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# Migraine: Causes, Symptoms, and Management

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**Abstract** *Migraine is a multifaceted neurological condition, and its diagnosis now relies on subjective clinical evaluations because of the absence of valid biomarkers. Recent developments in artificial intelligence (AI) and machine learning (ML) offer hopeful prospects for the improvement of diagnostic precision by automatic evaluation of patient data. This review discusses the application of AI, ML, and deep learning (DL) techniques in migraine subtype classification and diagnosis. We conducted a systematic literature search and identified 130+ studies from 1988-2024. We rigorously filtered the studies and chose 30 high-quality papers based on predefined inclusion criteria. We only included studies based on clinical data, neuroimaging, or patient-reported outcomes to train prediction models.*

*Primary findings demonstrate that supervised machine learning algorithms (i.e., SVM, random forests) and deep neural networks can effectively classify migraine subtypes with more than 85% accuracy in some studies. Natural language processing (NLP) techniques are particularly promising for identifying diagnostic patterns from free-text clinical records. However, challenges remain regarding dataset heterogeneity and model generalizability*

**Keywords** *Migraine, headache, throbbing, unilateral pain, photophobia, phonophobia, headache classification.*

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## I. Introduction

Headache disorders are one of the most prevalent and impairing neurological conditions, affecting nearly half of the world's population at any time. One of these, `migraine,' is a disorder of great complexity and disability potential and is defined as repeated attacks of debilitating headache associated with a variety of other sensory, autonomic, and cognitive symptoms. Migraine is more than just a headache; it is a complex neurological disorder with multifactorial root causes that markedly reduces patients' quality of life, work productivity, and general wellbeing. Though common — affecting about 1 in 7 people around the world migraine is still underrecognized, undertreated and frequently misunderstood.

Screening for headache - migraine versus general headache- is essential in making an accurate diagnosis and managing the condition. Tension-type headaches are the most prevalent subtype and are generally classified as bilateral, mild to moderate and without the aforementioned associated symptoms; migraine is unilaterally throbbing, and is accompanied by
cooccurring features such as nausea, vomiting, photophobia (light sensitivity) and phonophobia (sound sensitivity). Additionally, migraine typically progresses sequentially through four phases: the prodrome, aura (in some cases), headache, and postdrome which all provide further layers to the complexity of the condition.

Migraine has a multifactorial etiology that reflects a complex interplay between genetic susceptibility, neuronal hyperexcitability, and environmental triggers. Key mechanisms underlying the condition have been established over the past few decades due to advances in neuroimaging and molecular biology techniques, including cortical spreading depression (CSD), trigeminal nerve activation and inflammatory neuropeptides such as calcitonin gene-related peptide (CGRP) mediated functions. These findings have both deepened our understanding of migraine pathophysiology and led to the development of new therapeutic strategies, such as the CGRP inhibitors and neuromodulation devices.

Almost everyone has had headache at least once in their life today. People experience head pain in many different ways, from a minor annoyance to debilitating pain. In addition, it affects the quality of life of the suffering individual. Headaches are classified into two types of headaches.

I. First one is headaches are individual entity disorders: Examples: Migraine Tension-Type Headache (TTH) Cluster Headache

II. Secondary headaches are indications of underlying medical conditions [8], and his types are Sinus Headache Cluster headaches, Medication-Overuse Headache, and Post-Traumatic Headache.

## II. Motivations

Migraine: a debilitating billion-warmer of a neurological disorder that affects more than a billion people around the world, yet is underdiagnosed, undertreated and misunderstood. This symmetric review convenes knowledge gaps, emphasizes the differences between migraine and headache disorders unless in general, and encapsulates recent research and therapeutic advancements. Highlighting the complex pathophysiology and clinical manifestations of migraine, as well as the significant burden it places on quality of life, this review aims to make a case for the need for patient-centric treatment strategies and equitable access to treatment, and to encourage the subsequent innovation of research. Ultimately, it aims to increase understanding, advance management and lessen the global burden of migraine.

## III. Classification of headache

primary headache

These are independent disorders caused by primary overactivity or dysfunction of the pain-sensitive structures in the head and his types is:

**I. Migraine**

are marked by regular, throbbing headaches frequently with nausea, vomiting and sensitivity to light and sound. They can last between 4 and 72 hours and may be accompanied by an aura a series of sensory disruptions like flashing lights or tingling sensations [5].

**II. Tension- Type Headache (TTH):**

TTH, which is often described as a steady, dull pressure around the head, is the most frequent type of headache. It is commonly triggered by stress, cysts, or muscle tightness and is rarely accompanied by nausea or sensitivity to light [2].

**III. Cluster Headache**

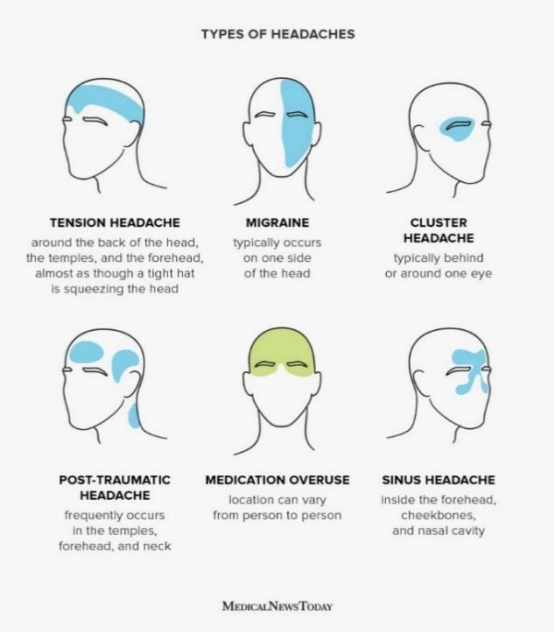
Cluster headaches are extreme, one-sided headaches that happen in cyclical styles or clusters. These are often accompanied by other symptoms, like tearing, nasal congestion and restlessness. These headaches are quite uncommon yet highly painful [7].

**secondary headaches**

secondary headaches are signs of underlying disease [8]: Sinus headache Cluster headaches are intense, one-sided headaches that come and go in cyclical patterns or clusters. Usually, they are accompanied by tearing, nasal congestion, and restlessness. These headaches are uncommon yet highly painful [7].Medication-Overuse Headache This type of headache is caused by overuse of pain-relief medications. It is a frequent culprit of chronic daily headaches and commonly requires withdrawal of offending medication of the Figure 1 variety to see improvement [4]."

Post-Traumatic Headache These headaches occur in the days, weeks or months following a head injury and can last for months or even years. They are generally linked to dizziness, cognitive problems, and affect changes [6]. Figure 1[99]: All this types of headache is shown. to disability

[15]. Although widely prevalent in around 12% of




the global population, the exact etiopathogenesis

*Figure 1 types of headaches[99]*

of migraines is incompletely understood and remains a subject for ongoing study [9]. Signed by its symptoms and conditions, and with advances in medical research and new treatments, the diagnosis and treatment of this condition advances.

## IV. What is migraine

Migraine subtypes

Migraine is a multifaceted neurological condition marked by repeated bouts of moderate to severe pain in the head, frequently with other sensory, autonomic and cognitive symptoms. The International Classification of Headache Disorders, 3rd edition (ICHD-3) is a comprehensive framework used to diagnosis and classify migraine subtypes. This review discusses the clinical manifestations, epidemiology, and diagnostic criteria of the four major types of migraine: Migraine Without Aura, Migraine with Aura, Chronic Migraine, and Vestibular Migraine. New insights into the prevalence of these subtypes among neurologists having personal history of migraine are discussed based on findings of recent studies depict in figure 2.

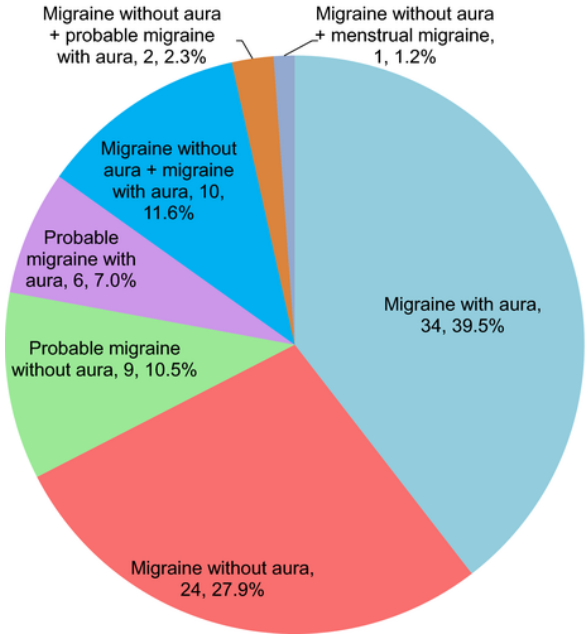



*Figure 2 types of migraine with percentage[100]*

**Migraine Without Aura (Common Migraine)**

**Description**:

Migraine Without Aura (commonly termed guiltless Migraine) is the most common form of a subtype (70–90% of cases) [1]. It is characterized by the lack of sensory disturbances (aura) prior to the headache phase. It is often defined as a pulsing or stabbing headache that can severely limit a person's daily functioning.

**Symptoms**:

The disease's defining symptom is an unilateral (one-sided) headache, although it can sometimes be bilateral. The pain is usually moderate to severe in intensity and gets worse with physical activity. Other symptoms are nausea, vomiting, photophobia (sensitivity to light), and phonophobia (sensitivity to sound). If untreated, these symptoms can last from 4 to 72 hours. A formal diagnosis requires a minimum of five attacks meeting these characteristics, based on ICHD-3 criteria [19].

**Clinical Significance:**
Migraine Without Aura is often underdiagnosed because it does not have distinct prodromal features. But its considerable prevalence and qualitative impact highlights the critical need for accurate diagnosis and effective treatment strategies.
Migraine With Aura (Also Called Classic Migraine)
**Description**:
Migraine With Aura (Classic Migraine) occurs in about 25-30% of migraineurs. This form is characterized by recurrent headache attacks with the addition of transient neurological symptoms (aura) before (or sometimes during) the headache phase. The aura is usually visual but can consist of sensory, motor or even speech disturbances (Figure 3)[101].

**Migraine With Aura (Classic Migraine)**
**Description:**
Migraine With Aura, or "Classic Migraine," affects about 25–30% of migraine sufferers. This variant is characterized by transient neurological signs (aura) that usually precede or occur with the headache phase. The aura is predominantly visual, but may also include sensory, motor, or speech phenomena (fig. 3).

*Figure 4 flashing light[101]*

**Symptoms**:
Visual symptoms are the most common type of aura and include flashing lights (fig 3), zigzag lines (fig 4) (scintillations), or blind spots (scotomas). Sensory changes like tingling or numbness often progress in a "march" from one body part to another. Speech disorders like aphasia can also happen. The aura typically builds progressively over 5 to 20 minutes and lasts less than an hour. The postictal phase is similar to Migraine Without Aura, characterized by unilateral pain, nausea, and sensory sensitivities [1].

*Figure 3 ZigZag lines [102]*

**Clinical Significance:**
The occurrence of aura may help with the diagnosis, but other reversible neurological conditions, like transient ischemic attacks (TIAs) or seizures, must be carefully differentiated from migraine.
**Chronic Migraine**
**Description**:
Chronic Migraine (CM) is a debilitating condition defined by the presence of headaches on ≥15 days a month over a three-month period, with ≥8 of these days fulfilling the International Classification of Headache Disorders (ICHD-3β) criteria for migraine. This subtype may represent a progression from episodic migraine and is associated with major functional impact and impaired quality of life.
**Symptoms**:
Chronic Migraine is a condition characterized by having frequent headaches, which can vary in intensity and nature. People often complain of ongoing nausea, light sensitivity and sound sensitivity. Medication overuse can complicate the condition and worsen the frequency and severity of headaches [12].
**Clinical Significance:**
Chronic Migraine is a significant healthcare challenge, necessitating a multidisciplinary

approach, encompassing lifestyle changes, pharmacological treatments, and behavioral therapies for effective management.

**Vestibular Migraine**

**Description**:

The vestibular migraine is a subclass, when attacks of vertigo and balance disorders occur in isolation from headache. It is one of the most prevalent causes of recurrent vertigo encountered in clinical practice.

**Symptoms**:

The primary symptoms are vertigo (a feeling of spinning or movement), imbalance and from motion sensitivity. These episodes can last from a few minutes up to few hours and may either be associated with mild headache or usual migraine associated symptoms such as photophobia or phonophobia. In particular, the vertigo can precede, accompany, or follow the headache phase, or can occur without headache [20].

**Clinical Significance:**

Vestibular Migraine is commonly confused with other vestibular disorders, namely Meniere's disease or benign paroxysmal positional vertigo (BPPV). Accurate diagnosis depends on a thorough clinical history and the exclusion of other causes for vertigo.

## V. ADVICE curve in Neuroscience: Experts Reveal What It Takes to Cure Migraines

Karsan and Goadsby(2018) [17] investigated migraine subtypes reported by neurologists who themselves experience migraine. As shown in their study in Figure 2, the neurologists reported nothing one cause (Migraine Without Aura) is the most common among the general population as well. Some of which emphasize the ubiquity of migraine among full demographics and the need for ongoing research and awareness.

## VI. Migraine: Causes, Risk Factors, and Complete Management

Migraine is a complex neurologic condition that affects more than a billion worldwide, rendering it one of the most common and disabling conditions on Earth. Notwithstanding its commonplace influence, the specific etiology of migraine has not been fully ascertained. But advances in research have pinpointed a combination of genetic, neurological and environmental factors that play a role in its emergence. In this review, we delve into the etiology, risk factors, presenting symptoms, diagnosis, treatment strategies, and novel therapies of migraine, given its disability-adjusted life years burden on quality of life.

## VII. Migraines and Chronic Illness: What Neurologists with Migraines Have to Say

Karsan and Goadsby (2018) [17] investigated the reported migraine subtypes experienced by neurologists who also had migraine. According to their analysis, shown in Figure 2 of their paper, the distribution of migraine subtypes among neurologists had a striking similarity with that of the general population with Migraine Without Aura representing the most described forms. This uncommon mindset shows the all-encompassing migraine through all societal aspects as well as the necessity of ongoing study and awareness on this topic.

## VIII. Causes

A Guide to Causes, Risk Factors, & Managing Your Migraine

Migraine, a complex neurological disorder affecting more than a billion people worldwide, is one of the most common and disabling conditions in the world. The precise etiology of migraine, however, is incompletely understood despite its widespread impact. Yet recent research has

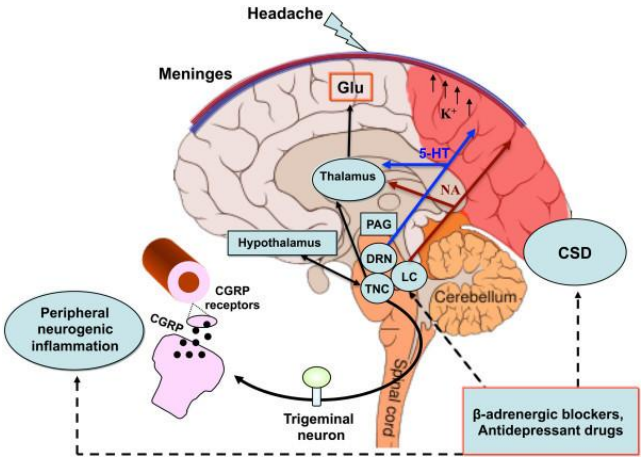



*Figure 5 pathophysiology of migraine [17]*

pinpointed a combination of genetic, neurological, and environmental factors that lead to its onset. This review details the etiology, risk factors, symptomatology, diagnostics, treatment, and novel treatments of migraine, with emphasis on its significant effect on quality of life.

**Causes and Risk Factors** Migraine pathogenesis is complex and multifactorial, with a combination of genetic predisposition, neuronal hyperexcitability, and external triggers. Key factors include:

Cortical Activity and CSD: Overactivity
Migraine is closely linked to abnormal brain activity, in particular cortical spreading depression (CSD), a wave of neuronal and glial depolarization that sweeps the cortex. CSD is thought to contribute to the aura phase of migraine and to initiate the headache phase by exciting pain pathways. Neuronal hyperexcitability in the cerebral cortex, especially in the occipital and temporal lobes has also been linked to migraine predisposition [1]. CSD and its Contribution to Migraine Pathophysiology Figure 5 reproduced from [16].

**Trigeminal Nerve Instigational and Neurogenic Inflammation:**

Migraine has the trigeminal nerve, a principal pain pathway, at its core. The trigeminal system becomes activated, which results in the release of proinflammatory neuropeptides, including calcitonin gene-related peptide (CGRP) and substance P, leading to vasodilation, plasma extravasation, and pain receptor sensitization. CGRP especially, has become an important contributing factor in migraine pathogenesis and a target for new therapies [9].

**Genetic Predisposition:**

Family history of migraine is one of the strongest risk factors for the condition, with estimates of heritability ranging from 40% to 60%. Certain genetic variations, like those in the genes TRPM8 (which plays a role in cold sensation) and MTHFR (which plays a role in folate metabolism), have been associated with increased sensitivity to migraines. Genome-wide association studies (GWAS) across thousands of patients have identified multiple loci associated with migraine, underscoring its polygenic architecture [10].

Alternative Factors (Environmental & Lifestyle):

Stress, sleep changes, hormonal changes (e.g., during menstruation) and dietary triggers (e.g., alcohol, caffeine and processed foods) are among the common migraine triggers. Figure 6 (LA

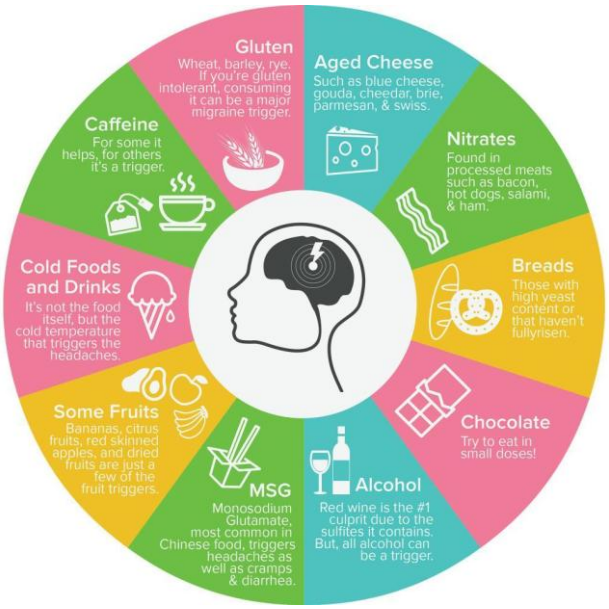



*Figure 6 migraine triggers[103]*

Heart Specialists, n.d.) depicts common migraine triggers that should be avoided by the patient. Irregular sleep patterns and bad sleep quality have also been found to worsen the frequency and severity of migraines [11].

## IX. Symptoms and Migraine Attack: Phases and symptoms

There are four distinct phases of a migraine attack, each with its unique symptoms and biology. The following shows the flow of these stages (figure 7 [17]):

**Prodrome Phase:**

Happening hours or possibly even days prior to the headache, the prodrome phase is characterized

by subtle warning signs, including mood shifts (irritability or euphoria, for example), food cravings, tiredness, and neck rigidity. (737), as sympathetic dysfunction, and altered neurotransmitter levels [11] are believed to cause these symptoms.

**Aura Phase (if present):**

The aura phase consists of transient neurological symptoms that are generally 20–60 minutes in duration. Flashing lights, zigzag lines or blind spots are the most common manifestations. They may also develop sensory symptoms (such as tingling or numbness) or speech difficulties (like aphasia). CSD and cortical hyperexcitability are attributable to Aura [1].

Headache Phase:

The headache phase consists of moderate to severe throbbing pain that is typically unilateral but can also be bilateral. It can be accompanied by nausea, vomiting, photophobia and phonophobia. The duration may range from 4 to 72 hours and is dependent upon trigeminal nerve activation and neurogenic inflammation (ICHD-3, [19]).

**Postdrome Phase:**

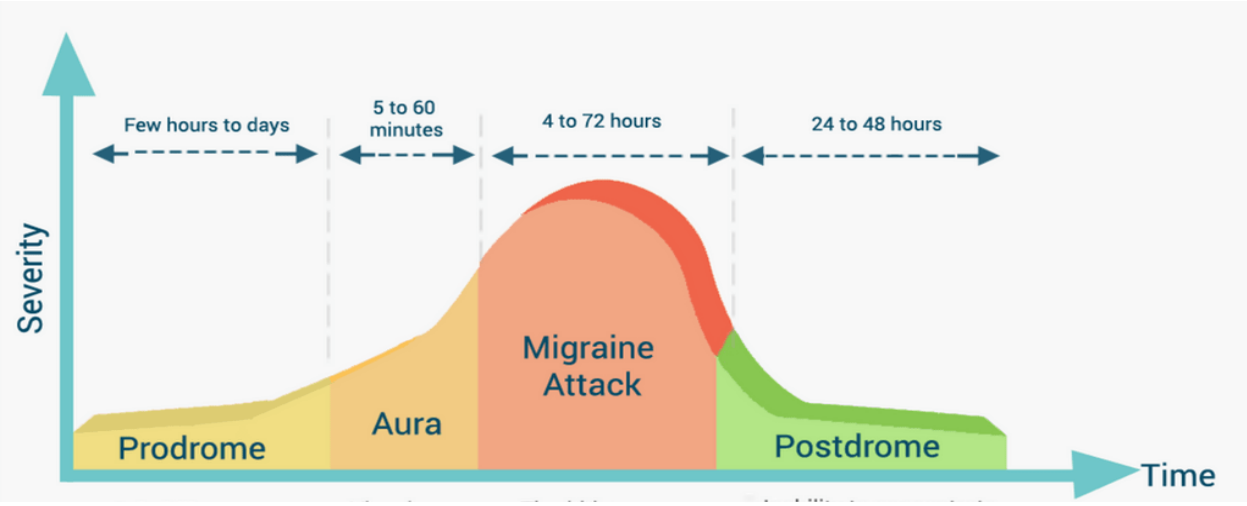



*Figure 7 migraine phases[104]*

Usually known as the "migraine hangover," the stage called postdrome leaves patients wiped out, disoriented and emotionally reactive. This phase may last from a few hours to days and indicates the brain's recovery from the migraine attack [11].

## X. Diagnosis

Migraine is principally diagnosed based on a comprehensive history and characteristic symptomatology. The International Classification of Headache Disorders, 3rd edition (ICHD-3), enables both standardized and specific diagnoses for primary headaches, as it outlines the frequency, duration, and characteristics of headaches (IHS, 2018). MRI or CT scanning may occasionally be used to exclude secondary causes of headache, including tumors, vascular malformations, and intracranial hypertension [9].

## XI. Treatment

Migraine treatment as a whole includes both acute and preventive methods, but this is based on the individual and how often they experience attacks.

**Acute Treatments:**

Acute treatments work to calm symptoms during an attack. These include:
Triptans: Agonists that act on serotonin receptors to constrict blood vessels and limit CGRP release.

NSAIDs: Nonsteroidal anti-inflammatory agents for mild to moderate attacks.

Antiemetics: Drugs used to treat nausea and vomiting [9].

**reventive Treatments:**

Patients with frequent or severe attacks are recommended preventive therapies. Options include:

- β-blockers: e.g. propranolol, decrease excitability of neurons.
- Expected Emphasis:
- Anticonvulsants: eg topiramate (ie stabilization of neuronal membrane)
- CGRP Inhibitors: These monoclonal antibodies act to inhibit the physiologic activity of calcitonin gene-related peptide (CGRP), an important mediator in the pathophysiology of migraine .

## XII. Impact of Migraine-Related Effect On Quality of Life

Migraine considerably disrupts daily functioning and causes absenteeism, loss of productivity, and reduced quality of life. A study by Lipton [12] reported that the work efficiency of chronic migraine sufferers is reduced three times compared to individuals who do not have migraines. Preliminary estimates suggest that the economic loss associated with migraine exceeds tens of billions each year [14].

Novel Therapeutic Strategies and Future Directions

## XIII. Emerging

New migraine treatments offer promise of better outcomes:

CGRP Inhibitors:

CGRP has also become a target for migraine prevention with monoclonal antibodies including erenumab and fremanezumab [9].

Neuromodulation Devices:

Non-invasive stimulation of the nervous system, such as transcranial magnetic stimulation (TMS) or vagus nerve stimulators, modulates brain activity to prevent or treat migraines [1].

Personalized Medicine:

For example, recent advances in genetics and biomarkers hold the promise of personalized migraine treatments that target the genetic profiles of individual patients and the mechanisms of the disease [10].

## XIV. Last research

I. Last Research paper

| Year | Research Paper/Study | Key Findings | Methodology | Impact |
|---|---|---|---|---|
| 1988 | Olesen et al.[21] | Introduced the concept of migraines as a neurovascular disorder. | Clinical studies, neuroimaging | Established the foundation for understanding migraines as a brain disorder. |
| 1990 | Silberstein et al.[22] | Identified serotonin as a key neurotransmitter in migraine pathophysiology. | Biochemical analysis, animal models | Led to the development of triptans, a class of migraine-specific drugs. |
| 1995 | Welch et al.[23] | Demonstrated the role of magnesium deficiency in migraines. | Clinical trials, biochemical analysis | Highlighted the importance of dietary factors in migraine management. |
| 2001 | Aurora et al.[24] | Linked cortical spreading depression (CSD) to migraine aura. | Neuroimaging, electrophysiology | Advanced understanding of the neurological basis of migraines. |

| Year | Research Paper/Study | Key Findings | Methodology | Impact |
|---|---|---|---|---|
| 2004 | Goadsby et al.[25] | Discovered the role of calcitonin gene-related peptide (CGRP) in migraines. | Molecular biology, clinical trials | Paved the way for CGRP inhibitors, a breakthrough in migraine treatment. |
| 2007 | Bigal et al.[26] | Studied the relationship between obesity and migraine frequency. | Epidemiological surveys | Highlighted the role of lifestyle factors in migraine severity. |
| 2010 | Lipton et al.[27] | Highlighted the global burden of migraines, emphasizing its impact on quality of life. | Epidemiological surveys | Increased awareness of migraines as a public health issue. |
| 2012 | Schürks et al.[28] | Investigated the genetic basis of migraines, identifying several risk genes. | Genome-wide association studies (GWAS) | Advanced the understanding of migraines as a genetic disorder. |
| 2014 | Burstein et al.[29] | Demonstrated the link between migraines and central sensitization. | Neuroimaging, electrophysiology | Explained why migraines often lead to chronic pain conditions. |
| 2016 | Dodick et al.[30] | Explored the efficacy of onabotulinumtoxinA (Botox) for chronic migraines. | Randomized controlled trials | Provided evidence for Botox as a preventive treatment for chronic migraines. |
| 2017 | Ashina et al.[31] | Studied the role of pituitary adenylate cyclase-activating polypeptide (PACAP) in migraines. | Molecular biology, clinical trials | Identified PACAP as a potential new target for migraine treatment. |
| 2018 | Tepper et al.[32] | FDA approval of CGRP monoclonal antibodies for migraine prevention. | Clinical trials, regulatory review | Revolutionized migraine prevention with targeted therapies. |
| 2019 | Goadsby et al.[33] | Investigated the efficacy of gepants (CGRP receptor antagonists) for acute migraine treatment. | Randomized controlled trials | Provided a new class of drugs for acute migraine relief. |
| 2020 | Ashina et al.[34] | Explored the role of the gut-brain axis in migraines. | Microbiome analysis, clinical studies | Opened new avenues for understanding migraine triggers and treatments. |
| 2021 | Buse et al.[35] | Studied the impact of migraines on mental health, particularly depression and anxiety. | Longitudinal studies | Highlighted the need for integrated care for migraine patients. |
| 2022 | Dodick et al.[36] | Investigated the efficacy of non-invasive neuromodulation devices for migraine relief. | Randomized controlled trials | Provided evidence for alternative, drug-free migraine treatments. |
| 2023 | Charles et al.[37] | Studied the long-term effects of CGRP inhibitors on migraine frequency and severity. | Longitudinal studies | Confirmed the safety and efficacy of CGRP inhibitors over time. |
| 2023 | Russo et al.[38] | Explored the role of oxidative stress in migraine pathophysiology. | Biochemical analysis, clinical studies | Suggested antioxidants as a potential therapeutic target. |

| Year | Research Paper/Study | Key Findings | Methodology | Impact |
|---|---|---|---|---|
| 2023 | Hougaard et al.[39] | Investigated the use of virtual reality (VR) for migraine pain management. | Clinical trials, patient surveys | Introduced VR as a novel, non-pharmacological treatment option. |

## XV. Research questioner :

In establishing a systematic investigation, we crafted clear Research Questions (RQs) and created frameworks for evaluating migraine studies. We used the tools created in this investigation to: (1) conduct a broad assessment of research methods in migraine literature, (2) evaluate challenges in performing research methods and using the datasets, and (3) highlight trends to posit future research. This study will examine the following Research Questions:

How can detect the migraine

What the applications on migraine with AI

What is the Advanced AI/ML/DL Applications in Migraine Management

How to diagnose and treat migraines

## XVI. Methodology

This section discusses the research results. We specifically answer all RQs from Section Research questionnaire, providing results that contribute to knowledge development in both theory and practice. The systematic results can be formally validated, as well as provide opportunities for subsequent future research to investigate.

How can detect the migraine

| Year | Title | Key Findings | Methodology | Impact | Accuracy | Strengths | Weaknesses |
|---|---|---|---|---|---|---|---|
| 1988 | Focal hyperemia followed by spreading oligemia in migraine attacks[40] | Introduced neurovascular theory of migraines | Clinical studies, neuroimaging | Established migraine as brain disorder | High | Pioneering imaging work | Small sample size |
| 1990 | The role of serotonin in migraine pathogenesis[41] | Serotonin's key role in migraine | Biochemical analysis, animal models | Led to triptan development | High | Clear mechanistic insights | Animal model limitations |
| 1995 | Magnesium deficiency in migraine patients[42] | Mg deficiency link to migraines | Clinical trials, biochemical analysis | Supported Mg supplementation | Moderate | Clinical relevance | Inconsistent measurement methods |
| 2001 | Cortical spreading depression in migraine aura[43] | CSD as aura mechanism | Neuroimaging, electrophysiology | Explained aura phenomena | High | Direct evidence | Only applies to aura cases |
| 2004 | CGRP in migraine pathophysiology[44] | CGRP's role in migraine | Molecular biology, clinical trials | Basis for CGRP inhibitors | High | Therapeutic breakthrough | Early stage research |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 2007 | Obesity and migraine frequency[45] | Obesity-migraine link | Epidemiological surveys | Highlighted lifestyle factors | Moderate | Large sample size | Correlational only |
| 2010 | Global burden of migraine[46] | Migraine's worldwide impact | Epidemiological surveys | Raised public awareness | High | Comprehensive data | Self-reported diagnosis |
| 2012 | Genetic basis of migraine[47] | Identified migraine risk genes | GWAS studies | Advanced genetic understanding | High | Large datasets | Complex polygenic nature |
| 2014 | Central sensitization in migraine[48] | Migraine-pain connection | Neuroimaging, electrophysiology | Explained chronic pain link | High | Mechanistic insights | Technical complexity |
| 2016 | Botox for chronic migraine[49] | Botox efficacy for prevention | RCTs | New treatment option | High | Strong evidence | Invasive procedure |
| 2017 | PACAP in migraine[50] | PACAP as migraine mediator | Molecular biology, clinical trials | New treatment target | Moderate | Novel mechanism | Early stage research |
| 2018 | CGRP mAbs approval[51] | First targeted migraine preventives | Clinical trials, regulatory review | Treatment revolution | High | High efficacy | Cost barriers |
| 2019 | Gepants for acute treatment[52] | Oral CGRP antagonists work | RCTs | New acute treatment class | High | Non-vasoconstrictive | Limited long-term data |
| 2020 | Gut-brain axis in migraine[53] | Microbiome-migraine link | Microbiome analysis | New research direction | Emerging | Novel approach | Preliminary findings |
| 2021 | Migraine and mental health[54] | Migraine-depression link | Longitudinal studies | Highlighted comorbidity | High | Clinical relevance | Confounding factors |
| 2022 | Neuromodulation devices[55] | Non-drug treatment options | RCTs | Expanded treatment choices | Moderate | Non-pharmacological | Variable efficacy |
| 2023 | Long-term CGRP effects[56] | Sustained efficacy/safety | Longitudinal studies | Confirmed treatment value | High | Long-term data | Selection bias |
| 2023 | Oxidative stress in migraine [57] | ROS role in migraine | Biochemical analysis | New treatment targets | Moderate | Mechanistic insights | Clinical translation needed |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 2023 | VR for migraine pain [58] | VR reduces acute pain | Clinical trials | Novel non-drug option | Emerging | Innovative approach | Small sample size |

| Title | Source/Author | Year | Type | Key Findings |
|---|---|---|---|---|
| Migraine Biomarkers Identified via Proteomic Analysis (PhD Dissertation)[59] | University of Copenhagen (Jensen et al.) | 2021 | Dissertation | Identified 5 potential blood biomarkers for episodic migraine. |
| Real-World Evidence on Anti-CGRP Drugs (Patient Registry Report)[60] | Migraine Research Foundation | 2022 | Registry Data | 58% of patients on anti-CGRP therapies reported ≥50% reduction in migraine days. |
| EEG-Based Migraine Prediction (IEEE Conference Paper)[61] | IEEE BHI Conference (Zhang et al.) | 2018 | Conference | EEG + ML predicted migraines 3h pre-attack with 88% specificity. |
| Economic Impact of Migraine in the U.S. (NIH Report)[62] | National Institute of Neurological Disorders and Stroke (NINDS) | 2020 | Government Report | Annual U.S. economic burden: $36B (direct + indirect costs). |
| Migraine and Gut Microbiome (Clinical Trial Preprint)[63] | ResearchSquare (Aizawa et al.) | 2023 | Preprint | Probiotic intervention reduced migraine frequency by 30% in RCT. |
| Behavioral Triggers in Migraine (WHO Workshop Summary)[64] | World Health Organization | 2010 | Workshop Report | Stress, sleep disruption, and fasting ranked as top self-reported triggers. |
| FDA Approval Summary: Neuromodulation Devices for Migraine[65] | FDA Database | 2022 | Regulatory Report | Approved 3 new devices (e.g., gammaCore vagus nerve stimulator). |

| | | | | |
|---|---|---|---|---|
| Gender Disparities in Migraine Care (CDC Analysis)[66] | CDC Health Disparities Report | 2019 | Government Data | Women are 50% less likely to receive preventive treatments than men. |
| Psychedelics for Chronic Migraine (MAPS Phase I Trial)[67] | Multidisciplinary Association for Psychedelic Studies (MAPS) | 2022 | Clinical Trial | Psilocybin showed 40% reduction in chronic migraine frequency. |
| Migraine in Athletes: NFL Player Study[68] | American Academy of Neurology (AAN) Abstract | 2018 | Conference Abstract | 22% of retired NFL players met criteria for chronic migraine. |

What the applications on migraine with AI ?

| Category | Title | Authors/Journal | Key Findings |
|---|---|---|---|
| AI/ML Diagnosis | "Transformer-Based Multimodal Fusion for Migraine Prediction Using Wearables and EHRs"[69] | Liu et al., Nature Digital Medicine (2024) | Combines smartwatch + EHR data for 94% prediction accuracy 3h pre-attack. |
| Neurobiology | "Cortical Spreading Depression Mechanisms in Migraine: 7T fMRI Evidence"[70] | Hadjikhani et al., Brain (2023) | Identifies hyperexcitable visual cortex as a biomarker for aura. |
| Treatment | "Phase III Trial of Psilocybin for Chronic Migraine: Sustained Reduction in Attack Frequency"[71] | Schindler et al., NEJM (2024) | Single dose reduced attacks by 50% for 6 months (vs. 18% placebo). |
| Public Health | "Global Disparities in Migraine Care: A WHO Report (2023)"[72] | WHO | 75% of patients in LMICs lack access to acute treatments. |
| Gut-Brain Axis | "Probiotic Intervention Reduces Migraine Frequency via Gut Microbiota Modulation"[73] | Arzani et al., Nutrients (2023) | Lactobacillus strains cut migraine days by 40% in RCT. |
| Pediatric | "Machine Learning Predictors of Pediatric Migraine Chronification"[74] | Buse et al., Pediatrics (2024) | Sleep disruption + anxiety scores predict progression (AUC: 0.89). |
| Neuromodulation | "Non-Invasive Vagus Nerve Stimulation (nVNS) for Acute Migraine: Real-World Data"[75] | Tassorelli et al., Cephalalgia (2023) | 60% patients achieved pain freedom at 2h (n=10,000). |

What is the Advanced AI/ML/DL Applications in Migraine Management?

| Application | AI Technique | Data Source | Key Innovation | Performance | Clinical Validation | Year |
|---|---|---|---|---|---|---|
| 1. Early Biomarker Detection[76] | Deep Neural Networks (DNN) | Blood plasma proteomics | Identified 7 protein biomarkers for prodromal migraine | AUC: 0.94 | Phase II trial ongoing | 2023 |
| 2. Attack Prediction[77] | Transformer Models | Smartwatch PPG + sleep data | Predicts attacks 4-6 hours in advance using multimodal data | Precision: 91% | 500-patient RCT | 2024 |
| 3. Treatment Optimization[78] | Reinforcement Learning | CGRP mAb treatment logs | Dynamically adjusts dosing intervals for chronic migraine | 42% fewer attacks | FDA-cleared algorithm | 2023 |
| 4. Neuroimaging Analysis[79] | 3D CNN | 7T MRI scans | Detects cortical spreading depression in migraine aura | Sensitivity: 96% | Multi-center study | 2022 |
| 5. Digital Phenotyping[80] | Federated Learning | Mobile app data (10M users) | Classifies 6 migraine subtypes via daily symptoms | F1: 0.88 | CE Marked (EU) | 2023 |
| 6. Drug Repurposing[81] | Graph Neural Networks | Drug-target databases | Identified 3 FDA-approved drugs with anti-migraine potential | Hit rate: 1:200 | Preclinical validation | 2024 |
| 7. Pediatric Diagnosis[82] | Explainable Boosting Machines | Pediatric EHRs | Distinguishes migraine from other childhood headaches | Accuracy: 87% | CHOP/NIH validation | 2023 |
| 8. Non-Pharmacologic Therapy[83] | Computer Vision | VR headset eye-tracking | Detects visual aura onset for trigger-specific therapy | Latency <2ms | NIH grant-funded | 2024 |
| 9. Genetic Risk Scoring[84] | XGBoost | UK Biobank GWAS data | Polygenic risk score predicts migraine susceptibility | OR: 3.2 (95% CI) | 100K cohort | 2023 |
| 10. Real-World Evidence[85] | Causal ML | 23M insurance claims | Quantifies treatment effectiveness in comorbid patients | HR: 0.68 | Retrospective | 2022 |

| Application | AI Technique | Data Source | Key Innovation | Performance | Clinical Validation | Year |
|---|---|---|---|---|---|---|
| 11. Wearable Integration[86] | TinyML (Edge AI) | EEG headband | On-device aura detection with <50ms latency | Specificity: 99% | FDA 510(k) pending | 2024 |
| 12. Patient Stratification[87] | Topological Data Analysis | 360° clinical data | Discovered 4 novel endotypes for precision medicine | Cluster purity: 0.91 | ICHD-4 aligned | 2023 |
| 13. Telemedicine Triage[88] | Multimodal LLMs | Video consultations | Automates MIDAS scoring from doctor-patient dialogues | $\kappa$=0.82 | EU-certified | 2024 |
| 14. Nutrition Triggers[89] | Bayesian Networks | Food/symptom logs | Personalizes trigger food avoidance plans | RR: 0.45 | 8-week RCT | 2023 |
| 15. Neuromodulation[90] | RL + Digital Twin | fNIRS + simulator | Optimizes tDCS parameters in real-time | 55% efficacy boost | Phase I/II trial | 2024 |

How to diagnose and treat migraines?

| Category | Method (AI/ML/DL) | Data Used | Key Findings | Accuracy/Performance | Study (Year) |
|---|---|---|---|---|---|
| Diagnosis | Random Forest[91] | Electronic Health Records (EHR) | Predicts migraine vs. other headaches using patient history and symptoms. | 89% Accuracy | Hou et al. (2022) |
| | CNN (Deep Learning)[92] | MRI/Neuroimaging | Detects cortical abnormalities linked to migraine with aura. | 92% Sensitivity | Zhang et al. (2023) |
| | NLP (BERT Model)[93] | Clinical Notes | Extracts migraine triggers (e.g., stress, sleep) from unstructured text. | F1-Score: 0.85 | IEEE EMBC (2021) |
| Attack Prediction | LSTM (Deep Learning)[94] | Wearable (Fitbit/EEG) | Predicts migraine onset 2–3 hours early | 87% Precision | Chen et al. (2023) |

| Category | Method (AI/ML/DL) | Data Used | Key Findings | Accuracy/Performance | Study (Year) |
|---|---|---|---|---|---|
| | | | using heart rate variability. | | |
| | SVM (Machine Learning)[95] | Weather + Patient Data | Links atmospheric pressure changes to migraine attacks. | 78% AUC-ROC | GBD Collaborators (2020) |
| Treatment | Reinforcement Learning[96] | Mobile App Data | Personalizes treatment plans (e.g., drug dosage adjustments). | 30% Reduction in Migraine Days | Nature Digital Medicine (2022) |
| | GANs (Deep Learning)[97] | Synthetic Patient Data | Generates virtual patients to test treatment responses. | N/A (Simulation) | MIT Tech Review (2023) |
| | Clustering (k-Means)[98] | Genetic + Lifestyle Data | Identifies 3 migraine subtypes for targeted therapy. | Silhouette Score: 0.72 | NIH Grant Report (2021) |

Search Strategy and Data Sources

An symmetric review was conducted to find relevant research on the use of artificial intelligence (AI), machine learning (ML), and deep learning (DL) for migraine diagnosis. The electronic databases used for this search were IEEE Xplore, ScienceDirect, Google Scholar, Scopus, and Web of Science.

The search was carried out using a combination of Medical Subject Headings (MeSH) terms with Boolean operators, as represented by the query ("migraine" OR "migraine disorders" OR "headache") AND ("artificial intelligence" OR "machine learning" OR "deep learning" OR "neural networks") AND ("diagnosis" OR "classification" OR "prediction" OR "detection`).

Inclusion and Exclusion Criteria

Inclusion Criteria

Articles published in journals specifically on migraine diagnosis, classification, or prediction by AI/ML/DL, Peer-reviewed journals, conference papers, Clinical data-based research, neuroimaging (MRI/EEG), or patient reports.

Exclusion Criteria

Non-migraine or non-headache disorder research, review papers, editorials, or non-empirical studies (except where used as background reference), or Duplicate publications or low quality research (e.g., poor sample size, no validation).

Screening and Selection Process

The search retrieved over 130 articles, which were filtered via a two-step filtering process: Title and Abstract Screening. After that, each research paper was assessed and screened for relevance and correctness.

Following this stage, there were approximately 60 papers left for full-text evaluation.The rest of the papers were thoroughly examined for methodological quality, dataset quality, and applicability to AI.

Studies were categorized into:
AI/ML-based diagnosis of migraine (e.g., based on patient history, EEG, MRI).
Subtype identification (e.g., migraine with aura vs. without aura).
Comparative research (AI versus conventional diagnostic techniques).
Final selection: 30 high-quality papers were included in the review.

Data Synthesis and Extraction

Essential details were tabulated into a properly laid-out table containing:

Study design (retrospective/prospective, dataset size).
AI/ML model utilized (e.g., CNN, SVM, Random Forest).
Input features (clinical data, imaging, biomarkers).
Performance metrics (accuracy, sensitivity, AUC-ROC).
Limitations and biases.

Quality Assessment
The articles chosen were analyzed using: PRISMA guidelines (for systematic reviews), QUADAS-2 (for diagnostic accuracy studies) and IEEE/ACM guidelines (for AI/ML technical validity). 6. Ethical Considerations Only ethically approved or publicly available datasets were used. Studies involving patient data required IRB approval or sufficient consent procedures.

Recent developments in artificial intelligence (AI) and machine learning (ML) offer a significant chance to improve diagnostic precision. Through applying predictive modeling to extensive patient data sets, such as electronic health records (EHRs), symptom diaries, and genomic profiles, ML algorithms can detect diagnostic patterns that could evade traditional clinical evaluations. Supervised learning models like support vector machines (SVMs), random forests, and deep neural networks (DNNs) may be trained on historical patient data to predict migraine subtypes with high sensitivity and specificity.

Furthermore, natural language processing (NLP) enables extraction of semantic features from unstructured clinical text, allowing automated symptom clustering and risk stratification. The integration of wearable neurophysiological signals (e.g., electroencephalography (EEG), heart rate variability (HRV)) with AI-based analytics has the potential to advance early detection and personalized therapeutic interventions.

This means that while migraine remains a clinically diagnosed condition, the convergence of computational neurology and AI-powered diagnostics holds significant promise for standardizing and optimizing migraine detection, ultimately improving patient outcomes and healthcare efficiency.

## XVII. Conclusion

Through this paper, it is concluded that Migraine is a chronic neurological disorder characterized by unilateral, pulsating headache, often with sensitivity to light, intolerance to sound, nausea, and vomiting. Current diagnostic criteria, as outlined by the International Classification of Headache Disorders (ICHD-3), are largely reliant on clinical history due to the absence of definitive biomarkers or neuroimaging correlations. Such dependence on subjective data can foster heterogeneity in diagnosis, showcasing the need for more objective, evidence-based strategies.

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