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Review Article

Evidence Based Practice: Transcranial Magnetic Stimulation for Major Depression

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Abstract: Transcranial Magnetic Stimulation (TMS) is defined as induction of an electrical current within the brain using fluctuating magnetic fields that are generated outside the brain close to scalp. In General, health care providers are interested in providing best health interventions to achieve effective outcomes and reduce unexpected results. This article formulated clinical questions about efficacy of TMS among patients with Major Depressive Disorder (MDD). The clinical question structure (PICOT) facilitates comparing TMS with other alternative interventions such as antidepressants or ECT. According available literature, among MDD patients the TMS is more effective compared to no treatments model. In addition to that, the evidences analysis showed that TMS is more effective than traditional antidepressants among MDD patients during in patient's periods. The literature also indicated that among MDD patients TMS is more effective than Electroconvulsive Therapy (ECT) especially for maintenance therapy during inpatient time.

Keywords: Transcranial Magnetic Stimulation, Major Depression, Electroconvulsive Therapy, Evidence Based Practice

1. Introduction

Mental health problems are international challenges that have significant contribution in illness burden worldwide [1]. Major Depressive Disorder (MDD) was one of common health problems and was estimated to affect 121 million adults worldwide [2]. The MDD currently represents second health problem regarding disability that is caused by illness in the world [2].

The MDD is defined as period of at least two weeks during which there were depressed mood and loss of interest or pleasure in most activities [3]. The MDD is associated with significant morbidity, mortality and disability that load the individual and his/ her family, contributed with impaired cognitive skills and deterioration of individual life aspects [1, 4]. Symptoms of depression include feeling of hopelessness and helplessness, loss energy, anhedonia, agitation, fatigue, withdrawn, weight loss or gain and inappropriate thinking [5].

Since 2000, Majority of published western guidelines have recommendations about all treatment phases of depression. The first line treatment is usually serotonin reuptake inhibitor, psychotherapy, or combination of psychotherapy and pharmacotherapy [6]. Actually, there is no exclusive effective therapy to treat MDD for every patient [4]. However, almost half of patients who are treated from MDD do not attain full remission of their symptoms, and they remain under risk of residual symptoms and relapse [7].

Tusaie & Fitzpatrick classified treatment modalities to psychotherapy, psychopharmacology and somatic therapy such as Electroconvulsive Therapy (ECT), Transcranial Magnetic Stimulation (TMS) and Vagal Nerve Stimulation (VNS) [8]. Specifically, TMS is defined as induction of an electrical current within the brain using fluctuating magnetic fields that are generated outside the brain close to scalp [9]. TMS is magnetic stimulation of the human motor cortex to produce depolarization of cortical areas. It was used before 20years ago as a therapy for MDD [10].

In General, health care providers are interested in providing best health interventions to achieve effective outcomes and

reduce unexpected results. One of most useful method to satisfy the solicitude in health care management is Evidence Based Practice (EBP) technique. EBP is defined as a problem-solving approach to deliver health care practice that is integrated with best evidence from studies, patient care data with clinician expertise, and patient preferences and values [11].

EBP has different level of evidences that reflect methodological rigor of their studies [12]. The level of EBP evidences started from systematic review or meta-analysis which indicates high strength evidence with less susceptible to bias. The low ranking level of EBP is opinion authorities or respected expert committees that is less rigor evidence and more susceptible to bias [12]. Indeed, the satisfied EBP is defined as practices and policies based on updated and most rigorous methodology evidences [13, 12].

2. Methodology

2.1. PICOT Question Form

Implementing EBP technique requires using of PICOT approach to formulate a clinical question. PICOT is defined as a method to formulate a clinical question and direct searching for evidences [14]. Using this format can help us to find best evidences available in a swift and more efficient manner [14]. Furthermore, PICOT question is consistent and systematic way to articulate components of a clinical issue to sustain practice effectively and quickly [11].

It is important to identify structures of a clinical question in terms of PICOT format. PICOT format consist of Population (P), Intervention or issue of interest (I), Comparing intervention or issue of interest (C), Outcome (O), and Time of implementing intervention (T) [11].

2.2. PICOT Question Regarding TMS for Patients with MDD

This article designated a clinical question about efficacy of TMS among patients with MDD. The clinical question structures facilitate comparing TMS with other alternative interventions such as antidepressants or ECT. The PICOT structures are illustrated in Table 1 as listed below.

Table 1. *PICOT format structures about TMS for MDD.*

Components	Clinical Question Elements
P	MDD patients
I	TMS
C	Without TMS or compared to antidepressant or ECT
O	Reducing severity of MDD and enhancing symptoms
T	Hospitalization period

Formulated clinical questions from the former PICOT format include all the following formulas that will be answered by evidences in next steps.

1. Among MDD patients, does the TMS effective in reducing depressive symptoms compared with no TMS during inpatient period?
2. Among MDD patients, does the TMS effective in reducing depressive symptoms compared with antidepressant during inpatient period?
3. Among MDD patients, does the TMS effective in reducing depressive symptoms compared with ECT during inpatient period?

To that end, the purpose of this paper is to answer the formulated PICOT questions that compared the efficacy of TMS with other treatment modality of MDD.

3. Literature Review

3.1. TMS Procedure and Mechanism of Action

In 1985, the TMS was introduced as somatic therapy technique to stimulate the cerebral cortex non-invasively [15]. It was classified as single pulse or repetitive therapy using either high frequency above one hertz for activation of brain cortex, or using low frequency below one hertz for inhibiting cortex [16, 17]. The TMS machine consists of large magnetic equalizer and locally applied coils to induce pulsating waves over located area with organized parameter to set frequencies, duration and thresholds [18, 9]. Clinically, TMS provides useful effect to treat many psychiatric and mental illness such as MDD, auditory hallucinations, and negative symptoms of schizophrenic patients [19, 20].

As stated by Baeken and Raedt, among MDD patients there is a pronounced shift in the homeostasis with diminished activity in the prefrontal cortex (dorsolateral and anterior cingulated) [18]. As a result of this, amygdala increases activity of stress system as loss of negative feedback on hypothalamic-pituitary-adrenal axis. After that the accumulation of cortisol level lead to hyper cortisolemia [18].

Applying TMS on dorsolateral prefrontal cortex suppresses hypothalamic and indirectly increase amygdala hyperactivity. Therefore normalization in the negative feedback system will be produced [18]. Furthermore, the antidepressant mechanism TMS may be reflected as inhibition of hyperactivity in the left temporal cortex and fusiform gyrus, perhaps through augmenting the function of anterior cingulum and the medial prefrontal cortex [21].

TMS enhance cerebral blood flow in the brain and improve oxygenation on multiple cerebral regions [22]. This action improves many cerebral functions without unpleasant changes in other regions of brain because of its focal effect [22]. As well, TMS provides stimulating or inhibitory effect to different functions of multiple brain regions as prefrontal cortex, cingulate gyrus, orbito frontal cortex or deeper limbic regions like the amygdala, insula and hippocampus [17].

3.2. Effectiveness of TMS for MDD Patients

A systematic review study of 29 randomized control trials (RCT) indicated that TMS was effective with 1371 subjects as a monotherapy [23]. The same study showed that TMS using recommended sessions of 8 to 12 over one month is effective in alleviating depressive symptoms and improving cognitive functions with favorable side effects [23]. One more systematic review study was consistent with the conclusion of the previous study and reported that TMS is effective and safe

therapy for MDD [24].

In addition, another systematic review and meta-analysis study of the TMS studies on depression with inclusion criteria included 13 initial studies (324 patients) and five studies for the recent meta-analysis (274 patients), suggested that TMS clinical trials have demonstrated antidepressant effect [25].

However, one systematic review and meta-analysis of RCT study demonstrated opposite conclusion. The study explored 10 RCT including 634 patients were deemed eligible for inclusion in that meta-analysis [26]. The results of the meta-analysis indicated that the clinical effectiveness of bilateral TMS was not significantly greater than that of unilateral TMS, but it was greater than sham TMS in patients with MDD [26]. It is recommended that bilateral TMS may not be a favorable stimulation model for treating MDD patients [26].

In a like manner, a systematic review and meta-analysis of 16 double blind, randomized, sham-controlled trials indicated that the high frequency TMS has only slight antidepressant effect and appears to be fostered by antidepressant medications [27].

In their RCT, Levkovitz and his colleagues have studied the antidepressant and cognitive effects generated by 4 weeks of high-frequency TMS over the prefrontal cortex of 65 medication-free patients with MDD [28]. A significant improvement in depressive symptoms scores was found when high stimulation potency was used with no adverse effect of treatment was observed [28]. The authors concluded that TMS over the prefrontal cortex region was found safe and effective in relieving depression [28]. In addition to that, an additional RCT of daily left prefrontal TMS as a monotherapy of 190 MDD patients found significant clinical antidepressant effect [29].

Not only antidepressant effect but enhancing antidepressant medication effect that what Isserlesa and his colleagues suggested in their RCT [30]. The authors observed depressive level of 57 patients with MDD after TMS sessions, and they concluded that TMS over prefrontal cortex proved to be safe and effective in treating MDD [30]. In contrary, a different RCT study of three compared groups of 41 medication free patients with MDD, suggested that TMS has no antidepressant effects [31].

In less strength evidence, a pilot study investigated the effect of high-frequency TMS on psychomotor retardation and agitation in MDD patients. The study investigated the effect of high frequency TMS on psychomotor retardation and agitation in 30 patients with MDD [32]. The authors found trend in dropping agitation level but not in relieving of retardation. In the same study the results showed no general additional antidepressant effect of TMS was observed [32].

3.3. TMS versus Antidepressants

A further systematic review study indicated that TMS among treatment resistant depressive patients after failed of traditional Antidepressants (AD), such as SSRIs, was effective in reducing depressive symptoms on Hamilton Depression Rating Scale [33]. TMS side effects were less compared to antidepressants drugs in addition to response and adherence that were more efficient in TMS [33]. In the same study, TMS demonstrated safe strategy with less dropout rate compared to traditional antidepressant medications.

Another systematic review study of eight RCT of 263 subjects concluded that TMS on left prefrontal cortex has significant effect on MDD patients, and it is more accepted to them more than traditional antidepressants [34]. Similar, one RCT of total 60 subjects compared TMS to venlafaxine ER among treatment resistant patients [35]. In this study the authors indicated that TMS was effective in improvement Depressive symptoms with little or no side effects compared to venlafaxine ER [35].

In the same way, one more observational study examined 307 patients with MDD concluded that TMS is an effective therapy for patients with MDD who did not respond to initial antidepressant medication [36]. Furthermore, one RCT showed that TMS has effective improvement on depressive level for both alcoholic and nonalcoholic MDD patients without drug interaction that can be seen in antidepressants [37].

3.4. TMS versus Electroconvulsive Therapy (ECT)

ECT defined as the safe induction of a series of generalized epileptic seizures for therapeutic purposes, using brief pulse stimulation techniques under anesthesia and muscle paralysis [38]. A Systematic review study about TMS and ECT for patients with MDD analyzed nine RCT studies of 350 patients. The study indicated that TMS on left or right cortex more effective in reducing of depressive symptoms and enhancing remission and response rate with less side effect than ECT [39].

Another systematic review study of 10 trials with total patients of 425 indicated that TMS had significant advantage on depressive patients in terms of remission, response, and improvement of depressive symptoms similar to ECT [40]. However, in the same study, authors reported that TMS has less side effects intensity than ECT, but ECT is more effective than TMS in short term treatment for psychotic depression [40].

In contrast, one RCT that compared ECT with right cortex TMS for 25 depressive patients has opposite results. The study showed that TMS was less effective than ECT but had lower side effect with MDD patients [41]. Authors also recommended using TMS only for patients who are drug resistant and medically unfit for ECT, and using ECT as first line treatment for life threatening cases [41].

Additionally, Bailine et al. in their RCT concluded that remission rate of ECT users in unipolar and bipolar depression was 60% greater than other drug modalities and TMS [42]. The study also reported that ECT did not induced mania in depressed patients.

3.5. Side Effects and Disadvantage of TMS

Generally, TMS has less or no side effects, compared to antidepressants or other somatic therapy, summarized as localized scalp pain and headache [43, 8]. Moreover, side effects include syncope, transient headache, local pain, neck pain, toothache, paresthesia, transient hearing changes and burns from scalp electrodes [44, 17]. In regard financial

burden, TMS is cost effective therapy that save patients money in contrary to psychopharmacotherapy [45].

Generalized tonic clonic seizure was observed after high frequency TMS therapy sessions in adolescent's depression cases [46, 43, 44]. In addition to that, high frequency TMS for depressive patients may induce hypomanic or manic shifting due to therapy [47, 44]. Specifically, induced hypomanic or manic shifting may associate with patients of ECT- induced mania history [48].

Furthermore, cardiovascular risks were seen in patients treated by TMS therapy, as high blood pressure and tachycardia [31, 49]. There were recommendations to avoid this therapy among patients who have cochlear implants or permanent metal devices to prevent destructions and unpleasant outcomes [44].

4. Discussion

There are many studies of first level of evidences concluded that TMS was effective in reducing symptoms of patients with MDD, prolonged remission and improvement of cognitive functioning. Studies that reported positive outcomes regarding TMS efficacy in MDD summarized in Table 2.

However, as shown in Table 2, some RCT and case control studies reported that TMS had no effect in reducing symptoms of MDD and it has side effects. Hence, the clinical questions, which investigate the efficacy of TMS, could be answered after evaluating all relevant studies.

Table 2. *Efficacy of TMS versus no treatment on MDD patients.*

Study	Objective/ aim	Design	Tool	N	Evidence level	Outcomes
Berlim et al., 2014 [23]	To assess efficacy of TMS on MDD patients	Systematic review	HDRS[1]	29 RCT	Level I	8 to 12 sessions of TMS is effective as monotherapy among depressive patients with less side effects
Gross et al., 2007 [25]	Efficacy of TMS on improvement of MDD symptoms	Systematic review	HDRS & BDI[2]	5 RCT	Level I	10 sessions of TMS had significant improvement on HDRS and BDI scales
Levkovitz et al., 2009 [28]	Effectiveness and safety of TMS in MDD	RCT	HDRS	65	Level II	10 sessions of TMS had several cognitive improvements, no serious adverse events.
Hoeppner et al., 2010 [32]	Efficacy of TMS on psychomotor function in MDD patients	Pilot study	HDRS & BDI	30	Level III	TMS provided enhancement on agitation and retardations
Isserlesa et al., 2011 [30]	Efficacy of TMS in treatment resistant MDD patients	RCT	HDRS	57	Level II	TMS provided effective therapeutic outcome and improved cognition
Zhang et al., 2015 [26]	Effectiveness of TMS on response and remission rate	Systematic review	HDRS	10 RCT	Level I	bilateral TMS may not be a favorable stimulation model for treating MDD patients
Hausmann et al., 2004 [31]	efficacy of TMS on MDD patients	RCT	HDRS	41	Level II	TMS had no significant improvement of HDRS for MDD patients
Ozten et al., 2013 [47]	Effectiveness and adverse events of TMS	Case control	HDRS	4	Level III	It induced mania or hypomania especially with antidepressants
Hu et al., 2011 [46]	Effect and adverse effect of TMS in MDD case	Case control	EEG[3] & HDRS	1	Level III	It induced seizure and with maintenance induced mania

[1]Hamilton Depression Rating Scale (HDRS)
[2]Beck Depression Inventory (BDI)
[3]Electroencephalogram (EEG)

Comparing of efficacy of TMS and traditional antidepressants was summarized in table 3. There are two upper level of evidences support using TMS as effective therapy among MDD patients. However, there are another two RCT studies showed no difference in efficacy between TMS and antidepressants agent, but TMS has less side effects.

Table 3. *Efficacy of TMS compared to antidepressants.*

Study	Objective/ aim	Design	Tool	N	Evidence level	Outcomes
Liu et al., 2014 [33]	comparing efficacy of TMS and traditional antidepressants for MDD patients	Systematic review	HDRS	7 RCT	Level I	TMS is more effective than traditional AD with less side effects
Berlim et al., 2013 [43]	comparing efficacy of TMS and standard AD for MDD patients	Systematic review	HDRS	8 RCT	Level I	TMS more beneficial and effective than standard AD
Rapinesi et al., 2014 [37]	comparing efficacy of TMS and AD for MDD- alcoholic patients	RCT	HDRS	23	Level II	TMS had significant improvement on HDRS as AD without drug interaction
Carpenter et al., 2012 [36]	Efficacy TMS on MDD comparing to advanced AD	RCT	HDRS	307	Level II	TMS effective in reducing depressive symptoms as AD agent but with less side effects
Bares et al., 2009 [35]	Efficacy of TMS compared to venlafaxine on MDD patients	RCT	BDI	60	Level II	TMS similar as venlafaxine in reducing depressive symptoms but with less side effects

Regarding efficacy of TMS and ECT, table 4 illustrates results of two upper level evidences supported TMS over ECT among MDD patients. In table 4, results showed that TMS has less side effect compared to ECT. However, there are only second level of evidences to support using of ECT over TMS especially in sever case and for short periods due to its adverse events.

Table 4. *Efficacy of TMS compared to ECT.*

Study	Objective/ aim	Design	Tool	N	Evidence level	Outcomes
Xie et al., 2013 [39]	comparing efficacy of TMS and ECT for MDD patients	Systematic review	HDRS	9 RCT	Level I	TMS is more effective than ECT in enhancing response and remission rate with less side effects
Ren et al., 2014 [40]	comparing efficacy of TMS and ECT for MDD patients	Systematic review	HDRS	10 RCT	Level I	TMS more effective than ECT with less side effects, they concluded to limit ECT just for short periods and sever suicidal behaviors as urgent action
Hansen et al., 2010 [41]	comparing efficacy of TMS and ECT for MDD patients	RCT	HDRS	25	Level II	TMS less effective than ECT but with less side effects, recommended to use TMS after failed of AD and ECT
Bailine et al., 2010 [42]	Efficacy ECT on MDD compared to AD and TMS	RCT	HDRS	220	Level II	ECT more effective than AD and TMS but had more cognitive side effects limited it to short and urgent cases

Actually, Strength and weakness of previous literature also assist in analyzing data for final decision and conclusion about clinical questions of using TMS among MDD. Table 5 summarized the strength and weakness of studied that have been used in literature review.

Table 5. *Strength and weakness of literature review.*

Study	Strength	Weakness
Systematic Review	-High level of evidence. -Primary resources of data. -Generalized. -Study of Berlim et al. [23] has double blind control, 29 RCT. -Study of Gross et al. [25] uses more specific inclusion criteria. -Study of Berlim et al. [43] compared to more than one type of AD.	-Shortage of test retest periods. -Lack of heterogeneous of quality of life for Berlim et al. [23] -Variation of stimulation process throughout selected studies for Zhang et al. [26] -Placebo effect of some cases as sham groups.
RCT	-Higher level than case control. -Primary resource of data. -Manipulation available. -Generalized. -Study of Carpenter et al. [36] has large sample size. -Study of Levkovitz et al. [28] has short follow up period	-Less than level I of evidence. -Hawthorn effect. -Study of Hausmann et al. [31] is old. -Study of Bailine et al. [42] has augmentation with more than one intervention.
Case control	-Specific case and primary resource of data.	-Least level of available literature. -Non generalized. -Non randomized and small sample.

As we can see in table 6, a comparison between advantage and disadvantage of the TMS according literature review was summarized.

Table 6. *Advantage and disadvantage of TMS.*

Advantage	Disadvantage
-Effective in improvement symptoms of MDD with high evidence practice. -Focal and selective effect. -Has additional effect on cognitive and emotional function. -Less or no drug to drug interaction or with alcohol. -Strengthening patient's adherence. -Can be used as maintenance and long term therapy. -Effective on comorbidity with other psychiatric and physiological illness. -Less serious side effects.	-Has side effect as any therapy. -Less effective in urgent situation. -Costive procedure compared to traditional. -Requires more studies and research for improve outcomes.

After all former summarized studies, the systematic review and RCT studies indicated significant and positive correlation between TMS and symptoms of MDD. Also high level of evidences supported using TMS as effective therapy for MDD patients, and low level of evidences (level II to III) were with negative efficacy. Hence, we can conclude that TMS may be considered as effective therapy among MDD patients compared to no treatment model according to vigorous evidences. That is to say, we answered the first PICOT question with statement of "among MDD patients the TMS is more effective compared to no treatments model".

To answer second PICOT question, the literature review demonstrated that due available high level evidence (level I and II) that support using TMS more than traditional antidepressants, TMS is significantly more effective than antidepressants. Antidepressant has only level II of similar efficacy to TMS and there was no study reported that TMS is less effective than antidepressants. Moreover, the TMS has plus feature as less side effects and drugs interactions therapy compared to antidepressants. In essence, second question can

be answered by stating that "among MDD patients TMS is more effective than traditional antidepressants during in patient's periods".

The last step, there are upper level (I and II) of evidences that confirmed using TMS is more efficient than using of ECT, and has less adverse events. On other hand, there are only second level evidences proved that TMS is less effective than ECT regardless minimum side effects of TMS. Accordingly, the third PICOT question can be answered by "among MDD patients TMS is more effective than ECT especially for maintenance therapy during inpatient time".

5. Recommendations

In the final analysis, TMS is considered effective treatment for MDD patient with low side effects compared to ECT and antidepressants. Many recommendations based on the literature review are stated in to enhance application of TMS therapy among MDD patients.

For instance, to apply TMS as somatic therapy, following steps according Rossi et al. must be performed; consent form must be taken from patient or family on case of uncontrollable, full physiological and medical assessment to patient, past medical and psychological history must be taken by physician, providing electroencephalogram monitor during and after procedure to assure safety and effective threshold of stimulation, reassessing patients vital signs and homeostasis after sessions [44]. Additionally, developing training programs for health care provider may enhance application and caring outcomes of TMS [15].

6. Conclusions

To summarize, TMS has significant efficacy in reducing MDD symptoms as monotherapy as well as less has low side effects according to robust evidences. Likewise, TMS can be used as long term therapy for chronic cases as presented in the literature compared to the other treatment modalities.

However, TMS is more efficient and has low risk rate than traditional antidepressants among MDD patients. As well as TMS is more effective and has low side effects than ECT therapy for MDD patients.

References

[1] Blake, H. (2012). Physical activity and exercise in the treatment of depression. *Frontier Psychiatrist*, *106* (3), 343-352.

[2] World Health Organization. (2012). *Global burden of disease report. Disease prevalence and disability*. Geneva: WHO; Retrieved from www.who.int/mediacentre/events/2012/wha65/journal/en/index4.html

[3] American Psychiatric Association. (2000). *Diagnostic and statistical manual of mental disorder DSM-IV-TR*. (4th Ed.). Washington, DC: Street, NW, Washington, DC.

[4] Nahas, R., & Sheikh, O. (2011). Complementary and alternative medicine for the treatment of major depressive disorder. *Canadian Family Physician*, *57* (1).

[5] Townsend, M. (2011). *Essential of Psychiatric Mental Health Nursing: Concepts of care in evidence-based practice.* (5th Ed.) F. A Davis. Philadelphia.

[6] Gelenberg, A. (2010). A review of the current guidelines for depression treatment. *Journal of Clinical Psychiatry*, 71 (7). DOI: 12.419/0878785.2013.7752.

[7] Solomon, D., Keller, M., Leon, A., Mueller, T., & Lavori, P. (2000). Multiple recurrences of major depressive disorder. *American Journal of Psychiatry*, 57 (2), 229–233.

[8] Tusaie, K. R., & Fitzpatrick, J. J. (2013). Advanced practice psychiatric nursing: Integrating psychotherapy, psychopharmacology, and complementary and alternative approaches. *New York, NY: Springer Pub. Co*.

[9] George, M., & Aston-Jones, G. (2010). Noninvasive techniques for probing neurocircuitry and treating illness: Vagus Nerve Stimulation (VNS), Transcranial Magnetic Stimulation (TMS) and transcranial Direct Current Stimulation (tDCS). *Neuropsychopharmacology, 35,* 301-316.

[10] Eitan, R., & Lerer, B. (2006). Nonpharmacological, somatic treatments of depression: electroconvulsive therapy and novel brain stimulation modalities. *Dialogues Clinical Neuroscience, 8,* 241-258.

[11] Stillwell, S., Fineout-Overholt, E., Melnyk, B., & Williamson, K. (2010). Asking the clinical question: a key step in evidence-based practice. *Advanced Journal of Nursing*, 110 (3), 58-61.

[12] Polit, D. F., & Beck, C. T. (2012). *Nursing research: Generating and Assessing Evidence for Nursing Practice* (9thed.). Philadelphia: Lippincott.

[13] Batista, T. (2010). A Case for Evidence Based Practice. *Columbia Social Work Review*, 1, 45-53.

[14] Stuart, G. (2001). Evidence based psychiatric nursing. *Journal of American Psychiatric Nurses association*, 7, 103.

[15] Najib, U., Bashir, S., Edwards, D., Rotenberg, A., & Pascual-Leone, A. (2011). Transcranial Brain Stimulation: Clinical Applications and Future Directions. *Neurosurg Clin N Am, 22* (2), 233-ix. DOI: 10.1016/j.nec.2011.01.002

[16] Cusin, C., & Dougherty, D. D. (2012). Somatic therapies for treatment-resistant depression: ECT, TMS, VNS, DBS. *Biology of Mood & Anxiety Disorders, 2* (14), 9 pages. Retrieved from: http://www.biolmoodanxietydisord.com/content/2/1/14

[17] Padberg, F., & George, M.S. (2009). Repetitive transcranial magnetic stimulation of the prefrontal cortex in depression. *Experimental Neurology 219*, 2–13. DOI: 10.1016/j.expneurol.2009.04.020

[18] Baeken, C., & Raedt, R. (2011). Neurobiological mechanisms of repetitive transcranial magnetic stimulation on the underlying neurocircuitry in unipolar depression. *Dialogues Clinical Neuroscience, 13*, 140-146.

[19] Bersani, F., Minichino, A., Enticott, P., Mazzarini, L., Khan, N., Antonacci, F., Biondi, M. (2013). Deep transcranial magnetic stimulation as a treatment for psychiatric disorders: A comprehensive review. *European Psychiatry, 28*, 30-39. Retrieved from: http://dx.doi.org/10.1016/j.eurpsy.2012.02.006

[20] Slotema, C., Blom, J., Hoek, H., & Sommer, I. (2010). Should we expand the toolbox of psychiatric treatment methods to include repetitive Transcranial Magnetic Stimulation (rTMS)? meta-analysis of the efficacy of rTMS in psychiatric disorders. *J Clinical Psychiatry, 71* (7), 873-884.

[21] Li, C., Wang, S., Hirvonen, J., Hsieh, J., Bai, Y., Hong, C., Su, T. (2010). Antidepressant mechanism of add-on repetitive transcranial magnetic stimulation in medication-resistant depression using cerebral glucose metabolism. *Journal of Affective Disorders, 127*, 219-229. DOI: 10.1016/j.jad.2010.05.028

[22] Mesquita, R., Faseyitan, O., Turkeltaub, P., Buckley, E., Thomas, A., Kim, A., Hamilton, R. (2013). Blood flow and oxygenation changes due to low-frequency repetitive transcranial magnetic stimulation of the cerebral cortex. *Journal of Biomedical Optics, 18* (6), 067006.

[23] Berlim, M., Eynde, F., Tovar-Perdomo, S., Daskalakis, Z. (2014). Response, remission and drop-out rates following high-frequency repetitive transcranial magnetic stimulation (rTMS) for treating major depression: a systematic review and meta-analysis of randomized, double-blind and sham-controlled trials. *Psychological Medicine,* 44, 225-239. DOI: 10.1017/S0033291713000512

[24] Hovington, C., McGirr, A., Lepage, M., Berlim, M. (2013). Repetitive transcranial magnetic stimulation (rTMS) for treating major depression and schizophrenia: a systematic review of recent meta-analyses. *Annals of Medicine,* 1-14. DOI: 10.3109/07853890.2013.783993

[25] Gross, M., Nakamura, L., Pascual-Leone, A., & Fregni, F. (2007). Has repetitive transcranial magnetic stimulation (rTMS) treatment for depression improved? A systematic review and meta-analysis comparing the recent vs. the earlier rTMS studies. *Acta Psychiatr Scand*, 116, 165-173. DOI: 10.1111/j.1600-0447.2007.01049.x

[26] Zhang, Y., Zhu, D., Zhou, X., Liu, Y., Qin, B., Ren, G., & Xie, P. (2015). Bilateral repetitive transcranial magnetic stimulation for treatment-resistant depression: a systematic review and meta-analysis of randomized controlled trials. *Brazilian Journal of Medical and Biological Research, 48* (3), 198-206. doi: 10.1590/1414-431x20144270

[27] Kedzior, K., Reitz, S., Azorina, V., & Loo, C. (2014). Durability of the antidepressant effect of the high-frequency repetitive transcranial magnetic stimulation (rTMS) in the absence of maintenance treatment in major depression. A systematic review and meta- analysis of 16 double-blind, randomised, sham-controlled trials. *Depression and Anxiety*, 0, 1-11. DOI: 10.1002/da.22339

[28] Levkovitz, Y., Harel, E., Roth, Y., Braw, Y., Most, D., Katz, N., Zangen, A. (2009). Deep transcranial magnetic stimulation over the prefrontal cortex: Evaluation of antidepressant and cognitive effects in depressive patients. *Brain Stimulation, 2*, 188-200. DOI: 10.1016/j.brs.2009.08.002

[29] George, M., Lisanby, S., Avery, D., McDonald, W., Durkalski, V., Pavlicova, M., Anderson, B., Sackeim, H. (2010). Daily Left Prefrontal Transcranial Magnetic Stimulation Therapy for Major Depressive Disorder. *Arch Gen Psychiatry*, 67 (5), 507-516.

[30] Isserles, M., Rosenberg, O., Dannon, P., Levkovitz, Y., Kotler, M., Deutsch, F., Zangen, A. (2011). Cognitive–emotional reactivation during deep transcranial magnetic stimulation over the prefrontal cortex of depressive patients affects antidepressant outcome. *Journal of Affective Disorders, 28*, 235-242.

[31] Hausmann, A., Kemmler, G., Walpoth, M., Mechtcheriakov, S., Kramer-Reinstadler, K., Lechner, T., Conca, A. (2004). No benefit derived from repetitive transcranial magnetic stimulation in depression: a prospective, single centre, randomised, double blind, sham controlled ‘‘add on’’ trial. *J Neurol Neurosurg Psychiatry, 75*, 320-322.

[32] Hoeppner, J., Padberg, F., Domes, G., Zinke, A., Herpertz, S., GroBheinrich, N., & Herwig, U. (2010). Influence of repetitive transcranial magnetic stimulation on psychomotor symptoms in major depression. *European Arch Psychiatry Clinical Neuroscience, 13*, 1-6.

[33] Liu, B., Zhang, Y., Zhang, L., & Li, L. (2014). Repetitive transcranial magnetic stimulation as an augmentative strategy for treatment-resistant depression, a meta-analysis of randomized, double-blind and sham-controlled study. *BMC Psychiatry*, 14 (342), 1-9. Retrieved from: http://www.biomedcentral.com/1471-244X/14/342

[34] Berlim, M., Eynde, F., & Daskalakis, Z. (2013). Clinically meaningful efficacy and acceptability of low-frequency repetitive transcranial magnetic stimulation (rTMS) for treating primary major depression: a meta-analysis of randomized, double-blind and sham-controlled trials. *Neuropsychopharmacology*, 38, 543-551.

[35] Bares, M., Kopecek, M., Novak, T., Stopkova, P., Sos, P., Kozeny, J., Hoschl, C. (2009). Low frequency (1-Hz), right prefrontal repetitive transcranial magnetic stimulation (rTMS) compared with venlafaxine ER in the treatment of resistant depression: A double-blind, single-centre, randomized study. *Journal of Affective Disorders, 118*, 94-100. DOI: 10.1016/j.jad.2009.01.032

[36] Carpenter, L., Philip, J., Aaronson, S., Boyadjis, T., Brock, D., Cook, I., Dunner, D., Demitrack, M. (2012). Transcranial magnetic stimulation for major depression: a multisite, naturalistic observational study of acute treatment outcomes and clinical practice. *Depression and Anxiety,* 29, 587-596.

[37] Rapinesi, C., Curto, M., Kotzalidis, G., Casale, A., Serata, D., Ferri, V., Pietro, S., Girardi, P. (2014). Antidepressant effectiveness of deep Transcranial Magnetic Stimulation (dTMS) in patients with Major Depressive Disorder (MDD) with or without Alcohol Use Disorders (AUDs): A 6-month, open label, follow-up study. Journal of Affective Disorders, 11 (15), 42-49. Retrieved from: http://dx.doi.org/10.1016/j.jad.2014.11.015

[38] Baghai, T., & Moller, H. (2008). Electroconvulsive Therapy and its Different Indications. *Dialogues Clinical Neuroscience, 10,* 105-117.

[39] Xie, J., Chen, J., & Wei, Q. (2013). Repetitive transcranial magnetic stimulation versus electroconvulsive therapy for major depression: a meta-analysis of stimulus parameter effects. *Journal of ECT,* 35 (10), 1084-1091.

[40] Ren, J., Li, H., Palaniyappan, L., Liu, H., Wang, H., Li, C., & Rossini, P. (2014). Repetitive transcranial magnetic stimulation versus electroconvulsive therapy for major depression: A systematic review and meta-analysis. *Progress in Neuro-Psychopharmacology & Biological Psychiatry,* 51, 181-189.

[41] Hansen, P., Ravnkilde, B., Videbech, P., Clemmensen, K., Sturlason, R., Reiner, M., Parner, E., & Vestergaard, P. (2010). Low-frequency repetitive transcranial magnetic stimulation inferior to electroconvulsive therapy in treating depression. *Journal of ECT*, *27* (1), 26-32. doi: 10.1097/YCT.0b013e3181d77645

[42] Bailine, S., Fink, M., Knapp, R., Petrides, G., Husain, M., Rasmussen, K., Kellner CH. (2010). Electroconvulsive Therapy is Equally Effective in Unipolar and Bipolar Depression. *Acta Psychiatric Scandinavia, 121*, 431-436. DOI: 10.1111/j.1600-0447.2009.01493.x

[43] George, M. (2010). Transcranial magnetic stimulation for the treatment of depression. *Expert Rev. Neurother, 10* (11), 1761-1772.

[44] Rossi, S., Hallett, M., Rossini, P., Pascual-Leone, A., & The Safety of TMS Consensus Group (2009). Safety, ethical considerations, and application guidelines for the use of transcranial magnetic stimulation in clinical practice and research. *Clinical Neurophysiology, 120* (12), 2008-2039. DOI: 10.1016/j.clinph.2009.08.016

[45] Simpson, K., Welch, M., Kozel, F., Demitrack, M., & Nahas, Z. (2009). Cost-effectiveness of transcranial magnetic stimulation in the treatment of major depression: A health economics analysis. *Adv Therapy, 26* (3), 346-368. DOI 10.1007/s12325-009-0013-x

[46] Hu, S., Wang, S., Zhang, M., Wang, J., Hu, J., Huang, M., Xu, Y. (2011). Repetitive transcranial magnetic stimulation- induced seizure of a patient with adolescent onset depression: a case report and literature review. *Journal of International Medical Research, 39*, 2039-2044.

[47] Ozten, E., Sayar, G., & Karamustafalioglu, O. (2013). Hypomanic shift observed during rTMS treatment of patients with unipolar depressive disorder: four case reports. *Annals of General Psychiatry, 12* (12), 1-5. Retrieved from: http://www.annals-general-psychiatry.com/content/12/1/12

[48] Philip, N., & Carpenter, S. (2013). Repetitive transcranial magnetic stimulation induced hypomanic symptoms in a woman with a history of electroconvulsive therapy induced mania: a case report. *F1000 Research, 2* (284), 1-4. DOI: 10.12688/f1000research.2-284.v1

[49] Sampaio, L., Fraguas, R., Lotufo, P., Bensenor, I., & Brunoni, A. (2012). A systematic review of non-invasive brain stimulation therapies and cardiovascular risk: implications for the treatment of major depressive disorder. *Frontiers in Psychiatry, 3* (87), 1-8.