High And Low Frequency Repetitive Transcranial Magnetic Stimulation In Smoking Cessation: A Systematic Review

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ABSTRACT

Repetitive Transcranial Magnetic Stimulation is a non-invasive brain stimulation process popularly used to treat psychiatric disorders. Multiple evidence shows effectiveness of rTMS in treating addiction, particularly in tobacco or cigarette users. This study consisted of review of current published literatures on repetitive transcranial magnetic stimulation following predefined eligibility criteria. The studies included evaluated at least one of the epidemiological parameters: (i) the meaning of repetitive transcranial magnetic stimulation (ii) Effectiveness of the Repetitive Transcranial Magnetic Simulation Over Behavioral therapy (iii) rTMS-associated adverse events among tobacco users.

Methodology

We included published studies discussing rTMS in smoking cessation which examined if these interventions were effective and identified whether it has a severe negative effect on the patients. A total of 104 related studies were identified through database searches (Pubmed, Elsevier, Cochrane). Of which, 53 duplicate studies were removed. Five studies were then excluded with more than 10 years in publication. A total of 28 papers were then included in the study.

Conclusion

We conclude that rTMS is more effective in treating addiction in terms of smoking compared to behavioral therapy and rTMS affects triggered desired circuit which may be crucial among tobacco users. Individual neuronal excitability in the specific region's subsequent induction may impact the therapeutic outcomes. With this, the high-frequency rTMS sequentially applied to the left superior medial frontal cortex and dorsolateral prefrontal cortex may be an effective tool for improving the cessation rate.

Keywords: Repetitive Transcranial Magnetic Stimulation, Transcranial Magnetic Stimulation, smoking cessation, tobacco user, cigarette consumption, and Repetitive TMS

INTRODUCTION

One of the most important public health risks in the world is smoking. It causes deaths of eight million people yearly, including nearly a million through exposure to secondhand smoke, making it the most significant preventable cause of disease and death globally.[1] Additionally, over 8% of the 1.3 billion smokers live in low and middle-income nations which shows that smoking exacerbates poverty by diverting household spending away from essentials like food and housing and toward cigarettes. The financial cost of using cigarettes is significant. It also includes loss of human capital due to mortality and morbidity attributable to tobacco use and high healthcare expenditures for treating diseases brought by cigarette use.[2] The most common drug use disorder worldwide involves tobacco use. It is characterized by withdrawal and yearning,

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compulsive use despite adverse consequences, and recurrent relapses. It is strongly associated with a number of health problems and failed quit attempts.[3] Despite improvements in public health, FDA-approved drugs, legislative changes, and psychotherapy choices, many smokers have trouble quitting. Other cigarette smokers who accept to treat their addiction tend to discontinue their decisions within one year, return to their old smoking habits, and use it as a reward after a long time of quitting. Most smokers who quit and return to smoking tend to experience delay discounting, a process where the patients "devalue" rewards as a function of when they will receive them. Due to increasing numbers of people who smoke, clinicians continuously look for ways to implement new interventions that can positively help patients to finally quit smoking for good[3]. Repetitive transcranial magnetic stimulation (rTMS), when used, can result in long-term behavioral changes by decreasing the craving in cigarette and consumption. The intervention also confirmed that it is efficient and safe for treating obsessive-compulsive disorder and depression. It can be an option for those unable to manage medication side effects or for those who were not adequately managed by psychotherapeutic or pharmacological options.[4]

Repetitive transcranial magnetic stimulation is a recognized treatment for depression though it is unknown whether it is also valuable for helping people stop smoking. Behavioral therapy is also known as one of the possible interventions to assess people who became addicted to nicotine or tobacco. In order to identify the possible interventions that will help people to stop smoking this study aimed to compare the effectiveness of the Repetitive Transcranial Magnetic Simulation over behavioral therapy and to evaluate the efficacy of repetitive transcranial magnetic stimulation (rTMS) in smoking cessation. It aims to present an overview of the research supporting the intervention for quitting smoking, and to lay out the steps for putting rTMS into practice in a primary care context.

The PICOS criteria shown in Table 1 were applied to determine the study purpose.

METHODOLOGY

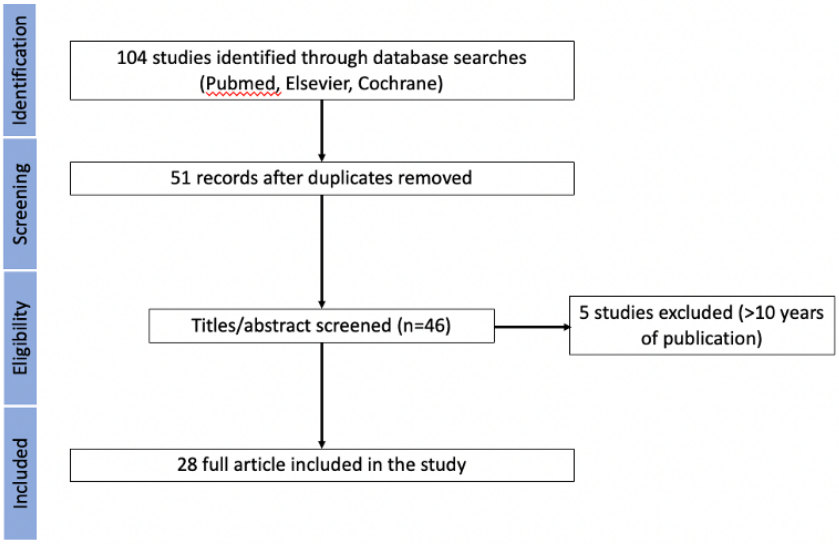
The review included papers published describing rTMS in smoking cessation and examined if these interventions were effective and whether it has a severe negative effect on the patients. The studies included evaluated at least one of the epidemiological parameters: (i) the meaning of repetitive transcranial magnetic stimulation, (ii) rTMS-associated adverse events, and (iii) Effectiveness of the Repetitive Transcranial Magnetic Simulation over behavioral therapy.

Table 1. PICOS criteria (Population; Intervention; Comparison; Outcome; Study design)

Population	Patient experience cigarette addiction
Intervention	High and low Repetitive Transcranial Magnetic Stimulation
Comparison	Effectiveness of the Repetitive Transcranial Magnetic Simulation Over Behavioral therapy.
Outcome	Improvement of smoking cessation
Study Design	Randomized clinical trials; Cohort studies

PubMed, Elsevier and Cochrane journals published from 2010 to 2022 were used in which the following terms were searched: "repetitive transcranial magnetic stimulation", "transcranial magnetic stimulation", "smoking cessation", "tobacco user", "cigarette consumption", cigarette craving", addiction medicine" and "repetitive TMS". Articles published in 2009 were excluded at the initial stage of screening. Before the full-text selected studies, research titles were independently reviewed and analyzed to find and omit articles that did not match the inclusion criteria.

Figure 1. PRISMA Flow Diagram



RESULTS

I. THE REPETITIVE TRANSCRANIAL MAGNETIC STIMULATION

One component of tobacco is nicotine, and smoking cigarettes can cause addiction. When nicotine interacts with nicotinic acetylcholine receptors, neurotransmitters like glutamate, dopamine, and gamma-aminobutyric acid are released. When a smoker stops smoking, they experience withdrawal symptoms like irritation and anxiety. Professional methods for helping people quit smoking typically target nicotine addiction and withdrawal symptoms[5]. TMS is a non-invasive technique that modifies cortical excitability by applying a relatively low or high-intensity magnetic field to brain tissue that can be utilized in smoking cessation. While repetitive transcranial magnetic stimulation (rTMS) refers to recuring TMS pulses to a specific region in the brain. Multiple psychiatric conditions as well as neurological problems may benefit from rTMS treatment. The neuromodulatory results depend upon several stimulation parameters such as intensity, frequency, cortical target, patient factor, duration. Patient factors include age, medication trial, disease state, and individual symptoms. High-frequency (>1Hz) rTMS was identified to increase cortical excitability, while low-frequency (1Hz) rTMS has been indicated to reduce cortical excitability.[6] Zhang, et al. in 2019 defined rTMS as one of the interventions used for rehabilitation of dysphagia and it directly delivers cortical stimulation, improved cortical neuroplasticity and swallowing function, thus, rTMS has attracted more attention in terms of rehabilitation especially in addiction. The study of Bickel and colleagues in 2018 and Khurshid in 2019 discovered that repetitive transcranial magnetic stimulation was the only available noninvasive therapy option for patients.[8,9] Moreover, it can positively affect the implicated neural areas. Different diseases, especially obsessive-compulsive disorder (OCD) symptoms and addiction, have been shown to benefit from TMS stimulation of several brain locations including the dorsolateral prefrontal, supplementary motor, dorsolateral prefrontal, anterior cingulate, and orbitofrontal cortex. Young and collegues in 2021 has defined the repetitive transcranial magnetic stimulation (rTMS) as a non-invasive, comparatively effortless, and pain-free process, which has been employed to investigate different cognitive functions and understand the association between the brain and behavior in healthy people and people

with a variety of neuropsychiatric disorders.[10] The study by Machado and colleagues in 2013 claimed that rTMS is currently a preferred method for researching several elements of human brain physiology, such as motor control, speech, sight, and the disease pathogenesis of brain illnesses.[11] For neuropsychiatric use in particular, it could be beneficial as a treatment tool. Depending on the stimulus parameters and the number of stimuli produced, the corticospinal system may experience prolonged up or down-regulation.

II.EFFECTIVENESS OF THE TREATMENT IN SMOKING CESSATION OVER BEHAVIORAL THERAPY

In the study of Hargiana, Keliat, & Mustikasari in 2018, it was stated that behavioral study was originally developed to treat borderline personality disorder and successfully used to treat people experiencing depression, bipolar disorder, PTSD and substance abuse.[12] Behavioral therapy skills are thought to have the capability to assess individuals to improve their ability to regulate emotions, negative emotions and tolerate distress. According to the study of Zamboni and colleagues in 2021, behavioral therapy consisting a combination of mindfulness, acceptance, and value-based therapeutic processes to foster psychological flexibility, which involves stepping back and mindfully watching inner experiences such as feelings, thoughts and bodily sensations. Based on the results of the study, behavioral therapy is to make patients able to engage in more value-focused lives and functional.[13] The study of Zangen and colleagues in 2021 stated that repetitive TMS intervention can help change the patient's behavior and mood which can last a long time[4]. With the tremendous impact of the intervention for managing obsessive-compulsive disorder and depression, different protocols and rules have been applied. Patients who experience depression and other disorders who cannot endure the adverse effect of treatment or those who do not have positive outcomes from psychotherapy and pharmacological treatment may have a chance to improve through rTMS. On the other hand, the evidence of the effectiveness of rTMS in treating cigarette addiction is still limited. Two hundred sixty-two chronic smokers in a multicenter were enrolled in Zangen et al's study - a double-blind randomized controlled trial. Active rTMS focusing on the insula and lateral prefrontal cortex led to a more significant acute reduction of the visual analogue scale (VAS) craving score, and the magnitude of the reduction predicted eventual quitting. It was found out that effective treatment with a stimulated craving circuit may be a vital component in the rTMS mechanism for the tobacco user and the individual neural excitability in the stimulated region will influence the clinical results. The proposed implementation of rTMS on the brain is further emphasized by inclusion of the insula and prefrontal cortex in functions calculated by the tobacco craving questionnaire (TCQ) domains. Both locations are involved in predicting rewarding outcomes (longing), rule overuse (compulsivity), and choice to smoke (purposefulness). Moreover, the emotionality domain is more limited and restricted to the insular cortex due to its deeper location, which may need a higher rTMS dose to apply long-term modifications. The researcher also found out that TCQ domains were affected by active rTMS stimulation as compared to sham treatment.

Da and colleagues in 2018 claimed that one of the causes of early death and avoidable death is smoking cigarettes[14]. It is known that most cigarette users find it challenging to stop smoking due to nicotine dependence. By attaching to the endogenous nicotinic acetylcholine receptors and disrupting the different brain activities controlled by the nAchRs, nicotine significantly negatively impacts the brain. Chronic nicotine exposure upregulates the nAchrs, specifically the nicotine high affinitive 42 subtype, which is more prevalent on dopaminergic neurons in the ventral tegmental area (VTA) and the projecting areas, including the ventral striatum, medial

Table 2 Effectiveness Of The Treatment In Smoking Cessations

Author	Dose/ Intervention	Cohort	Method	Result	Outcome
Hargiana, Keliat, & Mustikasari (2018)[12]	Quasi-experimental non-equivalent control group pretest-posttest design	Patients who experience Cigarette addiction	Cognitive Behavioral Therapy (CBT)	Reduce cue-induced craving in nicotine	CBT can effectively change smoking habits as well as reduce anxiety.
Zamboni, Centoni, Mantovani, & Fusina, (2021)[13]	N/A	Patients who experience Cigarette addiction	Cognitive behavioral therapies (CBTs), commitment therapy (ACT), dialectical behavior therapy (DBT), mindfulness-based cognitive therapy (MBCT), and schema therapy (ST).	Results seem to indicate that CBT and MBCT are effective interventions for SUDs	the studies showed a high degree of heterogeneity, so no exhaustive conclusions could be outlined at this time.
Zangen, et al. (2021)[4]	15 sessions over 3 weeks	Patients who experience Cigarette addiction	Double-blind, randomized, sham-controlled trial	Reduce cue-induced craving in nicotine and cocaine/ methamphetamine dependents	Improve smoking cessation
Da, et al. (2018)[14]	10 days and follow up for 25 days	Patients who experience Cigarette addiction	A frequency of 20 Hz rTMS was sequentially applied on the left dorso-lateral prefrontal cortex (DLPFC) and the superior medial frontal cortex (SMFC)	Reduce cue-induced craving in nicotine dependents	Improve smoking cessation
Shen, Cao, Tan, & Shan (2016)[3]	5 days	Patients who experience Cigarette addiction	Sham-controlled crossover study and 10-Hz Repetitive Transcranial Magnetic Stimulation of the Left Dorsolateral Prefrontal Cortex.	Improve smoking cessation/ Reduce cue-induced craving in nicotine and cocaine/ methamphetamine dependents	Improve smoking cessation
Tomova, Riecansky, & Lamm (2014)[15]	3-6 hours per session	Patient who experience Cigarette addiction	sham controlled study.	Hf rTMS applied to the left DLPFC reduces nicotine craving in short-term abstinent smokers.	Improve smoking cessation
Dinur-Klein, et al. (2014)[16]	13 daily sessions	Patients who experience Cigarette addiction	high-frequency, low-frequency and sham stimulation	High (but not low) frequency deep TMS treatment significantly reduced cigarette consumption and nicotine dependence	Improve smoking cessation
Li, et al., (2013)[17]	10-15 minutes daily sessions	Patients who experience Cigarette addiction	high-frequency, low-frequency and sham stimulation	One session of high-frequency rTMS (10 Hz) of the left DLPFC significantly reduced subjective craving induced by smoking cues in nicotine-dependent participants	Improve smoking cessation
Prikryl , et al. (2013)[18]	One-week sessions	Patient with Cigarette use disorder and schizophrenia	sham rTMS	High-frequency rTMS over the left DLPFC has the ability to decrease the number of cigarettes smoked in schizophrenia patients.	Improve smoking cessation
Huang, Shen, Zhang, & Xing (2016)[19]	N/A	Patient with Cigarette use disorder and schizophrenia	high-frequency, low-frequency and sham stimulation	High frequency (10Hz) repetitive transcranial magnetic stimulation on the left prefrontal cortex can reduce the number of cigarettes smoked in patients with schizophrenia	Improve smoking cessation
Ibrahim , Malik, Barr, Daskalakis, & Le Foll (2022)[20]	N/A	Patients who experience Cigarette addiction	transcranial magnetic stimulation (TMS), transcranial direct current stimulation (tDCS), and deep brain stimulation (DBS)	Improve smoking cessation and intervention	Improve smoking cessation
Shevorykin, et al. (2022)[21]	8-, 12-, or 16-day sessions	Patients who experience Cigarette addiction	20 Hz rTMS to the left dorsolateral prefrontal cortex (PFC)	Improve smoking cessation based on duration of session	Improve smoking cessation

orbitofrontal cortex (MOFC), anterior cingulate cortex (ACC), insula, amygdala, and dorsolateral prefrontal cortex. Abstinence from nicotine will significantly increase the availability of unbound 42 nAchRs due to the chronic nAchRs overexpression, which will cause a need for tobacco use and the subsequent relapse. Treatment for smoking has proven to be highly challenging because of these neurological alterations brought on by persistent nicotine binding. At six months following the start of treatment, the most successful therapies currently available, including drugs like varenicline, bupropion, as well as nicotine replacement therapy and psychotherapy, can still only produce abstinence rates of about 25%. In the study, instead of focusing on a single cortical area, the researcher concentrated on two: the left superior medial frontal cortex (SMFC) and dorsolateral prefrontal cortex (DLPFC). The orbitofrontal cortex, which is connected with impulsivity and is frequently implicated in drug cravings, including smoking. It has been found to be coupled with the SMFC and has been identified to be stimulated when resisting drug cravings. Stimulating the left SMFC and DLPFC can potentially increase the capacity to inhibit smoking and simultaneously decrease the urge to smoke, leading to more successful smoking cessation. The DLPFC is involved in inhibition control, which is known to be impaired in substance dependence. The researcher also gathered data regarding cerebral blood flow (CBF) in chronic cigarette users to determine if the rTMS treatment would change the baseline CBF in smokers. The affiliated hospital of Hangzhou Normal University's center for cognition and brain disorders served as the site of this investigation. Participants in the study included 14 smokers seeking therapy who smoked over ten cigarettes per day for over five years. The study found that a 20 Hz rTMS successively implemented to the left SMFC and DLPFC for ten days resulted in a high smoking cessation rate, supported by behavioral tests and fMRI results. rTMS also caused smoking cessation for the entire 25-day follow-up period, decreased craving to smoke, decreased brain entropy in the prefrontal cortex and insula, and decreased cerebral blood flow in the left hemisphere. The researcher concluded that high-frequency rTMS administered sequentially to the left SMFC and DLPFC might be beneficial to increase the cessation rate; measuring brain entropy and cerebral blood flow offer helpful ways to measure or evaluate the therapy effects.

In connection with this, the study of Shen and colleagues in 2016 found that high-frequency repetitive transcranial magnetic stimulation (rTMS) of the left DLPFC has been shown to drastically reduce appetite for nicotine in addicts by reducing cue-induced craving in cocaine and nicotine dependence. All subjects tolerated the rTMS, which consisted of a total of 2000 stimulation pulses, without experiencing any adverse side effects.[3]

Tomova, Riecansky, & Lamm in 2014 implemented rTMS of the left DLPFC to evaluate its effect on cue-induced nicotine desire and EEG spectral power. According to the results of rTMS of the left DLPFC, smoking cravings considerably decrease following verum stimulation compared to sham stimulation. The study confirms the hypothesis that rTMS of the left DLPFC reduces drug craving by simulating the effects of nicotine on the brain, which are likely mediated by changes in dopaminergic activity. The study concludes by demonstrating the significant potential for rTMS to reduce cigarette cravings when delivered to the left DLPFC. It also supports the notion that the dopaminergic brain reward system mediates stimulation-induced effects, which likely play a significant but perhaps not its sole role in this behavioral regulation. As a result, high frequency rTMS constitutes a good outcome for nicotine cessation therapy.[15]

Dinur-Klein and colleagues in 2014 also found out that deep high frequency rTMS of the lateral insula and prefrontal cortex reduces nicotine addiction and smoking with

long lasting abstinence rate in treatment resistant smokers.[16]

In addition, the study of Li and colleagues in 2013 identified that smoking-related exposure paradigm consistently improve subjective cravings for nicotine. Increased frequency of stimulation of the left DLPFC for 15 minutes significantly reduced cue-induced urges for tobacco use, likened to sham stimulation. The degree of nicotine reliance was positively related to the group's cue-induced desire reduction. In other words, those who used nicotine more frequently had more significant TMS-induced desire reduction. Cigarettes smoked daily and Fagerstrom Test for Nicotine Dependence (FTND) scores are common indicators of dependency. It was also found that the number of cigarettes smoked per day and a higher FTND score was positively connected with the decrease in cue-induced desire from rTMS. Comparatively speaking, users who smoke fewer cigarettes per day have a higher chance of quitting and maintaining their abstinence than smokers who consume more daily cigarettes.[17]

In connection with this, the study of Zangen and colleagues in 2021 and Ibrahim, Malik, Barr, Daskalakis, & Le Foll in 2022 also found out that rTMS effectively reduced cigarette consumption compared to the sham group as early as two weeks into the treatment.[4,20]

The study of Shevorykin and colleagues in 2022 revealed that the medium and duration for intensity for latency to relapse were two criteria that affected the efficacy of the rTMS intervention. Increasing time frame and increasing the intensity quadrupled the likelihood of abstinence. Increasing the duration raised the odds by a factor of 7 to 8. For the delay discounting rate, a modest impact size for intensity and a significant effect for duration were also identified.[21]

Furthermore, the study of Prikryl and colleagues in 2013 and Huang, Shen, Zhang, & Xing in 2016 aimed to determine whether high-frequency rTMS on the left prefrontal dorsolateral brain (DLPFC) could reduce the number of cigarettes smoked by schizophrenia patients. This research employed a randomized, double-blind, and supervised trial. A random number table was used to distribute participants to either the medication group or the control group, with an equivalent number of people in each group. The findings demonstrated a statistically significant difference: patients who receive rTMS treatment tend to smoke fewer cigarettes than those who do not. The follow-up data showed that the effect of rTMS on reducing cigarette smoking persisted for at least three weeks after the therapy was over. In addition, it was also found that people with schizophrenia consume more nicotine than those without the disorder and those who have faster metabolic rates, leading to a propensity for nicotine dependency. Moreover, smokers with schizophrenia have a lower success rate in quitting than smokers in the general population which is 42% as compared to 4% in persons with schizophrenia.[18,19]

III.rTMS-ASSOCIATED ADVERSE EVENTS

It is generally established that repetitive transcranial magnetic stimulation is a well-tolerated and safe interventional tool. However, there are several substantial inconsistencies between safety and rTMS stimulation. The presence of programmable devices, such as a pacemaker or implanted metallic material in the brain, is likely to be negatively impacted by strong magnetic fields. One of the main issues with using the treatment is that it may increase a person's susceptibility to seizure generation, especially in those patients with history of active brain illness, epilepsy, or significant alcohol or drug withdrawal. Standard stimulation techniques appear to have a meager chance of causing seizures and may be reduced by carefully choosing patients and strictly following established safety protocols.

Additionally, rTMS stimulation has the potential to cause a syncopal episode,

Table 3. Summary of rTMS-Associated Adverse Events

Author	Cohort	Method	Result	Adverse effect
Fitzgerald & Daskalakis (2013)[23]	Patient with depression	Repetitive transcranial magnetic stimulation (rTMS) treatment	The likelihood of seizure induction appears to be very low with standard methods of stimulation, and this can be limited by careful patient selection and by closely adhering to established safety guidelines.	chances of seizure but in a low level
Overvliet , et al., (2020)[25]	Older adults with depression	A systematic search	AE were reported in 12.4% of the older adults with a LLD treated with rTMS, serious AE in 1.5%. Headache (6.9%) and discomfort at the stimulation site (2.7%) are the most commonly reported AE.	Headache, discomfort at the stimulation site
Pereira, Müller, Gomes, Rotenberg, & Fregni (2016)[24]	patients with epilepsy	Research report	Found that seizure risk of 2.9% (95% CI: 1.3-4.5), given that 12 subjects reported seizures out of 410 subjects included in the analysis after data of patients with epilepsia partialis continua or status epilepticus were excluded from the estimate	Seizure
Tringali, Perrot, Collet, & Moulin (2012)[27]	All patients using TMS	Hearing thresholds and TEOAEs were recorded in 24 normal-hearing	No significant difference in hearing thresholds was observed between subjects exposed to real or sham rTMS. However, the difference in TEOAE amplitude between pre- and post-rTMS sessions increased significantly with rTMS noise for those subjects the least protected by earplugs, showing a post-rTMS slight decrease of TEOAE amplitude for high rTMS intensities and hence minor hearing function alteration.	Hearing loss
Lerner, Wassermann, & Tamircd, (2019)[28]	Different patient that uses rTMS	Surveyed laboratories and clinics about seizures and other events observed	Twenty-four seizures were reported (. 08/1000 sessions). TMS delivered within published guidelines to subjects without recognized risk factors caused 4 seizures (<.02/1000 sessions)	Seizure
Hauer, Sellner, Brigo, Sebastianelli, & Saltuari (2019)[29]	Patient experience alcohol and cigarette addiction	Systematic review	No evidence for cognitive adverse effects was found in all the included rTMS studies	N/A
Peterchev, Luber, Westin, & Lisanby (2017)[30]	Volunteer	Motor threshold and input-output (IO) curve of right first dorsal interosseus were determined in 26 and 12 healthy volunteers	All procedures were well tolerated with no seizures or other serious adverse events. Increasing pulse width decreased the motor threshold and increased the pulse energy and IO slope. The average strength-duration curve time constant is estimated to be 196 μs, 95% CI [181 μs, 210 μs]. IO slope is inversely correlated with motor threshold both across and within pulse width.	N/A

particularly in more susceptible people. There is no identified risk that rTMS may cause cognitive impairment and there had been no identified adverse effects on brain tissue. Both patients and medical professionals receiving rTMS treatment ought to wear hearing protection. More caution should be used when administering rTMS treatment to particular populations such as the young or expectant women.[22,23,24]

Tringali, Perrot , Collet, & Moulin in 2012 identified that rTMS can transiently affect hearing in normal, healthy patients even while following safety protocols and wearing of ear protection.[27] The study of Lerner, Wassermann, & Tamircd, 2019 concluded that applying TMS increases the chance of having seizure episodes at rate as of 0.8 per 1000 sessions. Most of the TMS related seizures are reported to happen in persons with risk factors such as anatomical lesion, congenital epilepsies and those who are using antiseizure medications.[28]

The study of Hauer, Sellner, Brigo, Sebastianelli, & Saltuari in 2019 found that rTMS affect the executive function and attention of patients.[29] In contrast to this, the study of Overvliet and colleagues in 2021 concluded that there were no adverse events even among older population with smoking addiction.[26] In the study of Peterchev, Luber, Westin, & Lisanby in 2017, it was noted that shorter TMS pulses (with an average 0.89-point increase on the discomfort scale for a pulse width of 30s compared to 120s) were perceived as slightly more uncomfortable than longer pulses. Although not stronger than longer pulses, the shorter pulses were noticeably sharper (2.95 points increase for 30s as compared to 120s pulse width). As anticipated, stronger and, to a lesser extent, sharper pulses were assessed as more uncomfortable and powerful. In addition, it was concluded that repetitive transcranial magnetic stimulation led to scalp discomfort for all types of patients[30]. Shen, Cao, Tan, & Shan in 2016 concluded that all patients admitted experienced headaches which immediately resolved after stimulation, with and without over-the-counter pain medications. It was also mentioned that some patients increased their use of over-the-counter pain medications to treat minor headaches after rTMS[3].

CONCLUSION

Repetitive transcranial magnetic stimulation (rTMS) is generally a safe procedure and is a potential therapy to treat smoking addiction. The deep high-frequency rTMS of the lateral insula and prefrontal cortex has the potential to decrease cigarette cravings. This study also identifies that rTMS reduces resting state insula activity and modulates functional connectivity of the orbitofrontal cortex in cigarette smokers. In addition, the triggered desire circuit might be a crucial part of the rTMS mechanism for the tobacco user. The individual neuronal excitability in the region's subsequent induction may have an impact on the therapeutic outcomes.

The high-frequency rTMS sequentially applied to the left SMFC and DLPFC is an effective tool for improving the cessation rate. Brain entropy and cerebral blood flow provide valuable means to quantify or monitor the treatment effects. Compared to behavioral therapy, the rTMS is more effective in treating smoking. The factors that affected the effectivity of the rTMS intervention were the duration and intensity of latency to relapse. Increasing duration increased the odds of abstinence 7-8-fold, and increasing intensity doubled the odds. While the adverse effects of using rTMS in smoking cessation include significantly increasing a person's risk of seizures, temporarily impairing hearing, affecting executive function, and causing headaches and scalp discomfort but these were observed in vulnerable population with preexisting neurological condition.

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DECLARATION OF COMPETING INTEREST

None.

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