



**Penn State College of Medicine
Continuing Education**

Neurology for the Non-Neurologist

Friday, March 28, 2025

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**Any names or ages used on the upcoming slides are fictitious
and not referring to an actual patient.**



PennState
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“Non-Medication” Options for Treatment of Headaches and Cephalgia

WILL JENS, DO FAAN
3/28/25

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Disclosure: ABBVIE, Eisai speaker

- ▶ Open for more

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Objective

- ▶ Redflags
- ▶ Snacky treatments
- ▶ Shocky treatments
- ▶ Stabby treatments
- ▶ “Swifty” Treatment with motion
- ▶ Sleepy

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SNOOP5 – REDFLAGS for headache

- ▶ Systemic signs – jaw claudication, fevers/chills, weight loss etc
- ▶ Neurologic signs – New weakness, numbness, ataxia, etc
- ▶ Old age >50: cancer vs GCA
- ▶ Onset: sudden: thunderclap
- ▶ Position: worse laying down, concern for high ICP
- ▶ Papilledema: sign of high ICP
- ▶ Pregnancy: growth,
- ▶ Progression: change in pattern is atypical
- ▶ Pulsatile: vascular issues, HTN



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How to choose preventative

Go for Effect

Depending on insurance if able to go for mAB, botox, gepant



Go for side effect

Use the common side effects as a treatment goal.

Anxiety? SSRI/Betablock
 Depression? Cyclic/SSRI
 Sleep? Cyclic
 BP issue: beta blocker
 Weight? Topamax
 Neuralgia? Topamax
 Systemic pain?
 Gabapentin vs SSRI/SNRI vs
 Tricyclic

Lifestyle

Push lifestyle changes

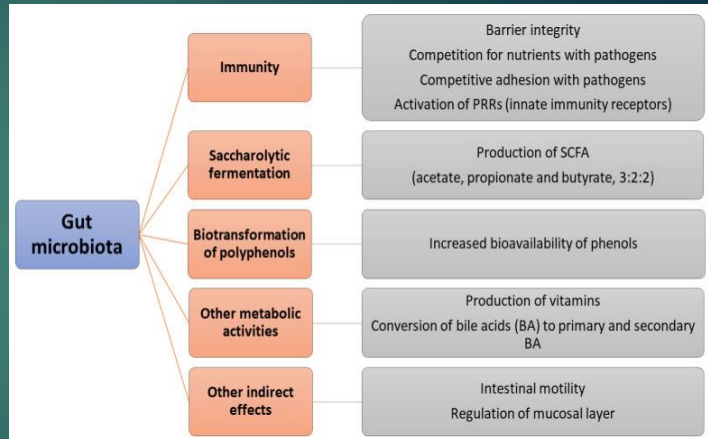
Not looking for you to become a VEGAN TRIATHLETE, but it could help.

Low inflammatory diet
 Exercise (30 min x 5 days)
 Hydration
 Avoid triggers
 Sleep (screen osa)
 Vision screen?
 Nutraceuticals
 Shocky-stabbies

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Diet: the microbiome

- ▶ Neuroinflammation (e.g., vagus nerve and cytokines ((IL1B, TNF, etc))
- ▶ gut-brain signaling (e.g., gamma-aminobutyric acid)
- ▶ metabolic function (e.g., short-chain fatty acids)
- ▶ MS showed a significant reduction in the variety and number of bacterial genera able to produce high amounts of SCFA, suggesting dysbiosis



Gazerani P, Papetti L, Dalkara T, Cook CL, Webster C, Bai J. The Brain, the Eating Plate, and the Gut Microbiome: Partners in Migraine Pathogenesis. *Nutrients*. 2024 Jul 11;16(14):2222. doi: 10.3390/nu16142222. PMID: 39064664; PMCID: PMC11280178.
 Altieri C, Speranza B, Carbo MR, Sinigaglia M, Bevilacqua A. Gut-Microbiota, and Multiple Sclerosis: Background, Evidence, and Perspectives. *Nutrients*. 2023 Feb 14;15(4):942. doi: 10.3390/nu15040942. PMID: 36839299; PMCID: PMC9965298.

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Migraine microbiome

- ▶ High correlation with Migraine in different gut disorders: IBS, Chrons', Celiacs etc.
- ▶ Manipulation: direct +(probiotics)/- (antibiotics), indirect (diet), replace
 - ▶ Supplementation hit or miss with relief , but higher hit
 - ▶ Antibiotic studies difficult to
 - ▶ Low fat diets (and some high omega3) as well as Low carbohydrate have shown reductions in migraine
 - ▶ Evidence showed an increase in CGRP plasma level of adult with obesity which is also pointed out in patients with migraine; studies on weightloss with GLP1s and bariatric surgery showed reduction in correlation with weight loss.

Gazerani P, Papetti L, Dalkara T, Cook CL, Webster C, Bai J. The Brain, the Eating Plate, and the Gut Microbiome: Partners in Migraine Pathogenesis. *Nutrients*. 2024 Jul 11;16(14):2222. doi: 10.3390/nu16142222. PMID: 39064664; PMCID: PMC11280178.

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Riboflavin

- ▶ Regulates the structure and function of flavoenzymes through its cofactors FMN and FAD
- ▶ protects the cells from oxidative stress, apoptosis, and inflammation
- ▶ 100 mg/d riboflavin supplementation during 3 months had a similar effect to propranolol intervention
- ▶ 400 mg/d riboflavin supplementation during 3 months had the same favorable effects as 500 mg/day sodium valproate
- ▶ AAN level A evidence

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Magnesium

- ▶ Mg+ deficiencies known to promote cortical spreading depression, alter nociceptive processing and neurotransmitter release
 - ▶ Mg+ ions antagonize NMDA receptors that are associated with nociception and the resulting neuroplastic changes in the trigeminal nociceptive neurons, as well as with regulation of cerebral blood flow
 - ▶ Production of NO can be inhibited by decreased magnesium levels, which is synaptic modulator, affecting nociceptive processing and bloodflow
 - ▶ Circulating CGRP levels have been shown to be decreased by the administration of magnesium in patients
- ▶ All migraine characteristics (such as frequency, intensity, duration of attacks and number of medications taken, and migraine disability) were significantly improved in the all groups. But the combination of magnesium and sodium valproate was more effective compared with other groups.



Chiu, H-Y, Yeh, T-H, Yin-Cheng, H, and Pin-Yuan, C. Effects of intravenous and oral magnesium on reducing migraine: a meta-analysis of randomized controlled trials. Pain Physician. (2016) 19:E97-E112. doi: 10.36076/ppj/2016.19.E97

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others

Feverfew

Parthenolide can inhibit the release of serotonin and prostaglandin.

This inhibits the dilatation blood vessels that can trigger migraine.

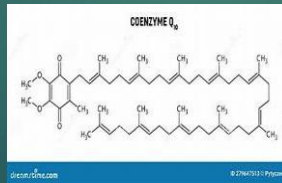
May help reduce the frequency and duration of migraine attacks.



CoQ10

Coenzyme Q10 is another essential player in mitochondrial electron transport chain and energy metabolism in the brain.

300 milligrams a day of CoQ10 can reduce migraine frequency in adults.



Omega-3s

Moderate evidence that fatty acid supplementation, particularly omega-3, improves migraine clinical outcomes



Guillermo García-Pérez-de-Sevilla, Ángel González-de-la-Flor, Impact of Fatty Acid Supplementation on Migraine Outcomes: A Systematic Review and Meta-analysis, *Nutrition Reviews*, 2025,, nuae219, <https://doi.org/10.1093/nutrit/nuae219>
Zahra Hojhashemy Z et al. Practical supplements for prevention and management of migraine attacks: a narrative review. *Front. Nutr.*, 29 October 2024. Volume 11 – 2024. <https://doi.org/10.3389/fnut.2024.1433390>

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“Shocky” treatments

- ▶ Electric stimulation
 - ▶ Gateway theory
 - ▶ Raise norepinephrine/epinephrine
 - ▶ Vagal suppression
- ▶ Magnet
 - ▶ Suppress CSD
- ▶ No use in epilepsy

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Cefaly

- ▶ Gateway theory for **Transcutaneous Supraorbital Nerve Stimulation**
- ▶ 67 episodic migraine patients; attack frequency, total headache days and acute drug use better, not severity
- ▶ prn: 60 min
- ▶ preventive: 20 min/day
- ▶ 18-65 No SCRIPT
- ▶ \$379 purchase, \$30 refills
- ▶ 90 day satisfaction guarantee



Relivion

- ▶ Gateway theory for **Transcutaneous Supraorbital Nerve and greater occipital Stimulation**
- ▶ RIME: pain freedom 2 hours post treatment, was superior to sham, 46% pain freedom vs 11.8% ($p < 0.001$)
- ▶ Prn 60 min
- ▶ > 18 yo
- ▶ \$75/mo x 24 mo

Yarnitsky, D., Dodick, D.W., Grosberg, B.M., Burstein, R., Ironi, A., Harris, D., Lin, T. and Silberstein, S.D. (2019), Remote Electrical Neuromodulation (REN) Relieves Acute Migraine: A Randomized, Double-Blind, Placebo-Controlled, Multicenter Trial. *Headache: The Journal of Head and Face Pain*, 59: 1240-1252. <https://doi.org/10.1111/head.13551>
 Sharon R et al. Efficacy of Relivion® MG in the Acute and Preventive Treatment of Migraine. Findings from Two Recent Studies. [P7-2.002]. *Neurology*. May 3, 2022
<https://doi.org/10.1212/NEP.0000000000000000>

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Gamma core

MOA

Vagal Nerve Stimulator
 Possible mechanistic explanations for nVNS efficacy in headache involving four core areas: Autonomic nervous system functions; cortical spreading depression inhibition; neurotransmitter regulation; and nociceptive modulation

Data/ Use

113 sham control study, greater 46%~24% 50% responder rate

prn: 2 x 2 min
 preventive: 2 x 2min tid

> 12 yo

Avoid/Cost

No seizure hx, active implantable devices, close to metal

\$575/mo



Najib U, Smith T, Hindiyyeh N, Saper J, Nye B, Ashina S, McClure CK, Marmura MJ, Chase S, Liebler E, Lipton RB. Non-invasive vagus nerve stimulation for prevention of migraine: The multicenter, randomized, double-blind, sham-controlled PREMIUM II trial. *Cephalalgia*. 2022 Jun;42(7):560-569. doi: 10.1177/03331024211068813. Epub 2022 Jan 9. PMID: 35001643.

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Nerivio

Action

Presumably, REN activates descending inhibition pathways that originate in the periaqueductal gray (PAG) and in the rostral ventromedial medulla (RVM) which globally inhibit pain by the release of serotonin and noradrenalin

DATA/USE

252 subjects, 66.7% ~48% of patients achieve pain relief, with 37.4% ~ 18.8% of patients achieve pain freedom

prn: 45 min

Prevent: QOD 45 min

> 8 yo

Avoid/Cost

No seizure hx, active implantable devices, close to metal

CHF, severe cardiac disease, severe cerebrovascular disease
not close to a cancerous lesion
not over open skin wound/rash

\$0-60

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MAGNETS!

sTMS delivers single low frequency electromagnetic fields
These non-invasive pulses signal the brain change the pattern of neuronal firing and inhibit cortical spreading depression.

164 sTMS or sham Pain-free response rates after 2 h were significantly higher with sTMS (32/82 [39%])

prn: 3 pulses prn preventive: 4 pulses bid
> 12 yo

\$1100 for 3 mo then \$350/mo

defibrillator, wearable cardioverter defibrillator

history of stroke, epilepsy, devices/implants, facial tattoos with metallic ink, not near explosive gases, gasoline or natural gas
not near flammable anesthetic, oxygen or nitrous oxide,
not while driving or in conjunction with dangerous activity



Lipton et al. Single-pulse transcranial magnetic stimulation for acute treatment of migraine with aura: a randomised, double-blind, parallel-group, sham controlled trial. *Lancet Neurol*, 9 (2010), pp. 373-380

Lloyd JO, Chisholm KI, Oehle B, Jones MG, Okine BN, Al-Kaisy A, Lambro G, McMahon SB, Andreou AP. Cortical Mechanisms of Single-Pulse Transcranial Magnetic Stimulation in Migraine. *Neurother* 2020 Oct;17(4):1973-1987. doi: 10.1007/s13311-020-00879-6. PMID: 32632772; PMCID: PMC7851313.

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Stabby Treatments

- ▶ Blocks
- ▶ Trigger point injections
- ▶ Cervical joint injections/CD treatment
- ▶ Botox
- ▶ TMJ
- ▶ Acupuncture
- ▶ Piercing

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**American Academy
of Neurology™**

- ▶ **2025 Annual Meeting | C25 - Skills Workshop: Interventional Headache Management: Botulinum Toxin, Nerve Blocks, and Trigger Point Injections**
 - ▶ Saturday 04/05/25 Time 12:00 PM - 04:30 PM PD

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ONB/Sphenopalatine Ganglion block



- Injections typically of local synesthetic and steroid to selected area
- 19 patients in the GON block group and 18 patients in the SPG block group were evaluated.
- Significant improvements in pain severity, duration, number HA days, and the need for acute medical treatment were observed in the 1st, 2nd, and 3rd months compared to baseline ($p < 0.001$).
- The GON block group showed a greater reduction in headache intensity, duration, number of headache days, and MIDAS scores ($p < 0.001$).
- Risks: Retroorbital bleed (SPN), bleeding, nerve irritation, pain/numbness, infection.



Unal HA, Basari A, Celiker OS, Cakar Turhan KS, Asik I, Ozgencil GE. Comparison of Greater Occipital Nerve Blockade and Sphenopalatine Ganglion Blockade in Patients with Episodic Migraine. J Clin Med. 2024 May 21;13(11):3027. doi: 10.3390/jcm13113027. PMID: 38892738; PMCID: PMC11173077.

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Trigger point

- ▶ Myofascial trigger points (MTrPs) are defined as a hyperirritable spot in a palpable taut band of skeletal muscle fibers
- ▶ May be provoked by trauma, overuse, postural faults, emotional psychological stress, degeneration or endocrine and metabolic deficiencies.
- ▶ Treatment options include dry needling (DN), wet needling (eg lidocaine injection and some local anesthetic injections), ischemic compression, laser and oral drugs.
- ▶ Risks: infection bleeding, pain

Travell JG, S.D., Simons LS, Travell and Simons' Myofascial pain and dysfunction: The trigger point manual, 2 ed, Vol. 1, 1999, Baltimore MD: Williams and Wilkens, Graff-Radford SB. Myofascial pain: diagnosis and management. Curr Pain Headache Rep. 2004;8:463-46

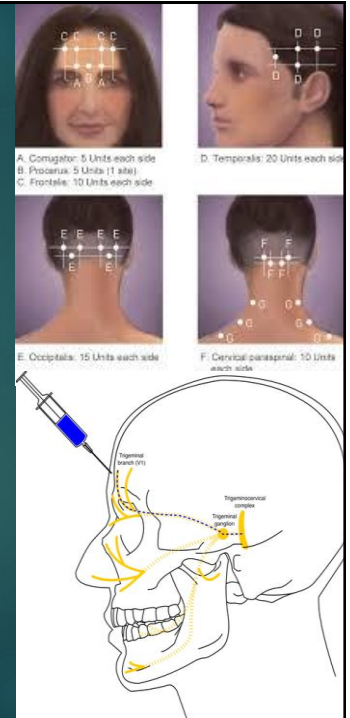
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Onabotulinumtoxin-A

- ▶ The mechanisms behind the effect of BoNT/A in chronic migraine may also include modulation of neurotransmitter release, changes in surface expression of receptors and cytokines as well as enhancement of opioidergic transmission
- ▶ transsynaptic transport after retrograde/anterograde axonal transport
- ▶ FDA approved treatment for Chronic Migraine
- ▶ Requires repeated treatments every 3 months (31 injections)
- ▶ Copay concerns

Dodick, D.W., Turkel, C.C., DeGryse, R.E., Aurora, S.K., Silberstein, S.D., Lipton, R.B., Diener, H.-C. and Brin, M.F. (2010). OnabotulinumtoxinA for Treatment of Chronic Migraine: Pooled Results from the Double-Blind, Randomized, Placebo-Controlled Phases of the PREEMPT Clinical Program. *Headache: The Journal of Head and Face Pain*, 50: 921-936. <https://doi.org/10.1111/j.1526-4610.2010.01678.x>

Do TP, Hvedstrup J, Schytz HW. Botulinum toxin: A review of the mode of action in migraine. *Acta Neurol Scand*. 2018 May;137(5):442-451. doi: 10.1111/ane.12906. Epub 2018 Feb 6. PMID: 29405250.



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Cervical injections

- ▶ Limited to Cervicogenic headaches
- ▶ localized, episodic pain projecting from the neck to the rest of the head, including ocular, occipital, frontal, and temporal regions in a C-shaped configuration.
- ▶ Characterized by a limited range of neck motion and pain from the neck radiating to the posterior and anterior regions of the head.
- ▶ Radio frequency ablations appear to work better than epidural steroids for lasting pain.
- ▶ 87 RF+ESI vs 57 ESI: The combination of PRF for the C2 dorsal root ganglion and ESI is a relatively safe therapy for CEH. This technique not only provides the sustained relief of pain symptom but improves the quality of life in patients with CEH.

Li, S.J., Feng, D. Pulsed radiofrequency of the C2 dorsal root ganglion and epidural steroid injections for cervicogenic headache. *Neural Sci* 40, 1173-1181 (2019). <https://doi.org/10.1007/s10072-019-03782-x>

Wang E, Wang D. Treatment of cervicogenic headache with cervical epidural steroid injection. *Curr Pain Headache Rep*. 2014 Sep;18(9):442. doi: 10.1007/s11916-014-0442-3. PMID: 25091129; PMCID: PMC4148620.

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Accupuncture

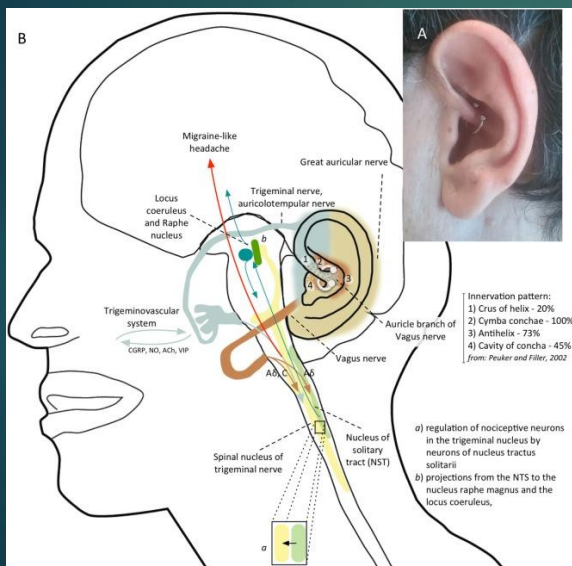
- ▶ "According to Chinese medicine, migraine is caused by six external evils, emotional disorders, dietary disorders, and dysfunctions of internal organs, etc., which lead to poor qi and blood circulation, impassable veins and channels, and ultimately triggers headache. Treatment is mainly aimed at regulating qi and blood, and balancing the functions of the internal organs to relieve symptoms."
- ▶ Vagal tone was elicited by AA or auricular acupressure
- ▶ Used as battlefield medicine, cancer treatment, MSK with some success
- ▶ Most studies seem to conclude combination of TCM+WCM is best.



Liu Y, Wang Y, Mi C, Wang Z, Han Y, Qi X, Ding X. Efficacy of Acupuncture-Related Therapy for Migraine: A Systematic Review and Network Meta-Analysis. *J Pain Res.* 2024 Mar 15;17:1107-1132. doi: 10.2147/JPR.S452971. PMID: 38505499; PMCID: PMC10950004.
 Mao JJ, Liou KT, Baser RE, Bao T, Panageas KS, Romero SAD, Li QS, Gallagher RM, Kantoff PW. Effectiveness of Electroacupuncture or Auricular Acupuncture vs Usual Care for Chronic Musculoskeletal Pain Among Cancer Survivors: The PEACE Randomized Clinical Trial. *JAMA Oncol.* 2021 May 1;7(5):720-727. doi: 10.1001/jamaoncol.2021.0310. PMID: 33734288; PMCID: PMC7974834.

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Daith Piercing



- Idea with constant pressure, should be better
- Meta analysis has not found any indication this is beneficial, but limited drawbacks.

Pradhan SK, Gantenbein AR, Li Y, Shaban H, Lyu X, Sevik A, Furian M. Daith piercing: Revisited from the perspective of auricular acupuncture systems. *A narrative review. Headache.* 2024 Feb;64(2):131-140. doi: 10.1111/head.14672. Epub 2024 Jan 29. PMID: 38284213.

Cascio Rizzo A, Paolucci M, Altavilla R, Brunelli N, Assenza F, Altamura C, Vernieri F. Daith Piercing in a Case of Chronic Migraine: A Possible Vagal Modulation. *Front Neurol.* 2017 Nov 27;8:624. doi: 10.3389/fneur.2017.00624. PMID: 29230190; PMCID: PMC5711775.

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Motion

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Primer

- ▶ Psychological elements, such as anxiety, depression, and pain catastrophizing, show a robust relationship with migraine disability
- ▶ Avoidance of physical activity, especially high-intensity exercise, is associated with a higher frequency of migraine attacks
- ▶ Reduced activity was correlated with a surge in both migraine and non-migraine headache prevalence

La Touche R, de Oliveira AB, Paris-Alemany A, Reina-Varona A. Incorporating Therapeutic Education and Exercise in Migraine Management: A Biobehavioral Approach. *Journal of Clinical Medicine*. 2024; 13(20):6273. <https://doi.org/10.3390/jcm13206273>

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Exercise

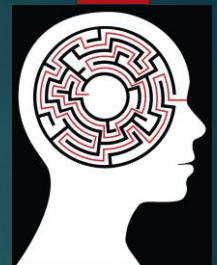
- ▶ 20 subjects; Exercise can attenuate inflammatory markers and how an aerobic exercise regimen can markedly diminish migraine frequency and intensity (Hagan K et al)
- ▶ 94 subjects; Exercise induced a decline in migraine days, anxiety levels, and plasma cytokine (interleukin-12p70) levels (Oliveira et al)
- ▶ 40 subjects; MIA exercises resulted in significant reductions in the intensity, frequency, and duration of headache attacks, as well as an increase in the aerobic power ($p < 0.001$)

Oliveira, A.B.; Bachi, A.L.L.; Ribeiro, R.T.; Mello, M.T.; Vaisberg, M.; Peres, M.F.P. Exercise-Induced Change in Plasma IL-12p70 Is Linked to Migraine Prevention and Anxiolytic Effects in Treatment-Naïve Women: A Randomized Controlled Trial. *Neuroimmunomodulation* **2017**, *24*, 293–299.
Hagan, K.K.; Li, W.; Mostofsky, E.; Bertisch, S.M.; Vgontzas, A.; Buettner, C.; Mittleman, M.A. Prospective cohort study of routine exercise and headache outcomes among adults with episodic migraine. *Headache J. Head Face Pain* **2021**, *61*, 493–499.
Pairo Z, Parnow A, Sari-aslani P, Eslami R. Effect of Moderate Intensity Aerobic Exercise on Migraine Headache Indexes and Quality of Life Improvement in Women with Migraine. *Intern Med Today* 2016; 22 (4) :291-297

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PT and headaches

- ▶ The approach to the crania-cervical-mandibular region reports significant effects in terms of decreasing the intensity of pain and frequency of headache episodes in the short and medium term



Repiso-Guardeño A, Moreno-Morales N, Armenta-Pendón MA, Rodríguez-Martínez MDC, Pino-Lozano R, Armenta-Peinado JA. Physical Therapy in Tension-Type Headache: A Systematic Review of Randomized Controlled Trials. *Int J Environ Res Public Health*. 2023 Mar 2;20(5):4466. doi: 10.3390/ijerph20054466. PMID: 36901475; PMCID: PMC10001815.

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Find ways to reduce/manage stress

- ▶ Yoga
- ▶ CBT
- ▶ Therapy
- ▶ Mindfulness
- ▶ Job changes
- ▶ Exercise

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Sleep

- ▶ Screen for OSA, particularly if AM headaches
- ▶ Ensure adequate sleep
- ▶ Help along with more natural aids (exercise, melatonin, avoidance of screens)
- ▶ Bed is for two things

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Basic treatment advice (applies to most things neuro)

SO EASY A KID CAN DO IT (PEDS)

- ▶ Psych – Find ways to reduce/manage stress with yoga, therapy, CBT
- ▶ Exercise - goal 30min x5days low moderate exercise
- ▶ Diet -avoid/screen for triggers, low inflammatory Mediterranean diet can help reduce flairs, hydration
- ▶ Sleep -screen OSA, ensure good quality & duration
- ▶ Your body likes routine, keep it healthy and consistent.