The Journal of International Advanced Otology

J Int Adv Otol 2019; 15(2): 321-5 • DOI: 10.5152/iao.2019.6022

Case Report

Functional Near-Infrared Spectroscopy to Probe tDCS-Induced Cortical Functioning Changes in Tinnitus

Rohit Verma, Amit Jha, Shuchita Singh

Department of Psychiatry, Brain Stimulation Unit, All India Institute of Medical Sciences, New Delhi, India (RV, AJ)
Department of Otorhinolaryngology, All India Institute of Medical Sciences, New Delhi, India (SS)

ORCID IDs of the authors: R.V. 0000-0001-7418-2511.

Cite this article as: Verma R, Jha A, Singh S. Functional Near-Infrared Spectroscopy to Probe Tdcs-Induced Cortical Functioning Changes in Tinnitus. J Int Adv Otol 2019; 15(2): 321-5.

There are limited treatment options for successful management of tinnitus, which is highly prevalent worldwide. The pathogenetic role of auditory cortex activation changes in tinnitus has been reported by various functional studies that suggest that the emerging neuromodulation techniques may pave way toward better treatment response. The current case report depicts the use of functional near-infrared spectroscopy (fNIRS) based on the assessment of improvement in auditory cortex functioning in chronic tinnitus by transcranial direct current stimulation (tDCS).

KEYWORDS: Tinnitus, tDCS, fNIRS, transcranial, infrared

INTRODUCTION

Tinnitus is a highly prevalent condition with no well-defined etiology [1, 2]. Its association with many forms of peripheral ear pathology, hearing loss, retrocochlear lesions, head and neck injury, dental and temporomandibular joint dysfunction, and drug toxicity leading to aberrant neural activity within the central auditory circuits is supported by the persistence of phantom sound perception following auditory nerve transection [2].

Functional changes in auditory cortex activity have been revealed in tinnitus using various imaging modalities, such as high-resolution electroencephalography and magnetoencephalography [3, 4]. Positron-emission tomography studies report an increased activity in the primary auditory cortex, unilateral left-sided or bilateral [5, 6]. Sound-evoked functional magnetic resonance imaging (fMRI) studies also showed an increased activity in the auditory cortex [7] or asymmetric activity [8]. Few resting state fMRI studies have reported an increased coherent activity of the auditory areas. There are also fMRI studies reporting no changes in the auditory cortex [9-12]. Very few studies have utilized the newer modality of optical imaging, i.e., functional near-infrared spectroscopy (fNIRS), for assessing brain hemodynamic activity in tinnitus [13-15].

With no respite offered by pharmacological therapies, there is an emerging literature suggesting the beneficial effects of neuromodulation therapies in tinnitus [16, 17]. Transcranial direct current stimulation (tDCS) is a non-invasive focal neurostimulation technique that involves the application of a low-intensity electric current utilizing surface electrodes for modulating the underlying cortical excitability by shifts in the resting membrane potential (depolarization and hyperpolarization) [18]. The potential beneficial effects of tDCS have been reported in the literature [17].

The current case reports the changes in functional cortical activity as assessed by fNIRS in a patient suffering from tinnitus managed by tDCS.

CASE PRESENTATION

Mr. R, a 28-year-old right-handed married man, educated up to higher secondary with well-adjusted premorbid personality with no family history of psychiatric or neurological illness, and working at a petrol pump, reported having progressively increasing symptoms of insidious onset since the last 5 years in which there was a slow onset diminution of hearing (right more than left) not associated with any

Corresponding Address: Rohit Verma E-mail: rohit.aiims@gmail.com

Submitted: 04.09.2018 • **Revision Received:** 29.09.2018 • **Accepted:** 16.10.2018 • **Available Online Date**: 24.07.2019
Available online at www.advancedotology.org

form of trauma, fever, discharge from the ear, fluid or wax collection, ear pain, dizziness, or gait instability. He did not have any history of diabetes, hypertension, hypothyroidism, seizure, any neurological illness, or any form of surgical intervention. During the initial 3 years, he was working normally with less interference in his everyday functioning even with hearing impairment. Over the last 2 years, he also started to have ringing in his ear, which gradually increased over 2-3 months. Ringing was continuous and more prominent in his right than in his left ear. Ringing would interfere with his work and interaction with people. It would increase in a noisy environment and when he would speak in a louder tone. However, it did not interfere with his sleep.

Thereafter, the patient sought treatment at the Department of Otorhinolaryngology where the initial work-up was done, finding no abnormalities in general physical and systemic examination and blood investigations, such as complete blood count, liver function test, renal function test, random blood sugar, thyroid profile, lipid profile, human immunodeficiency virus, hepatitis B surface antigen, anti-hepatitis C virus, antinuclear antibody, antineutrophil cytoplasmic antibodies, anti-double stranded DNA, and rheumatoid factor, followed by imaging studies. Tuning fork tests revealed conduction of sound to the left ear with no other abnormality. Pure tone audiometry revealed profound sensory neural hearing loss (>100 dB) in the right ear and mild conductive hearing loss in the left ear (Figure 1). MRI brain scan specifically focusing on the inner ear along with the temporal bone revealed no abnormality.

Over the next one and a half year, the patient was treated with multiple pharmacological approaches (gabapentin 600 mg (Gabalept; Micro Labs Ltd., Bangalore, India), amitriptyline 25 mg (Amitone; Intas Pharmaceuticals, Ahmedabad, India), antibiotic course, prednisolone up to 40 mg (Predcip; Cipla, Mumbai, India), and multivitamins) with no benefit and was thus referred to the Brain Stimulation Clinic, Department of Psychiatry. Since there was no improvement on medications, the patient had not been taking any medications from 2 months and was planned for tDCS. Tinnitus Handicap Inventory (THI) score was 60 (severe) at baseline. The patient was also planned for assessment over fNIRS before and after tDCS. Written informed consent was obtained from the patient for publication of this case study.

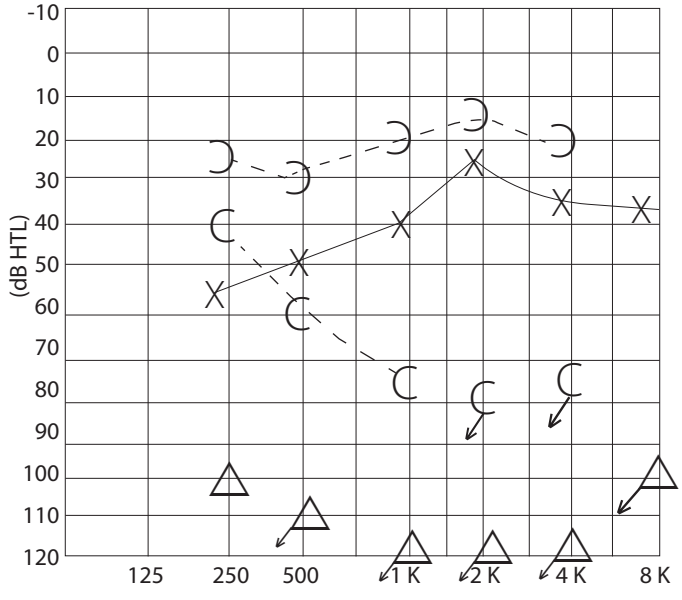

Figure 1. Pure tone audiogram of the patient.

fNIRS Experiment

The patient was assessed over fNIRS using an auditory task for assessing sound-evoked auditory cortex activity before initiating tDCS. The hemodynamic changes were obtained from the optical changes collected using a continuous-wave fNIRS system (NIRScout 8×8; NIRx Medizintechnik GmbH, Berlin, Germany). The system consisted of 8 light-emitting diode illumination sources (760 and 850 nm) and 8 fiber optic detectors placed on the region(s) of interest of the measuring cap (International 10-5 system) covering bilateral temporal cortical areas. The interoptode distances for channels (i.e., source-detector pairs) were kept at approximately 30 mm to guarantee an optimal balance between signal-to-noise ratio and cortical sensitivity [19]. The sampling rate for experiment was 15.625 Hz. The source-detector configuration used in the experiment is depicted in Figure 2.

In the auditory task, 6 blocks were presented comprising 12 trials in each block. Each trial consisted of a sound presented for 3 s, followed by 3 s of silence. A fixation cross was presented in the middle of the screen throughout the whole session. The patient was instructed to fixate on the cross the entire time during the session and press a button at the start of the stimulus to indicate the quickness of response to the sound. The patient received training prior to the actual data recording, and the training was repeated until he was 100% correct with button pressing.

All auditory stimuli were created using PRAAT 5.0.43 [20] and presented using the SuperLab version 4.5.1 (Cedrus, CA, USA). A Phillips head-

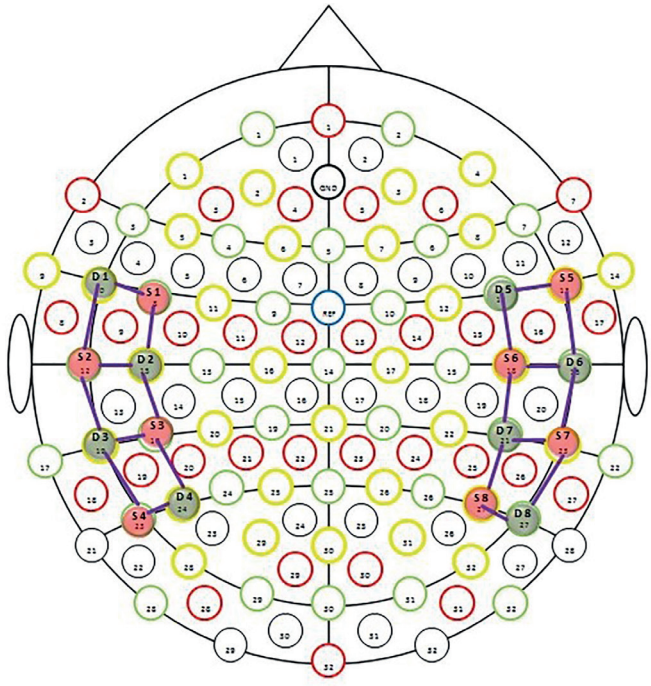

Figure 2. Configuration of channels (purple line) between source (S 1-8) and detector (D 1-8) pairs over the right and left cortical hemispheres. There are 8 detectors and 8 sources (at positions corresponding to the International 10-20 system), resulting in 10 channels per hemisphere overlying the auditory cortex.

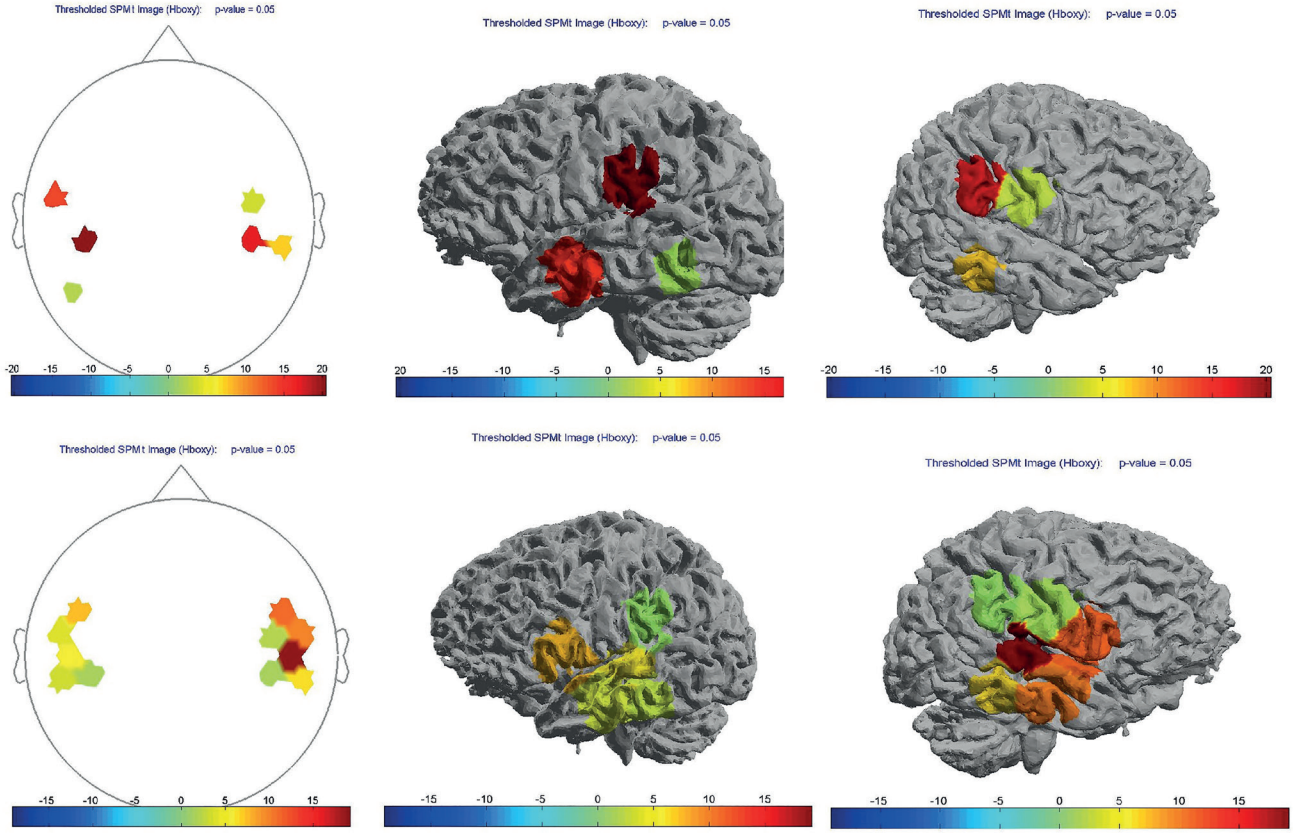

Figure 3. Changes in sound-evoked activity as indicated by brain oxygenation over the left and right cortical areas before tDCS (upper) and after tDCS (lower) corresponding to the overlying fNIRS channels.

phone was used to deliver the stimuli. The patient's responses were registered by using a compatible RB-844 response pad attached to the Cedrus StimTracker (Cedrus) connected to the fNIRS system.

tDCS Protocol

Stimulation via tDCS was delivered by a constant-current battery-operated stimulator unit (HDC Kit; Magstim, Whitland, UK) via two electrodes in conductive silicone (5×5 cm^2) kept under the sponge holding bag of plant cellulose (6×7.5 cm^2) soaked in a saline solution (NaCl 0.9%). The tDCS protocol included the placement of cathode at TP4 and anode at F4, delivering a current of 2 mA for 20 min with a ramp of 30 s, providing a total of 20 sessions at a rate of 2 sessions/day with an intersession interval of 3 h.

The patient reported a subjective symptomatic improvement of 40%-50% with a reduction of THI score to 26 after the completion of tDCS sessions. A repeat fNIRS assessment was conducted with the same baseline auditory experiment. The fNIRS data analysis was conducted using nirsLAB 17.06 (NIRx Medizintechnik GmbH, Berlin, Germany). There was a higher area of cortical activation observed for oxyhemoglobin (HbO) concentration bilaterally after tDCS than baseline, as well as a reduction in intensity of the hyperactivated areas (Figure 3).

DISCUSSION

Owing to the pathophysiological involvement of the auditory cortex in chronic tinnitus, the non-invasive brain stimulation method comprising tDCS was used as a possible treatment option in this case of chronic tinnitus that demonstrated a significant reduction in symptoms utilizing subjective and objective observations. Assessment of cortical functioning revealed a reduction in intensity of hyperactivated cortical areas, as well as a spreading of the cortical HbO concentration during the presentation of sound stimuli to a larger cortical area in comparison with baseline before receiving tDCS.

The literature reports variable effectiveness of tDCS in tinnitus. Forogh et al. placed anodal tDCS over the left temporoparietal area (LTA), whereas the current study provided cathodal tDCS over the right LTA [21]. There are other studies reporting positive outcomes with cathodal tDCS to LTA [17, 22], whereas others have demonstrated better outcomes with anodal Tdcs [23]. The positive responses to either stimulation could be due to a disruption of the ongoing neural hyperactivity that is independent of the inhibitory or excitatory effects. There might be a role of functionally connected cortical structures in modulating the response indirectly. Auditory deafferentation and/or deficit in noise cancellation have been proposed as a neurophysiological cause for tinnitus [24]. The duration and intensity of applied tDCS current might have filtered the response to different electrodes independent of the cortical areas involved.

Imaging studies using fMRI have mainly shown a left lateralization of the activity of the primary auditory cortex in tinnitus [3, 4, 6, 7]. We observed that sound-evoked hemodynamic activation was asymmetrically distributed over the bilateral auditory cortex region prior to tDCS, higher contralateral rather than ipsilateral to the tinnitus side

at baseline. While previous studies have also reported similar findings [16], few studies contradict the finding reporting reduced auditory activation contralateral to tinnitus in patients with unilateral tinnitus [8, 25]. The discrepancy with the previous results may be related to technical considerations, using fMRI machine, stimuli used to induce auditory cortex activation, or the number of epochs, or to the mechanisms at the origin of tinnitus. Impaired hearing in our patient could also have contributed to the discrepant findings.

Another possibility of discrepant findings could be differences between block- and event-related designs that have already been proposed as a potential explanation for limited reliability in fMRI research [26]. The current study utilized short duration sounds (3 s) in contrast to long-lasting sounds used in fMRI studies that may lead to differences in neural activation because the longer presentation of the same sound stimuli may make it irrelevant and presumably be inhibited through top-down mechanisms in accordance with prepulse inhibition and sensory gating models wherein a preceding stimulus decreases the novelty of the incoming information [27]. Previous literature has demonstrated the sensitivity of fNIRS for top-down mechanisms in the auditory domain [28]. Block-related designs have been associated with greater activation of the auditory region during fNIRS evaluation in tinnitus [13]. Another fNIRS-based study found a higher sound-evoked hemodynamic activity in the left hemisphere in patients with tinnitus than that in control participants [14]. The handedness of the participants was not determined in the majority of the studies, and it may account for this inconsistent finding.

In the current study, this contralaterally localized hyperactivity was reduced with regard to intensity, and there was a greater spread of HbO concentration observed over the bilateral auditory cortex region after receiving tDCS. In a study using low-frequency repetitive transcranial magnetic stimulation to manage tinnitus, sound-evoked fNIRS activity in the right temporal areas was higher in the patients than in the healthy controls, and left-sided temporal activity changed wherein higher baseline oxygenation was reduced and vice versa [13]. Enhanced connectivity is reported in both auditory and non-auditory regions in the brain after auditory stimulation in tinnitus [15].

CONCLUSION

fNIRS is a valuable tool to assess auditory cortex activation. There is an improvement in tinnitus symptoms after tDCS. In addition, there is an improvement in functional cortical activity as assessed by fNIRS in chronic tinnitus after tDCS.

Informed Consent: Written informed consent was obtained from the patient who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – R.V., S.S.; Design – R.V.; Supervision – R.V., S.S., A.J.; Resource – R.V., S.S., A.J.; Materials – R.V.; Data Collection and/or Processing – R.V., XS.S., A.J.; Analysis and/or Interpretation – R.V.; Literature Search – R.V., A.J.; Writing – R.V., S.S., A.J.; Critical Reviews – R.V., S.S.

Conflict of Interest: Dr Rohit Verma is supported by the Cognitive Science Research Initiative (CSRI) Grant by the Department of Science & Technology, Government of India (DST/CSRI/2017/186).

Financial Disclosure: The authors declared that this study has received no financial support.

REFERENCES

1. Coles RR. Epidemiology of tinnitus: (1) prevalence. J Laryngol Otol Suppl 1984; 9: 7-15. [CrossRef]
2. Levine RA, Oron Y. Tinnitus. Handb Clin Neurol 2015; 129: 409-31. [CrossRef]
3. Schlee W, Hartmann T, Langguth B, Weisz N. Abnormal resting state cortical coupling in chronic tinnitus. BMC Neurosci 2009; 10: 11. [CrossRef]
4. Moazami-Goudarzi M, Michels L, Weisz N, Jeanmonod D. Temporo-insular enhancement of EEG low and high frequencies in patients with chronic tinnitus. BMC Neurosci 2010; 11: 40. [CrossRef]
5. Song JJ, De Ridder D, Van de Heyning P, Vanneste S. Mapping tinnitus-related brain activation: an activation-likelihood estimation metaanalysis of PET studies. J Nucl Med 2012; 53: 1550-7. [CrossRef]
6. Schecklmann M, Landgrebe M, Poeppl TB, Kreuzer P, Männer P, Marienhagen J, et al. Neural correlates of tinnitus duration and distress: a positron emission tomography study. Hum Brain Mapp 2013; 34: 233-40. [CrossRef]
7. Leaver AM, Renier L, Chevillet MA, Morgan S, Kim HJ, Rauschecker JP. Dysregulation of limbic and auditory networks in tinnitus. Neuron 2011 Jan; 69: 33-43. [CrossRef]
8. Smits M, Kovacs S, de Ridder D, Peeters RR, van Hecke P, Sunaert S. Lateralization of functional magnetic resonance imaging (fMRI) activation in the auditory pathway of patients with lateralized tinnitus. Neuroradiology 2007; 49: 669-79. [CrossRef]
9. Lanting CP, De Kleine E, Bartels H, Van Dijk P. Functional imaging of unilateral tinnitus using fMRI. Acta Otolaryngol 2008; 128: 415-21. [CrossRef]
10. Schmidt SA, Akrofi K, Carpenter-Thompson JR, Husain FT. Default mode, dorsal attention and auditory resting state networks exhibit differential functional connectivity in tinnitus and hearing loss. PLoS One 2013; 8: e76488. [CrossRef]
11. Boyen K, de Kleine E, van Dijk P, Langers DR. Tinnitus-related dissociation between cortical and subcortical neural activity in humans with mild to moderate sensorineural hearing loss. Hear Res 2014; 312: 48-59. [CrossRef]
12. Davies J, Gander PE, Andrews M, Hall DA. Auditory network connectivity in tinnitus patients: a resting-state fMRI study. Int J Audiol 2014; 53: 192-8. [CrossRef]
13. Schecklmann M, Giani A, Tupak S, Langguth B, Raab V, Polak T, et al. Functional near-infrared spectroscopy to probe state- and trait-like conditions in chronic tinnitus: a proof-of-principle study. Neural Plast 2014; 2014: 894203. [CrossRef]
14. Issa M, Bisconti S, Kovelman I, Kileny P, Basura GJ. Human Auditory and Adjacent Nonauditory Cerebral Cortices Are Hypermetabolic in Tinnitus as Measured by Functional Near-Infrared Spectroscopy (fNIRS). Neural Plast 2016; 2016: 7453149. [CrossRef]
15. San Juan J, Hu XS, Issa M, Bisconti S, Kovelman I, Kileny P, et al. Tinnitus alters resting state functional connectivity (RSFC) in human auditory and non-auditory brain regions as measured by functional near-infrared spectroscopy (fNIRS). PLoS One 2017; 12: e0179150. [CrossRef]
16. Lefaucheur JP, Brugières P, Guimont F, Iglesias S, Franco-Rodrigues A, Liégeois-Chauvel C, et al. Navigated rTMS for the treatment of tinnitus: a pilot study with assessment by fMRI and AEPs. Neurophysiol Clin 2012; 42: 95-109. [CrossRef]
17. Verma R, Kumar N, Kumar R, Kumar S, Kathiresan P. Cathodal neuromodulation of dominant temporoparietal cortex with transcranial direct current stimulation for tinnitus: A case series. Noise Health 2018; 20: 27-9.
18. Nitsche MA, Liebetanz D, Antal A, Lang N, Tergau F, Paulus W. Modulation of cortical excitability by weak direct current stimulation-Technical, safety and functional aspects. Suppl Clin Neurophysiol 2003; 56: 255-76. [CrossRef]
19. Strangman GE, Li Z, Zhang Q. Depth sensitivity and source-detector separations for near infrared spectroscopy based on the Colin27 brain template. PLoS One 2013; 8: e66319. [CrossRef]
20. Boersma P, Weenink D. 2008. Praat: doing phonetics by computer Version 5.0.43 Computer program, retrieved 9 December 2017 from http://www.praat.org/.
21. Forogh B, Mirshaki Z, Raissi GR, Shirazi A, Mansoori K, Ahadi T. Repeated sessions of transcranial direct current stimulation for treatment of

chronic subjective tinnitus: A pilot randomized controlled trial. Neurol Sci 2016; 37: 253-9. [CrossRef]
22. Joos K, De Ridder D, Van de Heyning P, Vanneste S. Polarity specific suppression effects of transcranial direct current stimulation for tinnitus. Neural Plast 2014; 2014: 930860. [CrossRef]
23. Fregni F, Marcondes R, Boggio PS, Marcolin MA, Rigonatti SP, Sanchez TG, et al. Transient tinnitus suppression induced by repetitive transcranial magnetic stimulation and transcranial direct current stimulation. Eur J Neurol 2006; 13: 996-1001. [CrossRef]
24. De Ridder D, Vanneste S, Weisz N, Londero A, Schlee W, Elgoyhen AB, et al. An integrative model of auditory phantom perception: Tinnitus as a unified percept of interacting separable subnetworks. Neurosci Biobehav Rev 2014; 44: 16-32. [CrossRef]
25. Melcher JR, Sigalovsky IS, Guinan Jr JJ, Levine RA. Lateralized tinnitus studied with functional magnetic resonance imaging: abnormal inferior colliculus activation. J Neurophysiol 2000; 83: 1058-72. [CrossRef]
26. Bennett CM, Miller MB. MRI reliability: influences of task and experimental design. Cogn Affect Behav Neurosci 2013; 13: 690-702. [CrossRef]
27. Ehlis AC, Ringel TM, Plichta MM, Richter MM, Herrmann MJ, Fallgatter AJ. Cortical correlates of auditory sensory gating: a simultaneous near-infrared spectroscopy event-related potential study. Neuroscience 2009; 159: 1032-43. [CrossRef]
28. Plichta MM, Gerdes AB, Alpers GW, Harnisch W, Brill S, Wieser MJ, et al. Auditory cortex activation is modulated by emotion: a functional near-infrared spectroscopy (fNIRS) study. Neuroimage 2011; 55: 1200-7. [CrossRef]