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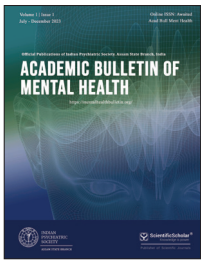

Letter to Editor

Accelerated Transcranial Random Noise Stimulation Improves Cognition in Traumatic Brain Injury: A Case Study

Sujita Kumar Kar[1], MD, Devika Raje[1], M Phil, Babli Kumari[1], MD

[1]Department of Psychiatry, King George's Medical University, Lucknow, Uttar Pradesh, India

*Corresponding author:
Dr. Sujita Kumar Kar,
Department of Psychiatry, King George's Medical University, Lucknow, Uttar Pradesh, India.

drsujita@gmail.com

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Dear Editor,

Transcranial random noise stimulation (tRNS) is a form of cortical electrical stimulation that delivers an oscillating current with random amplitudes, which alters the pathological oscillatory discharge of the neurons.[1] In addition, tRNS also causes alterations in the opening and closure of the sodium channels, latency of sodium currents, and amplification of sodium currents.[2] Long-term administration of tRNS (nine sessions over 5 weeks) in experimental animals (juvenile mice) resulted in enhancement of the excitatory effect and decrease in the inhibitory effect (mediated by a decrease in Gamma Amino-Butryric Acid (GABA) levels) without any alterations in the histopathology.[3] Administration of ten sessions of tRNS for cognitive impairment in an elderly individual with traumatic brain injury (whose cognitive symptoms show minimal improvement even after treatment with cognitive enhancers like donepezil and memantine) resulted in sustained improvement in cognitive flexibility, set-shifting (executive function), and visual attention.[4] A randomized controlled trial on a sample of nine patients with traumatic brain injury who were in subacute vegetative-unresponsive wakefulness state used tRNS over the dorsolateral prefrontal cortex (DLPFC) and there was no improvement in wakefulness reported after five sessions of tRNS intervention.[5] Evidence suggests that tRNS improves working memory in healthy individuals significantly than transcranial direct current stimulation (tDCS) and sham intervention.[1] In this case study, we highlight the relevance of tRNS intervention on cognition in a young patient with traumatic brain injury.

A moderately built 23-year-old adult male sought medical attention because of a troubling set of symptoms, which included increased irritability, crying spells, forgetfulness, and a reduced ability to concentrate. In addition, he would forget day-to-day events and events that happened before and after a traumatic brain injury. These symptoms had gradually worsened over a period of 7 months, beginning subtly and initially being associated with the head injury. Due to his persistent change of behavior, he consulted the neuropsychiatry specialty clinic. For the past 3 months, he had been prescribed the following medications: 50 mg of sertraline taken every night, 5 mg of melatonin before bedtime, and 50 mg of brivaracetam taken twice daily. It is worth noting that the patient had a history of using chewable tobacco for 2 years but quit this habit 7 months ago. There was no prior history of psychiatric disorders in the patient. The family history was insignificant. His premorbid personality was non-contributory. During the mental status examination (MSE), the patient displayed full awareness of time, place, and person. Based on the gathered medical history and the MSE findings, a diagnosis of post-concussional syndrome (F07.2) in accordance with the ICD-10 criteria was established. The patient was continued with sertraline and brivaracetam in

the same doses as before. In addition, quetiapine was added at 50 mg/day and later increased to 150 mg/day. Considering the persistently impairing cognitive deficits that were affecting his activities of daily living significantly, he was hospitalized and neuromodulation using tRNS was planned.

He underwent 20 sessions of tRNS over 10 consecutive days with two sessions daily. Each session lasted 30 minutes, and a current of 2 mA strength was used with an offset of 0.1 mA and ramp time of 10 seconds using electrodes of 5×5 cm^2 size. The anode was placed over the left DLPFC and the cathode was placed over cerebellar vermis (corresponding to Oz as per the 10–20 system of electrode placement in the electroencephalogram). Cognitive assessment was done at the baseline (before tRNS intervention) and 2 weeks following tRNS intervention using the same cognitive assessment tools.

Intelligence Quotient (IQ) Assessment: The IQ was assessed using performance tests and verbal adult intelligence scale of P.G.I. battery of brain dysfunction (PGI-BBD). Pre-intervention verbal quotient (VQ) was found to be "75–79" indicative of a borderline level of intellectual functioning, while during post-intervention, it increased to "85–89", indicating dull normal intellectual functioning. Performance quotient (PQ) could not be obtained as the patient was unable to comprehend the instructions of the test.

Neuropsychological Assessment: The assessment was done using PGI BBD. Subtests of NIMHANS (Digit vigilance

Table 1: Neurocognitive assessment of the patient before and after tRNS

Serial number	Test	Function	Percentile (Raw Score) Pre-intervention	Pre-intervention	Percentile (Raw Score) Post intervention	Post-intervention
1.	Digit Symbol	Mental Speed	Unable to comprehend	-	Unable to comprehend	-
2.	Digit vigilance	Visual Attention	Unable to comprehend	-	Unable to comprehend	-
3.	Controlled oral word association test	Verbal Fluency	Unable to comprehend	-	Unable to comprehend	-
4.	Verbal N back test	Working Memory 1 Back	Unable to comprehend	-	Unable to comprehend	-
5.	Auditory verbal learning test	Verbal Learning and Memory Immediate Recall Delayed Recall LTPR	Unable to comprehend	-	Unable to comprehend	-
6.	PGI-BBD	Immediate Retention of Similar Pair Dissimilar Pair Visual Retention Recognition	Dysfunction Rating = 3 Dysfunction Rating = 3 Dysfunction Rating = 3 Dysfunction Rating = 3 Dysfunction Rating = 3	Severe dysfunction Severe dysfunction Severe Dysfunction	Dysfunction Rating = 2 Dysfunction Rating = 3 Dysfunction rating = 3 Unable to comprehend Unable to comprehend	Moderate deficits Severe Dysfunction Severe Dysfunction - -
7.	VAIS	Information, Comprehension, Arithmetic, Digit Span	VQ=79	Borderline intelligence	VQ=88	Dull normal intelligence
8.	Nahor Benson test	Parieto-occipital functioning	Dysfunction Rating=3; Raw Score=5	Severe Dysfunction	Did not attempt	-
9.	BGT	Perception and visuomotor functioning	Dysfunction Rating=3; Raw Score=10	Severe Dysfunction	Dysfunction Rating=3	Severe Dysfunction

(*Cont...*)

Table 1: (Cont...)

Serial number	Test	Function	Percentile (Raw Score) Pre-intervention	Pre-intervention	Percentile (Raw Score) Post intervention	Post-intervention
10.	PGI-BBD	Remote memory Recent memory Mental balance Delayed recall Attention and concentration	Dysfunction Rating=3; Dysfunction rating=3 Dysfunction rating=3 Dysfunction rating=3 Dysfunction Rating=3	Severe Deficits Severe deficits Severe deficits Severe deficits Severe deficits	Dysfunction Rating=2; Dysfunction Rating=3 Dysfunction Rating=3 Dysfunction Rating=2 Dysfunction Rating=0	Moderate deficits Severe Dysfunction Severe dysfunction Moderate deficits No deficits

tRNS: Transcranial random noise stimulation, LTPR: Long Term Percent Retention, PGI-BBD: P. G. I. Battery of Brain Dysfunction, VAIS: Verbal Adult Intelligence Scale, VQ: Verbal Quotient, BGT: Bender Gestalt Test

and digit substitution) were attempted, but the patient was unable to comprehend the instructions [Table 1]. Before the intervention, the total dysfunction rating score was 30, which indicated severe cognitive dysfunction; post-intervention, the score was 18, which indicated significant improvement in cognitive dysfunction. The neuropsychological assessment revealed significant changes in domains of immediate recall, remote memory, delayed recall, and attention and concentration after tRNS intervention. We could not do any cognitive remediation during the course of neuromodulation as the patient was not getting engaged in the cognitive remediation therapy.

In addition, both the patient and his family were psychoeducated about the nature of the illness, with a focus on the importance of long-term adherence to the treatment plan. The patient was discharged after 3 weeks of hospitalization. In the 4-month follow-up, the patient was maintaining well and functioning was better with no worsening of symptoms.

In this case, it's noteworthy that the cognitive impairments were so severe that they significantly affected his activities of daily living. The unique feature was that he received two sessions of tRNS daily over 2 weeks (accelerated tRNS) for a total of 20 sessions. He did not report any side effects to tRNS during the course of therapy, which indicates that accelerated tRNS and extended sessions of therapy (up to 20 sessions) are well tolerable by the patients. Our patient showed improvement in some of the cognitive domains like attention, concentration, delayed recall, remote memory, immediate memory, and intelligence. The improvement in intelligence may be attributed to enhanced attention and concentration. Repeated tRNS sessions have shown long-term effects on the improvement of reaction time.[6] tRNS is known to improve perception and learning by boosting neuroplasticity,[7] which might have happened in this index patient by targeting specific brain areas which resulted in the improvement of cognitive function.

Emerging evidences suggest high-definition tRNS to be more effective than conventional tRNS and sham tRNS groups in enhancing complex task performance.[8] Future research should explore optimal protocols and accurate targets while using tRNS in the management of cognitive deficits due to traumatic brain injury. We have not evaluated the baseline functional connectivity and post-intervention change in functional connectivity, which might have given us a better insight to correlate the change in cognitive function in our patient.

Ethical approval

Institutional Review Board approval is not required.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Conflicts of interest

There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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