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REVIEW

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Influence of next-generation artificial intelligence on headache research, diagnosis and treatment: the junior editorial board members' vision – part 1

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Abstract

Artificial intelligence (AI) is revolutionizing the field of biomedical research and treatment, leveraging machine learning (ML) and advanced algorithms to analyze extensive health and medical data more efficiently. In headache disorders, particularly migraine, AI has shown promising potential in various applications, such as understanding disease mechanisms and predicting patient responses to therapies. Implementing next-generation AI in headache research and treatment could transform the field by providing precision treatments and augmenting clinical practice, thereby improving patient and public health outcomes and reducing clinician workload. AI-powered tools, such as large language models, could facilitate automated clinical notes and faster identification of effective drug combinations in headache patients, reducing cognitive burdens and physician burnout. AI diagnostic models also could enhance diagnostic accuracy for non-headache specialists, making headache management more accessible in general medical practice. Furthermore, virtual health assistants, digital applications, and wearable devices are pivotal in migraine management, enabling symptom tracking, trigger identification, and preventive measures. AI tools also could offer stress management and pain relief solutions to headache patients through digital applications. However, considerations such as technology literacy, compatibility, privacy, and regulatory standards must be adequately addressed. Overall, AI-driven advancements in headache management hold significant potential for enhancing patient care, clinical practice and research, which should encourage the headache community to adopt AI innovations.

Keywords Machine learning, Migraine, Virtual health assistants, Digital applications, Augmented reality, Ethical AI regulations

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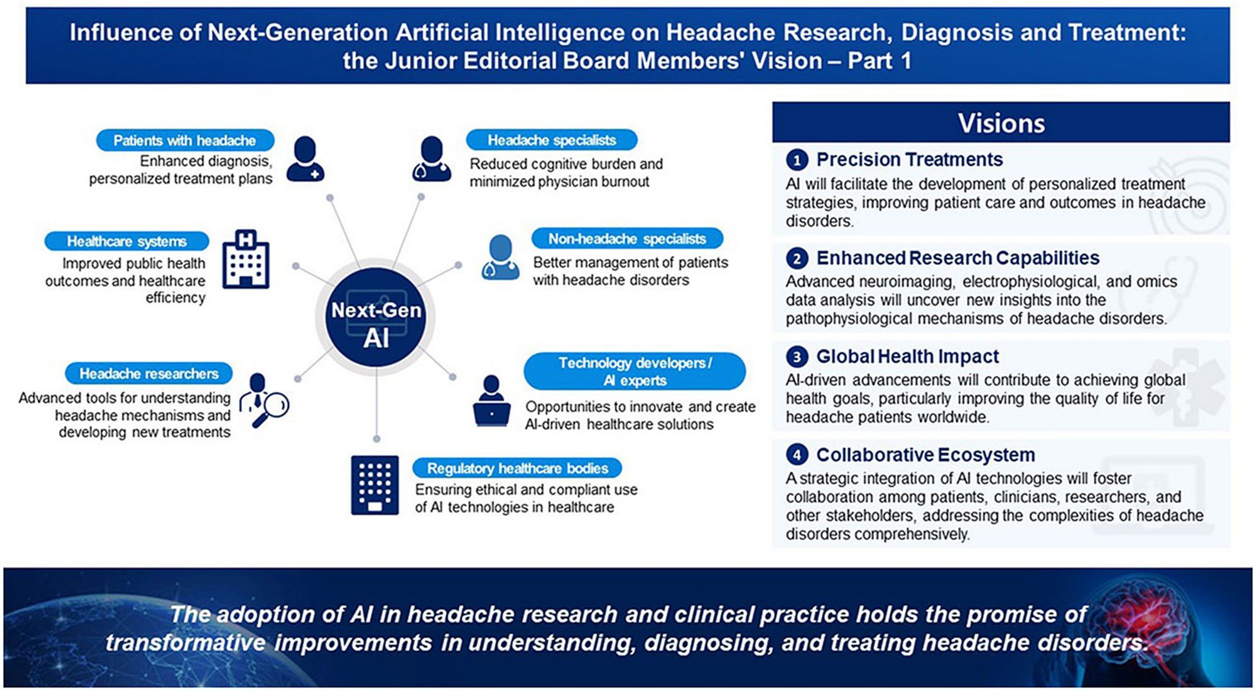
Graphical Abstract



Introduction

Artificial intelligence (AI) is a field of computer science that tries to mimic and outperform how the human brain learns, solves problems and makes decisions [1]. Medical AI is an area of emerging technology that leverages biomedical advances and AI to power discoveries for human health [2]. With the rapid developments in machine learning (ML) algorithms and improvements in hardware performances, AI technology is expected to play an important role in effectively analyzing and utilizing extensive amounts of health and medical data [2]. In particular, medical AI can help researchers discover new drugs, understand complex causes of disease, and predict how patients will respond to therapies [3–5]. In addition, AI tools could allow more precise and faster collection and analysis of medical data, augment and bridge research and clinical practice, and improve remote healthcare when patients do not need to interact with physicians directly when facing health issues related to previously established diagnosis [6]. Moreover, careful planning of using AI tools could improve public health outcomes and contribute to Gross Domestic Product (GDP) growth, providing a competitive advantage to countries that prioritize AI development [7].

Implementing next-generation AI in headache research, diagnosis and treatment becomes imperative because of its potential to transform and boost discoveries of the pathophysiological mechanisms and precision treatment of headache disorders, as well as improve outcomes of headache patients and facilitate clinical practice by reducing repetitive activities performed by clinicians, such as automate clinical notes by using large language models (LLMs) or fast identification of the right combination of drugs allowing earlier response to treatment; thus, reducing the cognitive burden and physician burnout and improve the physician-patient relationship [8–12]. Furthermore, AI-based headache diagnostic models may improve non-specialist diagnostic accuracy in everyday general medical practice [13]. Considering all the advantages of implementation of next-generation AI in headache research and treatment, embracing AI tools into research and clinical practice will have numerous impacts on the global community by helping in achieving the important third goal of the 2030 Agenda for Sustainable Development of the United Nations (ASD-2030) [14], specifically focused on means to improve worldwide health; as well as a great influence on the individual level, including headache patients, researchers and physicians who investigate and deal with headache disorders.

This document, written by a collaborative group of the Junior Editorial Board of the Journal of Headache and Pain, aims to highlight the current AI advantages that could be implemented in the research and treatment of headache disorders, especially migraine. Part 1 will cover challenges in remote healthcare of headache patients with a special focus on virtual health assistants, so-called chatbots [15], and new technologies driven by AI designed to prevent or block migraine attacks. In addition, we will highlight AI opportunities for healthcare assistance for physicians who deal with patients suffering from headache disorders. Also, various AI tools for analysis of collected data from people who suffer from headache, such as clinical descriptors, neuroimaging, electrophysiological and omics data, will be discussed in Part 1. Ethical and regulatory considerations of integrating AI technologies into healthcare for headache disorders are also discussed. Part 1 will serve as an introduction to continue our discussion in Part 2, which will cover drug discovery and development in the headache field boosted by AI, as well as AI-driven wearable healthcare technology designed to collect data about or treat headache attacks. In addition, Part 2 will cover the advantages of implementing a digital twin platform in the field of headache research and treatment of patients.

Our ultimate goal in sharing our vision is to draw attention to academic, clinical and patient communities to all AI opportunities that can revolutionize and reshape research and clinical practice in the headache field. Moreover, we hope that our initiative will instigate the headache community to bring innovation in AI from a headache perspective.

Virtual health assistants for patients who suffer from headache

Utilization of digital applications in headache patients

One of the important steps in migraine management is to record symptoms, triggers and days with headache [16, 17]. This method allows health professionals to better understand their patients and create a treatment roadmap, thereby increasing patient compliance [17]. AI algorithms could play a role in headache diagnosis and disease management. It is noteworthy that the number of health-related applications is quite high in the smartphone market. The study by Roesch et al. used an ICHD-3 criteria-based algorithm for classifying migraine and tension-type headache attacks in a headache e-diary [18]. The neurologist and the algorithm agreed on the diagnosis for 86 cases out of 102, which was found to be quite sufficient [18]. Recording disease patterns in diaries manually can be tedious and overwhelming for patients [17]. Stone et al. study stated that the compliance rate with e-diaries was 94%, whereas the compliance rate with paper diaries was 11% [19].

Digitalization, which goes beyond time and rises in all areas of life with the increase in Internet use, also provides advantages for migraine patients in the management of the disease [16]. It is supported by the literature that e-diaries help diagnose migraine [18, 20]. From the results obtained from the applications, it is understood that the disease burden and impact of migraine patients on their quality of life, work efficiency and general well-being are high [21], and these results can be determined from many different parts of the world at similar times [22]. The use of digital applications by migraine patients is useful both in managing a significant part of migraine care and in providing data for research [21, 22]. Studies emphasize that digital applications with algorithms that distinguish migraine headache days and symptoms are useful in diagnosing migraine [20], that digital diary monitoring for research allows more real-time data collection compared to paper diaries [21], and that these applications are necessary to provide reliable information considering situations that patients cannot remember [20, 23]. Additionally, these algorithms provide individualized mapping and reporting of triggers and symptoms [24], and patients can easily share these results with healthcare professionals [25].

Recently, different wearable devices and mobile applications have been developed not only to identify and monitor triggers but also to attempt to block such triggers. For example, as up to 90% of migraine patients experience photophobia during attacks [26], light sensitivity lenses have been designed to filter out ~80% of the wavelengths of light in the 480 nm (blue-green) portion of the spectrum [27]. The rationale is based on the study of Noseda et al., which revealed that blue, amber and red light exacerbate headaches, whereas green light reduces pain intensity [28]. The first small randomized double-blind trial showed that wearing the lenses resulted in a decrease in migraine-associated pain and light sensitivity [29]. However, the potential of integrating light sensitivity lenses with fully functional, self-contained augmented reality glasses remains to be determined.

Algorithms can also make new definitions of stress levels in the migraine cycle. In a study, thanks to digital application, three dominant patterns of perceived stress change throughout the migraine cycle were identified and it was emphasized that it would help healthcare professionals during the treatment phase [25]. Another study stated that progressive muscle relaxation provided by smartphone applications could be an accessible and effective treatment for migraine patients [30]. When the most used applications on mobile phones are examined, it can be seen that there are tracking applications on: migraine symptoms and triggers [22, 31], pain management-awareness-sleep-meditation-relaxation-biofeedback applications [16, 25, 31], presenting scientific articles [22], virtual headache specialist applications and social community applications. On the other hand, applications integrated with the menstrual cycle and weather and barometric pressure analysis are also preferred for reporting and blocking (with special earplugs) barometric triggers [22]. In a Delphi study, it was questioned what information was wanted to be collected from digital applications, and physicians reported that headache frequency, acute drug use frequency and functional disorder information should be collected [32]. From the patient's perspective, patients experiencing headaches prefer to fill out pain diaries on their smartphones [33]. They state that they want to have easy access to strategies for pain management, to reach other individuals experiencing headaches, and to be able to access experts when necessary [33]. Therefore, personalized and interactive applications suit their needs [33].

In addition to all these needs, desires and positive features, there may be some considerations to pay attention to. The concept of technology literacy is an important limitation for the use of digital applications and wearable technology [33, 34]. Best practice standards should be established when they are used [35]. Compatibility issues, psychometric testing of applications, wearable and application fees, security-privacy, ease of interface use of applications, and scientifically based development are considerations that require attention when recommending or selecting applications and wearable technology [23, 35–37]. Therefore, Food Drug Administration (FDA) regulations of digital medical applications and wearable technology are discussed through academics, clinicians, developers and patients [38].

As a result, AI algorithms offer advantages such as patient-medication-side effect monitoring to healthcare professionals in diseases such as migraine, where symptoms and triggers need to be well monitored, and patients to monitor themselves and reduce triggers with wearable and/or mobile phone they always carry with them and increase compliance with treatment. Applications are preferred for identifying migraine patients who do not contact healthcare professionals and are missed, for presenting real-world data, for saving time, and for detecting the migraine burden with a technological method that is perceived and reported by patients globally [17, 21, 23, 39]. We think that this new technology will enable patients and healthcare professionals to take part in migraine management together by providing healthcare professionals with real-world data in the light of science.

Utilization of augmented reality in patients who suffer from migraine

The recent worldwide diffusion of AI technologies in health care has brought about a significant change in the management of several diseases. Virtual and augmented reality (VR and AR, respectively) are expected to be more integrated in technologies assisting patients, having the potential to give new modalities to diagnose and treat diseases, and to remotely manage some conditions. The new conception of managing disorders both in standard and in highly realistic immersive ways, might represent an opportunity to improve the health care utilization in people with access difficulty, to give an early diagnosis of some clinical conditions and to make some procedures less invasive.

VR provides an immersive experience replacing the real-life environment, while AR shows a mixed reality with virtual elements in a live view [40]. VR/AR can be useful also to improve the ability of certain operators for more complicated procedures, and to reduce preoperative anxiety. Several devices have been developed in the context of surgery [41]. Moreover, AR in radiology by using deep learning training techniques is revolutionizing the way of evaluating disorders by imaging [42].

A limited number of devices are currently available in the neurology field, but drugless solutions, which can improve some neurological disorders such as migraine and limit the chronic use of analgesics, are currently needed. Relaxation techniques and mindfulness have been effective in mitigating anxiety, stress and burnout. Interestingly, immersive meditation with biofeedback and neurofeedback by using VR/AR devices directly at home is useful to eliminate ambient distractions and notifications, and nature-based virtual scenarios can have positive and relaxing effects. This is particularly true in people affected by post-traumatic stress syndrome such as veterans, which tends to affect their overall well-being and day-to-day functioning [43].

In chronic migraine, the frequent use of a portable biofeedback-virtual reality device has been associated with a significant reduction of acute analgesic consumption at 12 weeks of follow-up (65% in the experimental versus 35% decrease in the control group, respectively) and also in a reduction of depression score (35% decrease in the experimental versus 0.5% increase in the control group, respectively). Despite a significant reduction of monthly migraine days (MMDs) significant difference between the experimental vs. control groups has not been demonstrated. This platform might give additional benefits in the treatment of chronic migraine, especially in those patients where it is necessary to reduce the use of chronic analgesics [44].

Interestingly, extended reality (XR), which encompasses VR, AR and mixed reality, has been evaluated also in the preventive treatment of pediatric migraine, where the limitation of using antimigraine drugs and the low availability of preventive treatments make it necessary to find new tolerated approaches. In a study, it was investigated the acceptability of XR devices from pediatric migraine patients [45]. Ten to seventeen-year-old patients were instructed in three training conditions (fully immersive VR with or without neurofeedback, and AR with neurofeedback), and were equipped at home for one week of relaxation practice. Side effects were very mild (vertigo the most common), and the two fully immersive VR modalities were highly preferred over AR for relaxation training [45]. The effects of these devices in reducing the mean MMDs remain to be investigated, but these results encourage the study of XR devices in relieving pain in migraine patients (Table 1) [46].

Cultural misconceptions tend to underestimate migraine as a psychosocial disorder, increasing the social burden of the people who suffer from it [47]. By using AR devices with specific visual environments, also healthy subjects can experience some migraine symptoms such as visual distortions, light sensitivity and typical aura [48]. In a study, it has been demonstrated that participants experiencing migraine in a specific virtual environment show a significantly higher empathic reaction, compared to that of subjects who only imagine suffering from migraine. This could be useful to reduce the stigma associated with migraine, including social devaluation and the typical stereotype of an "easily solved disorder" [49]. Lessons from the recent pandemic have made it clear not to underestimate long-lasting, subtle symptoms such as headache, that can be disabling [50, 51].

Healthcare assistance for physicians

In managing chronic conditions like headaches, AI can enhance the efficiency of consultation, support the implementation of precision medicine, and improve the quality of patient care through telemedicine and digital visits. This will allow physicians to focus on more complex tasks and aid in the rapid and accurate treatment of headaches.

AI triage maximizes efficiency in emergency situations by quickly assessing and categorizing patients' conditions [52, 53]. Recent study using LLM has shown that AI predicts the Emergency Severity Index acuity level with an accuracy of 0.89 based on the clinical history from the medical records of first-time emergency department visitors [54]. For headache patients, AI triage could analyze symptoms and medical history to differentiate secondary headaches and assess urgency [55]. Yang et al. constructed an ML-based prediction model predicting secondary headaches with an accuracy of 0.74 in a dataset of 121,241 real-world emergency room cases in the UK [56]. Given that traditional red flags often show limited specificity in emergency department settings [57, 58], leading to unnecessary neuroimaging, AI triage can help reduce overcrowding and enable physicians to concentrate on more critical cases [59].

In outpatient settings, AI can assist in screening and classifying primary headache patients [55, 60]. ML classifiers based on patient surveys have accurately classified primary headaches, including migraine, tension-type headache, and cluster headaches [61–63]. Katsuki et al. demonstrated that an AI-based headache diagnostic model could enhance the diagnostic performance of non-headache specialists, aiding in referrals to headache specialists [13]. These AI-driven screening tools not only reduce the burden on physicians but can also be more satisfying for patients compared to manual screening [64].

Precision medicine is an approach that provides personalized treatment by considering the genetic, environmental, and lifestyle factors of individual patients [65]. For headache patients, a comprehensive analysis of genetic information, clinical data, and blood and imaging biomarkers can propose an optimal treatment strategy [66]. AI is naturally suited to handle the complex data processing involved in personalized approaches [67]. Gonzalez-Martinez et al. predicted the response to anti-calcitonin gene-related peptide treatment in migraine patients using ML-based models with headache characteristics [68]. Tso et al. conducted machine learning analyses of magnetic resonance imaging (MRI) data of cluster headache patients to predict their response to verapamil [4]. Kogelman predicted the response to acute and/or preventive medication based on the genetic data of migraine patients [69]. These studies suggest that

Table 1 Table shows some of the current available XR devices that could be employed in future trials for patients suffering from migraine

Name of device	Type of extended reality	Model type	Pros	Cons
Meta Quest 2, 3, PRO (Facebook)	VR/AR	Headset	- Affordable cost - Versatility and quality - Apps compatibility	Short battery life
Apple Vision PRO	VR/AR	Headset	- Versatility and quality - Apps compatibility	High Price
Playstation VR	VR	Headset	- Affordable cost - Quality	- Designed for gaming
Gear VR (Samsung)	VR	Headset	- Low cost	- Connection to the smartphone
Mira Prism	AR	Headset	- Quality	- Heavy to use
Microsoft HoloLens	AR	Headset	- Quality	- Short battery life
Google cardboard	VR	Headset	- Accessibility - Low cost	- Limited functions
Xreal AIR 2	Virtual monitor	Glasses	- Affordable cost	- Limited functions
ROKID	Virtual monitor	Glasses	- Affordable cost	- Limited functions

combining those modalities could soon enable us to provide more accurate optimal treatments for each patient [66]. Additionally, predicting drug-drug interactions in patients will also be a crucial aspect of precision medicine in migraine [70]. This approach can maximize the effectiveness of headache treatments and improve the quality of life of patients.

Telemedicine and digital visits provide a way for patients to receive medical services without meeting doctors in person. This is particularly useful for chronic conditions [71], such as headache patients [72]. Randomized controlled trials have shown that telemedicine for migraine patients improved patient convenience without significantly different clinical outcomes compared to in-person visits [73, 74]. During the COVID-19 pandemic, surveys of healthcare providers and patients in the US indicated that telemedicine for headache care increased patient satisfaction, convenience, and reduced costs, while also improving the no-show rate [75, 76]. AI-based telemedicine systems enable real-time symptom monitoring and immediate medical intervention through remote consultations [77]. For example, AI can analyze headache diaries to identify attack patterns and alert patients when an attack is anticipated. Stubberud et al. demonstrated an ML-based predicting model to forecast migraine attacks based on mobile phone diary and biofeedback data [78]. Through telemedicine and digital visits, patients can report their condition to doctors in real-time and receive necessary prescriptions or treatment advice [76, 79]. These systems can be especially beneficial for patients with mobility issues or those living in areas with limited access to healthcare [79].

In summary, AI can be a powerful tool for doctors in managing headaches. Considering that headache medicine specialists have one of the highest rates of burnout compared to other physician specialists [80], actively utilizing AI is essential for the future of headache management as it can significantly reduce physicians' workloads. Additionally, we believe that leveraging AI can enhance the overall efficiency of the current headache management system, thereby improving treatment outcomes for headache patients [81, 82].

Leveraging AI for data analysis of headache patients

In recent years, a growing body of research has employed AI to identify neuroimaging biomarkers with the potential to differentiate between headache subtypes, define disease prognosis and guide treatment decisions [9]. ML techniques are now widely used for medical image analyses. Many ML methods have been developed to identify structural, functional and molecular biomarkers from neuroimages such as MRI and positron emission tomography. ML approaches fall into two categories: supervised and unsupervised. Supervised algorithms learn to classify data into predefined groups (e.g., patients vs. controls), while unsupervised approaches, analyse unlabelled data to uncover hidden patterns without prior information [83, 84].

Many studies have employed supervised and unsupervised ML algorithms to test the accuracy of imaging biomarkers in differentiating people with migraine from healthy controls, and further stratifying migraine subgroups [9]. Supervised ML approaches using resting-state functional MRI (RS fMRI) have shown promise in differentiating migraine patients from controls. Studies report accuracies ranging from 86 to 91% by analyzing the functional connectivity (FC) within pain, visual, cognitive, and sensorimotor networks [85, 86]. Additionally, a positron emission tomography study employing a semi-supervised ML technique achieved similar accuracy (80–95%) in classifying migraine patients based on μ-opioid and dopamine receptor availability in brain regions associated with pain processing [87].

While supervised ML offers promise in differentiating migraine patients from controls, unsupervised approaches have yielded mixed results. An early study using brain morphometry failed to achieve clear separation [88]. However, a more recent study employing unsupervised deep learning on brain morphometry achieved 75% accuracy [89]. Notably, another investigation utilizing unsupervised deep learning models based on RS FC patterns achieved an even higher accuracy of 99% compared to previous supervised methods [90].

Despite being discouraged the electroencephalogram remains the most frequent complementary study performed in migraine patients. Outside its potential value for differential diagnosis in specific (and very limited) clinical situations, as in most clinical settings) won't be of any help in the evaluation of most migraine patients [91]. However, recent studies have shown the potential of machine learning to identify chronic migraine on magnetoencephalograms [92]. A classification model that employed a support vector machine was developed using the magnetoencephalographic data to assess the reliability and generalizability of chronic migraine identification. In the findings, the discriminative features that differentiate chronic migraine from healthy controls were principally observed from the functional interactions between salience, sensorimotor, and part of the default mode networks. The classification model with these features exhibited excellent performance in distinguishing patients with chronic migraine from healthy controls (accuracy: 86.8%, area under the curve (AUC): 0.9) and from those with episodic migraine (accuracy: 94.5%, AUC: 0.96). The model also achieved high performance (accuracy: 89.1%, AUC: 0.91) in classifying chronic migraine from other pain disorders [92]. Other study using the machine learning-multi-omic analyses approach found evidence for the role of glutamine, cyclic adenosine monophosphate regulation, and fatty acid oxidation in the molecular mechanisms of migraine and/or the effect of triptans [93]. This provides a new way for us to distinguish headache subtypes and prognosis by using multi-omics data artificial intelligence analysis.

ML approaches utilizing RS fMRI, morphometry, and diffusion tensor imaging (DTI) data have successfully differentiated migraine patients based on disease severity, including factors like disease duration, attack frequency, presence of cutaneous allodynia, and patients' disability [86, 88, 94–96]. This suggests their potential for identifying migraine subgroups with varying severity. Furthermore, recent studies demonstrated the ability of ML to differentiate migraine with aura patients from controls and even stratify migraine with aura subtypes based on aura complexity, achieving high accuracy (89–98%) and potentially surpassing traditional methods for predicting symptom severity [97, 98].

While migraine research dominates due to its prevalence, ML shows promise in differentiating other headache disorders. One study integrating clinical, structural, and functional MRI data achieved 98% accuracy in distinguishing cluster headache patients from controls [99]. Additionally, a similar high accuracy (99%) was maintained when classifying migraine from cluster headache patients. Notably, clinical features alone offered the best accuracy, highlighting the enduring value of clinical history despite promising AI approaches using imaging data. ML approaches effectively distinguished post-traumatic headache patients from controls (accuracy: 75-91%), using either morphometry data alone or combined with clinical data [89, 100]. Another study differentiated migraine from post-traumatic headache with 78% accuracy using a combination of psychological and cognitive tests, morphometry, and DTI [101]. Anxiety, decision-making, and microstructural features of thalamic and superior longitudinal tracts were most important for this classification.

ML offers promise for personalized headache treatment. Studies have shown high accuracy (83-93%) in predicting responders to nonsteroidal anti-inflammatory drugs and acupuncture using patterns of RS FC or gray matter volume in migraine patients [86, 102, 103]. On the other hand, a supervised ML algorithm incorporating clinical data and cerebellar grey matter volume only achieved moderate accuracy (66%) in predicting verapamil response in patients with cluster headache [4]. Some evidence combined degree centrality and support vector machines analysis, revealing a significant decrease in the degree centrality values of the bilateral inferior temporal gyrus among migraine sufferers. A positive linear correlation was found between the left inferior temporal gyrus and MIDAS (migraine disability assessment) scores. Support vector machine results indicated that the degree centrality value of the left inferior temporal gyrus has the potential to serve as an imaging diagnostic biomarker for migraine, with utmost diagnostic precision, sensitivity, and specificity rates of 82, 86, and 78%, respectively [104]. Finally, a recent study identified intracranial cerebral spinal fluid and ventricular volume as potential predictors of recurrence of spontaneous intracranial hypotension after an epidural blood patch [105].

While these findings highlight the potential of ML for headache diagnosis, subtyping, and treatment prediction, limitations warrant further investigation. Most studies included relatively small patient samples, potentially limiting generalizability. Furthermore, only two studies validated their results in independent cohorts, and just one demonstrated the specificity of its identified RS fMRI patterns for migraine (accuracy: 73% vs. other chronic pain conditions) [86, 89]. Future research necessitates larger cohorts, independent validation procedures, and evaluation of model generalizability across diverse clinical settings and scanners. Additionally, further studies should evaluate the specificity of ML-derived findings for headache compared to other chronic pain conditions.

Ethical and regulatory considerations of integrating AI technologies into healthcare for headache disorders

To integrate AI technology more extensively into research and clinical practice in the headache field, numerous ethical considerations must be adequately addressed [106]. First, ensuring the privacy and security of collected data from patients who suffer from headache disorder are critical aspects of integrating AI technologies into this healthcare field. It is also important to acknowledge that different countries have different data protection laws [107], different understandings of socially acceptable uses of data, different values, and different ethical standards [108]. Although some international data-sharing agreements exist, including biobanks and international consortia for medical imaging databases, most data used in developing AI technologies fall outside such agreements [109]. Therefore, a consensus paper for regulations of handling data, including medical records, genetic information, and real-time monitoring data of patients, for headache research should be of paramount importance, especially because AI heavily relies on the analysis of preexisting data. Second, the safety of AI-driven clinical practice and decision-making of headache patients' treatment are critical ethical considerations. While studies suggest that AI technology may enhance patient outcomes, still there is doubt that there are lack of standardization in reporting findings and the potential for unsafe recommendations for therapy optimization [110]. Further guidance and standard-setting by the regulatory agencies regarding transparency and data quality in AI-ML processes will be necessary to decrease risks and discriminatory outcomes in clinical trials [111]. Third, the implementation of AI in healthcare must address its potential influence on healthcare disparities, such as racial, socioeconomic, geographic, gender, age and cultural disparities [110]. Neglecting these disparities may increase the likelihood of having biases embedded in the AI algorithms, which could lead to unsafe recommendations when using AI tools that are not previously tested for their generalizability. It will also be important to ensure that when AI technology is used in underserved communities, these communities are not relegated to cheaper, less effective forms of AI tools that can further perpetuate health disparities [106]. Furthermore, without standardization of hardware, software, training data sets, and requirements for local adaptation, there is no guarantee that a model trained and designed in one country will achieve the same level of accuracy in another [109]. Therefore, all countries should aim for the same high standard of safety, efficacy, and ethics for AI tools in healthcare systems [112]. In addition, potential drawbacks of AI-driven application implementation in the headache centres are certainly related to data security and privacy, since the applications are usually hosted on third-party servers. One solution to this problem could be to improve client-side data encryption, and another is to employ federated learning to train models without data dispersion [113]. Certainly, better management of data locally could avoid legal problems. Furthermore, one typical criticism leveled toward AI systems is the so-called "black-box" problem. Deep learning algorithms typically lack the ability to provide convincing explanations for their forecasts [113]. However, building AI systems that can be understood by humans is still an active field of study, and future advancements in this field could significantly improve headache research opportunities and reveal new pathophysiological mechanisms and treatment methods in primary and secondary headache disorders.

Establishing trust in the physician-AI technology-patient loop is pivotal for the successful implementation of AI-driven healthcare. To achieve that goal, addressing concerns about data use, privacy, bias, and safety is crucial for fostering patient trust in AI-driven healthcare [114]. Furthermore, investment in AI education of physicians specialized in headache research and treatment will ensure responsible AI use and foster trust among patients and their physicians. Additionally, the present healthcare system assumes that all responsibility in case of inappropriate treatment lies in the hands of the medical staff. AI technology may affect treatment decisions for headache patients and may sometimes cause negative impacts. In such cases, liability issues would arise for responsible physician and healthcare institution. Hence, physicians need to learn how to better utilize and interpret AI algorithms and be aware of potential legal consequences associated with AI use in medical practice [115]. In addition, with the introduction of AI-driven applications and digital twins platforms, where the patient is required to provide crucial data for the AI tool to deliver the final result, some responsibility is also being placed on the patient. The overall goal is that over time AI policymakers will create frameworks that optimize the use of AI in making decisions while supporting clinicians who will remain in control of improved clinical processes and workflows.

Collaboration among headache societies, clinicians, researchers, industry, and regulatory bodies is essential for the ethical implementation of AI in headache research and clinical practice. In addition, stakeholders in the headache field should organize roundtables to discuss how to facilitate the collection of comprehensive multimodal data about patients who suffer from headache disorder and how to form an international big database for various primary and secondary headache disorders respecting all the above-mentioned ethical and regulatory considerations regarding emerging next-generation AI technologies. By addressing these challenges and advancing ethical AI practices, stakeholders in the headache field can harness the full potential of AI to improve research and clinical practice dealing with headache disorders while upholding ethical standards and protecting patient privacy and autonomy.

Conclusions

The integration of AI into the field of headache research and treatment represents a groundbreaking advancement with the potential to revolutionize both patient care and clinical practice. By leveraging AI technologies, researchers can uncover new insights into the pathophysiological mechanisms of headache disorders, particularly migraine, and develop more precise, personalized treatment strategies. The ability of AI to efficiently analyze extensive medical data sets can lead to faster and more accurate diagnosis, improved disease management, and enhanced patient outcomes.

AI-powered tools, such as large language models and ML algorithms, facilitate the automation of routine clinical tasks, reducing the cognitive burden on clinicians and minimizing physician burnout. This, in turn, allows healthcare professionals to focus more on direct patient care and strengthens the physician-patient relationship. Moreover, AI's potential to identify effective drug combinations quickly could lead to earlier and more effective interventions for headache patients.

The use of digital applications and wearable devices in headache management offers significant advantages, including higher patient compliance with symptom tracking and trigger identification, real-time data collection, and personalized treatment plans. These technologies also provide valuable insights into the disease burden and its impact on patients' quality of life, supporting more informed clinical decisions.

However, the successful implementation of AI in headache research and treatment requires careful consideration of ethical, regulatory, and practical challenges. Ensuring data privacy, addressing technology literacy gaps, and establishing best practice standards are critical for the widespread adoption of AI-driven solutions.

In conclusion, the adoption of AI in headache research and clinical practice holds the promise of transformative improvements in understanding, diagnosing, and treating headache disorders. By embracing AI innovations, the headache community will advance towards achieving significant global health goals and improving the quality of life for patients worldwide. The future of headache management lies in the strategic integration of AI technologies, fostering a collaborative approach between patients, clinicians, researchers and stakeholders to address the complexities of headache disorders comprehensively.

Abbreviations

AI	Artificial intelligence
ML	Machine learning
GDP	Gross Domestic Product
LLMs	Large language models
FDA	Food Drug Administration
VR	Virtual reality
AR	Augmented reality
XR	Extended reality
MMDs	Monthly migraine days
MRI	Magnetic resonance imaging
RS fMRI	Resting-state functional MRI
FC	Functional connectivity
DTI	Diffusion tensor imaging
AUC	Under the curve
MIDAS	Migraine disability assessment

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Not applicable.

Competing interests
All authors are Junior Editors of The Journal of Headache and Pain. IP also serves as Head of Imaging Section of the SN Comprehensive Clinical Medicine journal and as the Guest Editor in The Journal of Headache and Pain. Outside of this work, RM received honoraria for speaker activities and participating in advisory boards from Abbvie, Biomedia, Eli Lilly, Lundbeck, Pfizer and Teva.

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