



NERVOUS SYSTEM DISORDERS AND HEADACHE

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ABSTRACT

Neuropathology is the medical science that studies diseases of the nervous system with motility, sensitivity, and balance disorders. The brain can be affected by various disorders, such as stroke, epilepsy, multiple sclerosis, Alzheimer's disease, Parkinson's disease, brain infection, speech disorders, movement disorders, sleep disorders, encephalitis, aphasia, meningitis, and headache, which can affect the entire nervous system, including the spinal cord and nerves. Here in this paper, we will focus our study on headache, which are frequent and debilitating disorders of this medical branch. There are various etiologies of headache, and these diseases are important not only for their pathological severity but also for their emotional and social cost. About 13% of the population in Western countries suffers from headache, affecting more women than men. Various factors can trigger a headache, but in many cases, the reason why an individual has a headache is unknown. Some common foods that can be triggering factors include wine, alcohol, cheese, chocolate, and nuts. Other individuals may be sensitive to cigarette smoke, and headaches can also happen after physical exertion, stress, lack of light, continuous noise and hypertensive states. The characteristic headache is easily identifiable by its symptoms and can be followed by tiredness, vision disturbances, hypersensitivity to light, vomiting and nausea. Some studies report that pro-inflammatory cytokines, such as IL-1, IL-6, and tumor necrosis factor (TNF), are implicated in headache and increase during the acute phase. Headache can be episodic and unilateral and can occur more frequently in patients with asthma and allergies involving immune cells, including central nervous system (CNS) mast cells (MCs). Brain MCs can be activated by neurotransmitters such as substance P (SP) and neurotensin (NT), stimulators of pro-inflammatory cytokines. In addition, brain MCs can produce IL-6 and vascular endothelial growth factor (VEGF) capable of causing vasodilation. This article aims to provide an overview and update on headache and brain disorders.

KEYWORDS: neuropathology, headache, classification, migraine, cytokine, immune, brain disorder, inflammation

INTRODUCTION

Neuropathology is the branch of medicine that studies diseases of the nervous system concerning the brain, spinal cord, and nerves. Various pathologies affect the brain, such as stroke, epilepsy, multiple sclerosis, Alzheimer's disease, Parkinson's disease, infections, speech disorders, movement disorders, sleep disorders, encephalitis, aphasia, meningitis, and headaches.

Headaches, including migraine, are a common affliction worldwide responsible for significant disability and have emotional and economic repercussions. Prevalence rates in Western countries are high, with tension-type and general headache affecting 60-80% and migraine accounting for 15% of the population, with women affected more frequently than men (1).

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There are many different forms of headache, but they are broadly classified into two distinct categories, primary and secondary headaches, classifications defined by The International Classification of Headache Disorders 3rd edition (2). Primary headaches are not caused by another underlying condition and are the most prevalent form of headache experienced in the population. Secondary headaches are a symptom of a separate underlying disease or condition and occur much less frequently than primary headaches, although they can be related to life-threatening diseases. Therefore, headache is a complex disorder that involves both the peripheral and central nervous systems, with the additional involvement of cardiovascular and inflammatory mechanisms.

Types of headaches and their causes

Headache manifests in many forms and can be separated into two major categories: primary and secondary headaches. Primary headaches are disorders caused by independent pathomechanisms (not related to another disease) and account for most cases (about 98%) (3). The main types of primary headaches include migraine, tension-type headache, and trigeminal autonomic cephalalgias, such as cluster headache. These headaches can cause severe pain but are not caused by another underlying condition and, therefore, are not dangerous to the patient's life.

Following tension-type headache, migraine is the second most common type of headache, and it consists of diverse symptoms that are classified into four phases: the premonitory phase, aura phase, acute headache phase, and the postdrome phase that follows the resolution of the headache (4). A migraine is episodic and can last between 4 and 72 hours, and it is characterized by pulsating, throbbing pain, sensitivity to light and sounds, nausea, vomiting, and in many cases, visual disturbances called auras (5).

The pathophysiological basis for migraine is still being investigated, but evidence has suggested that it is caused by vascular and neurogenic mechanisms with the involvement of the immune system (6,7). It is associated with vasodilation, the involvement of serotonin and estrogen, altered brain regions functioning with distinct neuronal activation patterns, activation of the trigeminovascular system, pain sensitization of nociceptors, and an electrophysiological phenomenon of depolarization called cortical spreading depression (5,8).

Many different endogenous or exogenous factors can "trigger" a migraine headache, including stress, physical exertion, hypertensive states, menstruation, changes in weather or sleep, continuous noise, cigarette smoke, and certain foods such as cheeses or processed meats, alcohol (particularly red wine), chocolate, or nuts (9). However, a trigger is often not identifiable, and the reason for the headache is unknown.

Secondary headaches are a symptom of a separate underlying disease or condition that affects pain-sensitivity structures of the head and causes headache. These types of headaches need to be investigated immediately to identify the underlying problem, which can be severe and endanger the life of the sufferer. Many different disorders can cause headache, including the trauma of the head or neck, vascular disorders, epileptic seizures, intracranial infection, and intracranial neoplasms, amongst others (2).

Some common secondary headaches are caused by space-occupying lesions, central nervous system (CNS) infections such as meningitis or encephalitis, subarachnoid haemorrhage, giant-cell arteritis, cerebral venous thrombosis, and idiopathic intracranial hypertension (3).

Although they occur much less frequently, secondary headaches can be life-threatening. Some warning signs associated with secondary headaches include the sudden onset of intense pain, pain and stiffness in the neck, rash, fever, and changes in consciousness related to dangerous conditions.

Headache can cause pain in different areas, and the location of the pain is essential in determining the type of headache and arriving at a diagnosis. Pain can be unilateral, side-shifting, unilateral, bilateral, or unilateral, alternating with bilateral (10). The duration of pain further classifies headaches (lasting less than or more than four hours) and the number of days afflicted by headache (episodic versus chronic) (2).

Immunological aspects of headache

The immune system is also implicated in headache, particularly in migraine, where contributing immunological changes have been established. Neurogenic inflammatory agents are likely involved in the activation and sensitization of peripheral nociceptors, contributing to activation of the trigeminal nerves and inciting the release of vasoactive neuropeptides that contribute to inflammation (7).

Cytokines are immunomodulatory proteins which play an important role in innate and adaptive immunity and are involved in the physiological and pathological mechanisms of neuroinflammation and pain. Studies have shown a link between pro-inflammatory cytokines such as IL-1, IL-6, and tumor necrosis factor (TNF) (11-13) and headache, with increasing levels during the acute phase of an attack (14).

The action of these pro-inflammatory mediators on peripheral nociceptors is implicated in the sensitization of pain (15) and raised levels of these cytokines have been reported during migraine headache (13,16). The sensitization of nociceptors, partly mediated by inflammation and the immune system, can lead to persistent pain (17). Additionally, intracranial mediators such as nerve growth factor (NGF), Substance P (SP), and calcitonin gene-related peptide (CGRP) could also contribute to primary afferent nociceptor sensitization (18).

Headache can also have a higher rate of frequency in individuals with asthma and allergies, as it involves immune cells such as CNS MCs (19). MCs, derived from hematopoietic pluripotent bone marrow stem cells, migrate to reside near epithelial cells, nerves, and blood vessels. MCs are involved in innate as well as adaptive immune responses and produce and release different inflammatory mediators including cytokines (14).

Migraine occurs with neuroinflammation and involves the innate immune response in the CNS, activating different immune cells such as macrophages, microglia, dendritic cells, and MCs (14). These MCs can be activated by neurotransmitters, including SP and neurotensin (NT) which stimulate the release of pro-inflammatory cytokines and can produce IL-6 and vascular endothelial growth factor (VEGF) which can cause vasodilation.

CONCLUSIONS

Headache is a common and debilitating neuropathology that accounts for disability and economic burden around the world. Primary headaches are the largest types of headache experiences and include tension-type headache, migraine, and cluster headaches. Secondary headaches include those types with a separate, underlying cause in which the headache is a symptom. Often, they are linked with serious, life-threatening disorders, and it is imperative to identify the underlying cause for the health of the patient. In the case of secondary headaches, there is an identifiable cause and if treated, the headache usually subsides as a symptom. In the case of primary headaches, the reason for the headache is often unknown, although certain triggers may exist that bring about onset. These can be endogenous or exogenous factors such as stress, physical exertion, menstruation, changes in weather or sleep, or certain foods. The pathogenic mechanisms that induce primary headaches involve complex interactions between the neurological, vascular, and immune systems. Therefore, more research is still needed to further characterize the origin and nature of these interactions.

Conflict of interest

The author declares that they have no conflict of interest.

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