

# News etter Leading headache science, education and management globally

## Letter from the President - Continuing to build our future together

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## **Messoud Ashina**

Dear Colleagues

It has been my honour to serve as President of the International Headache Society.

Every day, I have learned from you. And I have been truly inspired by your commitment to continue providing care for your patients even in these troubling times. The COVID-19 pandemic has changed our lives and affected us all. My heart goes out to everyone, and especially to those who have lost loved ones. Please stay safe and I hope to see you all in person very soon.

I am also filled with gratitude that you have kept the IHS going strong in the face of struggle and loss. Thanks to your efforts, we are meeting the demands of a digital age. I would therefore like to share with you some of the accomplishments that you have been responsible for in the past 2 years.

First, we have increased the number of IHS members by more than 400 people since 2020. This is partly attributed to the membership campaign that was launched in February 2021. A total of 124 named representatives of neurological societies were contacted and we received an excellent response from many lower-income countries, increasing the number of IHS Associate members (from lower-income countries) to 1,500. The influx of new members from lower-income countries will help shape IHS into a more diverse and inclusive global organisation. Furthermore, it is expected that even more people will join IHS as we get closer to IHC 2021 in September.

Second, we have launched a new website in June 2020 and subsequently created an online Learning Centre and YouTube channel. The new website has averaged 32,000 page views over the past 3 months, compared with an average of 18,000 page views before the new website was launched. The great news is that more and more users of the website are from lower-income countries, such as Brazil, India, and Russia.

Third, we have made a concerted effort to develop our educational platform. Twentyfive videos, 16 podcasts and six webinars have been posted over the past year. The next step has already been initiated and involves creating a three-part video series on each headache disorder. Each video will have a duration of 3 minutes and the content will target a broad viewership that includes patients as well as healthcare professionals. The purpose is to provide open-access material that delivers a concise overview of the definition, prevalence, diagnostic criteria, clinical features, and therapies for each headache disorder. To underscore the global nature of IHS, we will post the video series



3-part video series will provide openaccess material to deliver a concise overview of the definition, prevalence, diagnostic criteria, clinical features and therapies for each headache disorder

Follow IHS on social media – help us raise awareness of headache disorders in a multitude of languages, such as English, Mandarin, Hindi, Spanish, Arabic, Russian, Portuguese, Turkish, German, and Italian.

Fourth, IHS is more active than ever before on social media platforms. The society currently has social media accounts on Twitter, Facebook, LinkedIn, Instagram, and YouTube. Our following has increased considerably since September 2020 and we have introduced a policy of one post per day on Twitter. Below, you will find a summary of the progress that has been made in large part thanks to the Electronic Media and Education Committees:

- Twitter Followers: 4,871 (from 4,334 in Sep 2020)
- Facebook followers: 8,315 (from 7,641 in Sep 2020)
- LinkedIn followers: 1,166 (from 928 in Sep 2020)
- Instagram followers: 3,419 (from 2,620 in Sep 2020)
- YouTube subscribers: 345

To help us in raising more awareness about headache disorders, I kindly ask you to follow/subscribe to IHS' various social media accounts. This will also allow you to receive instant updates on research grants, educational activities, and career development programmes that are offered by IHS. Furthermore, it should be noted that the 'Migraine Awareness Month' campaign ran through June 2021.

Fifth, IHS has decided to organise IHC 2021 in collaboration with the European Headache Federation (EHF). Due to the COVID-19 pandemic, IHC 2021 will be a fully virtual event that takes place from 8–12 September 2021. The main topic will be "Headache Science to Optimise Patient Care". On behalf of EHF President Zaza Katsarava and myself, we are pleased to invite you to attend the IHC 2021 and join us for the initial Presidential Symposium on new drug targets in migraine.

Lastly, I would like to thank the IHS Board of Trustees for their outstanding service to promote headache science worldwide. I would also like to thank administrative manager Carol Taylor who works tirelessly and provides invaluable assistance. Her commitment to the IHS is truly exceptional and second to none. Also, a final note of recognition and thanks to our outgoing Honorary Secretary Stefan Evers, Treasurer Wendy Thomas, and Co-Chair of the Education Committee Allan Purdy. They have been a source of energy and wisdom that has helped shape IHS into what we see today.

Professor Cristina Tassorelli will assume the IHS Presidency after the IHC 2021 in September. I am confident that Cristina will be great leader and I wish her as much success as possible. I encourage you to fully support her as we continue to build our future together.

Sincerely yours

Messoud Ashina
ashina@dadInet.dk



## **Update from the Honorary Secretary**



### **Stefan Evers**

I am pleased to give an update on IHS activities since the last Newsletter distributed in March 2021.

#### **Membership**

IHS membership numbers have increased again in 2021. This is as expected as members join to register for the forthcoming International Headache Congress (IHC) to be held virtually in September. We are particularly pleased to welcome many new Junior members from all over the world who have joined in recent weeks.

### Cephalalgia

I am pleased to report very successful data from *Cephalalgia*, our society's journal. The impact factor for 2020 has risen to 6.292 (2019: 4.868). *Cephalalgia* is now ranked 28 of 208 in Clinical Neurology and 48 of 273 in Neuroscience journals. Congratulations are offered to Editor-in-Chief, Arne May, Managing Editor, Wendy Krank, and the *Cephalalgia* Editorial Board and review team for their tireless contribution to our journals.

Cephalalgia Reports, the online silhouette journal to Cephalalgia, has now published almost 100 articles; the journal is listed in the Directory of Open Access Journals (DOAJ) and SCOPUS. Please consider publishing your research or views in Cephalalgia Reports. The journal actively encourages high quality papers in emerging observations with translational potential not yet realised, reports limited to regional relevance which may validate and add to existing studies, RCTs with negative outcomes, confirmatory studies, technical reports, articles with a more clinical emphasis, pilot trials which may stimulate therapeutic innovation and scientifically rigorous pathophysiological and pharmacological studies.

Please visit the **Cephalalgia Reports website** if you would like to submit your work to this exciting publication.

### **IHS guidelines**

IHS 'Guidelines of the International Headache Society for clinical trials with neuromodulation devices for the treatment of migraine' were published online-first in *Cephalalgia* in May.

Work is continuing on guidelines on idiopathic intracranial hypertension, cluster headache, registries on real life data and post-traumatic headache.

All IHS published guidelines including the IHS Classification of Headache Disorders (ICHD-3) and the International Classification of Orofacial Pain (ICOP) are freely available on the IHS and *Cephalalgia* websites. Translations of the ICHD-3 can be found on the IHS website.

### **Education activities**

The Education Committee continues to add content to the IHS website Learning Centre. There are now over 20 videos on various aspects of headache medicine, all of which are available with English, Spanish and Chinese subtitles, and almost 20 podcasts. The most recent podcasts are interviews with authors of key articles published in *Cephalalgia*.

Cephalalgia Impact Factor increased to 6.292

Guidelines for clinical trials with neuromodulation devices for migraine published



# Three IHS fellowships awarded in 2021

IHC advance registration deadline 4 August – register today!

IHS Junior members – register for IHC 2021 for free until 20 August The quarterly webinars are also available for view – the latest webinar was held in June and featured Professors Piero Barbanti and Anne MacGregor who talked about migraine treatment and migraine treatment in pregnancy and breastfeeding.

Most of the content is for IHS members only, and if you would like to gain access it is easy to join IHS through the website **Membership page**.

IHS is also grateful to our partner societies who have granted permission to include links to their online meeting presentations.

#### **IHS Electronic Media**

IHS continues to increase its online profile through the social media channels and under the guidance of the two Electronic Media Committee Co-Chairs the society is now more active than ever before. The most recent activity has been promotion of Migraine Awareness Month during June. Thanks are offered to all the Committee members who work daily to ensure the IHS has a strong online presence.

#### **Grants and fellowships**

The IHS fellowship attracted several excellent applications and three fellowships were awarded:

Erika Ivanna Araya, Argentina. Research title: Functional validation of microRNAs in migrainerelated behaviour in rodent models of chronic migraine. Institution: Vall d'Hebron Institute of Research, Spain – mentor: Patricia Pozo Rosich

Vimala Bharadwaj, India-USA. Research title: Translational studies towards understanding the involvement of hypothalamic kappa opioid receptors (KOR) in stress-induced migraine. Institution: Stanford University, USA – mentor: David Yeomans

Cedric Gollion, France. Research title: Transforming chronic to episodic migraine: an MRI study. Participation in the REFORM study. Institution: Danish Headache Center, Denmark – mentor: Faisal Amin

Introductions to the three Fellows can be read later in this newsletter.

#### **International Headache Congress**

### **IHC 2021**

We look forward to welcoming you to the IHC which will be held virtually from 8–12 September. There are 149 invited lectures; 563 abstracts were submitted – 60 have been selected for oral presentation, the remainder will be presented as e-posters, some of which will be accompanied by a short presentation. Six young investigators will take part in the Headache Science Excellence Tournament.

The complete Scientific Programme is available on the IHC website and includes all speaker names. Pre-congress registration is only open until 4 August so make sure you register soon!

Registration is free of charge for Junior IHS members – **but only until 20 August.** After that time you will need to pay the regular Junior registration fee.

### **IHC 2023**

Preparations are beginning on IHC 2023 which will be held in Seoul, South Korea. The congress will be Co-Chaired by Cristina Tassorelli and Min Kyung Chu, and the Scientific Programme Committee will meet in September to start discussing the programme.



Congratulations to newly elected IHS Presidentelect and Trustees

#### **IHS Board Trustee election results**

I am pleased to confirm the Board Trustee election results – we had a 38% member voting turnout to elect the President-elect and three Trustees. The successful candidate for President-elect was Rami Burstein from Boston, MA, USA, who will become IHS President from 2023–2025, succeeding Cristina Tassorelli. New Trustees Andrea Carmine Belin, Sweden, Aynur Özge, Turkey, and Jan Hoffmann, UK, were elected for their first 2-year term starting in September 2021. They will join the Trustees who were elected in 2019 who will remain for their second term in office, Fayyaz Ahmed and Gianluca Coppola. Lars Edvinsson, Immediate Past-President, Wendy Thomas, Honorary Treasurer, and myself as Honorary Secretary will retire, as will Mario Peres, Patricia Pozo Rosich and Todd Schwedt who have served two terms as Elected Trustees, however, it is intended to appoint Patricia Pozo Rosich as new Honorary Secretary and Fayyaz Ahmed as new Treasurer. Alexandra Sinclair has recently stepped down from the Board. The changes in the Board members will take place at the IHS Annual General Meeting to be held during the IHC in September. Congratulations to the successful candidates, and many thanks to the other candidates for standing, and to all retiring Board members.

#### **IHS Annual General Meeting**

The AGM is scheduled to be held virtually on Wednesday 8 September at 15.30 BST during the IHC. All members are invited to attend and the agenda and papers will be circulated in the next month. We hope many members will join us.

#### **Farewell**

This is the last Secretary's Update I will write for the Newsletter in my position as Honorary Secretary since I will leave office in September this year after 10 years in service. It was and still is a pleasure and a privilege for me to work for you and for our Society. Thank you.

#### **Stefan Evers**

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 Tassorelli C, Diener H-C, Silberstein S, et al. Guidelines of the International Headache Society for clinical trials with neuromodulation devices for the treatment of migraine. Cephalalgia 2021; https://doi.org/10.1177/03331024211010413.

#### **IHS Allied Specialities Scholarships 2021**

Applications are invited for the IHS Allied Specialities Scholarship

This initiative addresses the need to develop expertise in the field of headache for allied specialities e.g. nurses, therapists.

The Allied Specialities Scholarship will facilitate training through a short-stay scholarship for clinical training / research project in a major headache centre

Funding is provided for 8–12 weeks at a major headache centre in the home or another country

Applicants must be a qualified nurse or therapist – physiotherapist, occupational therapist, or psychotherapist – working at a primary or secondary headache care centre and a member of IHS

Visit the **Grants page of the IHS website** for more information

Deadline for applications: 30 October 2021





The International Headache Congress 2021 is going to take place in less than 2 months.

## **Teaching courses**

Sign up for one of our many teaching courses to broaden your knowledge of specific headache conditions or treatments. **Sign up for a course** 

## **Programme**

Check out the final IHC 2021 scientific programme online: Online programme

## **OnDemand**

Missed a Session? No problem. All sessions will be available OnDemand until **13 December 2021** for all registered participants.

## First information sheet

The most important information about The International Headache Congress 2021 at a glance. **Check it out** 

## **Videos**

Watch the welcome video, Zaza Katsarva´s invitation and Messoud Ashina´s invitation on our Homepage.

**Videos** 

www.headache-congress.org

## Advance registration deadline

Don't forget to take advantage of the advance registration fees and benefit from a **reduced registration fee** until **04 August 2021.** 

## **OnDemand**

Check out the interactive segment on our congress website and for the IHC 2021 and **win a free registration.**Special features

If you have any questions, feel free to contact the project team from our PCO Conventus via **headache-congress@conventus.de.** 



## **IHS Headache Trainee report**



## Yessika Milena Rojas Villegas, Colombia

Institution: São Paulo Headache Center, São Paulo, Brazil Mentor: Mario Peres

I was able to learn the clinical approach and performance of specialised consultation of headache First of all, I would like to thank IHS for giving me this amazing opportunity to use this grant and be able to perform this training even in the midst of the pandemic. I would like to thank Dr Mario Peres, Dra Thaiza Lima, Dra Vanda Lelis de Souza, Dr Juliane Peres, Dr Marcio Nattan, Dra Ida Fortini, Dr Gabriel Kubota, Dr Caio Grava, and all the people I interacted with during my stay in São Paulo for almost 5 months.

I would like to mention two parts of my fellowship programme, the clinical and the academic-scientific. São Paulo is a place with a population that is very similar to Colombia from the social, cultural and economic point of view, and both of them have very similar health systems.

I had the opportunity to be present during patient care in the public system and the private system with the challenges that each system has. In the private system, for most of the time I was observing consultations with Dr Mario in the "São Paulo Headache Center" and the "Hospital Israelita Albert Einstein". I was able to learn the clinical approach and performance of specialised consultation in headache, and the most important part was that Dr Mario shared with me his experiences and we discussed a lot of difficult clinical cases with an excellent approach to the comorbidities and newest



treatments such as monoclonal antibodies. I was able to observe ablative techniques performed by specialised anaesthesiology such as radiofrequency ablation for refractory trigeminal neuralgia and ultrasound-guided blocks for posterior neck pain. One of the objectives I had when I applied for the scholarship was to understand how an expert treats refractory headaches and how to provide adequate long-term care for these patients, and this is one of the many lessons I've learned from Dr Mario.

techniques such as acupuncture, puncture with dry needle, TENS and other orofacial pain treatments and interacted with allied specialities

**I learned** 

In the public system I was able to attend the outpatient headache consultation in the "Hospital das Clinicas" Fellow Program of the "São Paulo University". I met a team of professionals who are developing multidisciplinary work in headache. It was a great experience to understand techniques such as acupuncture, puncture with dry needle, TENS, and other orofacial pain treatments. I was able to interact with allied specialties such as odontology, neuro-ophthalmology and neurosurgery with a very important approach on secondary headaches. I also observed the anxiety outpatient consultation in the Psychiatric institute of the "Hospital das Clinicas".

In the second part of the fellowship I understood how a research team is articulated, regardless of geographic or even language barriers. Dr Mario was very helpful and made



I was involved in research projects which helped me understand essential details about the

instruments and

methodology

used

Connecting people at a regional level is a way to strengthen team work so together we can improve our approach to headache

me feel more comfortable every day, and he included me in two projects that we are still working on now. I was able to be present at research meetings online with people from Asia, Europe and the United States; these meetings happened virtually because of the pandemic. I was also present at academic meetings of the "Hospital das Clínicas" every week reviewing fundamental issues in headache.

During the fellowship I was very interested to understand better how to choose patients for each type of treatment, and specifically for monoclonal antibodies, in a health system similar to the one we have in Colombia, because at that time they were not being used in our country. We started a retrospective and prospective observational study that included patients who were treated consecutively with monoclonal antibodies in the Sâo Paulo Headache Center. We wanted to know the local conditions of access to medications, the patients' comorbidities, other medications used for patients during treatment in real life,



adherence to treatment, and results after follow-up. Carrying out the research preparation directly with Dr Mario and understanding essential details about the instruments used and the methodology have been very challenging, however Dr Mario has given me the necessary support to carry out the scientific work.

Visiting São Paulo Headache Center, Hospital Israelita Albert Einstein, Fellow Program Hospital das Clínicas and Psychiatric Institute of the Hospital das Clínicas has met all my initial aims. I think that in Latin America there is still the concept of individual work, and a



new way of creating remote teams is being born thanks to the networks that are being facilitated by virtuality. Understanding how countries like Brazil have developed the field of headache even with complex health systems made me think about new possibilities to continue the work locally and regionally. I believe that connecting people at a regional level is a way to strengthen team work so together we can improve our approach to headache. The training has given me a way to improve my knowledge, clinical skills and research skills, and I began to perceive things from another point of view.

This training helped me to grow as a professional and to start thinking more about the possible opportunities for the development of projects at a local level, not only in public practice but also in private practice. Now I continue to work with my mentor Dr Mario in the field of research and I understand the need we have in our countries, which is to improve our local information, and the impact this may have on patients.

Thanks to the chairs of the Electronic Media Committee, Dr Anna Andreou and Dr Arão Oliveira, now I'm a part of the committee, and this will also be a challenge for continuous learning.

Thanks to this training, I am part of the Headache Group of the Colombian Neurology Society and from my home town, Manizales in Colombia, I hope to continue contributing to the collective work that is so important in Latin America. I hope that more people in our region have opportunities like this and when they return to their countries they can contribute with their lessons learned as I intend to do.

Finally I would like to express my sincere appreciation and gratitude to Carol Taylor and Henrik Winther Schytz for all their help in this process, for their understanding with the



differences in language and for their professionalism. I would especially like to thank Dr Mario Peres for his unfailing support during my stay in São Paulo, for the support given in times of pandemic, for including me in all his activities, and his long explanations from his knowledge and the vast experience he has. Finally, I am so grateful to IHS; I truly appreciate everyone's efforts and commitment they have to improve access to information and access to this type of training that certainly has an impact in our countries.

## **IHS Fellowship report**



## Inge Loonen, Netherlands

The link between migraine aura and cerebrovascular endothelial dysfunction

Fellowship from November 2019 to April 2021 Neurovascular Research Lab, Department of Radiology, Massachusetts General Hospital, Harvard Medical School, Boston, USA Mentor: Cenk Ayata

**Overview** 

Migraineurs can have vascular dysfunction and are at significantly higher risk for ischaemic or haemorrhagic stroke, cerebral white matter disease and cardiovascular events. Migraine aura is a vascular risk biomarker but mechanisms underlying this association remain unknown. Cortical spreading depolarisation (CSD) can alter characteristics of cerebrovascular endothelium.

The aim of the study was to determine vascular endothelial features that are altered by migraine aura to understand the underlying mechanism. We hypothesised that the massive potassium increase during CSD traverses biological barriers to reach microvascular endothelial cells and induce a phenotype change resulting in blood-brain



barrier disruption and other yet unknown alterations, such as expression changes of adhesion molecules or endothelial anti-thrombotic and fibrinolytic factors, predisposing to cerebral ischaemic events.

We used non-invasive induction of cortical spreading depolarisation to prevent tissue injury and injury-related effects on neuronal cells and vasculature using optogenetics stimulation through intact skull of channelrhodopsin-2-positive mice, expressing light-sensitive ion channels in cortical

neurons. After recovery we will quantify adhesion molecule expression and pro/anti-thrombotic factors in the piriform cortex.

Our second experiment was to focus on CSD-induced transcriptome changes specifically in endothelial cells that were harvested from Tie2 mice with green fluorescent protein labelled endothelial cells, using RNA sequencing after FACS sorting.

The aim of the study was to determine vascular endothelial features that are altered by migraine aura to understand the underlying mechanism



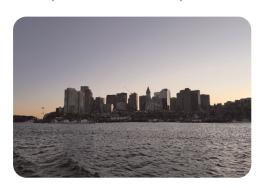
As well as my IHS research, I also had the opportunity to contribute to several other projects

The opportunity to work in this world-leading migraine research group was a great experience: I have learned new techniques, broadened my scientific knowledge, and strengthened my enthusiasm for translational research

### **Summary of research**

In Tie-2 mice, multiple CSDs were induced through thinned skull and detected non-invasively using optical intrinsic signals from white light illumination. Ipsi- and contralateral hemispheres were harvested separately and homogenised for FACS sorting of endothelial cells. Endothelial cell samples were grouped based on experimental condition: i) CSD induction hemispheres; ii) hemispheres contralateral to CSD induction sides as internal controls; iii) both hemispheres from sham experiments

as negative controls. The samples were sent to our collaborators at Leiden University in the Netherlands where RNA was isolated for RNA sequencing. Initial analysis of the first dataset looks promising, as we could identify the majority of genes known to be expressed specifically in brain endothelial cells. For some of these genes, samples collected from CSD hemispheres and control groups differed in expression levels. Additional data sets are being included to be able to state whether this trend will be significant.



In addition to my IHS project, I got the chance to contribute to several other projects in the lab - on synaptically triggered SD in migraine mutant mice, on SD as an innate antiseizure mechanism, and on the relation between SD and seizures.

#### **Outcome of research**

Initially, we aimed to determine whether non-invasive optogenetically-triggered CSD was able to induce an endothelial phenotype change and to identify CSD-associated gene expression changes and thereby molecular mechanisms responsible for disruption of the blood-brain barrier.

Since RNA sequencing and analysis of the results is still ongoing, it is hard to say whether our aims have been met at this point. Initial results do show CSD-associated changes in gene expression levels compared to control groups, but additional analysis will have to point out which genes are up- or downregulated and in which molecular pathways this will play a role.

### Conclusion

The opportunity to work in this world-leading migraine research group was a great experience in which I got to learn new techniques, broaden my scientific knowledge, and strengthen my enthusiasm for translational research. This will all help in finishing my PhD in the Netherlands and continue my career after that. The international experience will enhance my curriculum vitae which will be very valuable for my future career.



I would recommend future IHS Fellowship applicants make sure they are well prepared before starting the Fellowship abroad. For a smooth start, it definitely helps to familiarise yourself with the procedures you will be using. Also, it helps to ask what training you will have to follow or tests you will have to pass before you are allowed to start your experiments. It will save a lot of time if you can start those before or right after your arrival in the lab.



## **IHS Fellowship introductions**



Erika Ivanna Araya, Argentina

I am excited about the opportunity to continue my scientific career at a prestigious translational headache research institution

Functional validation of microRNAs in migraine-related behaviour in rodent models of chronic migraine

Fellowship from September 2021 to September 2022 Vall d'Hebron Institute of Research, Barcelona, Spain Mentor: Patricia Pozo Rosich

Recently, about a month after my PhD defence, I was awarded an IHS Clinical and Basic Science Headache Research Fellowship. The opportunity to continue my scientific career at a prestigious translational headache research institution, the Migraine Adaptive Brain Centre at the Vall d'Hebron Research Institute, makes me exultant. I am fully grateful for the possibility of training with experts in the field, which will enhance my research skills in exploring the central mechanisms involved in the pathophysiology of migraine.

I hold a licentiate in pharmacy from the University of Barcelona, Spain, where I had my first contact with research. Later, I concluded a Master of Science in Pharmacology at the Federal University of Paraná, Brazil, where I have also completed my PhD under the supervision of Dr Juliana G Chichorro. During my doctorate I had exposure to neuroscience in the study of the affective component of craniofacial pain disorders, through the evaluation of behavioural responses, molecular assays and analysis of ultrasonic vocalisations in rodents. In addition, I used a direct injection of calcitonin gene-related peptide (CGRP) into the trigeminal ganglion to promote migraine-related responses such as facial hyperalgesia, photophobia and anxiety-like behaviour. This complex mechanism of migraine has fascinated me. Therefore, I would like to dedicate my career as a scientist to do research in this field.

Migraine treatment is largely ineffective and clinically challenging for headache specialists. MicroRNAs (miRNAs) downregulate gene expression and may be involved in the generation and maintenance of migraine. The clinical group at the Migraine Adaptive Brain Centre led by Dr Patricia Pozo Rosich, has successfully identified two miRNAs serum biomarkers differentially expressed between migraine sufferers and healthy controls, which could potentially be used to improve target-driven therapeutics. Thus, the project aims to functionally validate the implication of these miRNAs in the pathophysiology of migraine in non-clinical models of migraine, which will allow their reliability to be used as biomarkers for migraine diagnosis or even as potential therapeutic targets.

Furthermore, it is an honour to work with Dr Patricia Pozo-Rosich, whose vast experience in headache research will shape my scientific future. This fellowship will broaden my knowledge of translational research methods and will open new horizons in my scientific career in the migraine field. Finally, I hope that my scientific contribution in the future may help to alleviate the suffering of migraine patients.

This fellowship will broaden my knowledge of translational research methods and will open new horizons in my scientific career in the migraine field





## Vimala Bharadwaj, India-USA

Translational studies towards understanding the involvement of hypothalamic kappa opioid receptors (KOR) in stress-induced migraine

Fellowship from September 2021 to September 2022 Stanford University, Stanford, USA Mentor: David Yeomans

I was awarded the IHS fellowship in summer of 2021 giving me an opportunity to work on an interdisciplinary translational project with leading experts at Stanford University. The project is built on my initial postdoctoral research work in Drs Frank Porreca and Trent Anderson's laboratories at the University of Arizona (U of A). The project involves PET imaging in migraine-like pain rodent models (pre-clinical) and migraine headache in migraineurs (clinical) to better understand the key transmitters in migraine pain generation. The critical technical skills and scientific expertise acquired during the IHS fellowship in Dr David Yeomans' laboratory will be vital for my early career development.

I grew up in India and completed my undergraduate studies in biotechnology. I came to the United States for my graduate studies and completed my PhD in Biomedical Engineering at Arizona State University (ASU). My doctoral work focused on preclinical studies investigating nanoparticle delivery across the blood-brain barrier after traumatic brain injury. For my research, I have received multiple outstanding achievement awards from the Society for Biomaterials. I received the outstanding mentor award from the Graduate and Professional Student Association, ASU, for my dedication to mentoring. In 2018, I joined Drs Porreca and Anderson labs at the U of A for postdoctoral training focused on migraine pain pathways and pathophysiology of stress-induced triggers of migraine headache. I was honoured as the Sursum fellow from U of A, obtaining an independent postdoctoral grant. Over the years, I have held several leadership positions, currently serving as the communications director for Stanford Postdoctoral Association, as a diversity, equity, and inclusion ally for the American Headache Society and associate editor team member for the *Headache* journal.

Migraine is a disabling primary headache disorder with over 45 million Americans affected. While the role of "triggers" in migraine is currently debated, about 70% of patients self-report the influence of external factors such as exposure to certain chemicals or emotional stress on their attacks. If migraine is considered as a threshold disorder, then normally subthreshold external stimuli could promote the activation of sensory afferents and pain. This multi-disciplinary translational project is intended to investigate the importance of hypothalamic kappa opioid receptor (KOR) activation as a link to stress and migraine headache. Our preliminary evidence suggests that stress increases dynorphin/KOR signaling in the hypothalamus promoting pronociceptive mechanisms in central and peripheral circuits in both male and female mice. This translational study will use radiotracer imaging techniques to examine stress-triggered changes in occupancy of hypothalamic KOR in an ex vivo rodent migraine model and in vivo in human migraineurs. Taken together, these studies should provide a better understanding of the mechanisms promoting transition from the interictal to ictal state and could thus allow for development of improved therapies for migraine prevention.

This multidisciplinary translational project is intended to investigate the importance of hypothalamic KOR activation as a link to stress and migraine

Preliminary
evidence
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in the
hypothalamus



The IHS fellowship will allow me to work with an outstanding team of mentors who will help me gain the necessary concepts and critical thinking required to become a successful independent researcher pursuing a career in headache research. It's an honour and a delightful opportunity to be working with Dr David Yeomans (expert in pain and headache physiology and therapy development) as my primary mentor, and Drs Rob Cowan (leading headache neurologist) and Sandip Biswal (leading radiologist) as my collaborative mentors.

My PhD studies have allowed me to study brain connectivity on restingstate functional MRI in migraine with aura patients

We will study
the functional
connectivity at
rest of chronic
migraine
patients who,
thanks to an
anti-CGRP
treatment,
switch to
episodic
migraine



## Cédric Gollion, France

Transforming chronic to episodic migraine: an MRI study. Participation in the REFORM study

Fellowship from November 2021 to October 2022 Danish Headache Center, Copenhagen, Denmark Mentor: Faisal Amin

During the summer of 2021, I was awarded the IHS fellowship to work for 1 year at an internationally recognised headache research centre, the Danish Headache Centre. I am very grateful for this unique opportunity to develop my knowledge in the field of headache and to deepen research in neuroimaging of migraine.

I am a neurologist graduated at the University of Toulouse and I have been practicing for 4 years as a fellow at the University Hospital of Toulouse in the department of stroke and headache. I am concluding a PhD in medical imaging on the research of MRI biomarkers of stroke risk in migraine with aura. The PhD, which I will defend at the end of 2021, has allowed me to study brain connectivity on resting-state functional MRI in migraine with aura patients.

Resting-state functional MRI has allowed many advances in the understanding of the pathophysiology of migraine, during the onset of the migraine attack, during the aura phase, in the mechanisms of chronicisation, and even in the prodrome phase. During the fellowship in Copenhagen, we will study the functional connectivity at rest of chronic migraine patients who, thanks to an anti-CGRP treatment (erenumab), switch to episodic migraine. These patients will be compared to patients who remain in chronic migraine despite anti-CGRP treatment and to non-migraineurs. Such research will allow us to better understand the mechanisms involved in the transition from chronic to episodic migraine, those involved in the persistence of chronic migraine, and to try to predict the response to treatment.

I look forward to joining the team of Professor Messoud Ashina and my mentor, Professor Faisal Mohammad Amin, to participate in this innovative research that aims to better understand the pathophysiology of chronic migraine. This research is part of an approach to personalising treatments. Conducting this research in this centre will give me the opportunity to benefit from their knowledge in migraine, in clinical pathophysiology studies, especially in neuroimaging, and from their experience in the field of headaches.



# Report of the 8th Asian Regional Conference of Headache (ARCH)





# Shuu-Jiun Wang and Wei-Ta Chen

More than 2,700 local and international delegates participated in this hybrid AOCN/ARCH meeting, 1,337 physical attendees and 1,424 virtual The 8th ARCH was initially scheduled to be held in 2020 but was postponed for 1 year and transformed to a hybrid form because of the COVID-19 pandemic. The proposed Hi-ARCH, which aims to provide a comprehensive educational programme for young clinicians and researchers interested in a career in headache, was also cancelled due to the COVID-19 pandemic. Despite these setbacks, in collaboration with the Asian Oceanian Association of Neurology (AOAN) and with the generous support of IHS, the 8th Asian Regional Conference of Headache (ARCH) and the 17th AOCN were successfully held from 1–4 April 2021 in Taipei, Taiwan. More than 2,700 local and international delegates participated in this hybrid AOCN/ARCH meeting, including 1,337 physical attendees and 1,424 virtual attendees.

The hybrid meeting of ARCH was held on 3 April with the main theme "Therapeutic armamentarium in headache disorders." The President of IHS, Professor Messoud Ashina, delivered the opening talk "Experimental human studies in headache disorders", which nicely summarised the knowledge and insights learned from in vivo experimental human migraine models. He also highlighted some potential novel therapeutic targets of migraine based on these experiments. Following the talk, Professor Wei-Ta Chen, the current President of the Taiwan Headache Society, addressed the difficult topic whether tension-type headache and migraine are two points on a continuum based on electrophysiological studies. Professor Tissa Wijeratne from Australia then gave a lecture regarding the established and emerging treatment of cluster headache. Professor Shih-Pin Chen from Taiwan addressed the pathophysiology of reversible cerebral vasoconstriction syndrome, a complex and enigmatic neurovascular disorder. Professor David Dodick, Past-President of IHS, provided a comprehensive review of migraine pathophysiology in individual phases of migraine. Professor Chi-ieong David Lau from Taiwan talked about neuromodulation in migraine, with specific focus on the role of abnormal neurophysiology and maladaptive plasticity. Professor Siwaporn Chankrachang from Thailand subsequently gave a talk regarding the ASEAN way of headache management. Following this, Professor Mi Ji Lee from South Korea delivered a lecture on the predictors and challenges in the treatment of medication-overuse headache, which concluded the morning session.

At the lunch symposium, President-Elect of IHS, Professor Cristina Tassorelli, provided a comprehensive review and update of headache treatment guidelines, with specific focus on the role of anti-CGRP monoclonal antibodies. Professor Fumihiko Sakai from Japan also shared the Asian experience in using anti-CGRP monoclonal antibodies for migraine treatment. In the afternoon session, Professor Chin-Sang Chung, Ex-President of ARCH, addressed the impact of comorbidity on the treatment and prognosis of headache disorders. Professor Jonathan Ong, current President of the Singapore Headache Society, shared his experiences of individualised treatment for migraine. Professor Yang Chun-Pai from Taiwan further talked about an interesting topic: whether the benefits of acupuncture on migraine are myth or science? Finally, Professor Allan Purdy from Canada delivered a wonderful perspective on the future of



There were presentations on many of the different headache disorders by renowned international experts as well as experts from the Asian region



headache treatment. All the audience enjoyed the wonderful and insightful lectures from these renowned experts.

In addition to the scientific session, Professor David Dodick and Professor Shuu-Jiun Wang, the current President of ARCH, both served as keynote speakers of the AOCN. Professor David Dodick gave a comprehensive update on anti-CGRP monoclonal antibodies as new therapies for migraine on the first day of AOCN, while Professor Shuu-Jiun Wang

provided the up-to-date review of spontaneous intracranial hypotension on the last day.

Following the ARCH conference, 26 delegates from the member countries attended the Virtual Business Meeting of the ARCH. Professor Shuu-Jiun Wang expressed his gratitude to all participants and members of the ARCH and appreciated the kind support from the IHS. Dr K Ravishankar was elected as the next President of the ARCH. The 9th ARCH will be held together with the 2022 Asian Oceanian Congress of Neurology (AOCN) from 3–6 November in New Delhi, India.



David Dodick and Shuu-Jiun Wang also gave keynote presentations in the main AOCN congress





## **Spotlight on IHS Affiliate Member Societies**

## **Mexican Association of Headache and** Migraine (AMCEMIG)

**AMCEMIG** was born from the need to create organisation formed primarily by neurologists related to the research. education, and clinical care of conditions characterised by headaches







Karina Velez-Jimenez, **Former President and Ildefonso Rodriquez-**Leyva, President

It is a privilege for us to have been selected by the Editorial Board of the IHS Newsletter to be part of this issue as its representative chapter in Mexico.

This association was born from the need to create an organisation formed primarily by neurologists related to the research, education, and clinical care of conditions characterised by headaches. Being a young organisation, it needs the enthusiasm and effort of its members to achieve common goals: a continuous medical education, especially of its associates. Furthermore, we strive to transmit our passion for the study of headaches to other specialists such as paediatricians, internists, family physicians, and others. We are promoting the use of a common language (proposed by IHS), maintaining a continuous update in the research and management of headaches, basing our studies on the characteristics of the population we seek to care for in our country. To achieve our goals, we have set out to educate ourselves with the support of the leading association in the study of headaches in the world, the IHS. With their help,

we have contacted experts who have shared their knowledge, experience and leadership with us.

We have held three annual meetings in which we have had more than 200 medical specialists in each one and at least 20 foreign professors. We held a Visiting Professors course last year in conjunction with the IHS Education Committee. We published a book on Headaches and Migraines, which was so successful that we are already working on the second edition. We also have a new publication on Migraine and Comorbidities that Leyva, Karina Velez-Jimenez, Carlos Bordini, we hope to release at our next annual meeting in which neurologists from Spain and Latin America will participate, giving more exposure



Jose Biller, Michel Volcy, Ildefonso Rodriguez-Alejandro Zermeño-Guerra Rector of the Universidad Autonoma de San Luis Potosi, at the 2nd International Congress of AMCEMIG.

to this publication. Before the pandemic, we initiated a long process of multiple sessions to finally publish "Comprehensive Management of Adults with Chronic Migraine. Clinical Practice Guidelines in Mexico". During the pandemic, we were actively participating in different virtual forums of continuing education, especially in the diagnosis and treatment of migraine, in which we achieved a strong diffusion. However, we are aware that there is still a long way to go and that there is much research to do and education of healthcare professionals to continue to help those who suffer from headaches.



This is why we will hold our annual meeting from 23–25 September where we will have the honour to have great professors such as Messoud Ashina, Cristina Tassorelli, Debora Friedman, Agustin Melo, Marcio Nattan, Julio Pascual, Carlos Bordini, Rami Burstein and Jose Biller, among others.

We are planning to hold an IHS Master School shortly (mid 2022) with the supervision and help of the IHS Education Committee Chairs, Allan Purdy and Henrik Schytz, who are responsible for this area in IHS.

We are confident that we will make the IHS proud to have us as their representatives in Mexico and that this relationship will promote the growth of headache knowledge and research in our country.



Workshop for the elaboration of Mexican Guidelines for diagnosis and treatment of Chronic Migraines.

# Australian & New Zealand Headache Society (ANZHS)



## Richard Stark, President

The ANZHS was formed in 2014. Its predecessor, the Australian Headache Society, had begun in 1985 and hosted the IHS scientific meeting in 1989, but in the 1990s the society became dormant. ANZHS was therefore formed afresh under the leadership of Alessandro Zagami, its founding President. Richard Stark was President-Elect and Vice President, Bronwyn Jenkins and Tissa Wijeratne were Honorary Secretaries, and Jane Prosser was Treasurer.

ANZHS had its first scientific meeting as a satellite meeting before the Australian New Zealand Association of Neurologists meeting in 2016, with about 40 attendees.

The society progressed rapidly from these small beginnings to hold an IHS Headache Master Class in Sydney in 2018. This was an enormous success with over 150 participants, including 50 from the wider Asian region. The event was made possible by generous support from IHS and from the pharmaceutical industry. High-profile internationally-based

**ANZHS** progressed from a first satellite meeting at the ANZ **Association of Neurologists** meeting in 2016, with 40 attendees, to hosting a **Master Class in** Sydney in 2018 with over 150 participants





speakers included Peter Goadsby, David Dodick, Allan Purdy, Shuu-Jiun Wang and Anne MacGregor.

ANZHS's first stand-alone scientific meeting was held in Melbourne in 2019. This was also a great success with 150 attendees. Guest speakers were Rigmor Jensen and Manjit Matharu.

Our scientific meetings for 2020 and 2021 were impacted by the COVID-19 pandemic, so they were run as virtual meetings. Adaptation to this mode of presentation has progressed

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and while attendees missed the pleasure of face-to-face interaction with colleagues, the reduced burden of travel enabled us to produce an outstanding programme with a list of speakers that would be the envy of any headache meeting anywhere in the world. They included, in 2020, Peter Goadsby, Allan Purdy, Alan Rapaport, Cristina Tassorelli and Elizabeth Loder, and in 2021, Andrew Charles, David Dodick, Peter Goadsby, Shuu-Jiun Wang, Alexandra Sinclair, Cristina Tassorelli and Arne May.

ANZHS has grown from its inception in 2014 to a thriving society with 193 members (a large

number considering that there are only about 600 neurologists in Australia and New Zealand). The society has a voice in government decisions, for example in advocating on funding of CGRP antibodies. ANZHS also engages with industry through a round table process to provide considered input from the profession towards our shared goal of

improved patient outcomes. ANZHS provides our members with newsletters, education and a forum for their views as well as providing them with a link to the international headache community through IHS.

With a paucity of formal training in headache in Australia and New Zealand (at present there is only one unit offering a funded headache fellowship), education has been, and will remain, a primary focus for ANZHS. We remain committed to advancing headache management in our region through collaborations with our international colleagues in research, advocacy and education.



The society now has 193 members and has a voice in government decisions such as advocating on funding of new therapies

through collaborations with our international colleagues in research, advocacy and education

We remain

advancing

headache

committed to

management

in our region



## **Danish Headache Society**



# Faisal Mohammad Amin, President

Internationally renowned headache experts are invited as keynote speakers to the society annual meeting

The Danish Headache Society was established in 1969 by a few active Danish scientists to promote all aspects of headache science in Denmark and to create a platform where novel scientific achievements can be discussed. Moreover, the goals of the society were to promote headache knowledge in physicians and other health workers who work with headache patients. Promotion of an evidence-based and ethical attitude to treatment of headache is a mainstay in the society's work.

During the years, the Danish Headache Society has been led by world-renowned top researchers, including two Past-Presidents and Honorary Life Members of IHS, Jes Olesen and Peer Tfelt-Hansen, as well as the current IHS president, Messoud Ashina. Moreover, the current Directors of the Danish Headache Center, Rigmor Højland Jensen and Lars Bendtsen, have both served as leaders of the Danish society.

One of the main activities of the society has been to organise the annual meeting, where internationally renowned headache experts are invited as keynote speakers. The meeting usually ends with young headache scientists' presentation tournament and a prize ceremony awarding the best presentation as well as the best scientific work of the year. This year's meeting will be held on 26 October, where Professors Michael Moskowitz, Peter Goadsby, Lars Edvinsson and David Dodick will be among the speakers. Due to COVID-19 restrictions only 100 persons will be allowed on site, but it will also be possible to attend the meeting virtually.

A young headache scientists' presentation tournament is held awarding the best presentation as well as the best scientific work of the year



Current and past Presidents of the Danish Headache Society taken at the annual meeting 2019 in the Domus Medica I Copenhagen (headquarters of the Danish Headache Society).

From left: Lars Bendtsen, Peer Tfelt-Hansen, Rigmor Højland Jensen, Jes Olesen, Birthe Krogh Rasmussen, Messoud Ashina, Henrik Winther Schytz and Faisal Mohammad Amin.



One of the society's short-term goals is to develop or facilitate headache outpatient clinics in all 16 governmental hospitals in Denmark which have a neurological department

One of the current board's short-term goals, within next 3 years, is to develop or facilitate headache outpatient clinics in all 16 governmental hospitals in Denmark which have a neurological department. To achieve this goal, the board has prioritised recruitment of new members among physicians, nurses, therapists, research fellows as well as medical students who are engaged in headache research or seeing headache patients. In the year 2021 alone, we have registered 31 new members who have also joined IHS, corresponding to a 40% increase of our IHS members. The next step is to promote the exchange of knowledge between already established headache clinics and new clinics, as well as to ensure that all members are aware of and using the national headache guidelines.

Moreover, within the past year the headache society has updated the second version of the national headache guidelines. The Danish Headache Society also took the initiative to develop a European Consensus Statement on the diagnosis and clinical management of migraine in collaboration with the European Headache Federation and the European Academy of Neurology. Our national guidelines have recently been published in the *Journal of Headache and Pain*, while the European consensus statement paper is published in the *Nature Reviews Neurology*.

In addition to the above mentioned activities, the board is in frequent contact with the health authorities and policymakers in Denmark as advisors on multiple issues concerning headache treatment in Denmark.

#### References

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- Eigenbrodt AK, Ashina H, Khan S, et al. Diagnosis and management of migraine in ten steps. Nat Rev Neurol 2021 Jun 18. Epub ahead of print, https://doi.org/10.1038/s41582-021-00509-5



# Calendar of events

Date	Event	Country	Contact/information
2021			
18-19 August	12th International Conference on Stroke, Neurology and Cerebrovascular Disease	Munich, Germany	Visit website
8–12 September	IHC 2021 – International Headache Congress – IHS and EHF joint congress 2021	Virtual meeting	Visit website
23–25 September	AMCEMIG (Mexican Headache Society) 3rd Headache Congress	Virtual meeting	Visit website
23–26 September	15th World Congress on Controversies in Neurology (CONy)	Virtual meeting	Visit website
24–25 September	Russian Headache Congress	Moscow, Russia	Visit website
3-7 October	XXV World Congress of Neurology	Virtual meeting	Visit website
28 November	American Headache Society – 2021 Scottsdale Headache Symposium	Scottsdale, AZ, USA	Visit website
2022			
17-22 April	74th Annual Meeting of the American Academy of Neurology	Seattle, WA, USA	Visit website
9-12 June	64th Annual Scientific Meeting of the American Headache Society	Aurora, CO, USA	Visit website
25–28 June	8th Congress of the European Academy of Neurology	Vienna, Austria	Visit website
8–11 September	Migraine Trust International Symposium	London, UK	Visit website
9-11 December	European Headache Federation Annual Congress	Vienna, Austria	Visit website

**Important note:** Events may be cancelled, postponed or go virtual due to the COVID-19 pandemic. Please check each event website for updated information.

If you would like IHS to include your meeting on the IHS website and newsletter please contact **Carol Taylor** with the details.



# New Open Access companion journal for Cephalalgia

## Cephalalgia Reports: A fully Open Access Journal

Published on behalf of the International Headache Society, *Cephalalgia Reports* is a peerreviewed, open access publication providing an international forum for original research papers, review articles, clinical perspectives, technical reports and short communications.

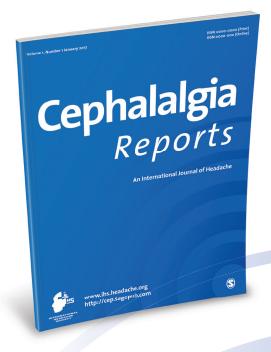
It actively encourages high quality papers in the following areas:

- Emerging observations with translational potential not yet realised
- Reports limited to regional relevance which may validate and add to existing studies
- Negative outcomes
- Technical reports
- Articles with a more clinical emphasis
- Pilot trials which may stimulate therapeutic innovation
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