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Review Article

Characterization of the White Matter Structures in Migraine and Healthy Patients using Brain MRI

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Received date: September 13, 2023; **Accepted date:** October 31, 2023; **Published date:** January 08, 2024

Citation: Abrar B. Elmalik, Amal M, Mohammed, Miada A. Abdelraheem, Nashwa A. Basheer, Alia A. Fadlallah, (2024), Characterization of the White Matter Structures in Migraine and Healthy Patients using Brain MRI, *Clinical Research and Clinical Trials*, 9(1); **DOI:10.31579/2693-4779/166**

Abstract:

Headache is a very common disorder of symptom complexity with multifactorial origin. Migraine-related intracerebral, deep white matter, the subcortical, the periventricular, and the callosal commissure locations are all involved in white matter lesions (WMLs), which are most likely microvascular and can be found in all four lobes. Migraine is a common neurological condition that is characterized by recurring headaches of moderate to severe intensity and related symptoms such as nausea, vomiting, and phonophobia, associated with increased reactivity to sound and light.

Aim: The purpose of this review is to examine how migraines affect the corpus callosum, deep white matter, and their appearance in brain MRI images.

Conclusion: The study concluded that migraine prevalence was found in the white matter (WHMs) of the brain showed as a subcortical and deep white matter lesion in MRI. Whereas most gender affected by migraine was females compared to males. The prevalence was found in the white matter hyperintense in 43.1% associated with nausea and dizziness. Also, this study found that the imaging protocol that was used in diagnosis was the T1-weighted SE sequence, T2-weighted FSE sequence, and FLAIR. Finally, the study found MRI plays a significant role in defining migraine according to the changes in the brain tissue which appear as a high signal intensity on the white matter either bilateral or unilateral.

Keywords: WHM (white hyperintense matter); MRI (magnetic resonance imaging); SE (spin echo-) FSE (fast spin echo)

Introduction

Headache is a very common disorder of symptom complexity with multifactorial origin. There are about 300 types of headaches identified still they are not classified. According to the International headache society (IHS) classification, headaches are classified into Primary headaches, Secondary headaches, and Unclassified headaches. The primary headache is classified

into Migraine headache, Tension-type headache, Cluster headache, and other types of headache and crania facial pain [1]. The IHS defined Migraine as a recurring primary headache disorder that typically affects one side, unilateral and pulsatile with moderate to severe pain, with attacks lasting for four to seventy-two hours these symptoms may result in changes to the cerebral cortex's structure and function [2]. The subcortical, the periventricular, deep white matter, and the callosal commissure site are all implicated in migraine-related intracerebral WMLs, which are most likely to be microvascular and can be identified in all 4 lobes. Migraine is a common neurological illness characterized by recurring headache attacks of moderate to severe intensity and concomitant symptoms such as nausea, phonophobia vomiting, photophobia, and heightened sensitivity to sound and light [3]. There are various stages of migraine: interictal, premonitory, aura, headache, and postdrome. Several cortical and subcortical brain regions, including the hypothalamus and brainstem nuclei that affect nociceptive transmission, interact intricately during the premonitory phase, which can start as early as three days before the headache phase. An aura phase may occur in one-third of patients during some attacks and, a cortical spreading depression like event; a slowly spreading wave of neuronal and glial cell depolarization and hyperpolarization is likely involved. Auras are brief neurologic symptoms that occur in around one-third of migraineurs and describe a type known as migraine with aura (MA). The well-researched tri gemino vascular system, is activated during the headache phase [4].

There are two types of migraine headaches. One is called "migraine with aura" and the other is called "migraine without aura". The difference between the two is whether or not someone experiences slowly spreading visual and sensory disturbances before the headache starts (1). About 15% of people suffer from migraines which cause lots of difficulties in daily life, including

missing work [5]. Migraines are a significant financial burden on healthcare systems around the world [6]. Women experience migraines more frequently than men do, them three times more frequently [7]. Those who have first-degree relatives who have aura are more likely to suffer from migraine with develop the disease unlike those who do not. Except for familial hemiplegic migraine, a primarily monogenic disorder, no single gene associated with migraine with aura has been identified. The most prevalent kind of aura is visual. Auras that are not visible include sensory, motor, and language issues [8].

Migraine is a frequent condition in the general community; nevertheless, the clinical phenomenology of migraine varies throughout time (in the corpus callosum and the white matter). Despite the pain and difficulty that migraine problems cause, white matter hyperintensities (WMHs) present in migraine sufferers' brain MRIs have not been examined. Migraine is frequently underdiagnosed and undertreated in clinical settings: one significant reason for this may be a lack of understanding among the general community of the migraine diagnosis aspects, namely the symptoms that aid in the differentiation of migraine vs non-migraine headache. In the Migraine Mechanism Headache, a fundamental neuronal malfunction, migraines were caused by number of intracranial and extracranial alterations that result in migraines. Migraine aura is hypothesized to be induced by depolarization of the glia and neurons that extends throughout the cerebral cortex [9]. This, then stimulates trigeminal afferents, altering the pain-sensitive meninges in an inflammatory manner, which use both cerebral and peripheral reflex pathways to cause migraine headaches.

In migraine patients, neuroimaging investigations have commonly found in ischemic and silent infarct-like lesions, WMHs, and volumetric abnormalities in gray and white matter [10-11]. WMHs are often little punctiform hyperintense lesions that are confined to periventricular deep, subcortical, and infratentorial tissues and have no mass effects. On MRI, WMHs are commonly found in T2 and FLAIR (fluid-attenuated inversion rescue weighted) sequences. WMHs are a common observation in migraine patients using T2-weighted and FLAIR sequences [12]. The aim of this study was to reviews for studies that looked at the influence of migraine headaches on the corpus callosum, deep white matter, and their appearance in brain MRI imaging.

Definition:

Migraine is an intense, chronic, repeated headache, that its basically occurred unilaterally, but it can be experienced as a generalized throbbing headache, which can extend to the neck or even the body [13], also its a common, disabling, mostly treatable headache, although remains under estimated and under treated. Migraine is 3 times more common in females, due to hormonal factors, with a 2:1 ratio, and tends to affect healthy people [14]. Migraine is the second neurological disorder that can be severely debilitating. It highly affects social and economic aspects [15]. It is a significant cause of morbidity in young people, particularly in students [16].

Classification:

International Headache Society classified migraine into 3 main conditions: primary forms of Migraine with aura type one: Migraine with typical aura, Migraine with brainstem aura, Hemiplegic migraine, Retinal migraine. 2. Migraine without aura. 3. chronic migraine (1).

Pathophysiology: Migraine is a neurovascular event which happens in people with genetically susceptible or sensitive nervous system. It's a sophisticated disorder with polygenic inheritance and environmental components [17]. There are many theories in its pathophysiology, the cortical spreading depression supposed it's a disease of the brain as angina is a disease of heart [18]. The second one is the disruption of normal brain functioning suggested to be the cause of migraine aura and pain. The last theory says it results from the widening the blood vessels that surround the brain. Migraine had been divided into phases: (premonitory, aura, headache, and postdrome l) which can occur in order or there may be an overlap [19]. Modulating the pain that results from the disruption of neural networks in the brain is part of the pathophysiology. Studies have shown the trigemino vascular system, which consist of afferent neurons that feed information to the trigeminal nucleus caudal and efferent neurons that supply vascular networks, is controlled by the brain stem and diencephalic nuclei. As a result of these networks being active, headache

e is interpreted as meningeal vasodilation and inflammation [20]. Causes: Exact cause of migraine is not clear, but there are several risk factors make people more susceptible to migraine, such as woman gender and depression (increases the although many patients with migraine don't have depression) [21]. Migraine trigger factors: are not quantifiable nor consistent in their effect (10). Mainly like, diet such as (cheese, tea, coffee, or nuts), strong odor, bright light, loud sounds, weather changes, stress, and more or less sleeping than usual (18). Risk factors: 1. Family history. 2. Age: tends to start in adolescence and reach its peak in the 30s. 3. Sex: women are three times susceptible to migraine than men. 4. Hormonal changes: for women with migraine, headache starts just before or after the onset of menstrual cycle (9). headache is commonly caused by a sudden fall in estrogen level prior to menstruation (11). Clinical picture: The presentation of migraine is in four phases: 1. Premonitory phase:(the prodromal) is known as the presence of symptoms that are not painful (12), which occur prior to headache onset, these symptoms like, yawning, food graving, thirst, mood changes, cognitive difficulties and sleepiness (13). 2.Aura: Aura is a precursor to over one-third of migraine. The third edition of the ICHD describes migraine with aura consisting of recurrent, minute-long attacks characterized by unilateral, reversible, sensory, visual, or other neurological abnormalities, headache follows after that, and other typical migraine signs. The most typical symptom is visual disturbance, however, there are also indications of sensory, linguistic, motor, and higher cerebral function impairment (4). 3. headache: Trigeminal sensory nerve activation, which produces migraine-like pounding pain, causes headaches (14). The postdromal phase: it's the period from headache recovery until the patient returns to normal (15). It lasts up to 72h and has non-headache symptoms, like fatigue, concentration difficulty, and neck stiffness (17). edition defined prodrome and postdrome as up to 48 hr form the onset rd The ICHD 3 of pain to a 48 h after pain relief [22].

Management:

For accurate diagnosis, consideration must be given to the clinical presentation of each type of migraine [23]. Aura-free migraine is characterized by repeated attacks of headaches for four to seventy-two hours, are generally unilateral, and are worsened by regular physical activity (1), and commonly with associated symptoms such as photophobia, phonophobia, nausea and vomiting, and also there may be a prodromal and postdromal indications [24]. Migraine with aura: Typically, aura comes before a headache, although it can sometimes occur during a headache attack [25]. The diagnosis of headache depends on the presentation history and physical exam (24). Medical history: should include (at least): age at the beginning of a headache, length, characteristic of pain, associated symptoms, aura, and history of medication use (24). Five or more attacks that meet the criteria B-D (1). B. headache bouts that last 4 to 72 hours (if not treated). C. a headache that possesses at least two of the following four elements: (1) location to one side. 2. pulsed quality. 3. discomfort that varies in intensity from modest to severe. 4. aggravating or encouraging aversion to exercise D. A headache that included at least one of the following: Nausea and/or vomiting. Photophobia and phonophobia are two examples of phobias. E. not better explained by another ICHD-3 diagnosis. Migraine accompanied by an aura: A. at least two assaults meet requirements B and C. B. 1 or more of the following aura symptoms that are entirely reversible: 1. The visual. 2. Senses. 3.speech & language. 4. motor. 5. The brainstem. 6. Retinal. C. at least 3 of the following 6 criteria: 1. at least 1 aura symptoms that spread gradually over 5 minutes or more. 2. 2 or > aura symptoms occur in sequence. 3. each symptom last five- sixty minutes. 4. at least 1 aura symptom is one side. 5. At least one condition is positive. 6. A headache appears concurrently with or earlier than the aura within 60 minutes. D. Not more adequately

explained by any ICHD-3 diagnosis. Investigation: In migraine sufferers with normal physical examinations, neuroimaging is not required. However, it may be considered in the case of an unusual, prolonged, or persistent aura; an increase in frequency, intensity, or change in migraine presentation; the first or worst migraine; a brainstem aura; a late-life migrainous accompaniment; a side-locked migraine; a migraine aura without a headache; or a migraine following a traumatic event [26]. There are several different ways that neuroimaging is used to diagnose headache and its overall yield is to identify significant abnormalities in patient presenting with headache was reported to be less than 8% [27]. The European Federation of neurological studies (EFNS) task force does recommend doing neuroimaging routinely in adult and pediatric patients with migraine with no changes in severity or pattern or with other focal neurological symptoms [28]. Although magnetic resonance imaging (MRI) and positron emission tomography (PET) imaging showed significant potential in revealing the pathophysiology of headache and determining the therapeutic effects (28). The frequent MRI finding is periventricular white matter, and subcortical bruises which are further common in migraineurs (12-48%) than healthy people (2-11%) [29]. Differential diagnosis: Other primary headaches, Tension type, and Cluster headaches [30]. Or some secondary headaches such as posttraumatic headaches (24). To differentiate between these types of headaches there are some features which distinguish them, include site of headache, quality, intensity, length of pain, associated symptoms, and behavior during attack (23). Tension- type headache is usually mild to moderate bilateral pain and doesn't have any migraine-associated symptoms, while cluster headache is severe one side pain with associated ipsilateral autonomic symptoms and last in less than 3 hours (23). Treatment: General principles: Evidence based guidelines from the United States, Canada and Europe recommend lifestyle modification, triggers avoidance and healthy cooperate mechanisms (24). Treatment for acute migraines: The best course of action is based on the patient's needs as well as the features of the headache, such as its frequency, severity, ability to interfere with daily activities, related symptoms, peak time, and any underlying medical conditions [31]. The first line: for mild to moderate is: acetaminophen and NSAID: Acetaminophen is less effective than NSAID, but it didn't cause gastritis or antiplatelet effect (24). Triptans, 5hydroxytriptamine receptor agonist is also effective as first line therapy, they are found in oral, nasal spray, and injectable forms. Triptans have more efficacy than oral NSAIDs in relieving pain within 2 hours [32]. The serotonin (triptans) is the first-choice therapy in moderate to severe migraine attacks that didn't respond to NSAIDs (32). The second line therapy: They were put in the second line because of their adverse effect, the potential of abuse, cost, and administrative route (24). Dihydroergotamine: it's a strong effective drug but have more side effects than triptan due to low receptor specificity, the main side effect is nausea so metoclopramide is given before it's administration (24). Opioids have moderate effectiveness its migraine treatment, but routine use is not recommended because it had a high abuse side effect (24). Acupuncture (form of traditional Chinese medicine which is applied by placing needles in specific location on the patient's skin to achieve therapeutic effect, one of its most common application is to treat chronic pain especially migraine pain. It has a measurable effect on migraine attack frequency and duration [33]. The best course of treatment for chronic migraine includes reducing risk factors, identifying triggers, treating comorbidities, and using acute and prophylactic medications as preventative measures. Acute migraine therapies are the same as those for episodic migraine [34]. Indications for drug treatment in the prevention of migraine include frequency, the effect on quality of life, and medication overuse. Beta -blockers, calcium channel blockers,and anti-convulsants showed effectiveness in preventing migraine attacks (34). Many studies showed that oxidative stress is involved in migraine, thus antioxidant appear to be helpful in its prevention (33). Vitamins and mineral including magnesium, coenzyme Q10 and fever few and riboflavin reduce the number of migraine attack days (33). In the case of chronic migraine, botulinum toxin type can reduce the number of migraine days per month by two days in patients with chronic migraine. Compared with the placebo group, there were no major side effects from the treated group [35].

Discussion

Migraine is a common condition among people, as it affects a person's performance during the day. Migraine prevalence was found in the white matter (WHMs) of the brain showed as a subcortical and deep white matter lesion in MRI. Whereas the most sex affected by migraine are females compared with males, the significance and correlation to migraine characteristics remain a matter of discussion. The age is one of the significant factors frequent among adults. A lot of previous studies showed no significant relationship between the time and duration of migraine by years which presence of WMHs [36].

Diagnosis

Migraine is detected by clinical examination, and brain magnetic resonance imaging is the best for diagnosis. The prevalence was found in the white matter hyperintensities in 43.1% with associated by nausea and dizziness [37]. The diagnosis imaging protocol was T1-weighted SE sequence, T2-weighted turbo SE sequence, and FLAIR. T2 weighted and flair shows high signals intensity on white matter either bilateral or unilateral [38]. In a recent study, it was discovered that brain regions associated with the visual, auditory, and somatosensory networks have a functional magnetic resonance that has linearly increasing sensory network connectivity over the pain-free interval, with a peak before the headache starts that "dropped" to the initial level during the headache [39].

Types

The accordance with previous studies migraine categories many much sub types; with aura and without * aura, and chronic which depend on how long time of occurring [40].

Treatment

Margarine should have been managed clinically by pharmacological therapy medications such as (NSAIDs). Although a study conducted by Ahmed, Sherihan Rezk et al.2022 found the association of MRI WMHs white matter hyperintense a weak response to acute headache medication. [41].

Conclusion:

The study concluded that migraine prevalence was found in the brain white matter (WHMs) showed as a subcortical and deep white matter lesion in MRI. Whereas most gender affected by migraine was females compared to males. The prevalence was found in the white matter hyperintense in 43.1% associated with nausea and dizziness. Also, this study found the imaging protocol used in diagnosis was T1-weighted SE sequence, T2-weighted turbo SE sequence, and FLAIR. Finally, the study found MRI plays a major role in the characterization of migraine according to the changes in the brain tissue which appear as a high signal intensity white matter either bilateral or unilateral.

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DOI:10.31579/2693-4779/166