13th European Headache Federation Congress (EHF)

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CONGRESS HIGHLIGHTS MAGAZINE
It is an exciting era for us headache and migraine experts.

The 13th annual congress of the European Headache Foundation (EHF) is over. For congress co-chair and Professor of Neurology Zaza Katsarava the event was a complete success, with over 900 engaged participants from around the world coming together to discuss migraine pathophysiology, epidemiology and novel treatments. There was a real sense that the rigorous scientific exchange that took place will further our understanding of headache and migraine, and translate into new treatments to improve the lives of patients.

Throughout this magazine, you will find key highlights and expect opinion from the congress. After reading, we are sure you will agree with Prof. Katsarava that the next EHF congress, taking place in Berlin on 3-5 July 2020, is not to be missed!
The role of the hypothalamus in migraine

In a presentation at the 13th annual congress of the European Headache Federation, Prof. Arne May (University of Hamburg, Germany) provided an overview of the role of the hypothalamus in cluster headache and migraine.

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Clinical features of visual aura symptoms

When diagnosing and treating patients with migraine, it is important to have a clear understanding of the symptoms and characteristics that a patient may be experiencing. This is especially true for migraine with aura - the diagnosis is purely clinical, and it is difficult to distinguish migraine with aura from other serious neurological disorders, such as transient ischaemic attack or epilepsy. During his presentation at the 13th annual congress of the European Headache Federation, Dr Michele Viana (Regional Hospital Lugano, Switzerland) provided insights into the clinical features of visual aura symptoms.
Visual disturbances are the most frequent symptom in migraine with aura, with 98% of migraineurs with aura experiencing them. Other symptoms are somatosensory (36% of migraineurs) and dysphasic symptoms (10%). Visual symptoms are multifaceted and spread gradually. Migraineurs report a variety of symptoms, that are often complex and multiple symptoms can occur during a single aura. Dr Viana highlighted the lack of clinical description of the plethora of visual symptoms, and continued with the current description of visual symptoms: zigzag figures assuming a laterally convex shape with an angular scintillating edge leaving scotoma in its wake. Results from a prospective, diary-aided study indicated that the five most frequent ‘elementary’, or individual, visual aura disturbances are flashes of bright light, foggy/blurred vision, zigzag/jagged lines, scotoma and phosphenes (small bright dots). Most aura have two visual symptoms and in 85% of aura, symptoms last for one hour or less.

Dr Viana proceeded by addressing the visual field in which aura occur. Visual aura typically begin at the periphery of the visual field (40%), followed by initiating in one half (27%) or in the entire (25%) visual field. Only 36% of visual aura are reported to occur on both sides of the visual field, indicating that the majority are unilateral. Dr Viana alerted the audience that while in most patients visual aura occur in both eyes, there is currently no clinical evidence supporting this observation. As for colours, half of migraineurs report always having black and white (30%) or black and silver (21%) visual aura. The remaining migraineurs described having both black and white and colourful (22%), colourful (18%) or no colour (9%) visual aura.

Dr Viana concluded by emphasising that migraine with aura is a multifaceted phenomenon and understanding its ‘hundred faces’ is of paramount importance for accurate diagnosis and treatment. Additionally, Dr Viana alerted the audience that an updated list of all evaluated visual symptoms of migraine with aura and their description will be promptly published in the Journal of Headache and Pain.

References


Prof. George Georgoudis (University of West Attica, Greece) described a biopsychosocial approach to treating headache, as well as clinical research to evaluate the benefits of this approach. In Prof. Georgoudis’ opinion, there is an opportunity for patients to benefit from a supplementary approach to headaches that incorporates physiotherapy.

Why include multidisciplinary treatment when organising the headache clinic?

At a teaching course at the 13th annual congress of the European Headache Federation, Prof. George Georgoudis (University of West Attica, Greece) described a biopsychosocial approach to treating headache, as well as clinical research to evaluate the benefits of this approach. In Prof. Georgoudis’ opinion, there is an opportunity for patients to benefit from a supplementary approach to headaches that incorporates physiotherapy.
Prof. Georgoudis described how patients attending headache clinics may present with a number of symptoms, including intense, bilateral pain that fails to deteriorate with regular physical activity. While patients often receive pharmacological interventions, incorporating physical therapy into patient management could provide a second opportunity to improve health outcomes. He further described targets for the management of physical therapy, including cervical spine manipulation or mobilisation, exercise to strengthen deep neck flexors and upper quarter muscles, thoracic spine thrust manipulation and exercise, and C1–C2 self-sustained natural apophyseal glide (SNAG). These treatments combine physiological benefits with cognitive and psychological benefits in patients.

During the presentation, Prof. Georgoudis described a pragmatic, randomised, controlled trial designed to investigate whether a biopsychosocial approach provides benefits for patients with TTH (tension-type headache) cephalagia. In the study, patients received ten treatment sessions within a four-week period, alongside a daily stretching regimen. Treatment sessions consisted of either acupuncture alone (control group) or acupuncture and physiotherapy (experimental group). Acupuncture was conducted at 17–20 acupuncture sites, of which 15–17 remained constant across patients, with the remainder being decided based on individual symptoms. Physiotherapy consisted of microwave diathermy and myofascial release with manual techniques. The primary outcome was mechanical pressure pain threshold (PPT) using a mechanical algometer to measure seven bilateral points, which were measured at baseline, after five treatments and after ten treatments.

In the opinion of Prof. Georgoudis, the observed results demonstrate that hands-on physiotherapy techniques, alongside acupuncture and stretching, can produce desirable physiological improvements in patients with TTH, alongside providing cognitive and psychological benefits. Considering this, a biopsychosocial approach to treating patients in the headache clinic could, therefore, complement existing pharmacological interventions.

References


The role of the hypothalamus in migraine

The role of hypothalamus in cluster headache is well established. In his presentation at the 13th annual congress of the European Headache Federation, Prof. Arne May (University of Hamburg, Germany) gave an overview of the role of the hypothalamus in cluster headache and recent clinical research into the nature of hypothalamic involvement in migraine.
Migraine is defined by the attack phase, however, the brain of migraineurs is also different from that of healthy controls outside of the attack.

Arne May (University of Hamburg, Germany)
of a migraine patient in the 24 hours immediately preceding a migraine attack. Combined, these results suggest that while the brainstem may be the ‘migraine generator’, the hypothalamus may play the role of mediator in the pathophysiology of migraine. Prof. May concluded that the different subregions of the hypothalamus play different roles in migraine – the anterior hypothalamus might be the driver of attacks, while the posterior hypothalamus is involved in acute migraine headache. Additionally, he indicated that beta-blockers, but not topiramate, may have an effect on hypothalamic control, which could, in turn, inform treatment decisions.

References

Advances in brain imaging have increased our understanding of migraine pathophysiology. But could brain imaging be used to predict migraine progression and how a patient will respond to treatment? At the 13th annual congress of the European Headache Federation, Prof. Todd J Schwedt (Mayo Clinic, USA) and Dr Anders Hougaard (University of Copenhagen, Denmark) discussed the past, present and future of migraine brain imaging.

Structural changes in migraine

Prof. Schwedt used his presentation to outline how structural brain imaging has contributed to understanding migraine pathophysiology and how imaging could be used for developing migraine biomarkers. He began by outlining techniques for comparing the brains of migraineurs with healthy controls, including magnetic resonance imaging (MRI), diffusion tensor imaging (DTI) and magnetic resonance (MR) tractography. A study using MRI has demonstrated cortical thinning in migraineurs compared with healthy controls, with differences observed bilaterally in the central sulcus, the left middle-frontal gyrus, the left visual cortices and the right occipito-temporal gyrus.1 Similarly, structural abnormalities of the brainstem have been observed in migraineurs, including smaller midbrain volume, inward deformation of the ventral midbrain and pons, and outward deformations in the lateral medulla and dorsolateral pons.2

In Prof. Schwedt’s opinion, understanding aberrant brain structure in migraine patients could lead to the development of objective, replicable biomarkers for migraine. These biomarkers could be beneficial for diagnostic and prognostic purposes, and may eventually be used to predict how a specific patient will respond to treatment.
Functional changes in migraine

Dr Hougaard used his presentation to highlight successes in using functional imaging to understand migraine. He began by discussing research in which brainstem activation was observed during a spontaneous migraine attack, with increased activity persisting after an injection was administered to induce complete relief from headache, phonophobia and photophobia. While researchers have used different techniques to explore the reproducibility of these findings, there is still a need to uncover precisely which brainstem subregions are involved in migraine, whether this evidence can be used to diagnose migraine, and the effect of different migraine therapies on brainstem activity. In Dr Hougaard’s opinion, functional imaging is a powerful approach for studying migraine pathophysiology. The example of research into brainstem activity during migraine attacks highlights the need for clinical evidence to be reproducible, and for researchers to build on existing research to gain greater insights into the underlying cause of migraine.

The future of brain imaging in patients with migraine

Brain imaging has been used to identify aberrant structures and alterations in brain activity in patients with migraine. Both Prof. Schwedt and Dr Hougaard highlighted the potential of brain imaging to identify biomarkers of migraine that can be applied at a patient level. While imaging can be used to identify migraine subtypes and to differentiate between headache types, there is more work to be done in this area. This may include using brain imaging to predict patient outcomes and responses to individual therapies, and combining structural and functional evidence to gain more powerful insights into migraine.

References

New peripheral targets in the treatment of migraine

Migraine treatments generally target the central nervous system (CNS) and potential peripheral targets are not investigated in depth. As part of the session entitled “New targets in migraine treatment” at the 13th annual congress of the European Headache Federation, Prof. Antoinette Maassen Van Den Brink (Erasmus University Rotterdam, Netherlands) emphasised the importance of investigating peripheral targets for migraine treatment and described the latest developments in this area.
Her presentation started with the blood-brain barrier (BBB), the semipermeable lining that ensures a tightly regulated exchange between the blood and the brain. She highlighted a study demonstrating that the trigeminal ganglion (TG) is more permeable than the brain,¹ a result suggesting that some migraine treatments might have peripheral, in addition to CNS, targets. Moreover, some triptans have the potential ability of crossing the BBB and, conversely, antibodies targeting the calcitonin gene-related peptide (CGRP) are not expected to permeate this tightly regulated barrier. Combined, these observations indicate that peripheral effects of existing treatments, and the investigation of new peripheral targets for migraine treatment, is of high importance.

Prof. Maassen Van Den Brink introduced new pharmacological peripheral targets – including the receptors: amylin, PACAP/PAC1, 5-hydroxytryptamine (HT)1F, purinergic and gamma-aminobutyric acid (GABA), as well as the transient receptor potential (TRP) channels – and proceeded with an overview of the latest developments. Recent research from her laboratory has shown that lasmiditan (a 5-HT1F agonist) inhibited CGRP release in the dura mater, the TG and the trigeminal nucleus caudalis (TNC). The efficacy of 5-HT1F agonists might, therefore, have both CNS and peripheral components. As for purinergic receptors, the P2X receptor mediates vasocontraction and induces CGRP release.² This receptor is expressed in the meningeal artery and the TG, and antagonists of the P2X3 receptor in particular, might be a viable new class of migraine treatment. Prof. Maassen Van Den Brink highlighted that while TRPV1, a member of the TRP channels, failed to show promising results in the clinic, these ion channels remain interesting targets.³ While only a few of the new peripheral targets were discussed during this presentation, there is much promise in this emerging field of migraine research.

References


Despite consensus among the scientific community that migraine is a prevalent and disabling condition, migraine remains both underdiagnosed and undertreated.¹ In her presentation at a Teva-sponsored satellite symposium that took place during the 13th annual congress of the European Headache Federation, Prof. Patricia Pozo-Rosich (Vall d’Hebron University Hospital of Barcelona, Spain) highlighted attempts that have been made to describe the epidemiology of migraine in Europe, alongside the negative impact of migraine on individuals and society.
We need to make sure societies and governments understand that migraine is a disease that needs to be treated.

Patricia Pozo-Rosich
(Vall d’Hebron University Hospital of Barcelona, Spain)
changing the perception of migraine among healthcare systems and employers. This includes educating clinicians, governments and workplaces about the devastating impact of migraine.

Moving forward: reducing the impact of migraine

Prof. Pozo-Rosich concluded with the positive message that treatment options are rapidly improving for migraineurs. New therapies are reducing the effect of migraine on functional ability, increasing health-related quality of life and decreasing the financial burden of migraine. However, to realise the benefits of an improved treatment landscape, it is vital that the need for new treatments is fully communicated to all relevant stakeholders.

References


Can anti-CGRP monoclonal antibodies be beneficial for other painful conditions?

The neuropeptide calcitonin gene-related peptide (CGRP) plays a significant role in chronic neuropathic pain, and the therapeutic benefits of anti-CGRP monoclonal antibodies (mAbs) in migraine treatment are well established. However, CGRP is not only expressed in the central nervous system, but also in nearly all human organs. In a presentation at the 13th annual congress of the European Headache Federation, Prof. David W. Dodick (Mayo Clinic, USA) provided a brief overview of recent studies on the use of anti-CGRP mAbs in non-migraine pain conditions.

Primary headache

Thus far, clinical trial results have not demonstrated a therapeutic benefit of anti-CGRP mAbs in cluster headache. Prof. Dodick questioned whether patient population and outcome measure selection could be improved to properly answer the research question, and emphasised that additional studies of anti-CGRP mAbs in cluster headache should be conducted.

Secondary headache

Animal studies have shown that concussions lead to headache and pain-related behaviours, and that the administration of anti-CGRP mAbs prevents allodynia in murine models of post-traumatic headache (PTH). Prof. Dodick highlighted an ongoing clinical trial (NCT03347188) that investigates anti-CGRP mAbs in patients with PTH. The results of this study are expected in October 2020.

Non-headache pain

A recent systematic literature review showed an association between measured CGRP levels and somatic, visceral, neuropathic and inflammatory pain. In particular, CGRP levels had a positive correlation with pain in somatic pain conditions. However, an initial investigation of anti-CGRP mAbs in patients with osteoarthritis knee pain failed to demonstrate a therapeutic benefit compared with placebo. In Prof. Dodick’s opinion, this was an unexpected result and he questioned whether the correct joint was targeted in this study. Prof. Dodick further commented that other pain syndromes that could be potentially addressed with anti-CGRP are those of visceral, inflammatory and neuropathic etiology.
Non-pain syndromes

The prophylactic administration of anti-CGRP antibodies was found to block CGRP-induced diarrhoea in mice. These preclinical results illustrate the potential of anti-CGRP mAbs as a novel therapeutic strategy for infectious diarrhoea and other gastro-intestinal pathologies, such as colitis and inflammatory bowel disease.

Prof. Dodick concluded his presentation with a call to action to track patients in clinical trials not only from a migraine standpoint, but to integrate measures that record other pain syndromes as well. Patient-reported outcome questionnaires were highlighted as appropriate tools for this purpose.

References


3. Porreca F and coworkers. manuscript in preparation


Patients with migraine report diminished functioning and well-being on health-related quality of life measures. Underdiagnosis and undertreatment means that the magnitude of the clinical economic burden to individuals, relatives and society may be underestimated. During a session at the 13th annual congress of the European Headache Foundation - chaired by Prof. Paolo Martelletti (University of Rome, Italy) and Dr Mark Braschinsky (University of Tartu, Estonia) - the invited faculty discussed the societal burden of migraine.
Migraine burden and barriers

Prof. Gisela Terwindt (Leiden University Medical Centre, the Netherlands) began her talk by highlighting that while migraine is the second most disabling disorder worldwide,3 it affects men and women very differently. She observed that not only is lifetime prevalence of migraine much higher in women than in men (33% vs. 13%, respectively),4 the risks associated with migraine are far greater for women. Migraine is a risk factor for stroke in women,5 with the presence of aura, smoking and regular use of oral contraceptives cumulatively increasing this risk. Similarly, women with migraine are at increased risk of white matter lesions compared with healthy controls, while men with migraine are not.6 Prof. Terwindt concluded by highlighting the disabling debilitating effect of migraine on women, especially those of working age. As such, migraine represents a significant barrier to the progression of women in the workforce.

Impact on working activity

Continuing the discussion of the societal impact of migraine, Prof. Paolo Martelletti emphasised the impact of migraine on working activity. Chronic migraine is associated with increased absenteeism, including missed work days and productivity loss.7 In Prof. Martelletti’s opinion, the fact that absenteeism is greater in young workers aged 18–34 years is of utmost concern.8 He concluded that the general population does not consider migraine to be a disability, despite the effects of migraine on workplace productivity and absenteeism being comparable with other major public health problems.

Economic cost of migraine

Prof. Paul McCrone (King’s College London, United Kingdom) finished the session by discussing the cost of migraine from a health economics perspective, and reviewing attempts to quantify and predict the economic cost of migraine for patients referred to specialists. In the UK, self-report data on healthcare resource use...
and lost employment over a 4-month period were acquired and used to estimate the economic costs of migraine.\(^9\) Prof. McCrone explained that alongside expenditure on healthcare services including inpatient, emergency department and other specialist care, individuals incurred large costs related to informal care. The latter accounted for 74% of the total migraine-related cost per person of £6588 over 4 months.

A need for greater evidence explaining the full cost of migraine During the question and answer session, all speakers agreed that there is a need for more evidence on the economic cost of migraine. However, the optimal way of presenting this evidence to regulatory and reimbursement bodies is still being debated.

References


