

Review Article

Digital Therapeutics for Migraine: Core Categories, Clinical Evidence, and Future Perspectives

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Abstract

Research Background: Migraine is one of the most common neurological disorders worldwide, with a prevalence of approximately 14–15%, and ranks second in terms of disability burden. Traditional pharmacological treatments face limitations in efficacy, adverse effects, and high costs, driving an increasing demand for non-pharmacological interventions. As evidence-based, software-driven therapeutic approaches, digital therapeutics offer a new direction for migraine management. **Research Objectives and Methods:** This study aims to systematically review the core categories, clinical evidence, and future development directions of digital therapies for migraine. A scoping review methodology was employed, with a literature search conducted in PubMed, Embase, and IEEE Xplore databases from 2018 to March 2026. Qualitative analysis of 48 articles was performed in accordance with the PRISMA-ScR guidelines. The study identified four major categories of digital therapeutics: digital cognitive behavioral therapy, digital neurostimulation technology, smart monitoring and early warning systems, and virtual reality combined with biofeedback therapy. Clinical evidence indicates that these interventions can effectively reduce headache frequency and improve comorbid symptoms such as anxiety and insomnia; however, limitations include methodological heterogeneity and varying evidence quality. **Conclusion:** It was concluded that digital therapies are an important component of comprehensive migraine management. Future efforts should focus on conducting large-scale, long-term randomized controlled trials to accumulate high-quality evidence, while simultaneously refining regulatory frameworks and developing personalized closed-loop adaptive systems, with the aim of providing better treatment options for hundreds of millions of patients worldwide.

Keywords

Migraine, Digital Therapy, Cognitive Behavioral Therapy, Neuromodulation, Artificial Intelligence

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1. Introduction

1.1. The Burden of Migraine and Challenges in Treatment

Migraine is one of the most common neurological disorders worldwide, imposing a heavy disease burden on patients and society. According to a review by Steiner and Stovner published in *Nature Reviews Neurology* in 2023, the global prevalence of migraine is approximately 14-15%, accounting for 4.9% of the global disease burden [1]. Research by Ashina et al. further indicates that approximately 1.1 billion people worldwide suffer from migraine, making it the second leading cause of disability [2].

An analysis by Safiri et al. based on the 2019 Global Burden of Disease database shows that the age-standardized prevalence of migraine is approximately 14, 107.3 per 100, 000 people, with a significantly higher prevalence among women than men (the male-to-female ratio is approximately 1: 3) [3]. Chronic migraine (CM), the most severe form within the migraine spectrum, affects approximately 1.4%-2.2% of the global population. Patients experience headaches on more than 15 days per month, severely impacting their quality of life [4].

Although significant progress has been made in acute treatments such as triptans and preventive medications like CGRP antagonists, a substantial proportion of patients still respond poorly to drug therapy or are unable to use medications due to contraindications, adverse reactions, or other reasons. Furthermore, the high cost and limited accessibility of drug treatments restrict their application in resource-limited regions. These treatment challenges have created an urgent need for non-pharmacological interventions, leading to the emergence of digital therapeutics (DTx).

1.2. Definition and Background of Digital Therapeutics

Digital therapeutics refer to treatment modalities that provide medical interventions through software programs based on evidence-based medicine. Hong et al. define them as “evidence-based therapeutic interventions driven by high-quality software programs for the prevention, management, or treatment of medical conditions or disorders” [5]. Unlike general health apps, Wang et al. further note that digital therapeutics must undergo rigorous clinical validation and regulatory approval processes [6].

The U.S. FDA has established a regulatory framework for digital therapeutics and has approved several digital therapeutic products for chronic pain and neurological disorders. Watson et al. note that the FDA is advancing the refinement of the digital therapeutics regulatory framework through the Pre-Cert Program and the Digital Health Centers of Excellence (DHCoE) [7]. Patel and Butte, meanwhile, highlight the unique challenges facing the clinical development of digital

therapeutics, including the need to balance rapid iteration with rigorous clinical trials [8].

1.3. Search Strategy and Eligibility Criteria

This scoping review was conducted to map the existing literature on digital therapeutics for migraine, identify research gaps, and guide future studies. Unlike systematic reviews, scoping reviews do not assess evidence quality or synthesize effect sizes, but rather provide a broad overview of the field.

We conducted a comprehensive literature search in PubMed, Embase, and IEEE Xplore databases from January 2018 to March 2026. Search terms included: ("digital therapeutics" OR "digital health" OR "mobile health" OR "mHealth") AND ("migraine" OR "headache"). Inclusion criteria were: (1) peer-reviewed articles on digital interventions for migraine; (2) published in English; (3) clinical studies, systematic reviews, or regulatory documents. Exclusion criteria were: case reports with <10 participants, non-clinical technical papers, and conference abstracts without full-text. A total of 215 articles were identified, of which 48 were included for qualitative synthesis. This review follows the PRISMA-ScR (Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews) guidelines.

2. Core Classification and Mechanisms of Digital Therapies for Migraines

2.1. Digital Cognitive Behavioral Therapy (dCBT) —Modulating Pain-related Cognitions and Emotions

Cognitive Behavioral Therapy (CBT) is the first-line behavioral treatment for migraine, supported by Grade A evidence. A study by Bae et al. demonstrated that CBT significantly reduces the frequency and severity of headaches in migraine patients [9].

Digital Cognitive Behavioral Therapy (dCBT) digitizes traditional CBT programs through mobile applications and internet platforms. Stubberud and Linde noted that the application of dCBT in migraine treatment includes modules such as relaxation training, stress management, sleep hygiene education, and cognitive restructuring [10]. A study by Minen et al. demonstrated that smartphone-based behavioral therapy for migraine has good feasibility and patient acceptance [11].

A study by Crawford et al. explored the application of digital cognitive behavioral therapy for insomnia (dCBT-I) in women with chronic migraine, finding that the therapy not only improved sleep quality but also reduced the frequency of migraine attacks [12]. Huang et al. further confirmed that digital CBT is as effective as face-to-face CBT in reducing the frequency of migraine attacks [13].

A randomized clinical trial published by Pach et al. evaluated the impact of a prescription digital health app on the number of migraine days. The results showed a significant reduction in migraine days in the intervention group, providing high-quality evidence for the application of dCBT in migraine management [14]. A systematic review published by Noser et al. also confirmed the effectiveness of digital headache self-management interventions [15].

2.2. Digital Neurostimulation — Modulating Pain Transmission Pathways

Neuromodulation technologies exert their anti-migraine effects by modulating the trigeminal vascular system and pain transmission pathways. Remote Electrical Neuromodulation (REN) is an emerging non-invasive neuromodulation technique that inhibits migraine-related pain signal transmission by targeting peripheral nerves in the upper limbs.

A real-world study by Tepper et al. evaluated the efficacy of REN in the acute treatment of migraine; the study demonstrated that the device, in conjunction with a companion app for recording patient migraine diaries, can effectively track treatment outcomes [16]. A large-scale real-world analysis by Ailani et al. further confirmed the safety and efficacy of REN [17].

A double-blind randomized controlled trial by Tepper et al. evaluated the efficacy of REN for migraine prevention, and the results showed a significant reduction in monthly migraine days in the active stimulation group [18]. A systematic review and meta-analysis by Alnajjar et al. comprehensively assessed the efficacy and safety of REN, providing high-level evidence for the application of this technology in migraine treatment [19].

Non-invasive vagus nerve stimulation (nVNS) is another important digital neuromodulation technology. Diener et al. evaluated the efficacy of the gammaCore nVNS device for migraine prevention through the PREMIUM study [20]. Barbanti et al. confirmed the feasibility of nVNS for the acute treatment of high-frequency and chronic migraine [21].

2.3. Digital Monitoring and Early Warning System — Identifying Precursors and Triggers

Migraine prediction systems based on wearable devices and

artificial intelligence (AI) represent a cutting-edge direction in digital therapeutics. Stubberud et al. investigated the use of machine learning algorithms to predict migraine attacks based on mobile diary and wearable device data, demonstrating the potential of AI in migraine prediction [22].

Kapustynska et al. explored the application of wearable biosensor technology in migraine prediction by monitoring changes in biomedical signals on the night before a migraine attack to predict its onset [23]. Lee and Chu provided a comprehensive review of AI applications in headache disorders, including diagnostic classification, treatment response assessment, and migraine prediction [24].

Petrušić described digital phenotyping as a “game-changer” for migraine research and management, highlighting the promising applications of wearable neuromodulation devices and personal AI agents in migraine management [25, 26]. Danelakis et al. further explored the emerging applications of AI, data science, and wearable devices in clinical headache care [27].

2.4. Virtual Reality/Biofeedback Therapy — Rewiring the Brain Through Behavioral Feedback

The combination of virtual reality (VR) and biofeedback offers an immersive experience for migraine treatment. Cuneo et al. evaluated the efficacy of a portable biofeedback-VR combination device as an adjunctive treatment for chronic migraine; the results showed that frequent use of the device was associated with a reduction in the number of headache days [28].

Shiri et al. explored the efficacy of a VR system combined with biofeedback for treating chronic headaches in children [29]. Subsequently, Lüddecke and Felnhofer conducted a comprehensive review of VR biofeedback applications in the health sector, highlighting its potential to overcome the challenges of traditional biofeedback [30].

Connelly et al. evaluated the acceptability and tolerability of extended reality relaxation training combined with wearable neurofeedback in pediatric migraine [31]. Paudel and Sah confirmed the efficacy of biofeedback for migraine, demonstrating that it significantly reduces headache frequency and severity [32].

Table 1. Summary of Evidence.

Intervention Category	Representative studies	Research Design	Sample size	Key Findings	Limitations of the evidence
dCBT	Pach et al., 2025	RCT	N=476(dCBT n=238, control n=238)	Reduce the number of migraine days	Short follow-up period
REN	Tepper et al., 2023	Double-blind RCT	N=248(active n=128, placebo n=120)	Significant preventive efficacy	The mechanism is unclear

Intervention Category	Representative studies	Research Design	Sample size	Key Findings	Limitations of the evidence
AI Predictions	Stubberud et al., 2023	Prospective development study	N=18(18 patients, 295 evaluable days)	Performance accuracy: AUC = 0.62	Lack of validation of the intervention
VR + Bio-feedback	Cuneo et al., 2023	Pilot RCT	N=50((VR+biofeedback+standard care n=25, standard care n=25)	Fewer days with headaches	Small sample size

3. Clinical Evidence and Efficacy Analysis

Clinical evidence supporting the use of digital therapies in migraine management is rapidly accumulating. A systematic review published by Tana et al. in 2026 comprehensively evaluated randomized controlled trials (RCTs) of digital and virtual interventions for migraine, covering a variety of intervention modalities such as virtual reality, mobile apps, digital neurostimulation/biofeedback, and digital cognitive behavioral therapy [33].

Multiple studies have demonstrated that digital therapies are significantly effective in reducing the number of headache days. Chen and Luo noted that digital therapies can effectively reduce the frequency of migraine attacks and the need for acute medication [34]. A study by Monteith et al. showed that frequent use of the REN wearable device among adolescent migraine patients yields preventive therapeutic effects [35].

Digital therapies have also demonstrated positive effects in improving comorbid conditions. Migraines often co-occur with anxiety, depression, and sleep disorders; dCBT can simultaneously improve these comorbid symptoms through cognitive restructuring and behavioral activation techniques. A study by Buse et al. combined Guided Instructional Relaxation (GIER) with REN for acute migraine treatment, highlighting the potential of integrated digital interventions [36].

However, current research still faces heterogeneity and methodological limitations. Yella et al. noted that new AI-driven interventions for migraine treatment require further validation through high-quality RCTs [37]. Heterogeneity among studies is reflected in diverse intervention formats, inconsistent control groups, varying outcome measures, and differing follow-up durations. Future research should adopt standardized outcome measures and more rigorous trial designs.

4. Challenges and Outlook

4.1. Data Privacy, Algorithmic Bias, and Prescription Regulation

The rapid development of digital therapeutics has raised

significant challenges regarding data privacy and algorithmic fairness. Chin et al. proposed guiding principles to address the impact of algorithmic bias on health disparities among racial and ethnic groups, emphasizing the importance of safeguarding autonomy and privacy in algorithm development [38].

Gianfrancesco et al. noted that machine learning algorithms using electronic health record (EHR) data carry potential risks of bias [39]. In 2024, Chen et al. conducted a comprehensive review of bias detection and mitigation strategies in EHR models [40].

Norori et al. called for addressing bias in health AI through open science approaches, proposing that privacy-preserving technologies such as federated learning can train AI algorithms while protecting patient privacy [41]. Subsequently, Rassi-Cruz et al. discussed the necessity of regulating digital therapeutics, emphasizing the need to develop products that are innovative, patient-centered, and safe [42].

4.2. Integrated Approaches Combining Medication and Non-pharmacological Therapies

Digital therapeutics should not be viewed as a substitute for traditional treatments, but rather as an integral component of comprehensive treatment strategies. Mathew et al. explored the integration of emerging pharmacological and non-pharmacological treatments for migraine [43]. Van de Graaf et al. noted that digital therapeutics may offer additional benefits when used as an adjunct to treatment at specialized headache centers [44].

Future integration pathways may include: adding dCBT to pharmacotherapy to improve treatment adherence; combining neurostimulation devices with mobile applications to achieve precision treatment; and utilizing AI predictive models to guide the individualized use of preventive medications. Such multimodal integration strategies are expected to achieve a synergistic effect where $1+1>2$.

4.3. Personalized Dynamic Intervention: From a “One-size-fits-all” Approach to a Closed-loop Adaptive System

The ultimate vision for digital therapeutics is to achieve a

truly personalized, closed-loop adaptive intervention system. Research has found that migraine patients exhibit significant disruptions in the MIND network associated with language, the cingulate-lateral prefrontal cortex, and the somatosensory motor system. These disruptions are linked to cognitive domains (such as memory, pain, and language) and can predict functional impairment ($r = 0.23$, $P_{perm} = 0.015$) [45]. Such neuroimaging biomarkers could inform future AI-driven closed-loop systems. In 2025, Pardo et al. explored the prospects of using AI and machine learning for predicting treatment outcomes in migraine [46]. Meanwhile, Natekar and Cohen discussed the application of AI and predictive modeling in the management of episodic migraine [47].

Key elements of this intervention system include: continuous physiological monitoring via wearable devices; machine learning-based attack prediction models; intelligent algorithms that automatically adjust intervention parameters based on the patient's real-time status; and a decision support system facilitating collaboration among patients, physicians, and algorithms [48].

5. Conclusion

As an emerging non-pharmacological pillar of chronic migraine management, digital therapeutics is transitioning from concept to clinical practice. This article reviews the four core types of digital therapeutics for migraine: digital cognitive behavioral therapy, digital neurostimulation, digital monitoring and early warning systems, and virtual reality/biofeedback therapy, and analyzes their respective mechanisms and clinical evidence.

Current evidence suggests that digital therapeutics play a positive role in reducing migraine attack frequency, improving comorbid symptoms, and enhancing quality of life. However, the field remains in a stage of rapid development and faces challenges such as data privacy protection, algorithmic fairness, and the refinement of regulatory frameworks.

Future directions include conducting more large-scale, long-term, multicenter randomized controlled trials to accumulate high-quality evidence; establishing pathways for integrating digital therapeutics with traditional treatments; and developing personalized closed-loop adaptive intervention systems. With technological advancements and the accumulation of evidence, digital therapeutics are expected to become an indispensable component of comprehensive migraine management, bringing new hope to hundreds of millions of migraine patients worldwide.

Abbreviations

CM	Chronic Migraine
DHCoE	Digital Health Centers of Excellence
dCBT	Digital Cognitive Behavioral Therapy (dCBT)
CBT	Cognitive Behavioral Therapy

REN	Remote Electrical Neuromodulation
nVNS	Non-invasive Vagus Nerve Stimulation
AI	Artificial Intelligence
VR	Virtual Reality
AUC	Area Under the Curve
GIER	Guided Instructional Relaxation and Education
EHR	Electronic Health Record

Author Contributions

Mengna Yang: Conceptualization, Methodology, Writing – original draft

Jinyan Shao: Validation, Writing – review & editing

Mario Fernando Prieto Peres: Investigation, Project administration, Supervision

Kaiming Liu: Formal Analysis, Funding acquisition, Project administration

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Conflicts of Interest

The authors declare no conflicts of interest.

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