“Chronobiological correlates of headache: three decades after”

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Abstract

“Primary headache belongs to a big group of neurological diseases in which there is not a discrete, structural lesion of the CNS but an impairment in the function of neuronal networks... Along with dysfunction in the pain control systems, there is an impaired ability of biological function to adjust, or better to display an adaptive response, to internal or external environmental change... Migraine and other primary headaches can be considered psychoendocrine disturbances of the adaptive responses to internal or external environmental change” [1]. Thus opened a communication delivered by Prof. Nappi at a symposium in Capri in 1983, which focused on the chronobiological correlates of headache. These few lines are enough to show that, three decades ago, there was already an awareness of the complexity of the problem of primary headaches (in terms of functional alterations of some adaptive networks) and above all of the relations between some of these forms and environmental changes. In particular, the concepts of periodicity and cyclicity, adapted to established timeframes (24 hours, seven days, the months, the seasons) became fundamental. For the first time in headache research, attention turned to “internal” factors of synchronization (or desynchronization), such as hormonal biorhythms and the sleep/wake cycle (the milieu interieur), and to “external” or environmental ones, such as the alternation of light and dark, geographical latitudes, lifestyles and habits (work shifts, mealtimes, etc.).

At that time, numerous studies were undertaken seeking to establish relations between these factors, primary headache patterns and changes in biohumoral, neurovegetative and neurophysiological parameters in man. However, many of these were abandoned after a few years due to various methodological limitations, linked mainly to the limited technology then available.

In more recent times, functional neuroimaging techniques have instead made it possible to demonstrate the correctness of these early insights. In 1998, almost 20 years after Prof. Nappi formulated the theory that the hypothalamic “clock” played a key role in the generation of cluster headache attacks (dyschronic hypothesis) and in their periodicity, a PET study [2] showed that cluster headache attacks are underlain by ipsilateral activation in the posterior hypothalamus. Much
more recently, it was shown that the hypothalamus is activated primarily in the early stages of migraine attacks [3]. The study that led to this finding was deemed so significant that it received the Harold G. Wolff Lecture Award by the American Headache Society at the latest IHS congress, which took place in June 2013 in Boston.

Another insight reported by Prof. Nappi et al. in 1983 was not only that environmental changes can lead to the triggering of headaches in susceptible patients, but also that this susceptibility can vary rhythmically over time. This, again, was a theory that was not confirmed until many years later, when it was demonstrated mainly through the neurophysiological studies conducted by the Liège group. Indeed, Prof. Schoenen and colleagues, in some elegant studies, showed that migraine patients have exclusive neurophysiological characteristics [4], and that these can vary depending on when the patient is investigated: in the intercritical period, during an attack, or just before an attack [5].

The purpose of this report on the chronobiological correlates of primary headaches is not only to point out the great achievements that have been made in the field of the pathophysiology of some primary headache forms, such as migraine and cluster headache, but also to provide an opportunity to think about how clinical observation, if performed carefully, rigorously and critically, can be fundamental in understanding the mechanics of the functioning of the central nervous system, which is the most complex and fascinating “universe” harbored by the human being.

Bibliography
