Repetitive transcranial magnetic stimulation (rTMS) is used to modulate local brain activity and thus modulating neurocircuitries involved in the pathophysiology of gambling disorders (GD) potentially resulting in therapeutic effects. Dopaminergic dysfunctions have been found to be critically involved in the development of GD, especially in presynaptic structures, in the reduced availability of dopamine transporters (DAT) in GD subjects. Stimulating the DLPFC with rTMS may restore a physiological basal dopaminergic activity and increase DAT levels, as well as modulate glutamatergic neurotransmission.

The aim of this review paper was to highlight possibilities for further research in determining efficacy of rTMS in the treatment of cravings in behavioral addiction, as well as recommendations for optimal stimulation settings and its clinical application.

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TREATING DEPRESSION IN PATIENTS WITH NEUROPATHIC PAIN AND DEMYELINATING DISEASE OF THE CENTRAL NERVOUS SYSTEM

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Transcranial magnetic stimulation (TMS) is a technique for noninvasive stimulation of the human brain. Stimulation is produced by generating a brief, high-intensity magnetic field by passing a brief electric current through a magnetic coil. The field can excite or inhibit a small area of brain below the coil.

Repetitive TMS has a modulatory effect on cortical excitability, which outlasts the stimulation period and can be used in a variety of indications, delivered to either motor or nonmotor brain regions. The impact of rTMS can be observed at the site of stimulation and mostly at a distance, according to the nature of the activated neural circuits.

Functional or clinical effects outlast the period of stimulation for minutes or hours, likely due to long-term depression (LTD) of synaptic transmission for low-frequency rTMS and long-term potentiation (LTP) for high-frequency rTMS.

Therefore by modifying brain functions, with after-effects lasting beyond the time of stimulation, rTMS opens exciting perspectives for therapeutic applications, especially in the domain of depression and chronic pain syndromes.

Neuropathic pain is caused by a lesion or disease of the somatosensory system, including peripheral fibres (AB, A δ and C fibres) and central neurons, and affects 7-10% of the general population. The somatosensory system allows for the perception of touch, pressure, pain, temperature, position, movement and vibration. Neuropathic pain is associated with increased drug prescriptions and visits to health care providers and can substantially impair quality of life as it often associates with other problems, such as loss of function, anxiety, depression, disturbed sleep and impaired cognition.

Progress in the understanding of the pathophysiology of neuropathic pain is spurring the development of new diagnostic procedures and personalized interventions, which emphasize the need for a multidisciplinary approach to the management of neuropathic pain. Repetitive sessions (5-10 sessions over 1-2 weeks) with high-frequency rTMS (5-20 Hz) have shown benefits in a mixture of central, peripheral and facial neuropathic pain states, with effects lasting >2 weeks after the stimulation. Contraindications of rTMS include a history of epilepsy and the presence of aneurysm clips, deep brain electrodes, cardiac pacemakers and cochlear implants.

Multiple sclerosis (MS) is a chronic inflammatory disease in which the fatty myelin sheaths around the axons of the brain and spinal cord are damaged, leading to demyelination and scarring as well as a broad spectrum of signs and symptoms. Multiple sclerosis (MS) associated neuropsychiatric disorders include major depression (MD), obsessive-compulsive disorder (OCD-MS), bipolar affective disorder, euphoria, pseudobulbar affect, psychosis, and personality change. A point prevalence of 15% to 30% and a lifetime prevalence of 40-60% of MD have been reported in MS patients; this rate of depression is 3 to 10 times that of the general population. H-coil rTMS is safe and well tolerated in patients with MS. The observed sustained reduction in fatigue after subthreshold MC stimulation warrants further investigation.

Our experience in treating depression in patients with demyelinating disease of the central nervous system also showed promising results on mood disorder.

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REPETITIVE TRANSCRANIAL MAGNETIC STIMULATION IN TREATMENT OF TINNITUS: META-ANALYSIS OF RANDOMIZED SHAM-CONTROLLED TRIALS

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Background: Tinnitus etiology and clinical presentations are highly variable. There is no stringent and universally accepted definition of the disorder, and objective diagnostic biomarkers are missing. There is no gold treatment standard, and the results of studies on various treatment effects are inconsistent. Clinical practice guidelines from 2014 stated that rTMS may not be recommended for the routine treatment of tinnitus neither, because of methodological heterogeneity/weaknesses, and inconsistencies of results of rTMS randomized controlled trials. Since 2014, more studies of rTMS efficacy on tinnitus have been published, but the results are still highly heterogenous, poorly reported, with low reproducibility, and non-conclusive. To access the efficacy of rTMS on idiopathic, chronic tinnitus disorder.

Study		Hedges g with 95% CI	Weight (%)
Smith, 2007		-0.37 [-1.76, 1.02]	1.50
Anders, 2010		-0.15 [-0.75, 0.45]	5.06
Marcondes, 2010		-0.75 [-1.68, 0.18]	2.87
Piccirillo, 2011		-0.06 [-0.80, 0.68]	3.97
Plewnia, 2012 B		0.08 [-0.77, 0.93]	3.29
Plewnia, 2012 A		0.04 [-0.81, 0.89]	3.29
Hoekstra, 2013		-0.24 [-0.80, 0.32]	5.49
Piccirillo, 2013		-0.24 [-1.00, 0.52]	3.84
Lee, 2013		-0.84 [-1.58, -0.10]	3.94
Barwood, 2013 –		-1.55 [-3.13, 0.03]	1.20
Langguth, 2014 C		-0.19 [-0.77, 0.39]	5.30
Langguth, 2014 B		-0.20 [-0.78, 0.38]	5.30
Langguth, 2014 A		-0.37 [-0.95, 0.21]	5.25
Yilmaz, 2014		-0.89 [-1.42, -0.36]	5.80
Folmer, 2015		-0.30 [-0.79, 0.19]	6.24
Billci, 2015 B		-1.01 [-1.95, -0.07]	2.82
Billci, 2015 A	_	-1.20 [-2.16, -0.24]	2.76
Wang, 2015 B		-1.38 [-2.86, 0.10]	1.35
Wang, 2015 A		-2.02 [-3.63, -0.41]	1.16
Schecklmann, 2016		0.23 [-0.59, 1.05]	3.43
Sahlsten, 2017		0.26 [-0.37, 0.89]	4.83
Landgrebe, 2017	-	0.04 [-0.28, 0.36]	8.32
Kyong, 2019 A		-0.09 [-0.93, 0.75]	3.32
Formanek, 2018		-0.40 [-1.13, 0.33]	4.04
Noh, 2019 A		-0.95 [-1.92, 0.02]	2.71
Li, 2019		-1.67 [-2.59, -0.75]	2.91
Overall	_	-0.39 [-0.57, -0.21]	
Favors rTMS Favors sham			
-4.00 -2.00 0.00 2.00			
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Figure 1. Forest plot of standardized mean differences (Hedges g) between active rTMS and passive sham coil in the effect on tinnitus severity measured immediately after the intervention; error lines in the summary measure represent 95% prediction interval (-1.00; 0.22); (n = 26 studies; 549 patients in active rTMS arms, 537 in passive sham arms); studies are sorted by the year of publishing of the first results in order starting with the oldest one