

# U NOVARTIS

A bimonthly newsletter for neurologists and other health care providers who manage migraine. VOLUME I ISSUE I

## MIGRAINE PATHOPHYSIOLOGY

Our understanding of how migraine attacks affect the brain and its chemicals, such as serotonin and CGRP, has advanced, offering new opportunities for diagnosis and treatment. In this issue, migraine pathophysiology and the phases of a migraine attack are reviewed to provide a clearer picture of how this neurological disease develops.

## THE NATURE OF MIGRAINE

Migraine is ranked as the third most common medical disorder on the planet, among over 300 diseases.<sup>1</sup> While a common presentation, migraine can be difficult to diagnose and treat. Dr. David W. Dodick, MD, FRCP (C), FACP, FAHS, Chair of the American Migraine Foundation, President of the International Headache Society, and Professor of Neurology at the Mayo Clinic in Arizona, United States, has explained why that is. "Neurologists are trained to look for a lesion as the cause of pain, but there's no lesion in migraine. It's a problem with function. not structure. Migraine can take over the normal anatomy of the brain and produce a whole host of different symptoms that lead to a substantial disability, but you can't take a picture of it."2

Researchers from the Headache Group in the Department of Neurology at the University of California, San Francisco, USA, have described migraine as a complex brain disorder with head pain as its key manifestation. The pathophysiology is not entirely clear but may be in part a dysfunction of subcortical structures, including the diencephalic and brainstem nuclei.3 The dysfunction of these nuclei, and their connections to other key brain centers, in the susceptible person may initiate a tide of events, resulting in other symptoms of migraine, such as sensitivity to light and sound. The many bidirectional connections in the brainstem and diencephalic nuclei create a brain state in which many symptoms can occur simultaneously.3

In an interview at the Migraine World Summit,<sup>2</sup> Dr. Dodick described the mechanics of migraine as a heritable disease that leads to a more responsive brain. It is known that migraine can be inherited, over 44 genes have been associated with migraine. In the migraine patient, that heritable condition makes the brain, which is constantly reacting to its environment, more responsive, and thus more sensitive to light, sound, smell, or sensation than other persons who don't have migraine. A migraine attack occurs as a response to a combination of biology and environmental factors.

### **MIGRAINE PHASES**

The prodromal phase of migraine is an important phase because it provides a warning that an attack is coming and is an ideal opportunity for early intervention, and for physicians to start treating early to prevent the down-stream effects. The prodromal phase occurs in about three-quarters of patients, but it may occur in more patients who are not aware of the symptoms. These include fatigue, yawning, nausea, neck pain, changes in mood, ability to concentrate, increased sensitivity, food cravings. The symptoms are heterogenous and all reflect dysfunction in the brain.

The prodromal and postdromal phases of migraine can last hours to days, and patients are not functioning well during those phases (Figure). When you consider the true start of the attack and the true ending of an attack, what was an 8- to 10-hour headache can turn into a 3-day attack.

## TIMELINE OF A MIGRAINE ATTACK

PRODROME FEW HOURS TO DAYS IRRITABILITY DEPRESSION YAWNING INCREASED NEED TO URINATE FOOD CRAVINGS SENSITIVITY TO LIGHT/SOUND PROBLEMS IN CONCENTRATING FATIGUE AND MUSCLE STIFFNESS DIFFICULTY IN SPEAKING AND READING NAUSEA	AURA 5-60 MIN VISUAL DISTURBANCES TEMPORARY LOSS OF SIGHT NUMBNESS AND TINGLING ON PART OF THE BODY	HEADACHE 4-72 HRS DRILLING ICEPICK IN THE HEAD BURNING NAUSEA VOMITING GIDDINESS INSOMNIA	POSTDROME 24-48 HRS INABILITY TO CONCENTRATE FATIGUE DEPRESSED MOOD EUPHORIC MOOD LACK OF COMPREHENSION

#### Figure. Timeline of a migraine attack.

Reproduced from the American Migraine Foundation. https://americanmigrainefoundation.org/understand-ing-mixgraine/timeline-migraine-attack/.

Dr. Dodick notes that "typically, we 'bookend' an attack by the beginning and the ending of the pain. When we treat from the start of pain to the end, we are doing patients a disservice by not addressing symptoms earlier on to prevent attacks and the postdromal phase."

However, it is often difficult, for the physician and the patient, to determine what is part of the prodromal phase and what is truly a trigger. According to Dr. Dodick, "Some patients will say they often crave a certain food, and if they eat it, they are destined to have an attack. It may seem like the migraine is triggered by eating that food. The area where migraine can begin in the brain is responsible for appetite and could lead to food cravings. Certain smells may trigger migraine, but it is unclear which ones."

Physicians need to be cognizant of the variety of migraine symptoms and help patients recognize their prodromal symptoms. While some patients may feel numbness on one side of their face, others may experience changes in language. Aura, which is due to an electrochemical event on the brain surface, spreads slowly; 90% of the time is starts in the occipital cortex, which controls vision, which is why patients experience a hallucination in their vision, such as spots, sparks, lights, or colors. The vision interruptions grow, starting in the periphery or center of the vision and expanding over 20 minutes or more.

The effectiveness of acute treatments of migraine is dependent upon identification of the specific symptoms a migraine patient has, and these symptoms can change with each migraine episode and over time.

#### **SUMMARY**

New perspectives on the nature of migraine are emerging that may transform the way migraine patients are evaluated and treated. The next issue will discuss the prevalence and burden of migraine for patients and their families.

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Quotes from Dr. Dodick on behalf of the American Migraine Foundation

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