European Psychiatry 28 (2013) 30–39

Available online at
SciVerse ScienceDirect
www.sciencedirect.com

Elsevier Masson France
EM|consulte
www.em-consulte.com/en

Review

Deep transcranial magnetic stimulation as a treatment for psychiatric disorders: A comprehensive review

F.S. Bersani [a,*], A. Minichino [a], P.G. Enticott [b], L. Mazzarini [d,e], N. Khan [a], G. Antonacci [f], R.N. Raccah [g], M. Salviati [a], R. Delle Chiaie [a], G. Bersani [c], P.B. Fitzgerald [b], M. Biondi [a]

[a] Department of Neurology and Psychiatry, Sapienza University of Rome, Rome, Italy
[b] Monash Alfred Psychiatry Research Centre, The Alfred and Central Clinical School, Monash University, Melbourne, Australia
[c] Department of Medical–Surgical Sciences and Biotechnologies, Sapienza University of Rome, Rome, Italy
[d] Neurosciences, Mental Health, and Sensory Organs Department, Sapienza University of Rome, Rome, Italy
[e] Department of Neuropsychiatry, Villa Rosa, Suore Hospitaliere of the Sacred Heart of Jesus, Viterbo, Italy
[f] Photonics Group, Department of Physics, Imperial College, London, UK
[g] ATID Ltd Advanced Technology Innovation Distribution, Rome, Italy

ARTICLE INFO

Article history:
Received 21 December 2011
Received in revised form 25 February 2012
Accepted 26 February 2012
Available online 3 May 2012

Keywords:
Deep transcranial magnetic stimulation
Transcranial magnetic stimulation
H-coil
Major depression
Autism
Bipolar disorder
Auditory hallucinations
Negative symptoms
Schizophrenia

ABSTRACT

Deep transcranial magnetic stimulation (TMS) is a technique of neuromodulation and neurostimulation based on the principle of electromagnetic induction of an electric field in the brain. The coil (H-coil) used in deep TMS is able to modulate cortical excitability up to a maximum depth of 6 cm and is therefore able not only to modulate the activity of the cerebral cortex but also the activity of deeper neural circuits. Deep TMS is largely used for the treatment of drug-resistant major depressive disorder (MDD) and is being tested to treat a very wide range of neurological, psychiatric and medical conditions. The aim of this review is to illustrate the biophysical principles of deep TMS, to explain the pathophysiological basis for its utilization in each psychiatric disorder (major depression, autism, bipolar depression, auditory hallucinations, negative symptoms of schizophrenia), to summarize the results presented thus far in the international scientific literature regarding the use of deep TMS in psychiatry, its side effects and its effects on cognitive functions.

1. Introduction

Deep transcranial magnetic stimulation (TMS) is a technique of neuromodulation and neurostimulation based on the principle of electromagnetic induction of an electric field in the brain [72]. This field can be of sufficient magnitude and density to depolarize neurons, and when TMS pulses are applied repetitively they can modulate cortical excitability, decreasing or increasing it, depending on the parameters of stimulation [26], even beyond the duration of the train of stimulation. This has behavioural consequences and therapeutic potential.

Deep TMS is used for the treatment of drug-resistant major depressive disorder (MDD) and there are ongoing studies of its use to treat a very wide range of neurological, psychiatric and medical conditions such as Alzheimer's disease, autism, Asperger's disorder, substance addictions, alcoholism, tinnitus, bipolar depression (BPD), post-traumatic stress disorder, migraine, cognitive deficits, Parkinson's disease, multiple sclerosis, neuropathic pain and schizophrenia. Deep TMS is a modification of standard TMS, which was originally invented by Barker et al. in 1985 and has been used from many years for medical and research purposes [2].

Standard TMS is mostly applied with an electromagnetic coil called a figure-of-eight coil (8-coil); deep TMS can be applied with different types of coils: the H-coil [71], the C-core coil [16] and the circular crown coil [18]. Among these, the only coil whose safety and effectiveness has been tested is the H-coil. Therefore it is the only one that has been used in clinical trials and the only one that will be reviewed in this text (Table 1).

Both standard TMS and deep TMS can modulate (positively or negatively) cortical excitability, inducing changes in those neural circuits that are assumed to be dysfunctional. The 8-coil, used in standard TMS is able to modulate cortical excitability up to a maximum depth of 1.5–2.5 cm from the scalp; the H-coil, used in deep TMS, is able to modulate cortical excitability up to a maximum depth of 6 cm [72] and is therefore able, not only to

* Corresponding author. Tel.: +39 3405165865; fax: +39 0649914728.
E-mail address: bersani.fs@tiscali.it (F.S. Bersani).

0924-9338/$ – see front matter © 2012 Elsevier Masson SAS. All rights reserved.
doi:10.1016/j.eurpsy.2012.02.006

modulate the activity of the cerebral cortex, but also the activity of deeper neural circuits.

Considering that treatment with standard TMS has been proved to be moderately effective in treating a wide range of neuropsychiatric diseases [51], it is reasonable to think that the deep TMS might be more effective, because the electromagnetic field generated by this technique can reach deeper brain regions. For this reason, deep TMS is gaining the attention of the global medical community as a possible therapeutic tool in the treatment of numerous pathological conditions.

The aim of this review is to illustrate the biophysical principles of deep TMS, to explain the pathophysiological basis for its utilization in psychiatric disorders, and to summarize the different findings presented thus far in the international scientific literature regarding the use of this therapy in the treatment of psychiatric disorders.

2. Biophysics of deep transcranial magnetic stimulation (TMS)

Biophysics of deep TMS relies on the electrical features of the nervous tissues. In particular, deep TMS functioning obeys Faraday's law of induction, which states that a closed electrical circuit Σ within an enclosed magnetic field B whose flux is time-dependent, will be subject to a variation of the electrical current E induced by the magnetic field itself. This law can be expressed as follows:

$$\oint_{\partial\Sigma} E \cdot ds = -\frac{d\phi_B}{dt} \quad (1)$$

where ϕ_B is the flux of the magnetic field. Equation (1) also shows also that the resulting electrical current propagates in the opposite direction to the variation of the magnetic field flux. In other words, the presence of a dynamic magnetic field leads to either an increase or a decrease in the intensity of the electric current of a closed electrical network. On the other hand, it is also true that an electric current whose intensity varies over time will also induce a second magnetic field. The induced magnetic field will interact with the one in which the electric circuit is immersed and it will be perpendicular to the plane where the enclosed electric circuit lies. Furthermore, the direction of B_{ind} will be uniquely fixed by the direction of propagation of the electrical current.

In agreement with these principles, a time-varying electrical current can thus generate a magnetic field able to change both the intensity and direction of a current propagating through a second electric circuit. In the case of the deep TMS used in neuropsychiatry, the electric circuit yielding a magnetic field is represented by the H-coil applied to the scalp whereas the conductor's subject to the induced electric current are the neuronal streams.

As mentioned before, magnetic stimulation with the 8-coil (standard TMS) has biological effects on the nerve cells within 1.5–2.5 cm from the scalp. Indeed, the induced electromagnetic field substantially decreases in intensity as it approaches deeper regions of the brain. Several studies on the 8-coil found an exponential decay of the electromagnetic signal as a function of the distance from the coil [15,23]. This fact is mainly due to the properties of the cerebral tissue, which acts as a conductor whilst both the air and the skull can be well approximated as insulating. As a consequence, beside the field E_I induced by the 8-coil, a concentration of electric charges on the cranial surface will yield a second field E_B whose direction will be opposite to E_I. Since the total electromagnetic field E_{TOT} will be given by the sum of the two field vectors:

$$E_{TOT} = E_I + E_B \quad (2)$$

it is straightforward to notice the attenuating effect led by E_B. Equation (2) implies also that, in order to stimulate deeper regions of the brain through the 8-coil, a high intensity of electric current would be required. This could lead to serious collateral effects to the facial nerves (e.g. pain, muscle contractions) as well as a high risk of seizure due to an excess of electrical charges on the cranial surface. Furthermore, several studies found that the efficiency

Table 1
Reviewed studies.

Study	Coil	Clinical target	Cortical target	Enrolled patients	Results
Enticott et al. 2011	Haut-coil	Social symptoms of Asperger's disorder	Bilateral medial prefrontal cortex	1	Improvement of self-report ToM scales
Krause et al. 2011	Haut-coil	Cognitive and affective ToM functions	Bilateral medial prefrontal cortex	16	Reduced affective ToM in patients with high empathy and increased affective ToM in patients with low empathy
Rosenberg et al., 2011	H1-coil	Hauditory allucinations of schizophrenia	Left temporo-parietal cortex	8	AHRS improved by 27.8% and SAPS improved by 13.75%
Levkovitz et al., 2011	H1-coil	Negative symptoms of schizophrenia	Left prefrontal dorsolateral cortex	15	SANS scores decreased by 16,82%
Levkovitz et al., 2009	H1-coil H2-coil H1L-coil	Major depressive disorder	Left prefrontal cortex and bilateral prefrontal cortex	65	Better efficacy of the higher intensity treatments. Greater response and remission rates induced by left rather than bilateral stimulation
Rosenberg et al., 2010	H1-coil	Major depressive disorder	Left prefrontal cortex	7	Reduction of more than 50% of HDRS in 3 patients; partial response in 1 patient
Isserles 2011	H1-coil	Major depressive disorder	Left prefrontal cortex	57	Efficacy of treatment in monotherapy; negative emotional directives caused important reductions in antidepressant outcome
Rosenberg et al., 2010	H1-coil	Major depressive disorder	Left prefrontal cortex	6	Reduction of more than 50% of HDRS in 2 patients who previously underwent ECT, including 1 who achieved full remission
Rosenberg et al., 2011	H1-coil	Major depressive disorder	Left prefrontal cortex	8	The magnitude of response in the second deep TMS treatment was smaller than in the first treatment course
Levkovitz et al., 2011	H1-coi H2-coil H1L-coil	Major depressive disorder	Left prefrontal cortex and bilateral prefrontal cortex	54	Deep TMS of the PFC affects both apathy and depression similarly
Harel et al, 2012	H1-coil	Major depressive disorder	Left prefrontal cortex	29	Deep TMS continuation treatment can help maintain an antidepressant effect for 18 weeks
Harel et al., 2011	H1-coil	Bipolar depression	Left prefrontal cortex	19	Reduction of more than 50% of HDRS in 12 patients (63,2%); 10 patients (52,6%) achieved remission
Bersani et al., 2012	H1-coil	Bipolar depression	Left prefrontal cortex	1	Efficacy of continuation of deep TMS treatments in maintaining euthymia

ToM: theory of mind; AHRS: auditory hallucinations rating scale; SAPS: scale for assessment of positive symptoms; HRDS: Hamilton depression rating scale; ECT: electroconvulsive therapy; TMS: transcranial magnetic stimulation.