Transcranial magnetic stimulation modalities for psychiatric disorders: Publication trends from 1985 to 2019

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Abstract
Aim: Transcranial magnetic stimulation (TMS) is a noninvasive brain stimulation technique that shows potential for treating psychiatric disorders. Although several studies have sought to investigate new TMS modalities for the treatment of various psychiatric disorders, no study has yet examined publication trends in research on TMS modalities for psychiatric disorders. This study investigated publication trends in TMS research for 13 psychiatric disorders, including addiction, dementia, major depressive disorder (MDD), and obsessive-compulsive disorder (OCD), and schizophrenia, as well as 9 TMS modalities, including bilateral stimulation, deep TMS, high-frequency stimulation, low-frequency stimulation, and theta burst stimulation.

Methods: Articles published in PubMed from 1985 to 2019 were searched to determine the number of published articles for each year in each category using the “Results by year” tool from the PubMed database.

Results: Over the past 30 years, an increasing number of articles were published regarding TMS research for the treatment of MDD, addiction, and dementia, which were among those most commonly investigated psychiatric disorders, whereas the number of articles addressing schizophrenia and OCD treated via TMS remained steady since 2015. Regarding TMS modalities, previous high-frequency stimulation, low-frequency stimulation, and bilateral stimulation were the most common topics, with research regarding deep TMS and theta burst stimulation having increased since 2000 and 2005, respectively.

Conclusion: TMS applications are rapidly developing and becoming increasingly ubiquitous in various psychiatric disorders. Determining publication trends in TMS research can be a useful method for monitoring TMS research interests and applications of new TMS modalities for psychiatric disorders.

KEYWORDS
major depressive disorder, psychiatric disorder, research publication trends, transcranial magnetic stimulation, transcranial magnetic stimulation modality
1 | INTRODUCTION

Transcranial magnetic stimulation (TMS) is a noninvasive brain stimulation technique that can modulate the excitability of specific brain areas. In 1985, Barker and colleagues developed the first TMS device and showed a motor evoked potential response by applying electrical stimulation to the motor cortex. Since then, TMS has been used to investigate the pathophysiology of several neuropsychiatric disorders, with studies suggesting its potential for use as a treatment for these disorders.

In 2008, the US Food and Drug Administration (FDA) approved the first repetitive TMS (rTMS) device for the treatment of major depressive disorder (MDD) in patients who had experienced poor response to at least one pharmacologic agent for the current episode. Currently, the standard TMS protocol for MDD consists of applying a 120% resting motor threshold with 10 Hz over the left dorsolateral prefrontal cortex (DLPFC). The treatment sessions delivered a total of 3000 pulses per day over a 5-day period for 4-6 weeks.

The use of deep TMS with an H7-coil for the treatment of obsessive-compulsive disorder (OCD) received FDA approval in 2018. Within the same year, intermittent theta burst stimulation (TBS) had been approved for the treatment of MDD, which could be attributed primarily to research regarding TMS for various psychiatric disorders and TMS modalities that had been conducted for decades. To date, however, only two studies have investigated TMS trends using bibliometric analysis, although several studies have examined publication trends in TMS research for psychiatric disorders and stimulation modalities. Therefore, the current study aimed to identify and analyze published TMS articles regarding psychiatric disorders and stimulation modalities from the PubMed database from 1985 to 2019. In this study, TMS modalities were defined as stimulation pattern, coil, and treatment schedule and did not include stimulation target site, intensity, device, total pulses per session, and so forth.

2 | MATERIALS AND METHODS

Publication trends in TMS research on 13 psychiatric disorders and 9 TMS modalities were investigated as listed in Table 1. In February 2020, a comprehensive search was conducted on the PubMed database to identify TMS articles published from 1985 to 2019, with the following search strategy:

- The “Results by year” PubMed database tool was used to determine the number of publications in a given year.
- Any available manuscript type, such as research article, review article, short report and letters, and case studies, was retrieved.
- No language restrictions were used.
- Analyses neither investigated unpublished TMS research nor excluded duplicate articles.
- Main key words were (“transcranial magnetic stimulation” OR TMS) AND psychiatric disorders AND TMS modalities.
- Key words searched for the 13 psychiatric disorders as follows:

  1. addiction
  2. anxiety
  3. attention deficit hyperactivity disorder
  4. autism spectrum disorder
  5. bipolar depression
  6. bipolar mania
  7. dementia
  8. eating disorder
  9. gambling disorder
  10. major depressive disorder
  11. obsessive-compulsive disorder
  12. post-traumatic stress disorder
  13. schizophrenia

- Key words searched for the 9 TMS modalities as follows:

  1. accelerated
  2. bilateral
  3. deep TMS
  4. high-frequency stimulation
  5. low-frequency stimulation
  6. priming
  7. quadripulse stimulation
  8. synchronized
  9. theta burst stimulation
  10. priming stimulation
  11. quadripulse stimulation
  12. theta burst stimulation

3 | RESULTS

Publication trends in TMS research showed a gradual increase in the number of articles from 1985 to 2000s but a rapidly increase in number of articles thereafter (Figure 1). Almost 1800 articles regarding the use of TMS modalities in psychiatric disorders were
published in 2019 alone. This trend is expected to continue given that TMS has been used for various neurologic and psychiatric diseases and will reach approximately 2000 TMS research articles in the near future.

As shown in Figure 2, the number of articles published for MDD, addiction, and dementia research using TMS modalities showed an increasing trend throughout the past 20 years. In particular, MDD was the most common topic in TMS research on psychiatric disorders. In contrast, the number of articles published for schizophrenia and OCD research using TMS have remained steady since 2015 (Figure S1, the top five psychiatric disorders with published articles on TMS research).

Over the past decades, the most commonly researched TMS modalities included high-frequency stimulation, followed low-frequency stimulation and bilateral stimulation (Figure 3). The number of publications on deep TMS has been increasing since 2000, and those on TBS have been increasing since 2005 (Figure S2, the top five TMS modalities with published articles on TMS research).

Most publications on TMS modalities for MDD from 2010 to 2014 involved high-frequency and low-frequency stimulation (Figure 4). Since 2015, the number of publications on deep TMS and TBS has been increasing. In contrast, the number of publications on low-frequency stimulation showed a decreasing trend. Other trends in the publication of research regarding TMS modalities for psychiatric disorders are described in the Supplementary information (Figure S3).

4 | DISCUSSION

To the best of our knowledge, this study has been the first to determine publication trends in TMS research for psychiatric disorders and stimulation modalities. Our findings showed that published articles on TMS modalities for the treatment of psychiatric disorders have increased year after year. Moreover, a trend toward increasing publication in TMS research and psychiatric disorders had been observed for MDD, addiction, and dementia. In particular, the publication of research on new TMS modalities, such as deep TMS and TBS, for MDD had shown a 5-year increasing trend since 2015.

The most widespread mental illness is MDD, which causes a substantial disease burden.\textsuperscript{8,9} Several studies have shown that approximately 33% of patients did not achieve remission with treatment, including pharmacologic and psychologic therapies.\textsuperscript{10} Thus, TMS research has continued to be conducted in order to identify possible alternative treatments for patients with treatment-resistant depression. Similarly, the number of patients with addiction and dementia has been increasing rapidly worldwide and is becoming a serious public health threat.\textsuperscript{11,12} Nevertheless, an effective treatment has yet to be established for either disease. Therefore, there is a public health need to further develop TMS as a novel protocol with modalities for MDD, addiction, and dementia.

A limitation of conventional TMS is the temporal constraint for patients. For instance, the typical 10-Hz high-frequency stimulation protocol for MDD lasts for approximately 37.5 minutes per session, 5 days a week for 20-30 sessions.\textsuperscript{4,5} In contrast, originally intermittent TBS is a newer and shorter protocol that can reduce treatment time to just 3 minutes per session, 5 days a week for 20-30 sessions. Moreover, a clinical trial showed that intermittent TBS was not inferior to 10-Hz high-frequency stimulation in terms of managing treatment-resistant depression.\textsuperscript{13} Moreover, the use of deep TMS, a next-generation stimulator using an H coil, has been studied in various clinical applications.\textsuperscript{3} The H coil can stimulate deeper and broader regions compared to the standard rTMS using a figure-8 coil.\textsuperscript{14} The H1-coil used for stimulating the left DLPFC has been approved by the FDA for clinical use and has been proven efficacious for the treatment of adults with late-life depression among whom different stimulation intensities are needed to address age-related functional changes in the prefrontal cortex,\textsuperscript{15} thereby optimizing new TMS modalities.

Recently, publication trends have been shifting toward TMS for MDD, with more articles on deep TMS and TBS involving low-frequency stimulation emerging since 2015. These results may be attributed to the FDA approval obtained by device and protocol for MDD. Similarly, the number of published articles for OCD had been
increasing since 2015. Thus, the timing of the TMS devices and protocols (four for MDD and one for OCD) approved by the FDA certainly had an impact on the publication trends in TMS research for psychiatric disorders.

This study has several limitations warranting discussion. First, the primary limitation of this study is that the literature search was based on only one database. Nonetheless, PubMed is the most comprehensive search engine for life sciences and biomedical publications and should therefore aggregate most of the published articles on TMS. Another limitation was that the analyses neither investigated unpublished TMS research nor excluded duplicate articles; however, this lack of analysis was considered to have had little effect on publication trends in TMS research.

5 | CONCLUSIONS

The current study showed an increasing trend in the publication of research on the use of TMS modalities for the treatment of psychiatric disorders.
psychiatric disorders from 1985 to 2019. Moreover, studied on the optimization of new TMS modalities for use in psychiatric disorders have been available. Publication trends in TMS research can be useful to monitor TMS research interests and applications of new TMS modalities to psychiatric disorders. We expected that TMS research in psychiatric disorders will continue to grow as modalities develop further. Nevertheless, further qualitative systematic reviews on TMS modalities for psychiatric disorders are needed.

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AUTHOR CONTRIBUTIONS
YM and SK have full access to all of the data in the study and bear responsibility for the integrity of the data and the accuracy of the data analysis. All authors approved the final manuscript. Study concept and design: YM and SK. Analysis and interpretation of data: YM, SK, and RY. Acquisition of data: YM and RY. Drafting of the manuscript: All authors. Study supervision: MS.

APPROVAL OF THE RESEARCH PROTOCOL BY AN INSTITUTIONAL REVIEW BOARD/ INFORMED CONSENT
Given that this study investigated publication trends, no ethics committee approval and informed consent was needed.

DATA AVAILABILITY STATEMENT
Data sharing not applicable to this article.

REFERENCES
1. Ridding MC, Rothwell JC. Is there a future for therapeutic use of transcranial magnetic stimulation? Nat Rev Neurosci. 2007;8(7):559–67.
2. Barker AT, Jalinous R, Freeston IL. Non-invasive magnetic stimulation of human motor cortex. Lancet (London, England). 1985;1(8437):1106–7.
3. Lefaucheur JP, Aleman A, Baeken C, Benninger DH, Brunelin J, Di Lazzaro V, et al. Evidence-based guidelines on the therapeutic use of repetitive transcranial magnetic stimulation (rTMS): an update (2014–2018). Clin Neurophysiol. 2020;131(2):474–528.
4. George MS, Lisanby SH, Avery D, McDonald WM, Durkalski V, Pavlicova M, et al. Daily left prefrontal transcranial magnetic stimulation therapy for major depressive disorder: a sham-controlled randomized trial. Arch Gen Psychiat. 2010;67(5):507–16.
5. O’Reardon JP, Solvason HB, Janicak PG, Sampson S, Isenberg KE, Nahas Z, et al. Efficacy and safety of transcranial magnetic stimulation in the acute treatment of major depression: a multisite randomized controlled trial. Biol Psychiat. 2007;62(11):1208–16.
6. Lawson McLean A. Publication trends in transcranial magnetic stimulation: a 30-year panorama. Brain Stimul. 2019;12(3):619–27.
7. Zheng KY, Dai GY, Lan Y, Wang XQ. Trends of repetitive transcranial magnetic stimulation from 2009 to 2018: a bibliometric analysis. Front Neurosci-Switz. 2020;14:106.
8. Murray CJL, Barber RM, Foreman KJ, Ozgoren AA, Abd-Allah F, Abraha SF, et al. Global, regional, and national disability-adjusted life years (DALYs) for 363 diseases and injuries and healthy life expectancy (HALE) for 188 countries, 1990–2013: quantifying the epidemiological transition. Lancet (London, England). 2015;386(10009):2145–91.
9. Kessler RC, Berglund P, Demler O, Jin R, Koretz D, Merikangas KR, et al. The epidemiology of major depressive disorder: results from the National Comorbidity Survey Replication (NCS-R). JAMA. 2003;289(23):3095–105.
10. Rush AJ, Trivedi MH, Wisniewski SR, Nierenberg AA, Stewart JW, Warden D, et al. Acute and longer-term outcomes in depressed outpatients requiring one or several treatment steps: a STAR*D report. Am J Psychiat. 2006;163(11):1905–17.
11. Khalili M, Rahimi-Movaghar A, Shadloo B, Mojtahabi R, Mann K, Amin-Esmaeili M. Global scientific production on illicit drug addiction: a two-decade analysis. Eur Addict Res. 2018;24(2):60–70.
12. Nichols E, Szeke CEI, Vollset SE, Abbasi N, Abd-Allah F, Abdela J, et al. Global, regional, and national burden of Alzheimer’s disease and other dementias, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet Neurol. 2019;18(1):88–106.

13. Blumberger DM, Vila-Rodriguez F, Thorpe KE, Feffer K, Noda Y, Giacobbe P, et al. Effectiveness of theta burst versus high-frequency repetitive transcranial magnetic stimulation in patients with depression (THREE-D): a randomised non-inferiority trial. Lancet (London, England). 2018;391(10131):1683–92.

14. Roth Y, Amir A, Levkovitz Y, Zangen A. Three-dimensional distribution of the electric field induced in the brain by transcranial magnetic stimulation using figure-8 and deep H-coils. J Clin Neurophysiol. 2007;24(1):31–8.

15. Kaster TS, Daskalakis ZJ, Noda Y, Knyahnytska Y, Downar J, Rajji TK, et al. Efficacy, tolerability, and cognitive effects of deep transcranial magnetic stimulation for late-life depression: a prospective randomized controlled trial. Neuropsychopharmacol. 2018;43(11):2231–8.

SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher’s website.

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