



Headaches: Causes, Cases, Cures

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Danger Signals



- New-severe headache
- Worst headache ever
- Headache with fever
- Headache with stiff neck
- Headache with weakness or numbness
- Headache that wakes from sleep
- Headache worsening over time
- History of head trauma

Migraine Diagnosis



Migraine is under-diagnosed

- 94% of patients seen by a primary care doctor with recurrent headache suffer from migraine
- Nearly 90% of “sinus headache” patients meet criteria for migraine
- Nearly 90% of “tension/stress” headache patients meet criteria for migraine

Migraine Diagnostic Questionnaire



- Has a headache limited your activities for a day or more in the last three months?
- Are you nauseated or sick to your stomach when you have a headache?
- Does light bother you when you have a headache?

Approach to headaches



- History
- Physical examination
- Neurological examination
- Differential diagnosis
- Laboratory and imaging tests
- Treatment

Treatment of migraine



General principles

- Establish correct diagnosis
- Eliminate triggers
- Lifestyle changes
- Non-pharmacological approaches
- Abortive and prophylactic drugs
- Botulinum toxin
- Devices

Treatment of migraine



Non-pharmacological treatments

- Sleep (sleep hygiene, treat sleep disorders, melatonin)
- Exercise
- Diet (low-carb, avoid trigger foods, gluten)
- Biofeedback, neurofeedback, or meditation
- Magnesium, CoQ₁₀, riboflavin, omega-3, alpha-lipoic acid
- Herbal: Feverfew, Boswellia, Butterbur, aromatherapy
- Acupuncture
- Music

Exercise and headaches



Physical activity and headache: results from the Nord-Trøndelag Health Study (HUNT). Varkey E, et al. *Cephalalgia* 2008.

A study of 46,648 subjects

“Low physical activity was associated with higher prevalence of migraine and non-migraine headache. In both headache groups, there was a strong linear trend ($P < 0.001$) of higher prevalence of ‘low physical activity’ with increasing headache frequency”

Exercise and headaches



Exercise as migraine prophylaxis: A randomized study using relaxation and topiramate as controls. Varkey E, Cider Å, J. Carlsson J, Linde M. *Cephalalgia* 2011;31:1428-1438.

91 patients divided into 3 groups:

- aerobic exercise (40 minutes three times a week)
- topiramate
- relaxation training

All three treatments equally effective. Only topiramate caused side effects, which occurred in 33% of patients

Treatment of migraine



Eliminate or reduce triggers

- Food
cheese, chocolate, sugar, wheat, dairy
- Environmental
light, noise, air pollution, weather
- Hormonal

Caffeine



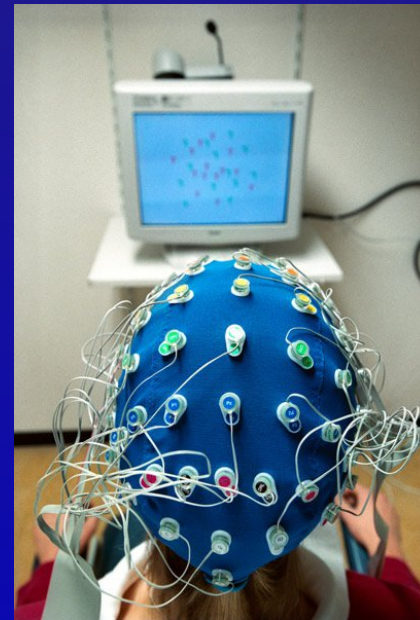
“Withdrawal syndrome after the double-blind cessation of caffeine consumption.”

- 52% moderate or severe headache
- 11% depression
- 11% low vigor
- 8% anxiety
- 8% fatigue

235 mg (2.5 cups) a day

(Silverman et al. *NEJM* 1992)

Biofeedback & neurofeedback



Meditation



Meditation-Based Treatment Yielding Immediate Relief for Meditation-Naïve Migraineurs. ME Tonelli, et al. *Pain Management Nursing*. 2014

A single intervention 33% decrease in pain and a 43% decrease in emotional tension

Meditation for Migraines: A Pilot Randomized Controlled Trial. RE Wells, et al. *Headache*, 2014.
10 meditated, 9 were controls;

Meditators had significant improvement in disability and other measures.

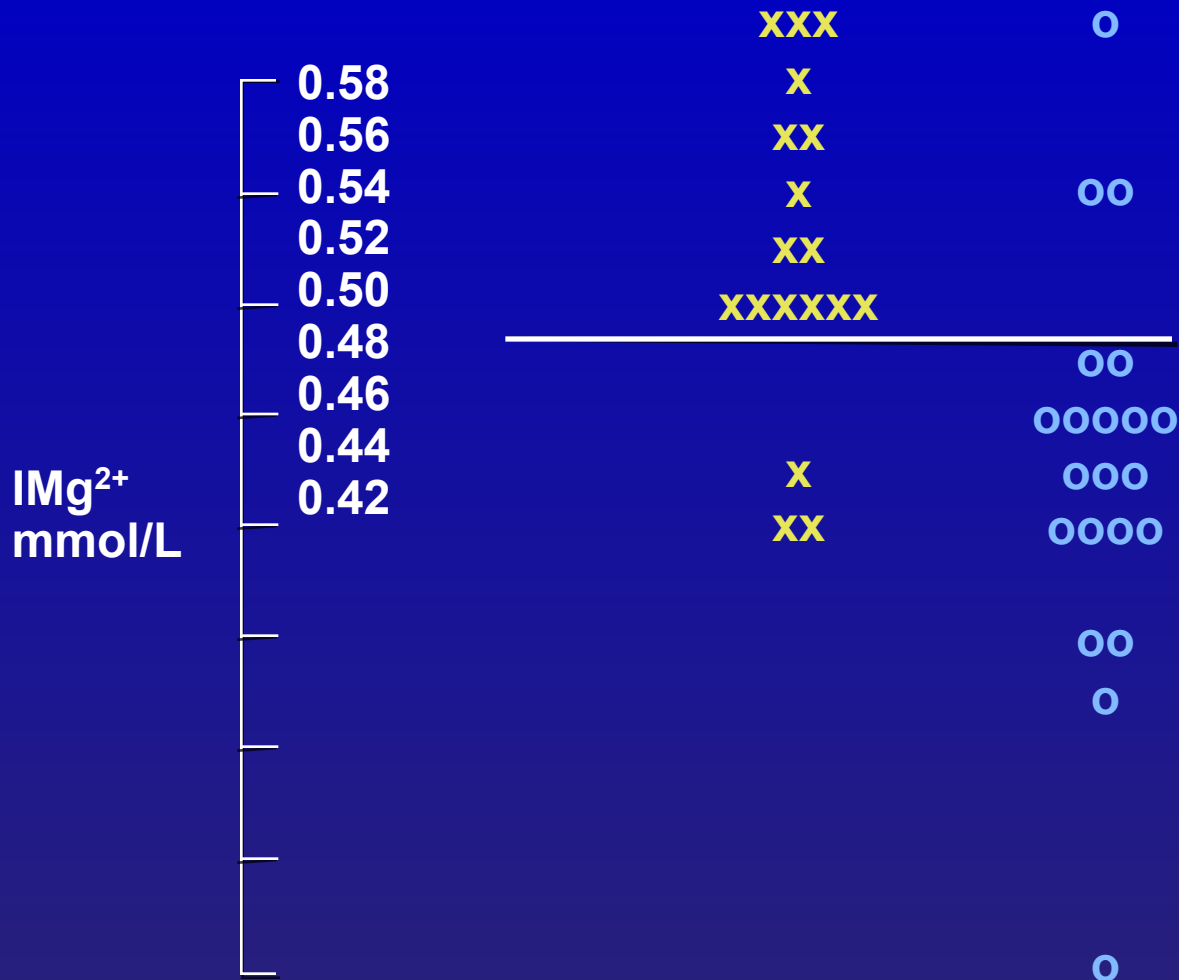
Magnesium and Migraine



Low brain magnesium in migraine

N.M. Ramadan, et al. *Headache* 1989.

IV MgSO₄ for Acute Migraine



x = non-responders

o = responders

A. Mauskop et al, *Clin Science* 1995;89:633-6

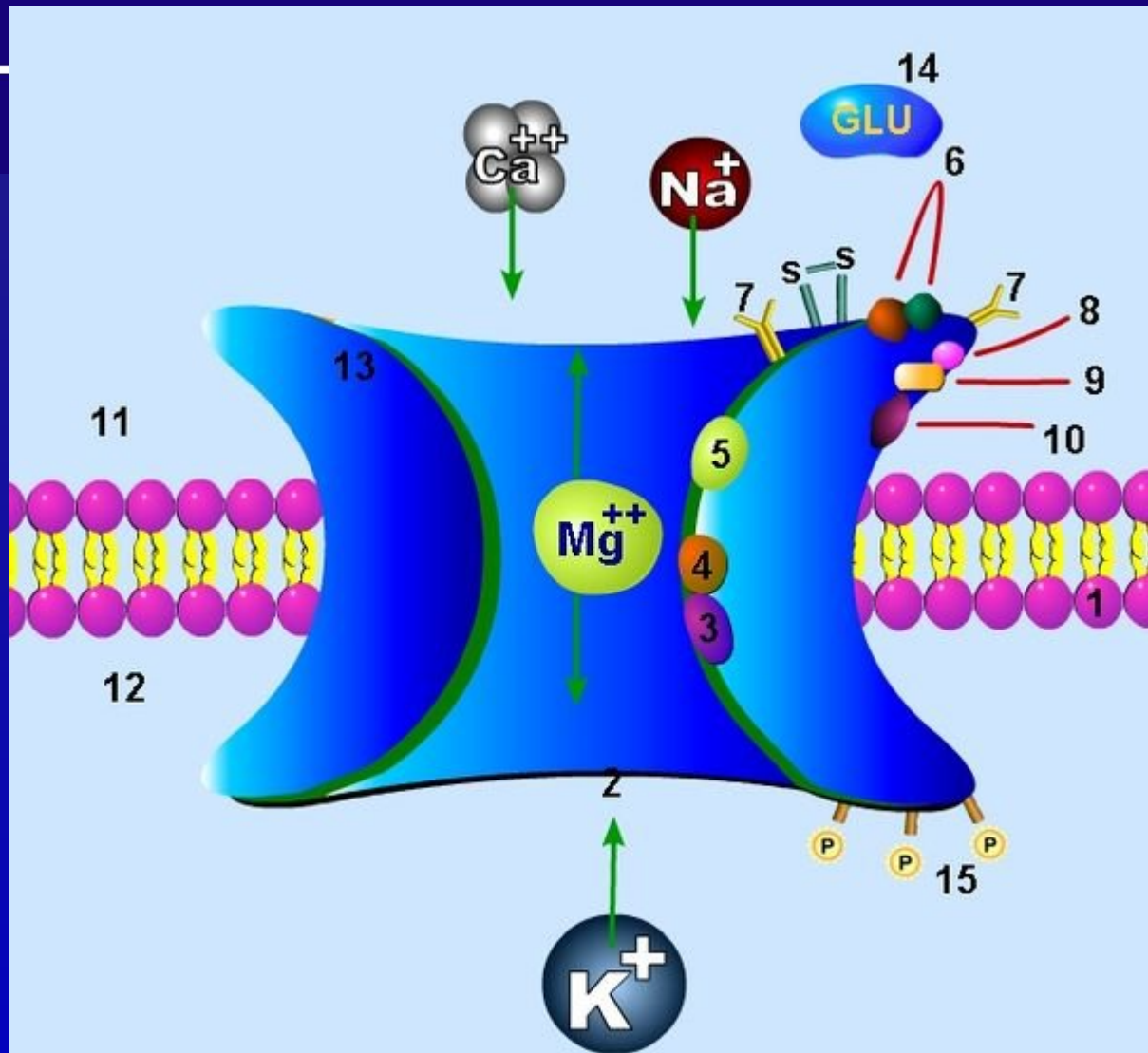
Magnesium and Migraine



Potential causes of magnesium deficiency

- Stress
- Alcohol & caffeine
- Genetics of absorption and renal excretion
- Low dietary intake
- Gastro-intestinal disorders (IBS, colitis, celiac)
- Chronic illness

NMDA receptor



Practical considerations



Clinical symptoms of hypomagnesemia

- Headaches
- Leg muscle cramps
- Coldness of extremities or body
- PMS
- Mental fog
- Irritability, depression

Headache genetics



The effects of vitamin supplementation and MTHFR (C677T) genotype on homocysteine-lowering and migraine disability. Lea R, et al. *Pharmacogenet Genomics*. 2009.

Daily supplementation for 6 months with 2 mg of folic acid, 25 mg vitamin B6, and 400 mcg of vitamin B12 vs placebo.

1. Homocysteine – ↓ by 39%, $p=0.001$
 2. Prevalence of disability – ↓ from 60% to 30%, $p=0.01$
 3. Headache frequency and pain severity ↓, $p<0.05$
- 1 and 2 were associated with MTHFRC677T genotype

Alpha-lipoic acid



A randomized double-blind placebo-controlled trial of thioctic acid in migraine prophylaxis

Magis D et al. *Headache* 2007

- 44 patients; α -lipoic acid 600 mg vs placebo
- 50% responder rate for attack frequency – no difference
- Improved: attack frequency, headache days, severity,
- No adverse effects reported



Coenzyme Q₁₀ deficiency and response to supplementation in pediatric and adolescent migraine

Hershey AD, et al. *Headache* 2007

- 1550 patients – 32.9% deficient
- Supplementation with 1-3 mg/kg/day
- CoQ₁₀ levels improved, $p < .0001$
- HA frequency improved from 19.2 to 12.5, $p < .001$
- HA disability improved from 47.4 to 22.8, $p < .001$

Butterbur (*Petasites Hybridus*)



Petasites hybridus root (butterbur) is an effective preventive treatment for migraine.

Lipton RB, Gobel H, Einhaupl KM, Wilks, K and Mauskop A.
Neurology 2004;63:2240-2244

- 245 patients
- Three groups: placebo, 100 mg & 150 mg
- Attack frequency reduced by: 48% in 150 mg group, 36% in 100 mg, 26% in placebo



Boswellia serrata



Long-term efficacy of *Boswellia serrata* in
4 patients with chronic cluster headache

C. Lampl, et al. J Headache Pain. 2013



Feverfew (*Tanacetum Parthenium*)



Efficacy and safety of 6.25 mg t.i.d. feverfew CO₂-extract (MIG-99) in migraine prevention – a randomized, double-blind, multicenter, placebo-controlled study.

Diener HC, et al.
Cephalalgia 2005





Effect of peppermint and eucalyptus oil preparations on neurophysiological and experimental algesimetric headache parameters

Gobel H, al. *Cephalagia* 1994.

Results



Combination of Peppermint Oil and Ethanol

- Analgesic effect
- Muscle relaxing effect
- Mentally relaxing effect

Music and the brain



- “Music training may strengthen a child's brain for a lifetime”
- Playing a musical instrument appears to have long-lasting brain benefits, particularly if a child starts practicing before age 7
- “Music has the unique ability to go through alternative channels and connect different sections of the brain”

November 13, 2013

Annual meeting of the Society for Neuroscience

Music therapy



- Butterbur root extract and music therapy in the prevention of childhood migraine: An explorative study. Oelkers-Ax R et al. European Journal of Pain. 2008.
- Butterbur (n=19) and music (n=20) groups did better than placebo (n=19) at 6 months follow-up. Only music group did better immediately after 12-week treatment period

Music therapy



Emotional valence contributes to music-induced analgesia. Roy M, et al. *Pain*. 2008.

18 volunteers subjected to pleasant music, unpleasant music and silent period;

Thermally-induced pain was reduced only by pleasant music.

Music therapy



Both happy and sad melodies modulate tonic human heat pain. Zhao H, et al. *The Journal of Pain*. 2009.

20 volunteers subjected to: baseline pain tolerance, pleasant sad music, pleasant happy music and, a lecture
Both happy and sad music resulted in significantly lower pain ratings.

Music therapy



Music modulation of pain perception and pain-related activity in the brain, brain stem, and spinal cord: A functional magnetic resonance imaging study. CE Dobek, et al. *The Journal of Pain*. 2014.

Conclusion: Music modulates pain responses in the brain, brain stem, and spinal cord, and neural activity changes are consistent with engagement of the descending analgesia system.

Acupuncture



Acupuncture in routine care. Jena S, Melchart D et al.

- 15,056 patients with migraine and tension-type headaches randomized to receive over three months either:
- conventional treatment (1,569) or
- conventional treatment plus up to 15 acupuncture treatments (1,613)
- the third group received acupuncture

Significant difference in QOL and in headache days per month:

two acupuncture groups – drop from 8.4 to 4.7 days

control group – 8.1 to 7.5 days

Improvement persisted for subsequent 3 months

Migraine: Symptomatic Treatment



- Pain
 - Ibuprofen
 - Naproxen
 - Acetaminophen

- Nausea
 - Ginger
 - Sea-Bands
 - Zofran

Migralex



A patented, rapidly dissolving combination of:

- Aspirin – 500 mg
- Magnesium oxide – 75 mg

Migralex



The usual dose is two tablets

(Aspirin – 1,000 mg and magnesium oxide – 150 mg)

- Both magnesium and aspirin relieve headaches
- Magnesium reduces GI side effects of aspirin
- Rapidly dissolving formulation
- Works for migraine, menstrual, tension, stress, sinus, allergy, neck-related, & hangover headaches

Prescription drugs



Non-triptans

- Cafergot - ergotamine/cafeine
- Migranol – dihydroergotamine nasal spray
- Fioricet, Esgic – butalbital/cafeine/APAP
- NSAIDs, COX-2
- codeine, hydrocodone, oxycodone
- Stadol NS – butorphanol nasal spray

Prescription drugs



Triptans

- Imitrex (Treximet) – sumatriptan (+naproxen)
- Zomig – zolmitriptan
- Maxalt – rizatriptan
- Amerge - naratriptan
- Axert - almotriptan
- Frova - frovatriptan
- Relpax - eletriptan

Consider prevention when:



- Migraine significantly interferes with patient's daily routine despite acute treatment
- Frequency attacks >2 /week with risk of acute medication overuse
- Contraindication to, failure, adverse events, or acute medication overuse
- Patient preference

Preventive Treatment



Choice is based on:

- Patient's preferences
- Headache type
- Drug side effects
- Presence of coexisting conditions

Preventive drugs



-  -blockers: Inderal (propranolol)
- Antidepressants: Elavil (amitriptyline)
Cymbalta (duloxetine)
- Epilepsy drugs: Depakote (divalproex)
Topamax (topiramate)

History of Botox use in migraine



- Anecdotal reports of reduced migraines from patients receiving BTX-A treatment for other indications
- A retrospective review of patient charts suggested migraine relief was associated with certain injection sites
- This information was used in designing early clinical studies

Botox for chronic migraine: Phase III trials



Botulinum neurotoxin type A for treatment of chronic migraine

Aurora et al. Cephalalgia 2009

Botulinum neurotoxin type A for treatment of chronic migraine.

Dodick et al. Cephalalgia 2009

Safety Summary



- Botox was very well tolerated
- All treatment-related adverse events were local and transient
- Most common were
 - Headache
 - Neck pain
 - Ptosis (droopy eyelid)
 - Injection site weakness
 - Skin tightness
- There were no serious treatment-related adverse events

Peripheral nerve stimulation



Cefaly - TENS

TMS for migraine



Cerena TMS by eNeura Therapeutics

Vagus nerve stimulation



Gammacore



- Acute treatment of up to 4 migraine attacks
- Treatment consisted of two, 90-second doses, at 15-minute intervals.
- Of 30 enrolled, 26 treated 79 migraines headaches.
- At 2 hours, 46 of 79 headaches (58%) responded, and in 22 out of 79 (28%) pain was completely gone.
- Of 26 patients 20 (77%) reported mild or no pain at 2 hours, for at least one treated headache

Approach to migraine patients at the NYHC



- aerobic exercise, neck exercise
- biofeedback / neurofeedback / meditation
- magnesium
- CoQ₁₀
- dietary approaches
- Botox
- acupuncture
- medications: abortive, prophylactic

Case 1



- ❖ **Chief Complaint:** Severe headaches.
- ❖ **History of Present Illness:** 35-year-old woman, headaches since age 15. Headaches: frontal and periorbital, severe, pulsatile, with nasal congestion, at times nausea, often with sensitivity to light, but not noise; and made worse by light physical activity. Occur once a month and last three days. No aura or other neurological symptoms. She has been seeing an ENT and takes decongestants, and at times antibiotics or steroids with some relief; Sinus surgery suggested by ENT, despite normal CT scan

Case 1



- ❖ **Review of Organ Systems:** anxiety, occasional insomnia
- ❖ **Past Medical History:** negative
- ❖ **Social History:** no tobacco use or alcohol abuse; married with 3 children; works full time
- ❖ **Family History:** Positive for headaches.
- ❖ **Physical Examination:** Normal

Case 1



❖ Assessment:

Migraine headaches (nasal congestion is not an uncommon occurrence in migraines)

❖ Treatment:

Sumatriptan, 100 mg – excellent relief with disability score dropping from severe to none.

Case 2



- ❖ **Chief Complaint:** Severe headaches.
- ❖ **History of Present Illness:** 40-year-old woman, headaches since age 8. Headaches: unilateral, severe, pulsatile, with nausea, sensitivity to light and noise, not made worse by light physical activity. Occur four times a week and last one day.

No aura or other neurological symptoms.

Triggers: stress and menstrual cycle.

Rx: Imitrex, 100 mg: good, but incomplete relief.

Excedrin Migraine, 2-4 tablets almost daily

Case 2



- ❖ **Review of Organ Systems:** constipation, decline in memory, cold hands, PMS, back and neck pains.
- ❖ **Past Medical History:** negative
- ❖ **Social History:** no tobacco use or alcohol abuse, 4 cups of coffee; married with 2 children; works full time
- ❖ **Family History:** Positive for headaches.
- ❖ **Physical Examination:** Neck muscle spasm

Case 2



❖ **Assessment:**

Intractable chronic migraine headaches

Severe disability (MIDAS -22, over 20 - severe disability).

Excessive caffeine consumption - major contributor.

Presence of coldness of extremities and PMS suggest magnesium deficiency

Case 2



❖ Plan:

Stop all caffeine (coffee and Excedrin)

Regular aerobic exercise

Biofeedback

Magnesium oxide, 400 mg and CoQ10, 300 mg

For abortive therapy: rizatriptan (Maxalt), 10 mg PRN

If ineffective, try other triptans with an NSAID.

If headaches persist consider:

Botox injections or prophylactic medications



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