

## Guest editorial

Despite intense research efforts and technological advances, migraine remains a sphinx. Nevertheless, migraine is no longer a complete mystery as it was some decades ago.

Epidemiological studies have emphasized the impressive disrupting effects of migraine on the quality of life. Migraine is often characterized by a stereotypical noci-vegeto-affective cliché that implies a convincing conclusion: this disease is due to an excess of physiological functions having similar clinical expressions linked to both the same anatomical sites and the same operating neurotransmitters. Such a pathology does not consist in the phenomena themselves, which all are physiological; the pathology consists in their spontaneity, not in their being automatic.

This is personal opinion which, nonetheless, seems to be only capable of reducing the sphinx's ironic smile towards human efforts to understand the essence of this disorder. Given the complexity of the topic, it is easy to understand the proposals of a jungle of theories. From a speculative, ethnological point of view, it is interesting to observe how the pragmatic Anglo-American mentality has been obstinately oriented to a vascular-peripheral mechanism, in contrast to the Galileian, imaginative Mediterranean mentality which ignored this theory and which preferred to focus on headache as a pri-

mary brain disorder. In fact, the pragmatic vascular theory has little convincing scientific support and has given rise to even fewer therapies. Instead, the revolutionary central theory led researchers to achieve a major number of interpretative and therapeutic goals which started with the original serotonin holistic central theory. The double-magic moment occurred when a molecule was discovered by an Italian pharmacologist and when the fundamental role of serotonin in migraine was revealed by a Tuscan researcher. Nonetheless, much excellent, extraordinary evidence for this theory has been recently offered by researchers from other countries.

There is a new trend in the investigation of "headache": it is not a simple muscular or vascular disease (like Raynaud disease involving only the cephalic segment), but a disease concerning sensory neuraxial sites. Thus, it is a condition of non-organic deafferentiation, genetic in nature. Today, this is no longer just personal speculation. Despite the paradoxical feeling of inferiority of Hesperia's people, the numerous Mediterranean successes are justly mentioned here. Besides the discovery of the 5-HT molecule and the formulation of a novel holistic, central serotonergic theory of migraine, one ought to remember:

- i) A sensory transmission disorder is a clue in serious chronic migraine

and central panalgesia. This latter was the original name of primary fibromyalgia so erroneously labeled. As a matter of fact, hyperalgesia is its main clinical, pathological feature. Noteworthy, a hyperalgesic state is also the chief characteristic of migraine.

- ii) The central and peripheral supersensitivity to agonists such as 5-HT, dopamine, opioids, and acetylcholine (which inhibit pain transmission) is demonstrated by the unquestionable pharmacoclinical observation. That seemingly explains the dramatic effect of sumatriptan, a 5-HT-like molecule. This drug is capable of initiating the central activation of some of the above analgesic systems. Indeed, this drug, vicarious of the natural 5-HT central analgesizing principle, can cross the blood-brain barrier and is measured in cerebrospinal fluid for a long time following oral assumption in man.
- iii) Chronic migraine diathesis due to an excess of “pain memorization” and the consequent excellent results with ionotropic NMDA

antagonists. The discovery of “third genetic visceral hyperalgesia” is also relevant.

Lastly, there is a new trend in curing headache by means of second-generation anti-acetylcholinesterases capable of acting at the level of the central nervous system, so significantly ameliorating migraine course.

The birth of a novel journal regarding the ever-young theme of migraine and primary pain confirms the increasing attraction and interest for this pathology, which involves problems regarding basic and clinical sciences. The architecture of this journal is quite suitable to the enterprise of maintaining the flexing nature of this argument on a double track: one in agreement with rigidity of pragmatic rules, the other on a more classic track in agreement with the exigency of re-newed trends and suggestions which research requires as its vital breath. Compliments to the Editor-in-Chief for his courage, and overall a warm prayer to the stars of the Italian sky that keep on enlightening the romantic fatigue of researchers.