'Further elucidation of the mechanisms underlying the cognitive benefits of tDCS will help understand the pathophysiology of cognitive disturbances pertinent to many psychiatric conditions, and develop more effective and safer methods to treat these dysfunctions.'

COGNITIVE IMPAIRMENT

Schizophrenia is a serious mental disorder that has a devastating effect on the way patients think, feel and act. Not only will schizophrenia patients exhibit distinct psychotic symptoms related to the disorder they suffer from, but they will also experience a profound decline in their cognitive functioning. 'Despite the fact that it has been over a century since this chronic disease was initially defined and characterised, the precise aetiology and pathophysiology of this disease – but also of most psychiatric disease – is yet to be fully unravelled and understood,' highlights Sumiyoshi. He continues that diagnosis for most psychiatric conditions relies heavily on clinical interviews, which by

default hamper the interpretation, but also our understanding, regarding various clinical manifestations such as cognitive impairment. 'The paucity of objective markers to predict progression to psychoses and mood disorders comes as a result of the above situation, posing a distinct challenge against early intervention into psychiatric conditions', he says. Therefore, it has become evident that novel approaches and innovative methods need to be employed in order to treat cognitive impairment of psychiatric illnesses, with tDCS holding much potential.

In principle, tDCS is a contemporary non-invasive neuromodulatory method of delivering low electric currents to the patient's scalp. 'Informally known as a brain-hacking technique, tDCS is based on the application of a positive and a negative current by using electrodes to a given area, thus changing the electrical gradient between inside and outside of the membrane of a neural cell,' outlines Sumiyoshi. 'In neuroscience, synaptic plasticity, such as the ability of synapses to strengthen or weaken in accordance to external stimuli, is the basis

If the benefits of tDCS on social functioning are confirmed, this technique will increase the chance of functional recovery for patients receiving conventional treatments

of our learning and memory skills.' In other words, tDCS augments synaptic plasticity and can be used to improve cognitive functions such as memory, language and attention. This is exactly the reason why the efficiency of this technique is now being investigated on psychiatric patients in order to facilitate higher-level functional outcomes, including daily-living skills reflecting cognitive function. 'If the benefits of tDCS on social functioning are confirmed, this technique will increase the chance of functional recovery for patients receiving conventional treatments, such as antipsychotic drugs, especially for those who exhibit intolerance to these medications,' he says.

Sumiyoshi's interventional study intends to employ a randomised controlled design. More specifically, psychiatric patients will be separated into two groups, one receiving active stimulation from the tDCS (active group) and one receiving sham stimulation (control group). 'Functional capacity will be evaluated by the UCSD Performance-based Skills Assessment-Brief (UPSA-B) as a primary outcome,' he explains. 'Cognition, as measured by the Brief Assessment of Cognition in Schizophrenia, and psychotic symptoms, as measured by the Positive and Negative Syndrome Scale, will also be evaluated.'

COLLABORATION AND SUPPORT

This study uses a novel medical device, which is not approved for clinical practice in Japan. Therefore, the respective research design and protocols had to be subjected to various regulations and ethical committees in order to ensure the development of a legal framework that will allow the use of this device in clinical trials. Sumiyoshi confirms that this process was time consuming but also expensive as investors and investigators needed to cover a substantial amount of related fees in addition to management service and insurance. 'I am very grateful for the assistance of the National Centre of Neurology and Psychiatry (NCNP) who provided us with great support towards the implementation of our clinical studies,' remarks Sumiyoshi.

Collaboration is a key parameter for the realisation of this research. In fact, and to highlight the importance of multidisciplinary collaboration for this project, this interventional study requires the assistance of project/study managers, a biostatistician, a data manager, monitoring staff and clinical research coordinators in order to maintain and ensure optimal quality. 'Educating and working with young researchers is a large and important part of my work,' says Sumiyoshi. 'As Chair of the World Psychiatric Association Section on Psychoneurobiology, I support the promotion of worldwide interactions among researchers and clinicians on cognitive sciences, psychopharmacology, neurophysiology, neuromodulation and related fields.'

More specifically, Sumiyoshi and his team are carrying out their clinical studies in research institutes and medical facilities both inside and outside of NCNP. For instance, the Hospital of NCNP is providing this research with valuable assistance, especially in terms of recruiting psychiatric patients and in performing the respective clinical experiments, whereas the Translational Medical Centre has been providing data management services.

FUTURE PLANS

The primary objective of Sumiyoshi's research is to validate current findings regarding the efficiency of tDCS in treating impairment of daily-living skills in patients with schizophrenia by means of randomly assigned sham-stimulation controlled trial. However, and owing to Sumiyoshi's background and expertise, his research interests are not solely limited to schizophrenia, but also to mood disorders and developmental disorders, such as autism. 'Furthermore, I am planning to work on the development of preventive intervention methods for these psychiatric conditions, based on data from preclinical and clinical studies on neurobiological substrates responsible for vulnerability and progression to overt mental diseases,' he concludes. ●

Project Insights

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COLLABORATORS

- Kenji Hatano (MD, PhD)
- Takuma Inagawa (MD)
- Kazushi Maruo (PhD)
- Kazuyuki Nakagome (MD, PhD)
- Zui Narita (MD, PhD)
- Takamasa Noda (MD, PhD)
- Hideki Ohi (PhD)
- Aya Shirama (PhD)
- Kazuki Sueyoshi (MS)
- Ayumu Wada (MS)
- Yuji Yamada (MD)

CONTACT

Dr Tomiki Sumiyoshi (MD, PhD)

T: +81 42 3412711

E: tomikisumiyoshi840@gmail.com

W: www.linkedin.com/in/tomiki-sumiyoshi-0730668/?originalSubdomain=jp

BIO

Dr Tomiki Sumiyoshi is Director of the Department of Preventive Intervention for Psychiatric Disorders, National Institute of Mental Health, National Center of Neurology and Psychiatry. His research interests include investigating neurobiological substrates responsible for cognitive impairment, implementing methods for early intervention and discovering effective therapeutics to facilitate social outcomes in patients with psychosis or mood disorders.

