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REVIEW ARTICLE **OPEN ACCESS**

Transcranial Magnetic Stimulation: A New Possibility in Obesity Treatment

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Abstract:
Obesity is a major public health challenge and results from the complex interaction of many etiopathogenetic factors. However, food-related hedonic stimuli and poor inhibitory control often appear to be specific maintenance factors, and conventional treatments are sometimes ineffective. Transcranial magnetic stimulation is emerging as a promising treatment option. Targeting specific brain regions, such as the dorsolateral prefrontal cortex, was found to be effective in modulating acute food craving and improving cognitive control. This review traces the evolution and development of transcranial magnetic stimulation and presents the results of recent randomized clinical trials conducted in obese subjects. These suggest that repetitive transcranial magnetic stimulation and deep transcranial magnetic stimulation may be effective in reducing body weight, BMI and food cravings. The neural circuits involved and the underlying mechanisms of action of this neurostimulation technique are also reviewed. Finally, outstanding questions and future research directions are identified to further understand and develop this promising therapy.

Keywords: Transcranial magnetic stimulation, Obesity, Weight management, Dorsolateral prefrontal cortex, Reword mechanism, Executive functions, Inhibitory control.

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1. INTRODUCTION

The increasing prevalence of obesity is a major global public health challenge. Excess body weight significantly increases the risk of a number of chronic diseases, such as type 2 diabetes mellitus, non-alcoholic fatty liver disease, hypertension, and cardiovascular disease, including myocardial infarction and stroke. Obesity is also strongly associated with a wide range of health problems, including osteoporosis, joint disease, renal dysfunction, dyslipidaemia, obstructive sleep apnoea, and certain cancers. It can also lead to musculoskeletal problems and rapid cognitive decline [1-6]. These negative effects underscore the importance of maintaining a healthy weight.

Obesity is a complex condition shaped by a variety of influences, including physiological, metabolic, psychological, and environmental factors [7-10]. The hedonic aspect of eating, characterised by strong cravings and challenges in resisting certain foods, adds another layer of complexity to the problem. In addition, although lifestyle modification, pharmacotherapy, and bariatric surgery offer potential benefits, their effectiveness is limited and may not be appropriate for all individuals [11, 12].

Transcranial magnetic stimulation (TMS), a non-invasive method of modulating brain activity, is emerging as a promising new treatment for obesity and associated eating disorders. TMS targets specific brain regions involved in the regulation of intense food cravings and dietary control and has shown promise in facilitating weight loss [13-16]. Studying obesity through the lens of TMS is challenging due to the complex nature of the disorder and the significant role of neurobehavioral factors [17, 18].

TMS is a potential intervention for modifying neural circuits that are essential for controlling appetite, reducing food cravings, and regulating impulses. These components are closely linked to the development and treatment of obesity [14, 19]. Preliminary studies have shown that TMS has a profound effect on eating behaviour and metabolic functions, opening up new avenues for treatment [20].

These investigations suggest that obesity may result from imbalances in brain networks, with some pathways associated with gratification mechanisms and others involved in cognitive control and impulse inhibition [21-23]. The increasing importance of neural function and control mechanisms in weight management, beyond metabolic or lifestyle factors, is now recognised [17, 18]. In particular, the dorsolateral prefrontal cortex (dlPFC) is a key neural site for modulating hunger and satiety signals and plays an essential role in regulating impulses and food choices [24, 25]. This region has become a specific target of neurostimulation techniques for addictive behaviours and eating disorders because of its role in the executive functions that manage the cognitive regulation of food consumption [26-28]. However, the specific cognitive mechanisms affected by the dlPFC that are modulated by TMS remain largely undefined. It has been theorised that such dynamics may include changes in reward valuation [29], attentional biases [30], or inhibitory control [31]. Whether TMS is effective in reducing food cravings in the long-term has not been conclusively established. Further research is needed to determine the most appropriate use of this technology in the treatment of obesity and related eating disorders, as the current scientific evidence does not provide precise guidelines [32, 33]. Initial research on TMS provides convincing evidence of its therapeutic potential and underlying mechanisms. These findings are a fundamental prerequisite for more in-depth investigations into the use of TMS as an innovative strategy in the treatment of obesity.

This review summarises the current state of knowledge on the use of TMS in the treatment of obesity, examines the efficacy of common TMS techniques in obese subjects enrolled in randomised controlled clinical trials, explores potential mechanisms of action, and highlights areas of uncertainty that require further scientific investigation.

2. NEURAL MODULATION BY TRANSCRANIAL MAGNETIC STIMULATION

TMS employs electromagnetic induction to elicit localized electrical currents within the brain, thereby modulating neuronal activity [34]. Initially developed to treat stubborn psychiatric conditions such as mood disorders, substance abuse, and post-traumatic stress disease [35-39], the application of TMS has subsequently expanded to encompass a range of neurocognitive disorders [40-43] such as schizophrenia [44], dementia [45], and eating disorders [46, 47]. Repetitive Transcranial Magnetic Stimulation (rTMS) and deep Transcranial Magnetic Stimulation (dTMS) constitute the core methodologies within the TMS framework [48-50]. The rTMS protocol employs a figure-of-eight electromagnetic coil to generate focal magnetic pulses or sequences of pulses that target discrete cortical regions to a depth of approximately 1.5 cm below the scalp. These magnetic pulses can modulate cortical excitability, either augmenting or diminishing the electrical activity within the targeted neuronal circuits. Conversely, dTMS is characterised by the use of an H-coil, which is designed to extend stimulation to both cortical and subcortical structures, achieving penetration depths of 4.5 to 5.5 cm from the cranial surface [41, 51-53]. In both rTMS and dTMS modalities, the use of high-frequency stimulation (≥5 Hz) is associated with an excitatory effect on neuronal excitability, whereas low-frequency stimulation (≤1 Hz) is associated with inhibitory effects [30, 54, 55]. Further diversification within TMS techniques includes intermittent theta burst stimulation (iTBS) and continuous theta burst stimulation (cTBS). iTBS, characterised by its high-frequency burst pattern, is postulated to induce an increase in cortical excitability, whereas cTBS is associated with a decrease in cortical excitability [56, 57]. As it has been reported, these stimulation protocols have been found to provide a range of modulatory effects on neural circuits, which highlights the potential usefulness of TMS in the therapeutic modulation of neurocognitive and neuropsychiatric conditions. TMS is highly valued within the clinical paradigm for its ability to induce lasting therapeutic changes beyond the temporal limits of the stimulation sessions themselves [58]. The significance of the neurophysiological changes induced by TMS is highlighted by its capacity to induce long-term synaptic plasticity [59]. Further, rTMS can be classified into single-session and multi-session approaches. The former, a single-session application, is extensively employed in experimental research to evaluate the immediate neurophysiological effects of rTMS. The latter method involves multiple sessions delivered over consecutive days and is primarily used in clinical settings for extended therapeutic interventions [34].

The efficacy and specificity of TMS interventions

depend on the precise localization of the targeted brain region. Neuroimaging techniques, such as electroencephalography (EEG) or structural magnetic resonance imaging (MRI), are necessary for this purpose. These techniques should be complemented by neuronavigation technologies, a methodology that has been extensively documented in the literature [60, 61]. Precision in targeting is essential to optimize the therapeutic outcome of TMS. TMS is considered a safe and non-invasive method that is generally well-tolerated [62, 63]. However, it has been reported that the incidence of side effects was approximately 5%. The most common were headache (46%), lightheadedness (22%), muscle twitching (10%), and a general feeling of lightheadedness (10%) [64]. It is important to note that the main safety concern with TMS is epileptic seizures, although these are very rare and may only be a risk for those with a pre-existing epileptic condition [62-64].

3. TRANSCRANIAL MAGNETIC STIMULATION FOR THE TREATMENT OF OBESITY: A SYNTHESIS OF RANDOMIZED CONTROLLED TRIALS

In line with the latest scientific literature [27, 65, 66], this section will provide an overview of studies investigating the effects of TMS in obese individuals. The focus will be on two specific TMS techniques, rTMS and dTMS. This chapter examines rigorous Randomized Controlled Trials (RCTs) comparing active neuromodulation techniques with sham interventions to determine the impact of such stimulations on key indicators of interest in the field of obesity research. The particular metrics being monitored are body weight, body mass index (BMI), and cravings for food.

3.1. Repetitive Transcranial Magnetic Stimulation and Obesity

According to a study conducted by Kim and colleagues in 2018 [32], 57 individuals between the ages of 18 and 65 were randomly assigned to two groups in a two-week, single-blind trial. Of the participants, 29 received rTMS, while 28 received sham treatment. The rTMS sessions, each lasting 20 minutes at a frequency of 10 Hz, targeted the left dlPFC. The study results indicated significant weight loss in the rTMS group, accompanied by reductions in BMI, visceral fat, and calorie intake.

Continuing from the previous study, the research group [67] conducted a four-week study on 43 patients who were classified as obese and aged between 18 and 70. The participants were divided into two groups: 21 individuals received eight 20-minute sessions of rTMS at 10 Hz, while the remaining 22 individuals received sham treatments. The study results indicate that individuals who received rTMS treatment experienced a significantly greater weight loss (2.75 kg, SD 2.37) compared to those who received the sham treatment (0.38 kg, SD 1.0). Furthermore, the rTMS group also showed significant reductions in fat mass and visceral adipose tissue by the fourth week. Additionally, after treatment, the rTMS group demonstrated reduced daily kilocalorie and carbohydrate consumption compared to the control group.

In a study conducted in 2019, the effects of combining rTMS with a low-carbohydrate diet were tested on 37 overweight or obese patients [15]. The participants were randomly assigned to two groups: 18 followed the diet with rTMS, and 19 followed the diet with sham rTMS. After 17 sessions of 10 Hz rTMS to the left dlPFC, the treatment group showed significant reductions in body weight and food cravings, as well as improvements in anxiety symptoms, physical functionality, and body image.

In 2020, a study was conducted on 29 obese Filipino patients aged between 15 and 65. The patients were randomly assigned to either a treatment group (15 subjects) or a sham group (14 subjects). They received four 20-minute rTMS sessions at 10 Hz to the left dlPFC over two weeks in a single-blind, monocentric setting [13]. Upon completion of the study, the treatment group exhibited a significant decrease in BMI (-0.6, SD 0.6) and body weight (-1.3 kg, SD 1.3). It is worth noting that the weight reduction did not appear to be sustained beyond the 6-12 week treatment period.

3.2. Deep Transcranial Magnetic Stimulation and Obesity

A pilot study was conducted on 33 obese individuals (9 men, 24 women, mean age 48.1 years, SD 10.6) [33]. The participants were divided into three groups: 13 underwent a 5-week high-frequency dTMS treatment (18 Hz; HF group), 10 received low-frequency dTMS (1 Hz; LF group), and 10 received placebo treatments (sham group). The stimulation targeted the bilateral Prefrontal Cortex (PFC) and Insula, consisting of 15 sessions, each lasting 30 minutes. Food cravings, metabolic indicators, and neuroendocrine measures were assessed at baseline, after 5 weeks of treatment, and at follow-up sessions (1 month, 6 months, and 1 year post-treatment). The findings showed a significant decrease in both body weight (-7.83 kg, SD 2.28) and BMI (-2.83, SD 0.83) in the HF group compared to the sham group. Additionally, there was a significant trend towards reduced food cravings in the HF group compared to the LF and sham groups. The HF group also demonstrated significant improvements in metabolic variables and physical activity.

In another study involving 22 obese individuals (17 female; mean age 44.9 ± 2.2 years; BMI 37.5 ± 1.0 kg/m^2) [68], the same researchers suggested that dTMS may have the potential to influence both the pathways of the brain-gut communication and the composition of the gut microbiome. The study involved randomising participants into three groups, each attending 30-minute sessions three times a week for five weeks. They received either high-frequency (18 Hz - HF), low-frequency (1 Hz - LF), or sham dTMS treatments, respectively, with the stimulation site being the bilateral PFC and Insula. After 5 weeks, the HF group showed significant weight loss compared to the LF and sham groups (HF: -4.1 kg, SD 0.8 *vs.* LF: -1.9 kg, SD 0.8 *vs.* sham: -1.3 kg, SD 0.6). Moreover, it appears that HF dTMS treatment has had a positive impact on the gut microbiota composition, reversing previous changes and

promoting bacterial species with anti-inflammatory properties.

A preliminary randomized, double-blind, placebo-controlled study [14] was conducted to investigate the resting-state functional connectivity (rsFC) in obese patients after 15 sessions of 30-minute treatments. Nine participants underwent high-frequency (18 Hz - HF) dTMS treatment, focusing on the bilateral PFC and Insula, three times a week for five weeks, while 8 were given placebo treatments (sham TMS group). Out of the 17 participants, 6 were diagnosed with Type 2 Diabetes (T2D). The results indicate that the experimental group experienced a significant decrease in body weight and BMI, which persisted through a one-month follow-up. Additionally, there was an observed enhancement in the functional brain connectivity within the medial Orbitofrontal Cortex (mOFC), coupled with a reduction in connectivity with the occipital pole. These findings indicate a potential brain mechanism behind weight loss, characterized by diminished responsiveness to bottom-up visual sensory inputs and an increased dependence on top-down cognitive decision-making processes.

A study was conducted to examine the correlation between psychological symptoms and neuroendocrine parameters in individuals with obesity [69]. The study also investigated the effects of a 5-week treatment regimen involving 30-minute high-frequency (18 Hz) stimulations targeting the bilateral PFC and Insula using dTMS. A study was conducted on 45 patients who were obese, out of which 33 were female. The patients had an average age of 48.8 years (SD 9.9), body weight of 97.6 kg (SD 14.2), and BMI of 36.2 (SD 4.2). The patients were randomly assigned to two groups, out of which 26 patients received high-frequency (HF) dTMS, while 19 underwent sham stimulation. The study found that the HF group showed a significant reduction in body weight and BMI, along with a decrease in impulsivity levels. Additionally, a positive correlation was observed between decreased impulsivity and leptin levels. These results indicate that dTMS was effective in reducing both BMI and impulsivity, improving inhibitory control of the PFC, and impacting the neuroendocrine system, particularly with regard to leptin.

4. MECHANISMS OF ACTION OF TMS IN THE TREATMENT OF OBESITY

These studies suggest that both TMS methods are effective in reducing body weight and BMI, with high-frequency stimulation of the dlPFC showing particular promise, which is in line with previous research [18, 70-72]. However, further research is required to investigate the effects on food cravings [27]. The current evidence suggests that by reducing the frequency and intensity of food cravings, it may be possible to decrease calorie intake and facilitate fat loss [32, 67]. In other words, by strengthening cognitive regulatory competencies, individuals may be better equipped to exercise discipline in their dietary practices. This enhancement provides the opportunity to choose healthier food options instead of those prompted by impulsive or emotional consumption patterns, which can aid in the weight loss process [73-77]. The phenomenon of craving, characterized as an intense and uncontrollable urge to consume, is believed to be influenced by dysfunction in frontostriatal brain circuits that are involved in both substance abuse and overeating [78]. High-frequency rTMS can selectively activate dlPFC while reducing activity in deeper regions such as the orbitofrontal cortex (OFC) and anterior cingulate cortex (ACC) [79, 80]. However, the effects of TMS on food cravings appear to be a topic of debate, with some studies highlighting the ambiguity of treatment responses. A study was conducted to evaluate the effectiveness of high-frequency rTMS targeting the left dlPFC in reducing food cravings in a group of 28 female participants [81]. Both real and sham rTMS sessions were administered before and after participants were exposed to highly palatable foods. The results indicated that self-reported craving remained unchanged after the real rTMS treatment but increased in the sham condition. However, it should be noted that no significant variations in snack consumption were observed during the brief 5-minute post-stimulation period, regardless of the type of rTMS administered. In another study, the effect of rTMS on the left PFC in 10 healthy women was investigated using an improved sham condition 82]. The participants were randomly allocated to one of two groups and were unaware of which treatment they were receiving. Both conditions demonstrated a noteworthy decrease in craving, with no significant difference observed between real and sham rTMS, even after taking into account the time elapsed since the last meal. However, it was found that prefrontal rTMS did not prove to be superior to the sham condition in reducing craving. It has been suggested [78] that the mild discomfort induced by both real and simulated rTMS may contribute to the reduction in food cravings, suggesting that this reduction may not be solely due to the specific effects of rTMS. Further research is necessary to establish whether the decrease in food cravings caused by rTMS is directly affected by the uncomfortable sensation it produces or if it occurs through an indirect mechanism. Craving is an adaptive mechanism that signals the organism's nutritional needs. It has been considered essential for human survival, especially in an evolutionary context, as it facilitated the accumulation of food supplies in anticipation of times of scarcity [83]. For example, a growing appetite for iron-rich foods, such as meat, has been documented in response to shortages of this essential nutrient [84]. However, it is worth noting that the widespread availability of sugary and fatty foods has transformed these previously adaptive cravings into potential contributors to the development of obesity or uncontrollable eating behaviour [85]. There is a growing body of evidence to suggest that cravings are a key factor in the obesity epidemic [86-88]. Some studies indicate a correlation between obesity, binge eating behaviour, and self-control issues. According to research, a lack of control and an increased desire for food, especially palatable or high-calorie foods, may result in a loss of control over food intake, leading to weight gain. Additionally, studies have

indicated that higher food cravings are linked not only to increased body weight but also to lower success rates in weight loss programmes [89-91]. According to experimental studies, there may be common neuro-biological bases between addiction and morbid obesity, particularly in the phenomenon of craving [92]. It has been observed that certain regions of the brain, such as the OFC, are involved in both food craving and addiction control. The OFC plays an essential role in assessing the rewarding properties of stimuli, which suggests that both food and substances can activate it in a similar way. Furthermore, it should be noted that there appears to be a correlation between heightened activation of the OFC and increased food cravings in individuals with normal weight [93]. However, the full impact of brain stimulation on food cravings is not yet fully understood. As previously described [65], there are various potential mechanisms that could be responsible, such as improved cognitive control, alterations in reward perception, or heightened dopaminergic activity. The role of the dlPFC is particularly intriguing in this context. It has been suggested that reduced activity in the dlPFC may contribute to weight gain, as it has been linked to satiety and craving [94, 95]. On the other hand, stimulation of the dlPFC has been shown to enhance cognitive control and effectively suppress the compulsive urge to eat [96]. Furthermore, research has indicated that the interaction between the dlPFC and mOFC may affect the evaluation of food stimuli, leading to a reduction in attractiveness and more regulated food choices [29]. The correlation between improved inhibitory control and reduced cravings suggests that neuromodulation may be able to enhance brain networks involved in behavioural food control by increasing the ability to resist food-related stimuli [97]. According to research, it has been found that the stimulation of the dlPFC can enhance cognitive control and reduce food cravings [98]. It has been observed that the dlPFC, OFC, and ACC together form the executive control network that is critical for desire management and decision-making. Additionally, these regions interact with the orexinergic system [99-103]. Another plausible hypothesis is that neurostimulation of the dlPFC may stimulate dopamine production in the corpus striatum [104]. It is suggested that dopamine levels may increase either directly, through corticostriatal projections, or indirectly, through cortical projections to mesostriatal dopamine neurons located in the midbrain [105-107]. Research has indicated that PFC stimulation in animal studies can activate both the striatum and Ventral Tegmental Areas (VTA), suggesting that both pathways are sensitive to neurostimulation [108, 109]. Additionally, dTMS has been shown to rebalance the dopamine-cortisol ratio during alcohol withdrawal [110]. It is well established that dopamine plays a significant role in inhibitory control, and abnormalities in this area can lead to behavioural disorders such as obesity [111]. Indeed, a correlation has been found between BMI and a decrease in the availability of dopamine D2 receptors [112]. This could potentially lead to pathological eating behaviour as the brain attempts to compensate for reduced activity in motivational and reward circuits. Hence, it may be suggested that individuals who experience intense food cravings and/or obesity could potentially benefit from modifying their dopamine levels through non-invasive brain modulation techniques. Moreover, it has been shown that dTMS is associated with changes in leptin levels and behavioural impulsivity [69]. Leptin, a hormone produced by adipocytes and intestinal enterocytes, plays a crucial role in regulating energy homeostasis [113]. The regulation of leptin levels may have a positive impact on appetite and food intake, while leptin resistance may be linked to increased food intake and the onset of obesity [114]. Specifically, a 5-week course of radiofrequency dTMS treatment led to significant changes in the gut microbiome composition of obese subjects [68]. These changes helped to normalize the microbiota, bringing it closer to that found in normal-weight subjects, and also favored an increase in bacterial species with anti-inflammatory properties. These findings suggest that this intervention may have therapeutic potential in the treatment of obesity. Although there are many theoretical insights to explain the effects of neurostimulation on weight loss, identifying the exact mechanisms remains a challenge.

CONCLUSION AND FUTURE DIRECTION

This review examines the potential of TMS as a new approach to treating obesity. The review suggests that non-invasive neuromodulation may be an effective standalone treatment or may improve therapeutic outcomes when used in combination with other strategies, such as diet. The theoretical basis for this approach is supported by experimental results that demonstrate the complex interplay between neurophysiology and obesity. It proposes a paradigm shift towards specific interventions aimed at modulating and normalising neural circuits using advanced neuromodulation techniques [20, 93, 100, 115-117]. However, it may be beneficial for future research to address the limitations and unresolved questions surrounding the potential applications of neuromodulation in eating behaviour. To gain a more complete and accurate understanding of the role of TMS in dysfunctional eating behaviour, researchers could consider focusing on the following key aspects.

In experimental neuromodulation research, it is essential to enhance study blinding. It is recommended that participants remain unaware of the treatment they are receiving, whether real or sham, to prevent any potential bias in their behaviour or responses. It has been observed in some neuromodulation studies that participants were able to correctly identify experimental conditions with 79% accuracy [82, 118]. Therefore, it is suggested that future research should explore the use of parallel methods to enhance blinding.

Another important aspect is to consider using more meaningful outcome measures. While some studies rely on self-report measures directly reported by participants, others use weight indices that may be outdated, making their true clinical relevance uncertain. For example, the

BMI has been criticised for its inability to distinguish between muscle mass and fat mass, as well as for its inability to measure regional adiposity [119-121]. In contrast, it could be argued that waist circumference is a more sensitive measure of visceral adiposity [122-124].

Further research is needed to fully understand the interaction between neuromodulation and gender. Neuropsychological evidence suggests that gender may have a significant impact on prefrontal executive performance [125]. It has been observed that men and women exhibit different abilities in specific subdomains, such as attention, planning, inhibition, and verbal fluency [126-132]. However, it is important to note that these differences do not necessarily imply systematic differences between the sexes. Instead, they reflect differences in the cognitive strategies employed during cognitive tasks [133]. These differences could be due to variability in the anatomic-functional characteristics of the brain and the involvement of neurotransmitter systems, including dopamine and serotonin [134-141].

Moreover, when studying feeding processes and mechanisms, it is crucial to take into account the fluctuations in brain activity that may be associated with metabolic conditions. Therefore, it is recommended that studies explicitly state the time since the last meal and its effect. The review reports that hunger and satiety conditions may produce significant differences in hormonal and neurotransmitter systems. Similarly, when considering the effects of neuromodulation, it is important to take into account the individual's previous or current diets, including their duration and any possible relapses [143]. It is worth noting that individuals who suffer from eating disorders and obesity often follow strict diets, which can significantly affect brain excitability and responsiveness to neuromodulation. Additionally, it is crucial to report whether participants are currently losing weight or maintaining a stable weight. The passage presents data that has implications for both the brain's resting state and its response to neuromodulation [20]. Furthermore, it is worth noting that an individual’s unique anatomical features may affect the propagation of electromagnetic signals [143]. Therefore, it is important to investigate the impact of intracranial adipose tissue on current density distribution, as adipose tissue is known to be more resistive [63, 144].

As shown in this review, TMS offers a promising perspective for the study and treatment of neural vulnerabilities associated with obesity. However, while neurostimulation techniques were originally developed to address the lack of effective treatments in neurology and psychiatry, the application of neuromodulation to the modification of eating behaviour is a more recent development in the field. TMS has been shown to produce temporary and long-term changes by actively affecting the strength of synaptic connections. The primary target of TMS is the dlPFC, a complex brain region associated with executive function and cognitive control of food intake. It can influence the balance between craving and the ability to exercise cognitive control, potentially reducing the rewarding mechanisms that drive excessive eating. It is worth noting that research in the area of actively manipulating the human brain is still in its early stages, and no definitive conclusions are available. Moreover, it is essential to bear in mind that transcranial devices should not be treated as playthings and must be used responsibly [143].

LIST OF ABBREVIATIONS

TMS	=	Transcranial magnetic stimulation
dlPFC	=	Dorsolateral prefrontal cortex
rTMS	=	Repetitive Transcranial Magnetic Stimulation
dTMS	=	Deep Transcranial Magnetic Stimulation
iTBS	=	Intermittent theta burst stimulation
cTBS	=	Continuous theta burst stimulation
EEG	=	Electroencephalography
MRI	=	Structural magnetic resonance imaging
RCTs	=	Randomized Controlled Trials
BMI	=	Body mass index
HF	=	High Frequency
LF	=	Low frequency
PFC	=	Prefrontal Cortex
rsFC	=	Resting-state functional connectivity
T2D	=	Type 2 Diabetes
mOFC	=	Medial Orbitofrontal Cortex
OFC	=	Orbitofrontal cortex
ACC	=	Anterior cingulate cortex
VTA	=	Ventral Tegmental Areas

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CONFLICT OF INTEREST

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