



Welcome to the Q4, 2022 issue of the Migraine World Summit (MWS) Quarterly Research Report. This report highlights recent research publications related to migraine and headache. We hope you find it a helpful way to discover some of the latest findings that may be relevant to you.

Each report is intentionally brief in order to provide a quick overview. The goal is to give you an idea of current research and to share some insights that may improve your understanding of migraine.

Consult your headache specialist or primary care physician to discuss how any of the research findings might apply to you.

Some medical publications don't provide free online access. In some cases, your health care professional may be able to print a copy for you.

Please note that our volunteer support team members are patients themselves and are not able to answer questions about the research or comment on these medical studies.

Authors highlighted **in bold** are those who have spoken at the Migraine World Summit.

Quotes are taken directly from the research paper.

We welcome your feedback on this report. Please share via email to info@migraineworldsummit.com

Disclaimer: The views reflected in this research report do not represent the views of the Migraine World Summit. This report is not designed to replace a consultation with your doctor. Seek medical advice before making any changes to your treatment plan.

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Research Title

Association Between Computer Vision Syndrome, Insomnia, and Migraine Among Lebanese Adults: The Mediating Effect of Stress

Publication Date

2022

Medical Journal

Prim Care Companion
CNS Disord

RESEARCH OVERVIEW

Computer vision syndrome (CVS) is a catchall term for visual and non-visual symptoms that can result from extended viewing of digital device screens.

In this study, researchers gathered information using an online survey of 749 people in Lebanon. They conducted the study during a period of COVID-19 lockdown, when screen usage was higher than normal. Migraine was assessed using the Migraine Disability Assessment Scale (MIDAS). The study population was 66% female, 34% male, with a mean age of 24 years.

Just over 70% of the people surveyed reported CVS, and the researchers found a significant association of CVS with migraine. Stress mediated the correlation between CVS and migraine, confirming prior studies that show a relationship between excessive computer use and migraine



QUOTES

“The blue light emitted from computer screens not only causes insomnia but also worsens or triggers migraine attacks.”

“Our research revealed that the presence of CVS was significantly associated with more migraine.”

“Thus, we can conclude that computer screens frequently cause headache in [healthy participants] and trigger or exacerbate migraine attacks in patients with a history of migraine.”

“In our results, stress also mediated the correlation between CVS and migraine. Many studies showed that excessive computer use can trigger or worsen migraine attacks via visual stimulation of the trigeminovascular route, leading to dysregulation of the nociceptive pathway responsible for migraine.”



OUR TAKEAWAY

This study adds to the evidence that computer usage, and especially extended usage, can be a migraine trigger. Although the mechanisms for this effect have not been definitively established, the dominant blue-light frequencies of digital screens apparently leads to a cascade of events that result in stimulation of the trigeminal system.

That finding suggests that there is a “double jeopardy” effect because this and other studies report that extended periods of screen use also exacerbate insomnia, which in turn is a contributing factor to migraine onset.



RESEARCH LINK & AUTHORS

Full article available free at

<https://www.psychiatrist.com/pcc/sleep/association-between-computer-vision-syndrome-insomnia-migraine-among-lebanese-adults-mediating-effect-stress/>

Akiki M, Obeid S, Salameh P, et al. Association between computer vision syndrome, insomnia, and migraine among Lebanese adults: the mediating effect of stress. *Prim Care Companion CNS Disord.* 2022;24(4):21m03083.



Research Title

The Importance of an Early Onset of Migraine Prevention: An Evidence-Based, Hypothesis-Driven Scoping Literature Review

Publication Date

2022

Medical Journal

Ther Adv Neurol Disord



RESEARCH OVERVIEW

This study is a review and summation of the data from 18 studies about the rate of onset migraine relief for patients who are given one of the CGRP inhibitor medications.

Compared to placebo, erenumab [Aimovig] (three studies) reduced weekly migraine days within 1 week; fremanezumab [Ajovy] (six studies) increased reports of no headache of at least moderate severity on Day 1 and significantly reduced migraine frequency within 1 week; galcanezumab [Emgality] (three studies) significantly reduced the mean number of patients with migraine beginning Day 1 and each day of the first week; eptinezumab [Vypti] (four studies) significantly reduced migraine attack likelihood on Day 1 by > 50% *versus* baseline; and onabotulinumtoxinA [Botox] (two studies) reduced headache and migraine days within 1 week. Four publications described function, disability, and quality of life improvements as early as Week 4.



QUOTES

“Migraine prevention is an important component of overall migraine management; it is recommended not only to reduce migraine attack frequency, severity, duration, and related disability but also to improve responsiveness to acute medications (and avoid escalation in use and reduce reliance on them), to improve health-related quality of life, and to reduce headache-associated distress, psychological symptoms, and overall costs.”

“Anti-CGRP monoclonal antibodies (erenumab, fremanezumab, galcanezumab, and eptinezumab) and a chemodenervation agent (onabotulinumtoxinA) provide clinically relevant benefits during the first treatment week.”

“Recently approved migraine preventive therapies facilitate rapid control of migraine activity, potentially improving patients' lives and minimizing the societal burden of migraine.”



OUR TAKEAWAY

Clinical trials usually measure therapeutic effect after 12 weeks, since that was generally the minimum time required to see benefits of older medications. The newer CGRP inhibitor medications, however, are demonstrating a far more rapid onset of relief from migraine symptoms. This literature review confirmed that each of the CGRP medications brings rapid relief to many people with migraine disease.

One of the shadow benefits of rapid relief onset is that it provides feedback and encouragement. Older medications, with their slower onset, often lead to people feeling that “It isn’t working,” and then switching or abandoning preventive medications.



RESEARCH LINK & AUTHORS

Abstract and full article available free at <https://pubmed.ncbi.nlm.nih.gov/35662957/>

Gottschalk C, Buse DC, Marmura MJ, Torphy B, Pavlovic JM, Dumas PK, Lalvani N, Blumenfeld A. The importance of an early onset of migraine prevention: an evidence-based, hypothesis-driven scoping literature review. *Ther Adv Neurol Disord.* 2022 May 31;15:17562864221095902. doi: 10.1177/17562864221095902. PMID: 35662957; PMCID: PMC9160905.



Research Title

Decrease Retinal Thickness in Patients with Chronic Migraine Evaluated by Optical Coherence Tomography

Publication Date

2022

Medical Journal

Diagnostics (Basel)



RESEARCH OVERVIEW

This study uses state-of-the-art technology to demonstrate that there are significant alterations in retinal thickness among people with chronic migraine disease.

Recognizing that the trigeminal vascular system — known for its involvement with migraine disease — innervates the eye as well as other structures, the researchers used optical coherence tomograph (OCT) to compare the thickness of different retinal layers between chronic migraine patients and healthy controls (90 of each).

Statistically significant differences were found in the mean macular thickness, which was thinner in migraine patients than in healthy controls. Macular thickness was significantly lower ($p \leq 0.05$) in the main quadrants (superior, inferior, peripheral inferior, temporal, and nasal) of migraine patients compared with the controls, except for the central quadrant.



QUOTES

“In the pathophysiology of a migraine, activation and sensitisation occurs episodically in the trigeminal vascular system, which is also found in extracranial structures, such as the retina and choroid. Its activation causes inflammation, in addition to causing vasodilation and subsequent vasoconstriction in both structures. It is known that this vascular narrowing and the lack of blood supply is temporary, both at the cerebral and ocular level, but the chronic nature of migraine may be the cause of permanent structural and functional alterations.”

“The quantification of the axonal damage could be used as a biomarker to help in the diagnosis and monitoring of this pathology.”

“. . .the longer one suffers from CM, the thinner the macular and [ganglion cell layer].”



OUR TAKEAWAY

This is an important study, because it demonstrates that chronic migraine can have an impact on retinal tissue.

While the dilation and subsequent vasoconstriction of vessels that occurs during a migraine are temporary, a concern for people with migraine disease is always whether or not *permanent* damage is occurring to any area affected by the migraine.

It should be noted that this study was entirely of people with chronic migraine (>15 migraine days/month). Effects on those with less-frequent, episodic migraine are unknown.



RESEARCH LINK & AUTHORS

Abstract and full article available free at

<https://pubmed.ncbi.nlm.nih.gov/36611297/>

Raga-Martínez I, Povedano-Montero FJ, Hernández-Gallego J, López-Muñoz F. Decrease Retinal Thickness in Patients with Chronic Migraine Evaluated by Optical Coherence Tomography. *Diagnostics (Basel)*. 2022 Dec 20;13(1):5. doi: 10.3390/diagnostics13010005. PMID: 36611297; PMCID: PMC9818823.



Research Title

Migraine and the Risk of Stroke in a Middle-Aged and Elderly Population: A Prospective Cohort Study

Publication Date

2023

Medical Journal

Cephalalgia



RESEARCH OVERVIEW

Research has shown that patients with migraine have a higher risk of stroke, but definitive data on the presence and extent of risk for older individuals has been lacking.

As part of an ongoing, prospective population-based study (the Rotterdam Study), researchers identified the presence of migraine using a validated questionnaire in a structured interview between 2006 and 2011. This formed the baseline for analyzing the association between migraine and the risk of stroke.

A total of 6,925 (mean age 65.7 +/- 11.3 years, 57.8% females) stroke-free participants were included. At baseline, 1,030 (14.9%) participants had a lifetime history of migraine. During a median followup of 6.2 years, 195 participants developed a stroke.

There was an “association” between stroke and a history of migraine, but the results were not statistically significant.



QUOTES

“Our results suggest an association between migraine and the risk of stroke in a middle-aged and elderly population, although this was not statistically significant. Likewise, our data suggested a similar association of migraine and ischemic stroke, albeit again not statistically significant.”

“In the elderly, a history of migraine may not be a risk factor for stroke except in current smokers and individuals with late-life migraine onset.”



OUR TAKEAWAY

The literature on stroke and migraine has been indecisive, with reports of both an increased risk and no difference in risk for older (>50 years) people.

This study benefitted from being part of a prospective, ongoing population study with a depth of data, excellent followup, and specific criteria for defining the presence of migraine and stroke.

The researchers note that the results could be affected by the fact that almost all migraine onset occurs prior to age 50, and that in an older population cardiovascular risk is high enough that it may obscure risk attributable only to long-term migraine disease. .



RESEARCH LINK & AUTHORS

Abstract and full article available free at

<https://journals.sagepub.com/doi/full/10.1177/0333102421132008>

Acarsoy C, Fani L, Al-Hassany L, Berghout B, Koudstaal PJ, **Maassen Van Den Brink A**, Ikram MK, Bos D. Migraine and the risk of stroke in a middle-aged and elderly population: A prospective cohort study. *Cephalalgia*. 2023 Jan;43(1):3331024221132008. doi: 10.1177/03331024221132008. PMID: 36622876.



Research Title

Postural Orthostatic Tachycardia Syndrome and Migraine: A Narrative Review 2022

Publication Date

2022

Medical Journal

Headache



RESEARCH OVERVIEW

Migraine disease is the most common comorbidity of postural orthostatic tachycardia syndrome (POTS). POTS is a disorder of the autonomic nervous system characterized by positional changes that result in either an increase in heart rate of >30 beats/minute or a heart rate of >120 beats/minute. Other symptoms can include headache, fatigue, migraine, and cognitive dysfunction. POTS is a debilitating illness with few effective treatments.

The high prevalence of migraine in patients with POTS may be explained by common pathologic mechanisms. There is evidence that dysregulation of the sympathetic nervous system, alterations in central and peripheral hemodynamics, and central sensitization increase vulnerability to both POTS and migraine. Non-pharmacologic and pharmacologic treatments that target these shared mechanisms may provide significant benefit for the patient with POTS and migraine.



QUOTES

“The high prevalence of migraine in patients with POTS may be explained by common pathologic mechanisms.”

“Migraine is the most common comorbidity in patients with POTS.”

“Migraine treatments that decrease peripheral and central sensitization, including onabotulinumtoxinA and calcitonin-gene-related peptide antagonists, may improve POTS symptoms, but this has not been studied.”

“For individuals with migraine with comorbid POTS, β -blockers may improve the symptoms of both conditions.”



OUR TAKEAWAY

This article summarizes experimental and clinical evidence demonstrating connections between POTS and migraine.

Vagal nerve stimulation (VNS), which has been approved for treatment of migraine disease, is also being tested as an intervention for POTS. Given the high rate of comorbidity, this tends to affirm the likelihood of a shared physiological pathway.

Central sensitization, an important feature of migraine, has recently been demonstrated in patients with POTS (both with and without migraine) and may be a significant shared pathophysiology. Central sensitization in POTS and migraine may involve elevations of pro-inflammatory cytokines.



RESEARCH LINK & AUTHORS

Abstract available free at

<https://doi.org/10.1111/head.14365>

Mueller, B. R., & Robinson-Papp, J. (2022). Postural orthostatic tachycardia syndrome and migraine: A narrative review. *Headache*, 62(7), 792-800.



Research Title

Prevalence and Clinical Characteristics of White Matter Hyperintensities in Migraine: A Meta-Analysis

Publication Date

2023

Medical Journal

Neuroimage Clin.



RESEARCH OVERVIEW

White matter is found in the deeper tissues of the brain. It consists of nerve fibers surrounded by a covering of myelin, which gives white matter its color. White matter lesions with hyperintensities (WMHs) are subclinical brain injuries that represent damage to the brain's small vessels, including arterioles, capillaries, and venules. These are seen as areas of higher intensity on MRI imaging.

The reported prevalence of WMHs in those with migraine disease varies widely across studies, ranging from 9.9% to 78.4%. The correlations between WMHs and demographic or migraine characteristics (e.g., migraine subtypes and attack frequency) are also inconsistent across studies. The aim of this systematic review and meta-analysis was to explore the pooled prevalence of WMH and the associations of WMHs with clinical characteristics in patients with migraine.



QUOTES

“The overall evidence suggests that the prevalence of WMHs in migraineurs (44%) is significantly higher than that in healthy controls, which may offer important insights into the early stage of stroke and dementia in migraine.”

“Evidence suggests that persons with an extensive WMHs burden have an increased risk of stroke and dementia in the future. This may explain the increased risk of stroke and dementia in patients with migraine. Considering that the presence of WMHs precedes stroke and dementia, it is plausible that preventing the formation and progression of WMHs could thereby reduce the risk of stroke and dementia in patients with migraine.”

“[Because] the pathogenesis of migraine affects WMH, comorbid hypertension and diabetes mellitus are likely to result in WMHs.”



OUR TAKEAWAY

This study reinforces the importance of *preventing* migraine episodes, not only to reduce the quality-of-life impact, but also to prevent cumulative vascular damage that may potentially increase the risk of stroke or dementia.

This study used data from 30 studies involving 3,502 people with migraine disease. The pooled WMHs prevalence was 44%, 45%, and 38% in migraine, migraine with aura, and migraine without aura groups, respectively.

As with all meta-studies that pool published data, there are inconsistencies in methods, measurement, study design, and statistical analyses in the studies used.



RESEARCH LINK & AUTHORS

Abstract and full article available free at

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9827384/>

Zhang W, Cheng Z, Fu F, Zhan Z. Prevalence and clinical characteristics of white matter hyperintensities in Migraine: A meta-analysis. *Neuroimage Clin.* 2023 Jan 3;37:103312. doi: 10.1016/j.nicl.2023.103312. Epub ahead of print. PMID: 36610309; PMCID: PMC9827384.



Research Title

A Qualitative Evidence Synthesis of Patient Perspectives on Migraine Treatment Features and Outcomes

Publication Date

2023

Medical Journal

Headache



RESEARCH OVERVIEW

What patients want from treatment outcomes and what the medical community offers do not always align.

The research used data from 19 studies, reporting on 459 patients. The researchers identified eight overlapping themes relating to the migraine treatment process: (1) shared decision-making, (2) a tailored approach, (3) trust in healthcare professionals, (4) inclusion of knowledge and options, (5) a holistic approach, (6) ease of communication, (7) a non-undermining process, and (8) a process that includes reciprocity.

Seven themes relating specifically to the treatment itself were identified. These were (1) nonpharmacologic treatment, (2) high effectiveness, (3) rapidity of action, (4) long-lasting effect, (5) lower cost and more accessibility, (6) abortive and prophylactic treatment, without clear preference between the two, and (7) self-management/self-delivery option.



QUOTES

“There are data that ‘prescribing migraine education’ makes an impact on migraine frequency and quality of life. Per this review, individuals with migraine who participated in a prospective, migraine education program were more likely to have fewer headache days and also have improved headache-related disability scores over 12 months.”

“Patient values and preferences were individually constructed, varied widely, and could be at odds with conventional medical perspectives and evidence of treatment effects.”

“Findings highlight the complex and nuanced nature of migraine treatment. People living with migraine described their struggle to find a treatment that satisfied their expectations and needs.”



OUR TAKEAWAY

The findings point to a need for improvements in alignment of patient and healthcare provider treatment goals and strategies for attaining them, as well as the importance of migraine education, which includes efforts such as Migraine World Summit.

One of the notable findings was that “The diagnosis of migraine is based on clinical features rather than test results. As such, patients expressed feeling as though they did not understand the cause for their symptoms, and/or that their clinicians did not provide adequate or clear explanations for their symptoms.” Patients know they have migraine disease; they want to know *why*, and they want to know how and why certain treatments work.



RESEARCH LINK & AUTHORS

Abstract and full article available free at

<https://headachejournal.onlinelibrary.wiley.com/doi/10.1111/head.14430>

Urtecho M, Wagner B, Wang Z, **VanderPluym JH**, **Halker Singh RB**, Noyes J, Butler ME, Murad MH. A qualitative evidence synthesis of patient perspectives on migraine treatment features and outcomes. *Headache*. 2023 Jan 5. doi: 10.1111/head.14430. Epub ahead of print. PMID: 36602191.



Research Title

Polymorphisms of the Proinflammatory Cytokine Genes Modulate the Response to NSAIDs But Not to Triptans in Migraine Attacks

Publication Date

2022

Medical Journal

Int J Mol Sci.



RESEARCH OVERVIEW

At present, a significant portion of patients do not obtain a satisfactory response to acute pain-relieving therapies, including NSAIDs and triptans. At least for those with episodic migraine, the answer may be found in genetics.

Pain relief by administration of NSAIDs or triptans for three consecutive migraine attacks was evaluated. The researchers found a significant association between one version of a gene for a substance known as tumor necrosis factor- α promoter (TNF- α) and a lack of efficacy after NSAID administration. Remaining genetic variations had no significant effect on pain relief, and there was no association between any genetic variation and responsiveness to triptans.

The study showed that a functional variation in the TNF- α gene significantly modulates the clinical response to NSAID administration in acute attacks.



QUOTES

“This is the first study demonstrating a lack of efficacy after NSAID administration in migraine attacks in migraineurs carrying a functional polymorphism in the TNF- α gene. . .”

“In our patients with episodic migraine without aura, it could be hypothesized that migraineurs carrying the A allele showed a significantly lower anti-migraine effect of NSAIDs due to higher production of the active cytokine during stress.”



OUR TAKEAWAY

Considerable research attention is being focused on cytokines — immune system substances that play a role in the body’s inflammatory response to challenges such as migraine. Tumor necrosis factor alpha is one of those substances.

There are several variations (polymorphisms) of a gene that encodes TNF- α . This study reports that when one of those variations is present in people with episodic migraine (less than 15 migraine days/month), the use of nonsteroidal anti-inflammatory medications is less effective.



RESEARCH LINK & AUTHORS

Abstract and full article available free at

<https://www.mdpi.com/1422-0067/24/1/657>

Urtecho M, Wagner B, Wang Z, **VanderPluym JH**, **Halker Singh RB**, Noyes J, Butler ME, Murad MH. A Rubino E, Marcinnò A, Grassini A, Piella EM, Ferrandes F, Roveta F, Boschi S, Cermelli A, Gallone S, Savi L, Rainero I. Polymorphisms of the Proinflammatory Cytokine Genes Modulate the Response to NSAIDs but Not to Triptans in Migraine Attacks. *Int J Mol Sci*. 2022 Dec 30;24(1):657. doi: 10.3390/ijms24010657. PMID: 36614097; PMCID: PMC9820603.