MICRO REPORT

NEUROPSYCHOPHARMACOLOGY
REPORTS

WILEY

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.[1] In 1985, Barker and colleagues developed the first TMS device[2] 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.[3]

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.[4,5]

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.[3] To date, however, only two studies have investigated TMS trends using bibliometric analysis,[6,7] 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 were as follows:

TABLE 1 Psychiatric disorders and transcranial magnetic stimulation (TMS) modalities included in this study

Psychiatric disorder	TMS modality
Addiction/Substance abuse	Accelerated TMS
Anxiety disorder	Bilateral stimulation
Attention deficit hyperactivity disorder	Deep TMS
Autism spectrum disorder	High-frequency stimulation
Bipolar depression	Low-frequency stimulation
Bipolar mania	Priming stimulation
Dementia	Quadripulse stimulation
Eating disorder	Synchronized TMS
Gambling disorder	Theta burst stimulation
Major depressive disorder	
Obsessive-compulsive disorder	
Post-traumatic stress disorder	
Schizophrenia	

1. (addiction OR "substance abuse" OR craving OR alcohol OR nicotine OR methamphetamine)
2. ("anxiety disorder" OR "generalized anxiety disorder" OR GAD OR "social anxiety disorder" OR SAD OR "panic disorder")
3. ("attention deficit hyperactivity disorder" OR ADHD)
4. ("autism spectrum disorder" OR ASD)
5. ("bipolar depression" OR "bipolar depressive episode")
6. ("bipolar mania" OR "bipolar manic episode")
7. (dementia OR "mild cognitive impairment" OR MCI OR "Alzheimer's disease")
8. ("eating disorder" OR "anorexia nervosa" OR "bulimia nervosa")
9. "gambling disorder"
10. ("major depressive disorder" OR MDD)
11. ("obsessive-compulsive disorder" OR OCD)
12. ("post-traumatic stress disorder" OR PTSD)
13. schizophrenia

- Key words searched for the 9 TMS modalities were as follows:
  1. accelerated
  2. bilateral
  3. (deep OR "H coil")
  4. ("high frequency" OR "rapid rate")
  5. ("low frequency" OR "slow rate")
  6. priming
  7. ("quadripulse stimulation" OR QPS)
  8. synchronized
  9. ("theta burst" OR "θ burst" OR TBS)

3 | RESULTS

Publication trends in TMS research showed a gradual increased 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.[8,9] Several studies have shown that approximately 33% of patients did not achieve remission with treatment, including pharmacologic and psychologic therapies.[10] Thus, TMS research has continued to be been 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.[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.[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.[13] Moreover, the use of deep TMS, a next-generation stimulator using an H coil, has been studied in various clinical applications.[3] The H coil can stimulate deeper and broader regions compared to the standard rTMS using a figure-8 coil.[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,[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
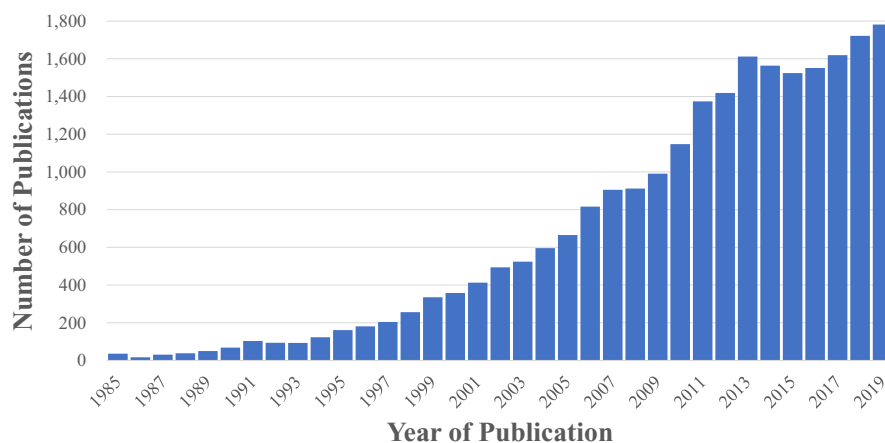

FIGURE 1 Overview of publication trends in transcranial magnetic stimulation (TMS) from 1985 to 2019. The published TMS articles have been increasing steadily as evidence by the upward curve
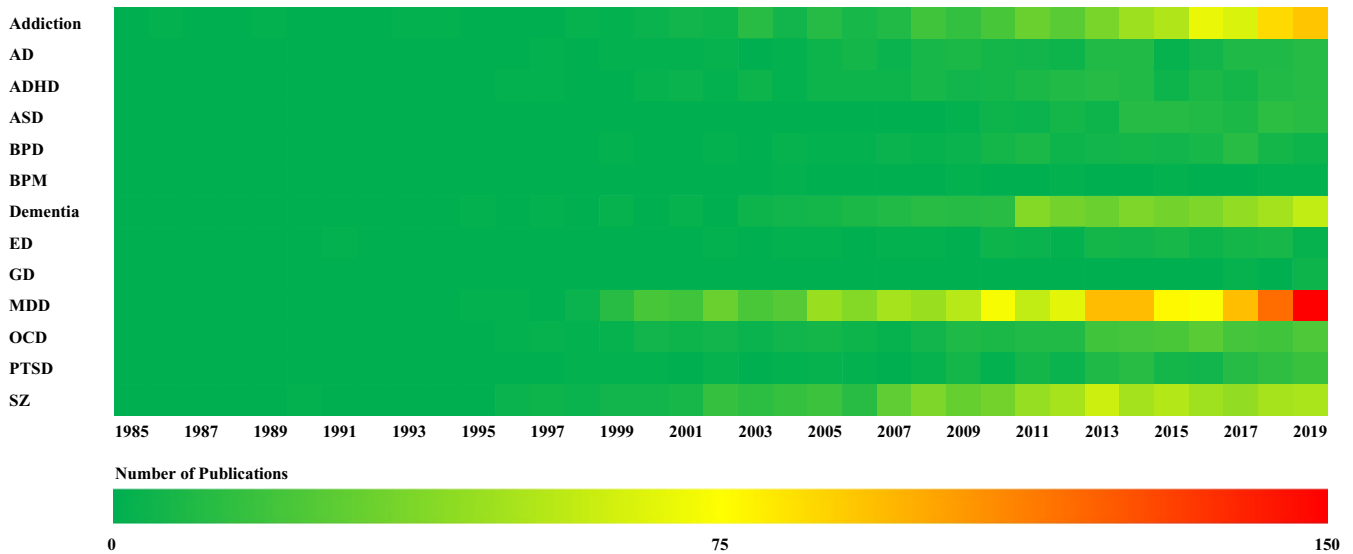
FIGURE 2 Publication trends in transcranial magnetic stimulation (TMS) for psychiatric disorders. AD, anxiety disorder; ADHD, attention deficit hyperactivity disorder; ASD, autism spectrum disorder; BPD, bipolar depression; BPM, bipolar mania; ED, eating disorder; GD, gambling disorder; MDD, major depressive disorder; OCD, obsessive-compulsive disorder; PTSD, post-traumatic stress disorder; SZ, schizophrenia
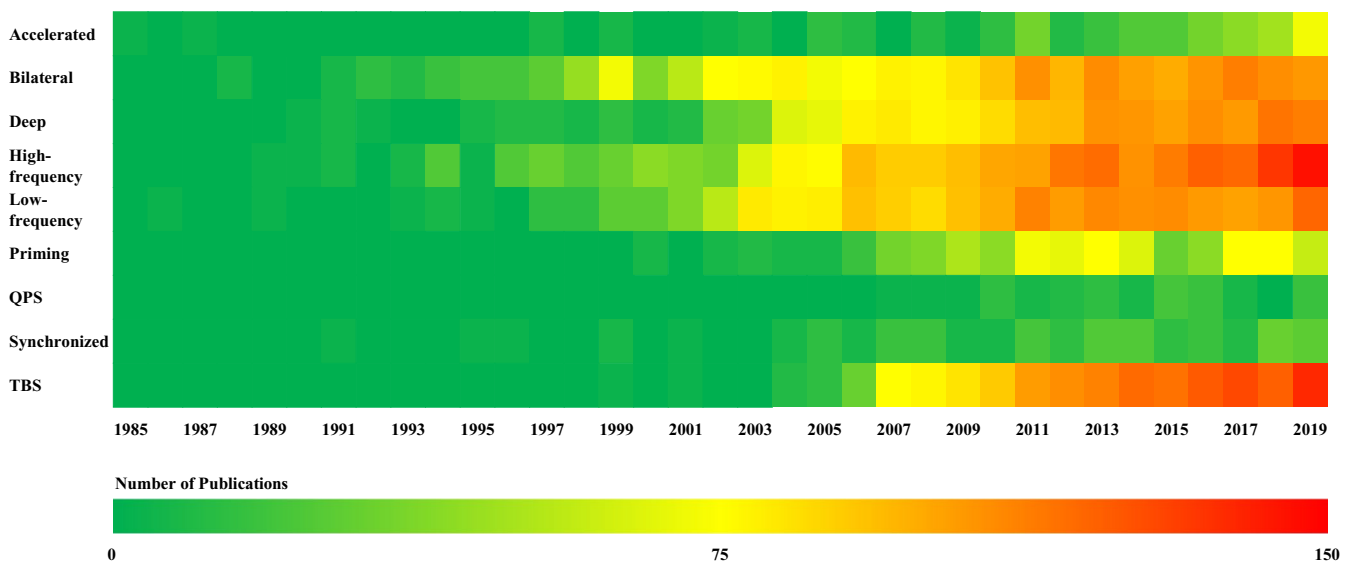

FIGURE 3 Publication trends related to transcranial magnetic stimulation (TMS) modalities. QPS, quadripulse stimulation; TBS, theta burst stimulation

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
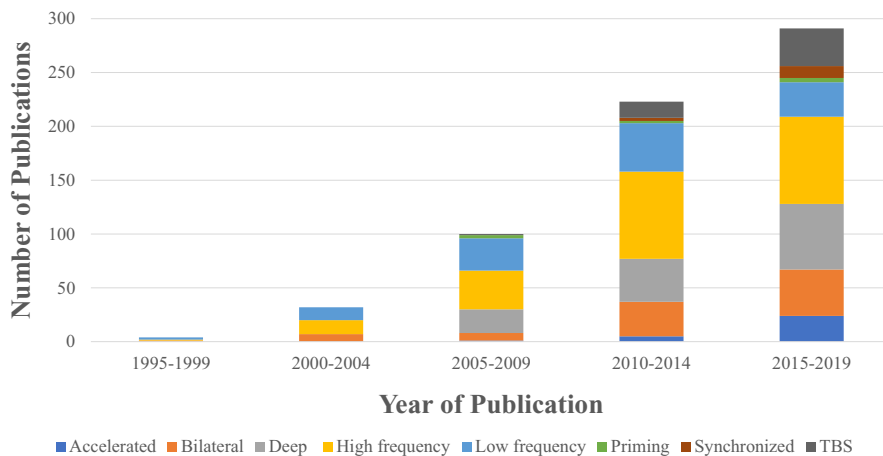
FIGURE 4 Publication trends of transcranial magnetic stimulation (TMS) modalities for major depressive disorder. TBS, theta burst stimulation

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.

CONFLICT OF INTEREST

SK reports research grants, speaking fees, or advisory board work with Century Medical, Inter-Riha, and Teijin Pharma. RY reports personal fee from Inter-Riha, outside the submitted work. The other authors have no financial disclosures or conflicts of interest to report.

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.

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SUPPORTING INFORMATION

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