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Headaches: A Historical Background

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Abstract
Headaches are widespread recurrent or chronic pain disorders. Every aspect of daily life, from work performance to social and family relationships, can be severely affected and many individuals feel this problem is even more unbearable than the pain itself. The prehistoric era showed the first indications of a headache deemed so unbearable that a hole had to be drilled in the head. Indeed, cranial drilling is the oldest surgical operation, as attested by palaeopathological evidence. In the Neolithic period (7,500 - 5,300 BC) drilling was practised widely; the oldest drilled skull in Europe was found in Ensisheim, Alsace and in the Neolithic necropolis of Loisy-en-Brie (France), a drilled skull with a bone flap to close the hole was discovered. Examples of drilling can also be found in Italy, such as the Catignano skull dating back to the fifth millennium. These finds indicate how headaches have afflicted humankind since the earliest times: the notion that stress is typical of the contemporary world must be revised, while the idea that 'sickness of living' has affected humankind throughout its long history must be accepted. In the 4th century B.C. Hippocrates described a migraine with aura, while in the 1st century A.D. Areteus of Cappadocia codified a syndrome he called heterocrania, the symptoms of which were unilateral pain, nausea and vomiting. The term hemicrania was later coined by Galen, who attributed the disease to yellow bile, one of the four humours hypothesised by Hippocrates as responsible for the disease. Today's clinical instruments can accurately measure disability parameters, whose significant reduction is increasingly the focus of drug trial end-points.

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Introduction

Headaches are a widespread disorder characterised by localised pain in the skull caused by stimulation of pain-sensitive intracranial structures. In some cases it is a rare disorder; however it more often manifests itself in a frequent and intense way, to the extent that it impairs the sufferer's ability to work or enjoy family and social life [1]. Although in a certain number of cases the headache may be related to intracranial or severe systemic pathologies (with potential life-threatening consequences), for the vast majority, pain is the principal feature and therefore not sustained by any known condition. However, despite their substantial benignity in prognostic terms, the significant impact these forms can have on the quality of life of sufferers is notable, as they can significantly reduce the ability to function from both a working and social perspective [2]. Of over 35 types and subtypes of primary headaches [3], migraines are the most clinically relevant and the most significant for women of childbearing age [4]. Migraines are characterised by recurrent attacks of intense, mono or bilateral head pain that lasts from several hours to days and can be accompanied by various other symptoms such as nausea, vomiting, photophobia and phonophobia. The pain and associated disturbances are considerably worsened by movement, forcing the patient to seek relief in stationary rest, away from light or sound stimuli, until the crisis passes, usually within 72 hours of onset. The total (albeit temporary) disability that a migraine attack can entail significantly impacts the quality of life of frequent sufferers [5]. The impossibility of accurately

predicting those days at risk is a source of further discomfort in terms of quality of life, making planning for work commitments or other activities problematic. For these reasons, in recent decades clinician and researcher attention to the problems of disability induced by primary headaches, particularly migraines, has increased significantly [6]. Despite their severity, migraines are still a poorly understood disorder and are frequently misdiagnosed, going untreated or undertreated. One of the consequences of this attitude is the transformation of episodic forms into chronic, treatment-resistant forms, a phenomenon often sustained by excessive or improper use of analgesics. Several factors still limit headache sufferers' access to adequate diagnosis and treatment. At every level, one of the principal elements is the persistence of genuine cultural prejudices, such as that which sees migraine as a simple somatic expression of psychological problems [7]. Other aspects include a patient's fatalism about the chronic nature of the illness, reticence linked to disappointing previous pharmacological experiences and even a lack of empathy and collaboration on the part of the treating doctor, who may sometimes reductively categorise this disorder. These considerations are compounded by other logistical and economic details that further limit a migraine patient's chances of receiving proper and timely treatment.

Headaches have afflicted humanity since the dawn of time, as evidenced by the signs of skull-cap drilling found in fossil finds dating back to the Neolithic period. This primordial form of neurosurgery was intended to rid the patient of evil spirits that were thought to dwell in his head. The oldest documents in which it has been possible to trace specific references to a form of headache accompanied by visual disturbances date back to 3000 B.C., from Mesopotamia. One of these describes migraine symptomatology as a bowed head with pain gripping the temples and eyes afflicted with blackness and haziness [8]. Other references are apparent in Greek mythology. Zeus, for example, is struck by terrible headaches immediately after devouring his pregnant wife Metis in order to prevent the prophecy that his first male child will oust him. Hephaestus (Vulcan to the Romans) is summoned, and with an axe cuts open Zeus's head to free him from suffering. However, the result is that the fully-armed goddess of war Athena appears out of the god's head with a mighty cry. Hippocrates accurately describes a migraine with a regressed aura after vomiting [9]. However, it was not until the first century A.D. that Areteus of Cappadocia explicitly defined the characteristic pattern of unilateral pain, nausea and vomiting that characterises migraines, which he called heterocrania [10]. Hippocrates believed that a headache attack could be caused by exercise and sexual activity. Plato hypothesised that headaches were related to the overuse of one's body [11]. Celsus believed that abuse of wine, gastrointestinal disorders and temperature variations were at the root of a migraine. More modern descriptions hypothesised different origins ranging from toxic vapours [12] from the stomach to a melancholic mood that 'bored the heart and infected the brain' [13]. On the other hand, it is to Galen that we owe the term *hemicrania*, which still retains its initial descriptive efficacy today. This was one of the first etiopathogenic hypotheses according to which attacks were caused by yellow bile, one of the four humours proposed centuries earlier by Hippocrates. Yellow bile, originating from the liver, was also considered responsible for the choleric temperament to signal possible comorbidity between headaches and character disorders. From Galen onwards, the term hemicrania (referring to a painful unilateral head disorder associated with nausea, vomiting and photophobia) remained unchanged, often recognisable even among radically different languages. Liveing wrote the first monographic text devoted to migraine in 1873, entitled 'On Migraine, Nauseous Headache and Associated Disorders: a Contribution to the Pathology of Nervous Storms'. Meanwhile, etiopathogenetic interpretations multiplied and it is worth mentioning here the visions of Hildegard von Bingen, a charismatic Benedictine abbess who lived in the early Middle Ages. Many authors of the past grappled with the causes of migraine and traces of their numerous theories remain, largely reflecting the cultural influences and level of knowledge [14] of the eras in which they were formulated. In the 20th century, modern research contributed to a considerable expansion in knowledge of the causes of headaches, which has also led to significant advances over the last twenty years at therapeutic level. Deyl attributed the pain to pituitary gland swelling with consequent trigeminal nerve compression, while at the same time his contemporary Spitzer suggested that headaches were caused by a blockage of the interventricular foramen with dilation of the lateral ventricle [15]. In 1938, John Graham and Harold Wolff demonstrated that the efficacy of ergotamine in the treatment of migraine was linked to its vasoconstrictor effect, and this formed the basis of the so-called vascular theory, according to which pain is caused by an uncomfortable dilation of the arteries of the skull. Despite a degree of crudely incomplete detail, the vascular theory of migraine remained the most accepted theory for a long time and it was only in the early 1980s that this was succeeded by the neuro-vascular theory based on Moskowitz's brilliant histochemical and neurophysiological studies. Thanks to advances in functional neuroimaging techniques [16], we now consider primary headaches as complex disorders involving a set of central nervous structures [17], the pain matrix, which include specific areas of the neocortex and subcortical centres and pathways involved in the control of central neurosensory traffic [18]. There is still a long way to go for the majority of sufferers to receive an entirely correct diagnosis and effective treatment [19]. However, it is hoped that in the near future the issue of pain control and disability reduction for headache sufferers will form part of public health service priorities through patient education programmes.

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