Closing remarks: what future prospects can we expect in migraine management?

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Abstract The future prospects that we can expect in migraine management are both exciting and challenging. Obviously, the future cannot be predicted fully; however, the science related to migraine pathogenesis, diagnosis and treatment has increased exponentially over the past two decades and continues to direct future research and clinical care. More than any time in the recent past, it now may be more possible to define better what migraine is and how it relates to other neurological disorders and other diseases. This overview will look at future prospects for management of migraine and how they relate to the migraine diathesis, and ways that might provide a better understanding of how it might be possible to calm the excitable brain. This meeting examined potential future developments in the management of migraine patients, with emphasis on disability, quality of life, and the role of patient personality in episodic and chronic migraine with substance/analgesic overuse. This meeting precedes the main theme of the seminar, which explores the relationships between pain, emotion and headache in light of recent findings, which show that pain and emotion are closely interrelated and contribute to the pathophysiology of headache. Thus, it is important to understand about future migraine management prospects in terms of known migraine pathophysiology, as current data provide support for the concept that migraine is a brain disorder.

Keywords Migraine · Behavior · Pain · Personality · Disability and management

Introduction

Migraine is a complex disorder with increasingly clearer neurobiological underpinnings in terms of pain and other anatomical pathways involved brain structure and function [1]. However, migraine is more than headache and has relationships and co-morbidities many of which direct emotions and behaviors to the extent they cannot be separated clinically from the pain of migraine.

The modern pathophysiological understanding of migraine [1, 2] suggests the many ways it hijacks the normal anatomical pathways of the brain to create its myriad symptoms and signs. To date remarkable basic science and clinical work has been done which underscores what happens during the migraine attack and interictally [3, 4]. In an oversimplification, it would appear that a cortical event, probably in the form of a cortical spreading depression [5], triggers afferent nociceptive pathways for pain via the brainstem and thalamus back to the sensory cortex to explain the evolution of the pain of migraine. In addition, a more recent view of pain suggests that our feeling of pain is both a distinct sensation and a motivation—that is, a specific emotion that reflects homeostatic behavioral drive, similar to other basic biological drives [6].

Discussion

The spread of the cortical events tends to recruit and engage eloquent cortex of the brain in a manner that produces a plethora of neurological symptomology in patients with aura

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in particular [7]. Obviously, stimulation of the occipital cortex produces the typical aura of migraine, with subsequent involvement of sensory or motor modalities [7, 8]. Other structures are involved to produce the very complex symptomology that can occur during a migraine attack.

The further elucidation of the pathophysiology of migraine will direct further understanding and management in the future. This will inevitably lead to more biological and pharmacological targets being sought for new therapies for the treatment of acute migraine or prevention of recurrent attacks [9–11]. Despite remarkable clinical success of the triptans in the treatment of migraine [12] therapy will evolve [13] to include new targeted therapies such as 5-HT(1F) receptor agonists, calcitonin gene-related peptide (CGRP) antagonists, nitric oxide synthetase inhibitors, and ion channel antagonists, as well as a recent development is the creation of antibodies to CGRP and its receptor for migraine prevention [13].

The biobehavioral model of migraine as a pain disorder may not necessarily be different than other forms of acute or chronic pain [14]. Probably neuroimaging will guide the way here as further exploration of the pain matrix within the central nervous system and their connectivities are elucidated [15]. Already important work has been done to show that there are obviously functional changes in the cortex, subcortical and brainstem structures and there are significant volumetric changes in the cortex of the migraine brain [16]. Functional changes are seen in the visual cortex in migraine [17], and in chronic migraine there appears to be some degree of reversibility particularly after overuse of medication is reversed [18].

To appreciate future concepts, it is important to emphasize the connectivity of pain and emotion from the neuroanatomical view predominantly, as well as conceptually. The pain network is defined as a matrix [14] that encompasses normal pain pathways for the sensory appreciation of pain as well as limbic connections for affective responses to pain. This mesolimbic network appears conceptually to be well suited to explain migraine pain and its relationships to emotion. It also may help facilitate our understanding of the role that stress may play in altering our homeostatic mechanisms [19] to produce an episodic or chronic migraine state.

It might be useful to think that when certain CSD thresholds are surpassed, that migraine neurological symptoms may present depending on the degree of CSD activation [7]. The lower the threshold for CSD activation then the more prominent would migraine symptomology and possibly the co-opting of emotional circuits occurs as well, especially as at some point it would appear that migraine crosses over from a bothersome infrequent paroxysmal disorder to a chronic disease with allodynia, and increasing comorbidities [20, 21]. The brain bulk changes

in critical areas occurring during migraine chronification [22] and interictally as well along with the presence of neural networks being established above and beyond default networks and remaining functional make the migraine brain more dynamic than was thought according to recent research in this area [23].

Brain changes seen in chronic migraine on medication are of great interest and show that they actually change the brain in a fundamental way, which appears from recent research to have some reversibility as noted above [18]. Importantly, sensory pain centers appear hypoactive in this study [18] although the mechanism for that remains unknown; however, this finding raises the question that this new state might allow other pain pathways to be more active or at least more prominent. Maybe, and this is speculation, that turning off somatic pain pathways lead to more limbic pain involvement. There is some support for this concept in the pain literature [24]. So we have a unique migraine brain with alterations in functional networks. You need a brain for pain, and migraine is one pain disorder or disease that appears to be genetically predetermined, but adaptable and somewhat plastic in its nature.

All clinicians who see migraine patients realize that migraine does have a spectrum of presentations from the occasional debilitating headache to the presence of daily headaches, the latter associated with more behavioral consequences [25]. Using multiple management modalities is a necessity with some treatments better suited to one patient more than another. As outlined in this meeting, it truly is the individual patient with migraine that needs to be managed. Management of certain personality types as discussed, along with complementary and alternative therapies might work for some but sooner or later medication and more sophisticated biobehavioral techniques are frequently needed [26]. What works for one patient might not work for another. In the future, one has to think that the antiepileptic drugs or AEDs hold the greatest chance of working in calming the excitable brain [27] as they do in epilepsy; however, on other occasions, simple understanding and explanation might prove just as valuable as well as handling stress and other triggers [28]. Addressing disability of the individual and quality of life has to be a larger part of management in the future [29] and is not employed by all clinicians on a regular basis. Migraine is more than headache to patients as it can affect their lives and livelihood, and although not life threatening in most instances is certainly life altering.

Concluding remarks

Importantly future concepts will depend on answering many questions. What is it about migraine that intrigues so

many physicians and researchers that merits such detailed epidemiological, clinical, basic science research? Is migraine part of the human condition, representing a survival mechanism that has evolved over centuries, or is it just another neurological disorder. Are all human beings capable of having a migraine attack under the right circumstances? Genetics play a key role along with nurture in structuring the migraine attack; however, is migraine fundamentally a disorder or a disease?

There are more questions about migraine and its understanding and management in the future than there currently are answers. There is great potential for further investigation, understanding and therapeutic interventions. Migraine has been around for centuries and has a lot to teach us about the function of the brain now and in the future. One suspects that migraine will be around for many more centuries, more will be learned about this fascinating disorder and more insights obtained as to whether cure is possible or not; however, this topic is beyond the limits of this current discussion [30].

Here lies the excitement for the future. Will migraine lead us down a path, which not only improves our abilities to manage migraine better but also allow us to better understand how our brain works? At present, some of the management strategies for migraine are still considered to be an art and not a science. Certainly, the science is improving, but there still is an art to management that must be taught and learned so that future generations can manage patients with migraine, as migraine patients learn more about managing their own migraine.

In closing, genetics, epidemiology, pathophysiology, pharmacology, therapeutics, clinical neurology, neuroimaging, behavioral neurology, pain medicine and medicine in general will all benefit from a clearer and complete understanding of this most common of neurological disorders. So, once again the future prospects for migraine management are numerous and endless. There is great hope that, as we understand the brain and pain, the management of this particular disorder will continue to improve.

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