Note on Resources

• PPTs
• Scripps Resource Sheet phone #
• National Headache Foundation
  – http://www.headaches.org
• Annals Internal Medicine HA tool kit
  – Patient Resources: HA diary, etc
• Scripps Guidelines in process
# Faculty Disclosure

<table>
<thead>
<tr>
<th>Company</th>
<th>Nature of Affiliation</th>
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<tr>
<td>McNeil Consumer Health Health</td>
<td>Consultant</td>
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</table>
• In 1886, Pharmacist John Pemberton developed Coca-Cola - a non-alcoholic version of his previous French Wine Coca.

• He claimed it cured:
  – Headache
  – Neuralgia
  – Opioid addiction
  – Hysteria
  – Melancholy
  – Impotence
Integrative Therapy Overview

- Background
- Rationale
- Goals
- Prevalence & Approach to Treatments
- Integration: Putting it all together
- Conclusions
Large, Costly Problem

>30 million in US suffer with HA
>$30 Billion (lost productivity)
~10% of all lost job productivity

http://www.allianceforheadacheadvocacy.org/
Burden of illness and satisfaction with care among patients with headache seen in a primary care setting

• “..we observed across the sites a consistent need for improvement in headache management.”

• Migraine patients are satisfied or very satisfied with current care options 21% of the time

The Impact of Migraine and the Effect of Migraine Treatment on Workplace Productivity in the United States and Suggestions for Future Research

WAYNE N. BURTON, MD; STEPHEN H. LANDY, MD; KRISTEN E. DOWNS, MSPH; AND M. CHRIS RUNKEN, PHARM.D

- Evidence suggests that, despite the debilitating effects of migraine, the condition is underdiagnosed and undertreated.

Guidelines and Classifications Galore

- Intern. Headache Society (HIS) Classification of Headache Disorders (180 pages)
- Inst. for Clinical Systems Improvement. Diagnosis and Treatment of Headache. 2013 (92 pages)
- Headaches: diagnosis and management of headaches in young people and adults. (NICE) 2012 (360 pages, abridged = 38 pages)
- American Academy of Neurology 2012; multiple guidelines

Editorial

When West Meets East: Is It Time for Headache Medicine to Complement “Convention” With Alternative Practices?
Goals - Simplify

• Provide a comprehensive, practical guide to headache management in the Scripps System
• Start focus on the adult migraine patient,
• Also highlight subpopulations:
  – Chronic Daily Headache
  – HAs in Children / Adolescent & Pregnancy
  – Headache with co-morbidities:
    • Muscle tension
    • Depression
    • Genetic / Nutrient Abnormalities
Goals - Integrate

• Discuss utilization of an integrative approach to optimize outcomes:
  
• Part I:
  – Diagnosis and Approach
  – Pharmacological
  – Interventional

• Part II:
  – Diet
  – Stress Management
  – Supplementation
  – Physical Therapy/ Manual Therapy
  – Acupuncture . . .
Scripps Migraine Management in Primary Care

Establish **Diagnosis & Treatment Needs** (History, 1 Diary, MIDAS etc)  
→ Complicated Migraine / Stroke-like symptoms  
→ Refer to Neurology

**Low Tx Needs**

1-2 HA days/mo  
Mild to moderate pain  
**Abortive:**  
Naproxen 550, Diclofenac 50 mg, short acting triptan (oral, nasal, SQ) or Migranol Nasal Spray  
**Alternatives:**  
Tramadol 50-100mg  
Butalbital with caffeine – no more than 6 days per month  
**Nausea:**  
Ondansetron, Phenergan or Compazine (suppository)

**Medium Tx Needs**

Less than 15 days/mo  
**Moderate Pain**  
**Preventative:**  
If sleep disturbance present, Elavil 10 mg-30 mg as tolerated  
If no sleep disturbance:  
Namenda XR 7-28 mg titration  
Topamax 25-100 mg titration  
Propranolol LA 80-240 mg  
SSRIs, Neurontin of lesser benefit  
**Abortive meds to be used only 2 days per week**

**High Tx Needs**

Greater than 15 days/mo, UCC visits  
**Meds:**  
Prophylaxis along with Medication Overuse Protocol using prednisone and taper from analgesics  
**Additional:**  
Botulinum toxin  
Consider Ketoralac injections/nasal spray  
Occipital and Trigeminal Nerve Blocks

**Acute Management**

**Treatment in Primary Office:**  
Differentiate from  
1 chronic pain found newly intolerable  
2. New illness of great pathologic significance (SAH, temporal arteritis, cranio cervical disease)  
Acute Rescue IM: Toradol 30-60 mg IM, Phenergan 25 mg IM, TPI, Sumatriptan 6 mg SQ: If fails, Demerol  
Acute Rescue IV: Magnesium 1000mg, Toradol 30 mg, Depacon 500 mg, Decadron 10 mg, Phenergan 25 mg,

**3 Injection / Intervention:**  
Botulinum Toxin A  
ONB without steroid  
Trigeminal Blocks without steroid  
TPIs

**4. Imaging:** Indicated if exam abnormal, history atypical (explosive onset, worsens with Val Salva or cough), onset over age 40. CT with and without indicated, if posterior fossa or vascular lesion suspected, MRI/MRA indicated

---

**1 Diagnosis:**  
a. Nausea with HA?  
b. HA limited ADLs ≥ day / 3 months?  
c. Light bothersome during HA?  
2 / 3 = PPV 93%; 3 / 3 : PPV 98%  
Lipton RB et al. Neurology, 2003

**1 History is Key:**  
Age of onset, description  
Triggers  
FHx  
SHx(stressors)

---

Christy Jackson MD, Robert Bonakdar MD
# Scripps Migraine Management in Primary Care

## Education, Self Management & Non-Pharmacological Care:
(consider options for optimizing behavioral, physical and cardiometabolic issues in all patients)

### Triggers / Comorbidities

- **BEHAVIORAL**
  - Stress
  - Depression
  - Anxiety
  - Sleep

- **PHYSICAL**
  - Mechan./Myofascial
    - Cervicalgia
    - TMJ
    - TrPs
    - Decond...

- **CARDIO-METABOLIC / DIETARY**
  - Deficiency
  - Fatigue
  - Obesity
  - DM/CV Dz.

### TX Support: Course of up to 10 treatments:
- Biofeedback
- Cognitive-Behavioral
- Behav. therapy (MBSR)
- Other Relaxation / (Sleep eval)

### TX Support: Course of up to 10 treatments:
- Physical Therapy
- Cranial Sacral Therapy
- Acupuncture
- Graded Exercise Program
- Yoga
- (Topicals)

### TX Support:
- Dietary consult/testing
- Trigger Elimin Diet
- Low G.I./∞-inf. Diet
- Supplementation typically 12-16 wks

### SUPPLEMENT

<table>
<thead>
<tr>
<th>DEFICIENCY</th>
<th>DAILY DOSE</th>
<th>Notes</th>
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<tbody>
<tr>
<td>Magnesium</td>
<td>200-600+ mg</td>
<td>PG,PD</td>
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<tr>
<td>Riboflavin (Vit B-2)</td>
<td>400 mg</td>
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<td>Co-enzyme Q10</td>
<td>100-200 mg</td>
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### INFLAMMATORY

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<td>Ginger (Zingiber officinale)</td>
<td>500-1000+</td>
<td>PG (≤1 GM) *GI</td>
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<td>Omega-3s (fish oils)</td>
<td>1-4 GMS</td>
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<td>Feverfew (Tanacetum parthemium)</td>
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<td>Peppermint oil</td>
<td>10% extract topically</td>
<td>Tension component</td>
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<tr>
<td>Melatonin</td>
<td>1-6+ mg</td>
<td>*Sleep onset</td>
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<tr>
<td>Vitamin D3</td>
<td>1000 iu +</td>
<td>Target 40 ng/ml</td>
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</tbody>
</table>

*PG: appears safe in pregnancy, esp after 2nd trimester
*PD: not safe in pregnancy
*PD: Evaluated in Pediatric population
*Allergy: consider in those with comorbid allergy
*GI: consider in those with sig. GI symptoms

### Assoc.
- IBS
- MDD
- FMS
- CSS
- POTS

### Notes

- **PG**: appears safe in pregnancy, esp after 2nd trimester
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- **PD**: Evaluated in Pediatric population
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Integrative Therapy Overview

• Background
• Rationale
• Goals
• Prevalence & Approach to Treatments
• Integration: Putting it all together
• Conclusions
The Migraine Cycle: Patient Burden of Migraine During and Between Migraine Attacks

Jan Lewis Brandes, MD

• Depression
• Anxiety
• Panic

• Missed School/Work
• Loss Productivity
• Worry about next Headache

References:
Neurologic and psychological disorders share some overlapping pathophysiologic mechanisms with vascular disorders.
Magnitude, impact, and stability of primary headache subtypes: 30 year prospective Swiss cohort study

- Migraine without aura: 24.6%
- Migraine with aura: 4.9%
- Tension-type headache: 36.4%

BMJ 2011;343:d5076
Crossing over

- **87%** of migraine sufferers during the first decade of study met criteria for another subtype … during the 20 years f/up
- Likewise, **84%** of those with tension-type headache presented with migraine or another … subtype …

BMJ 2011;343:d5076
Body Mass Index and Episodic Headaches

A Population-Based Study

Marcelo E. Bigal, MD, PhD; Amy Tsang; Elizabeth Loder, MD; Daniel Serrano, PhD; Michael L. Reed, PhD; Richard B. Lipton, MD; for the American Migraine Prevalence and Prevention Advisory Group

Figure 1. Percentage of subjects with migraine who ever used a migraine prevention medication (for migraine purposes or for other medical reasons) according to body mass index (BMI) category.
Generalized neck-shoulder hyperalgesia in chronic tension-type headache and unilateral migraine assessed by pressure pain sensitivity topographical maps of the trapezius muscle

C Fernández-de-las-Peñas¹,²,³, P Madeleine², AB Caminero⁴, ML Cuadrado³,⁵,⁶, L Arendt-Nielsen² & JA Pareja³,⁵

¹Department of Physical Therapy, Occupational Therapy, Physical Medicine and Rehabilitation of Universidad Rey Juan Carlos, ³Aesthesiology Laboratory of Universidad Rey Juan Carlos, ⁵Departments of Neurology of Fundación Hospital Alcorcón and Universidad Rey Juan Carlos, Alcorcón, ⁶Neurology Department, Hospital Clínico San Carlos and Universidad Complutense, Madrid and ⁴Neurology Department of Hospital Avila, Avila, Spain, and ²Centre for Sensory-Motor Interaction (SMI), Department of Health Science and Technology, Aalborg University, Aalborg, Denmark

Figure 1 Schematic representation of the 11 points for pressure pain threshold assessment.
• Trigger points found
  – 93.9% migraineurs &
  – 29% controls (P < 0.0001)

• # TrPs related to:
  – Frequency & Duration of Disease

The Bowel and Migraine

• What appears to link migraine, IBS, and CD is a disease model of a genetically sensitive nervous system transformed into one that is hypervigilant, and that over time can often develop disabling and pervasive disease.

Brain–Gut axis

- Sensitizing event

Genetically hyperexcitable nervous system

Hypervigilant Limbic/ENS augmentation

IBS
Enteric sensitization

Migraine
Trigeminal vascular sensitization

Celiac disease
Immune sensitization
The omics in migraine

Luana Lionetto¹, Giovanna Gentile², Elisa Bellei³, Matilde Capi¹, Donata Sabato¹, Francesco Marsibilio⁴.

Genomics
- ADARB2, EDNRA, GABRG2, GNOS, GRIA2, HTR7, KCNQ3, MTHFR, OPRM1, TRPV,

Proteomics
- AMBP, CYTC, IGKC, ITH4, UROM, ZAZG

Metabolomics
- BDNF, CRP, Lactate, NAA, PCT, sCD40L

The “omics” synergism in migraine
Mitochondrial Dysfunction in Migraine

William R. Yorns Jr, DO, *; † and H. Huntley Hardison, MD *; †
Serum levels of $N$-acetyl-aspartate (NAA) in the main primary headache types and controls

The low NAA in the serum may be a sign of neuronal dysfunction predisposing to migraine, probably based on reduced mitochondria function.

• Prevalence of depression (PHQ-9)
  – 9.2% in the general population
  – 17.2% in episodic migraine
  – 30.2% in those with chronic migraine

• 2-year incidence of new-onset migraine
  \(3.4X\) \(\uparrow\) in those with depression (9.3% vs 2.9%)

• 2-year incidence of new-onset depression
  is \(5.8x\) \(\uparrow\) in migraineurs (10.5% vs 2%)

Rationale: Integrative Approach

- Unimodal approach unlikely to fully address the burden of illness
- Approaches that understand the complex and expanding nature of the condition—i.e., "genetically sensitive nervous system"—may better address the expanding needs of the migraine patient
Integrative Therapy Overview

- Background
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- Conclusions
The US Headache Consortium

• Nonpharmacologic Tx well suited for those with:
  1. Preference for such Tx
  2. Poor tolerance for pharma Tx
  3. Contraindications for specific pharma Tx
  4. Insufficient or no response to pharma Tx
  5. (planning to be) pregnant or nursing
  6. H/O long-term, frequent, or excessive analgesic or acute medications
  7. Exhibit significant stress or deficient stress-coping skills

Goals of Behavioral & Preventive Treatments

1. ↓ frequency and severity of headache
2. ↓ headache-related disability
3. ↓ reliance on poorly tolerated or unwanted pharmacotherapies
4. ↑ personal control of migraine
5. ↓ headache-related distress and psychologic symptoms

**Scripps Migraine Management in Primary Care**

**2. Education, Self Management & Non-Pharmacological Care:** (consider options for optimizing behavioral, physical and cardiometabolic issues in all patients)

### Triggers / Comorbidities
- Stress
- Depression
- Anxiety
- Sleep

### Behavioral
- Biofeedback
- Cognitive-Behavioral
- Behavioural therapy (MBSR)
- Other Relaxation
- (Sleep eval)

### Physical
- Physical Therapy
- Cranial Sacral Therapy
- Acupuncture
- Graded Exercise Program
- Yoga
- (Topicals)

### Cardiometabolic / Dietary
- Deficiency
- Fatigue
- Obesity
- DM/CV Dx.

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### Inflammatory

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CAM Prevalence in Headache

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<th>Country and first author</th>
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<td>Relaxation training</td>
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USA 50% Mind-Body 30
Wells et al. 2011 Herbal/Dietary Supplements 27
Wells et al. 2011 Massage/Manipulation 21

Prevalence, pattern and predictors of use of CAM in migraine patients

- CAM use correlated with:
  - Higher education, comorbidities: anxiety, pain
- Therapies perceived beneficial by 39.5%
- Most common reason for CAM use:
  - 'potential improvement of headache' (47.7%)
- Most common source of information:
  - a friend or relative (52.7%)
- 53%-61% of CAM users had not informed clinician


Integrative Approaches to Headache Management

BY ROBERT BONAKDAR, MD, FAAFP, and CHRISTY JACKSON, MD
NIH, National Center for Complementary / Alternative Med.

“Integrative Medicine Combines Mainstream Medical Therapies & CAM Therapies for Which There is Some High-Quality Scientific Evidence of Safety and Effectiveness.”

NCCAM groups CAM practices into four domains, recognizing there can be some overlap. In addition, NCCAM studies CAM whole medical systems, which cut across all domains.

http://nccam.nih.gov/
The 4 P’s

• Preventive
• Personalized
• Predictive
• Participatory

– Leroy Hood coined term “P4 Medicine,”
– http://p4mi.org
Migraine Triggers  

- Stress (79.7%)
- Hormones (65.1%)
- Not eating (57.3%)
- Weather (53.2%)
- Sleep disturbance (49.8%)
- Perfume or odor (43.7%)
- Neck pain (38.4%)
- Light(s) (38.1%)
- Alcohol (37.8%)
- Smoke (35.7%)
- Sleeping late (32.0%)
- Heat (30.3%)
- Food (26.9%)
- Exercise (22.1%)
- Sexual activity (5.2%)

Kelman L. Cephalalgia. 2007 May;27(5):394-402. The triggers or precipitants of the acute migraine attack.
**SHED Your Triggers**

- **S**
  - Stress & Tension
  - Stimuli (lights, sound, odors)
  - Sleep disruption

- **H**
  - Hormones
  - Habits (skipped meals, poor posture, etc)

- **E**
  - Exercise (lack of / irregular)
  - Environmental (weather, mealtime) change

- **D**
  - Diet
  - Deficiency
  - Dehydration
  - Drugs
Integrative Considerations

- Trigger management
  - S
  - H
  - E
  - D

- Dietary Supplements
  - Riboflavin
  - Magnesium
  - CoQ10
  - Feverfew
  - Butterbur
  - Ginger . . .

- Mind-Body & Behavioral Therapies
  - Biofeedback
  - CBT
  - Guided Imagery
  - Visualization
  - Relaxation / Breathing

- Modalities
  - Exercise
  - Manual therapy / Manipulation
  - Yoga / MBSR
  - Acupuncture
  - Healing Touch
Headache

Nonpharmacologic Treatments for Migraine and Tension-Type Headache: How to Choose and When to Use

Robert A. Nicholson, PhD
Dawn C. Buse, PhD
Frank Andrasik, PhD
Richard B. Lipton, MD

<table>
<thead>
<tr>
<th>Intervention type</th>
<th>Specific procedure</th>
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<sup>a</sup>Class I = strongest evidence; Class IV = weakest evidence  
<sup>b</sup>Petadolex (Weber & Weber USA; Orlando, FL)  
CAM complementary and alternative medicine; EMG electromyography
Italian guidelines for primary headaches: 2012 revised version

Paola Sarchielli · Franco Granella · Maria Pia Prudenzano · Luigi Alberto Pini · Vincenzo Guidetti · Giorgio Bono · Lorenzo Pinessi · Massimo Alessandri · Fabio Antonaci · Marcello Fanciullacci · Anna Ferrari · Mario Guazzelli · Giuseppe Nappi · Grazia Sances · Giorgio Sandrini · Lidia Savi · Cristina Tassorelli · Giorgio Zanchin
Table 17 Preventive non-pharmacological treatments for migraine

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Level of evidence</th>
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<th>Clinical effectiveness</th>
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<td>+</td>
<td>–</td>
<td>III</td>
</tr>
<tr>
<td>Acupuncture</td>
<td>A</td>
<td>++</td>
<td>+</td>
<td>Rare</td>
<td>II</td>
</tr>
<tr>
<td>Transcutaneous electrical nerve stimulation (TENS)</td>
<td>–</td>
<td>–</td>
<td>?</td>
<td>–</td>
<td>IV</td>
</tr>
<tr>
<td>Transcranial magnetic stimulation (TMS)</td>
<td>C</td>
<td>+</td>
<td>+</td>
<td>Rare</td>
<td>III</td>
</tr>
<tr>
<td>Physical activity</td>
<td>–</td>
<td>–</td>
<td>?</td>
<td>–</td>
<td>IV</td>
</tr>
<tr>
<td>Anaesthetic blockade</td>
<td>C</td>
<td>?</td>
<td>?</td>
<td>Rare</td>
<td>IV</td>
</tr>
<tr>
<td>Diet</td>
<td>–</td>
<td>–</td>
<td>?</td>
<td>–</td>
<td>IV</td>
</tr>
<tr>
<td>Other drugs</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Riboflavin</td>
<td>400</td>
<td>B</td>
<td>++</td>
<td>Rare, not severe</td>
<td>III^b</td>
</tr>
<tr>
<td>Magnesium</td>
<td>400–600</td>
<td>B</td>
<td>++</td>
<td>Rare, not severe</td>
<td>III^b</td>
</tr>
<tr>
<td><em>Petasites hybridus</em></td>
<td>100–150</td>
<td>B</td>
<td>++</td>
<td>Rare, not severe</td>
<td>III^e</td>
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<tr>
<td><em>Tanacetum parthenium</em></td>
<td>18.75</td>
<td>B</td>
<td>+</td>
<td>0/+</td>
<td>Rare, not severe</td>
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<tr>
<td>Thiotic acid</td>
<td>600</td>
<td>B</td>
<td>+</td>
<td>Rare, not severe</td>
<td>III^e</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Level of evidence</th>
<th>Scientific strength of evidence</th>
<th>Clinical effectiveness</th>
<th>Adverse events</th>
<th>Level of recommendation</th>
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<tr>
<td>Biofeedback</td>
<td>A</td>
<td>++</td>
<td>++</td>
<td>−</td>
<td>I</td>
</tr>
<tr>
<td>Cognitive-behavioural treatment</td>
<td>−</td>
<td>−</td>
<td>+</td>
<td>−</td>
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<tr>
<td>Strategic short-term psychotherapy</td>
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<td>−</td>
<td>+</td>
<td>−</td>
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</tr>
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<td>Chiropractic osteopathy</td>
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<td>+</td>
<td>+</td>
<td>−</td>
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</tr>
<tr>
<td>Physiotherapy</td>
<td>C</td>
<td>+</td>
<td>+</td>
<td>−</td>
<td>III</td>
</tr>
<tr>
<td>Acupuncture</td>
<td>A</td>
<td>++</td>
<td>+</td>
<td>Rare</td>
<td>II</td>
</tr>
<tr>
<td>Transcutaneous electrical nerve stimulation (TENS)</td>
<td>−</td>
<td>−</td>
<td>?</td>
<td>−</td>
<td>IV</td>
</tr>
<tr>
<td>Physical activity</td>
<td>−</td>
<td>−</td>
<td>?</td>
<td>−</td>
<td>IV</td>
</tr>
<tr>
<td>Pranotherapy</td>
<td>−</td>
<td>−</td>
<td>?</td>
<td>−</td>
<td>IV</td>
</tr>
<tr>
<td>Orthodontic and gnathological techniques</td>
<td>C</td>
<td>+</td>
<td>+</td>
<td>−</td>
<td>IV</td>
</tr>
</tbody>
</table>
Role Diet and Supplements in HA

GOALS:
- ↓ HA burden
- Diet that:
  - Optimizes weight
  - Health Promoting

Triggers / Excess
Deficient
Optimize Support

Optimal Diet
Dietary Triggers & Headache (individual)

A - Foods

- Allergy (gluten)
- Allergenic Trigger (histaminic response)
- Additives (MSG, . . . )
  - Fast food, frozen, canned, processed, packaged
- Artificial (sweeteners)
- Aged
  - Tyramine (cheese, wine, sauerkraut)
- Alcohol
- Other (chocolate, caffeine, etc)
## Fat in the Diet – Amount and Type

<table>
<thead>
<tr>
<th>AMOUNT</th>
<th>TYPE</th>
</tr>
</thead>
<tbody>
<tr>
<td>↓ Dietary fat from 66 G/day to 28 g/day</td>
<td>↓ Trans</td>
</tr>
<tr>
<td>Significant reduction (P &lt; 0.0001) in:</td>
<td>↓ Omega-6</td>
</tr>
<tr>
<td>– Frequency</td>
<td>↑ Omega-3</td>
</tr>
<tr>
<td>– Intensity</td>
<td>↑ Polyunsaturated</td>
</tr>
<tr>
<td>– Duration</td>
<td>↑ Monounsaturated</td>
</tr>
<tr>
<td>– Medication Use</td>
<td></td>
</tr>
</tbody>
</table>

Summary HA Diet Suggestions

↓ Excess fat/calories
↓ Saturated fat
↓ A – Foods

↑ Mono & Poly
↑ Unsaturated Fats
↑ Fresh foods
↑ Unrefined Foods
Role Diet and Supplements in HA

Optimize Support

Magnesium CoQ10 Vitamin D...

Triggers / Excess

Optimal Diet

GOALS:
- HA burden
- Diet that:
  - Optimizes weight
  - Health Promoting
<table>
<thead>
<tr>
<th>SUPPLEMENT</th>
<th>DAILY DOSE</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Magnesium</td>
<td>200-600 mg</td>
<td>Base formula on GI</td>
</tr>
<tr>
<td>Vitamin D3</td>
<td>1000 iu +</td>
<td>Based on level</td>
</tr>
<tr>
<td>Riboflavin (Vit B-2)</td>
<td>400 mg</td>
<td>GI Side Efx</td>
</tr>
<tr>
<td>Co-enzyme Q10 CoQ10</td>
<td>100-200 mg</td>
<td>Cost, absorption</td>
</tr>
<tr>
<td>Omega-3 fatty acids (fish oils)</td>
<td>1-4 grams</td>
<td>GI Side Efx</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Blood thinning at ↑ dose</td>
</tr>
<tr>
<td>Butterbur (Petasites Hybridus)</td>
<td>100 mg-150 mg</td>
<td>Formulation: Petadolex</td>
</tr>
<tr>
<td>Feverfew (Tanacetum parthemium)</td>
<td>50-100 mg extract</td>
<td>Formulations vary</td>
</tr>
<tr>
<td>Ginger (Zingiber officinale)</td>
<td>500-1000mg+</td>
<td>Anti-nausea, anti-inflam.</td>
</tr>
<tr>
<td>Peppermint oil</td>
<td>10% extract topically</td>
<td>Tension</td>
</tr>
<tr>
<td>Melatonin</td>
<td>1-10 mg</td>
<td>Cluster/Migraine</td>
</tr>
</tbody>
</table>
Magnesium – Functions

- Anti-Inflammatory mediator
- Calcium channel blocker
- Skeletal and Smooth Muscle tone
- Energy reactions involving ATP
- Platelet aggregation
- -----
- ↓CSF Mg levels associated poor neurovascular tone
- ↓Mg and ↑Ca/Mg ratio may modulate cerebral serotonin receptors

Among US adults, 68% consumed less than the recommended daily allowance (RDA) of magnesium, and 19% consumed less than 50% of the RDA.

Adults who consumed < RDA were 1.48 – 1.75 X more likely to have ↑ CRP.
Magnesium Deficiency / Insufficiency Equivalents

- **Symptoms**
  - Constipation
  - Myalgia
  - Ext Cramps and
  - ↓ Mood
  - Paresthesia
  - Palpitations
  - Extremity Temp ↓

- **Chronic Disease**
  - CV, GI, Renal, DM, Heme . . .

- **Medications:**
  - PPIs - OCPs
  - Corticosteroids
  - Diuretics - Digoxin
  - Cisplatin - Aminoglyc.
  - Amphotericin B

- **Metabolic / Lab**
  - ↓ Vit D
  - ↓ Calcium
  - ↓ Potassium
  - ↑ hsCRP
Mag Oxide in Ped. Migraine

• R DB PC PG Trial 7 Kaiser clinics; N=118
• Ages 3-17 y.o. with wkly mod-sev migraine
• 9 mg/kg / day PO TID with food x 16 wks
• 70% of Mg & 76% placebo completed
• Intention-to-treat analysis:
  • ↓ Freq Mg (P = .0037); placebo (P = .086)
  • ↓ Severity (P = .0029) vs placebo

Brief Communications

Chronic Tension-Type Headache With Vitamin D Deficiency: Casual or Causal Association?

Sanjay Prakash, DM; Nilima D. Shah, MD
Pharmacological doses of vitamin D increase Mg absorption in both vitamin D-deficient and vitamin D-replete animals.
Vitamin D Deficiency Promotes Skeletal Muscle Hypersensitivity and Sensory Hyperinnervation

Sarah E. Tague,1,4 Gwenaëlle L. Clarke,1,4 Michelle K. Winter,2,4 Kenneth E. McCarson,2,4 Douglas E. Wright,3,4 and Peter G. Smith1,4

Departments of 1Molecular and Integrative Physiology, 2Pharmacology, Toxicology and Therapeutics, and 3Anatomy and Cell Biology, and 4Kansas Intellectual and Developmental Disabilities Research Center, University of Kansas Medical Center, Kansas City, Kansas 66160
CoEnzyme Q10 and Riboflavin: The Mitochondrial Connection

Herbert G. Markley, MD, FAAN, FAHS

Riboflavin (B-2) → Flavin Adenine Dinucleotide (FAD) → FAD deficiency has been linked to poor cerebrovascular tone

Riboflavin (Vitamin B-2)

- N=55 (RDBPCT intention to treat analysis)
- 400 mg/day of B2 vs. placebo for 3 months
- Those subjects who ↓ HA days by > 50%
  - = 15% placebo
  - = 59% B-2 \( (p = .002) \)
- **NNT=2.3** Side effects= rare diarrhea
- No significant change in intensity and duration

- **Valproate NNT=1.6**
- **Valproate NNT for ADVERSE EFFECT = 2.4**
  - riboflavin's NNT for ADVERSE EFFECT = 33.3

Riboflavin

The graph shows the number of attacks per month for a placebo group and a riboflavin group. The riboflavin group shows a significant decrease in the number of attacks over the months, while the placebo group shows no such decrease.
This study provides some early evidence that lowering homocysteine through vitamin supplementation reduces migraine disability in a subgroup of patients.

Pharmacogenet Genomics. 2009 Jun;19(6):422-8
“Riboflavin appears to be more effective in patients with migraine with non-H mitochondrial DNA haplotypes. …could be related to the association of haplogroup H with increased activity in complex I, a major target for riboflavin. Haplogroup H is chiefly found in the European population.

Neurology® 2009;72:1588–1594
Figure: Mean frequency of attacks per month before and after prophylactic treatment with riboflavin (400 mg QD) in the total population of patients and in mitochondrial DNA haplogroup H and non-H subgroups.
CoQ10 level of 1550 patients (avg. age=13.3)  
- 32.9% were below the reference range  
  - Recommended 1 to 3 mg/kg per day of CoQ10 in liquid gel capsule  
- ~3 mo. f/u: CoQ10 level ↑ to 1.20 (P < .0001)  
- HA frequency ↓ from 19.2 → 12.5 (P < .001)  
- Headache disability (PedMIDAS) improved from 47.4 → 22.8 (P < .001)
• By month 3, CoQ10 superior to placebo for
  – Attack-frequency
  – Headache-days
  – Days-with-nausea
• 50%-responder-rate for attack frequency was
  14.4% for placebo and 47.6% for CoQ10
• Well tolerated
• **number-needed-to-treat NNT: 3**
Role Diet and Supplements in HA

**GOALS:**
- **↓** HA burden
- Diet that:
  - Optimizes weight
  - Health Promoting

**Triggers / Excess**

**Optimal Diet**

**Magnesium CoQ10 Vitamin D...**

**Feverfew Butterbur Ginger...**
Butterbur

(*Petasites Hybridus* root)

- **Constituents**
  - Sesquiterpene
  - Petasin
  - Isopetasin
  - Volatile oils
  - Flavonoids
  - Tannins
  - Pyrrolizidine alkaloids*

- **Activity**
  - Antispasmodic effects on smooth muscle and vascular walls.
  - \( \downarrow \) leukotriene & histamine synthesis
Butterbur (Petadolex)

Butterbur dosing

• Petadolex brand

• **Dosing:** 50 / 100 / 150

• **Adults:** 150 mg/day

• **Peds:** 6-9 years  25 mg twice daily
  Older Peds:  50 mg twice daily

• **S.E.:** Mild GI events (eructation)

• ? Hepatic adv effects with other brands
<table>
<thead>
<tr>
<th>Level A: Medications with established efficacy (≥2 Class I trials)</th>
<th>Level B: Medications are probably effective (1 Class I or 2 Class II studies)</th>
<th>Level C: Medications are possibly effective (1 Class II study)</th>
<th>Level U: Inadequate or conflicting data to support or refute medication use</th>
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<tbody>
<tr>
<td>Herbal preparations, vitamins, minerals, and other</td>
<td>NSAIDs</td>
<td>NSAIDs</td>
<td>NSAIDs</td>
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<td><strong>Petasites</strong></td>
<td><strong>Fenoprofen</strong></td>
<td><strong>Flurbiprofen</strong></td>
<td>Aspirin</td>
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<td><strong>Ibuprofen</strong></td>
<td><strong>Mefenamic acid</strong></td>
<td><strong>Indomethacin</strong></td>
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<tr>
<td><strong>Ketoprofen</strong></td>
<td>Herbal preparations vitamins, minerals, and other</td>
<td>Herbal preparations vitamins, minerals, and other</td>
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<tr>
<td><strong>Naproxen</strong></td>
<td><strong>Co-Q10</strong></td>
<td></td>
<td>Omega-3</td>
</tr>
<tr>
<td><strong>Naproxen sodium</strong></td>
<td><strong>Estrogen</strong></td>
<td></td>
<td>Other</td>
</tr>
<tr>
<td>Herbal preparations, vitamins, minerals, and other</td>
<td><strong>Antihistamine</strong></td>
<td></td>
<td>Hyperbaric oxygen</td>
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<tr>
<td>Magnesium</td>
<td>Cyproheptadine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MIG-99 (feverfew)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Riboflavin</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>
• Traditional Use

• Properties:
  – Serotonin Receptor Modulation
  – Anti-nausea effects (on a regular basis)
  – Anti-inflammatory
  – GI-protective

• Sublingual ginger for acute use

• 250-1000 mg/day
Comparison Between the Efficacy of Ginger and Sumatriptan in the Ablative Treatment of the Common Migraine
Other Supplements

• Omega-3 (EPA/DHA) 1-3 grams/day
• Melatonin: 1-3 mg
• Alpha Lipoic Acid 600 -1200 mg/day
• Ginkgo Biloba 120 mg/day
• Ginger 250 -1000 mg/day
• Topical and Intranasal options
  – Capsicum
  – Peppermint…

Figure 3 An algorithm for “stratified” and “step-wise” preventive anti-migraine treatment based on available data on efficacy/tolerance ratios and on personal experience.
Arcana Pharmacy
• Biofeedback
• Guided Imagery
• Hypnosis
• Cognitive Behavioral Therapy
• Meditation / Breathing
• Relaxation training
• Stress Management

Autonomic Dysregulation in HA

- Measurements of HRV, skin temp, skin cond. & respirations vs matched controls
- *Headache subjects have* ↑ sympathetic nervous system & ↓ parasympathetic activity *compared to non-headache controls*
- *Headaches subjects also showed greater emotional distress, fatigue & sleep problems.*

Behavioral Therapy Summary

• Relaxation training,
• Thermal biofeedback with relaxation train.
• EMG biofeedback, and
• CBT
• have been shown in RCTs to reduce migraine frequency by 30%–50%

# Biofeedback - The Feedback and Tools

<table>
<thead>
<tr>
<th>Feedback</th>
<th>Tool</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin Temperature</td>
<td>Digital Thermal Gauge</td>
</tr>
<tr>
<td>Galvonic Skin Response</td>
<td>GSR meter</td>
</tr>
<tr>
<td>sEMG</td>
<td>Electromyography</td>
</tr>
<tr>
<td>Heart Rate variability</td>
<td>Pulse / Respiratory Monitor</td>
</tr>
<tr>
<td>Respiratory rate</td>
<td></td>
</tr>
</tbody>
</table>
The Benefits of Biofeedback

Sleep and Pain

Stress and sleep duration predict headache severity in chronic headache sufferers.

- 2 days of either ↑ stress or ↓ sleep were strongly predictive of headache, 2 days of ↓ stress or adequate sleep were protective.

Primary Approach
- Understand etiology
- Understand Stress
- Sleep Hygiene
- CBT
- Mind/Body Tools

Effect of preventive (β blocker) treatment, behavioural migraine management, or their combination on outcomes of optimised acute treatment in frequent migraine: randomised controlled trial

Kenneth A Holroyd, distinguished professor,12 Constance K Cottrell, assistant research professor,12 Francis J O'Donnell, clinical assistant professor,234 Gary E Cordingley, associate professor,4 Jana B Drew, assistant research professor,12 Bruce W Carlson, associate professor,1 Lina Himawan, biostatistician1
Optimised acute treatment plus:

- Placebo
- \(\beta\) blocker
- Placebo + behavioural migraine management
- \(\beta\) blocker + behavioural migraine management
Incorporating biofeed/relaxation

- Clinic treatments
  - 3-4 wkly treatments

- Home treatments
  - Guided Imagery CDs
  - Computer Programs
    - Wild Divine / Heart Math …

- On-line: University of Minnesota
  - http://www.takingcharge.csh.umn.edu/conditions/migraine
  - Mobile / Smartphones
Movement & Headache
Changing the Tissue & Beyond

- Exercise
- Stretching
- Massage & Manual Therapy
- Physical Therapy
- Manipulation / Cranial Sacral Therapy
Exercise as migraine prophylaxis: A randomized study using relaxation and topiramate as controls

- Exercise 40 min 3 x/ wk vs relaxation vs topiramate (max 200 mg/day) x 3 mo.
- Attack # reduction noted in all 3 groups and no significant difference b/w groups
- Exercise significant ↑ max. O₂ uptake
- Exercise may be an option …in patients who do not benefit from or do not want to take daily medication.
• N= 384 office workers with chronic HA/neck pain, randomized to UC vs:
  – Relaxation exercises
  – Stretches
  – Awareness

VS controls at 6 months

- 40% ↓ in monthly HA frequency
- ↓ neck and shoulder pain
- ↓ in medication intake
Effectiveness of Yoga Therapy in the Treatment of Migraine Without Aura: A Randomized Controlled Trial

P.J. John, PhD; Neha Sharma, MSc; Chandra M. Sharma, MD, DM; Arvind Kankane, MD

- **N = 72 migraine without aura**
- **Yoga therapy or self-care x 3 months**
  - Yoga postures & *breathing* (*Pranayama*)
  - *Relaxation exercises*, meditation, *Neti Pot cleansing*
  - 5x/week + at prodromal stage (relaxation exercises and deep relaxation)
  - At f/u: ↓ in HA frequency, duration & severity; medication use, McGill Pain and HADS (anxiety and depression) (*P*<0.001)
Craniosacral therapy for migraine: Protocol development for an exploratory controlled clinical trial

John D Mann*¹, Keturah R Faurot², Laurel Wilkinson³, Peter Curtis⁴, Remy R Coeytaux³,⁴, Chirayath Suchindran⁵ and Susan A Gaylord²
NIH Consensus 1997

“Acupuncture may be useful as an adjunct treatment or an acceptable alternative or be included in a comprehensive management program”

- Myofascial pain
- Osteoarthritis
- Low back pain
- Headache
- Menstrual cramps
- Tennis elbow
- Fibromyalgia
- Carpal tunnel syndrome
- Addiction
- Stroke rehabilitation
- Asthma

The NIH Consensus Development Program. Available at:
Acupuncture for Migraine Prophylaxis
Cochrane Review

• 22 trials (n=4419); Effective for prevention of migraine HA, & may be slightly better than pharmacotherapy; strength of evid.=A

• 4 trials vs. beta blockers, calcium channel blockers, or valproic acid

• ACP demonstrated slightly better outcomes at 2, 4, and 6 months after randomization, with fewer adverse effects.

Acupuncture versus topiramate in chronic migraine prophylaxis: A randomized clinical trial

- 12 weeks of treatment:
- Decrease in the mean monthly number of moderate/severe headache days
- ACP: $20.2 \pm 1.5 \rightarrow 9.8 \pm 2.8$
- Topiramate: $19.8 \pm 1.7 \rightarrow 12.0 \pm 4.1$
  \(- (p < .01)\)

A 6-week randomized controlled trial with 4-week follow-up of acupuncture combined with paroxetine in patients with major depressive disorder.
The insertion of a semi-permanent needle in these zones allowed stable control of the migraine pain...within 30 min and persisted at the same levels 24 h later (p<0.01)
A sham-controlled trial of acupuncture as an adjunct in migraine prophylaxis

• In patients with migraine unresponsive Rx:
• True acupuncture outperformed sham ACP
• Max benefit at end of active tx
• Reduction in benefit, but continued significance, at 4 months after treatment
• Ongoing “tune up” treatment necessary

Choice of initial acute treatment

- All patients should be provided with behavioural and/or physical therapies, such as:
  - relaxation
  - biofeedback
  - stress reduction strategies
  - cervical manipulation
  - massage
  - exercise
  - the avoidance of migraine triggers
Acupuncture in Guidelines: NICE

• For Tension Type and Migraine HA:

1.3.9 Consider a course of up to 10 sessions of acupuncture over 5–8 weeks for the prophylactic treatment of chronic tension-type headache.

Integrative Therapy Overview

- Background
- Rationale
- Goals
- Prevalence & Approach to Treatments
- Integration: Putting it all together
- Conclusions
• Group program for migraine 6 weeks with
  – 18 group-supervised exercise sessions
  – 2 group stress management and relaxation therapy lectures
  – 2 massage therapy sessions
  – 1 group dietary lecture session

• At 6 wks & 3 mo follow-up with intention to treat analysis, significant (P < 0.001) benefit in:
  – Pain frequency, intensity, and duration
  – Functional status, quality of life, health status, pain-related disability, and depression

• “Positive health related outcomes in migraine can be obtained with a low cost, group, multidisciplinary intervention in a community based nonclinical setting”

Clinical Trial of Integrative Medicine Treatment Approaches for Migraine and Headache Disorders – A Subgroup Analysis of SIMTAP

R. Bonakdar1, R. Coeytaux2, R. Roberts3; on behalf of the BraveNet Practice Based Research Network
1Scripps Center for Integrative Medicine, San Diego, CA; 2Duke Clinical Research Institute, Durham, NC

BACKGROUND

Integrative Medicine and Headache

Nearly half of adults with headache report use of complementary and alternative medicine (CAM) with the common reason being desire to find additional relief. However, there has been no prospective research on the effectiveness of coordinated CAM or integrative medicine (IM) approaches.

OBJECTIVES

- To determine whether use of an integrative treatment approach for headache can reduce disability as measured by the Migraine Disability Assessment (MIDAS).
- To explore predictors of treatment response, including CAM use and IM.

METHODS

- SIMTAP is a prospective research study conducted by the BraveNet Collaboratives practice-based research network for integrative medicine. SIMTAP's objective is to evaluate the feasibility of assessing the impact of IM interventions on chronic pain.
- The study design involves randomization of participants to treatment groups.

Study Design

- SIMTAP enrolled 142 subjects with headache disorders at 9 clinical sites between May 2009 and October 2010.
- A subset of these subjects (n=38) who used headache treatments referred to the Outpatient Center for Integrative Medicine by a neurologist were analyzed for a 24-week period.

Analysis

- The primary efficacy analysis was performed using a repeated measures analysis of variance, utilizing the statistical change score defined as a decrease of at least 20% in MIDAS or IMI scores between any two given time points.

Assessment

- Baseline variables included:
  - Gender
  - Age
  - BMI
  - History of Migraine
  - Previous treatment history

RESULTS

- Of the 142 subjects enrolled, 138 were assessed at 24 weeks, follow-up rate = 96%.
- Baseline characteristics are presented in Table 1.
- At the end of the 24-week study, 38 subjects completed the follow-up assessment.

<table>
<thead>
<tr>
<th>Table 1. Baseline Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subjects (n=38)</td>
</tr>
<tr>
<td>Mean age (range)</td>
</tr>
<tr>
<td>Number (%) female</td>
</tr>
<tr>
<td>No. of years with relevant chronic pain, mean (range)</td>
</tr>
<tr>
<td>BMI, mean range</td>
</tr>
<tr>
<td>% Relief from Current Pain/Treatment/Medication</td>
</tr>
<tr>
<td>Expected level of improvements, mean (range)</td>
</tr>
<tr>
<td>MIDAS score, mean (range)</td>
</tr>
<tr>
<td>CES-D score, mean (range)</td>
</tr>
<tr>
<td>Subjects with CES-D &gt; 16 (%clinically depressed)</td>
</tr>
</tbody>
</table>

Table 2. TREATMENT OVERVIEW

<table>
<thead>
<tr>
<th>Treatment at Baseline (% of subjects) (n=38)</th>
<th>Treatments at 24 weeks (% of subjects) (n=38)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Massage (29%)</td>
<td>Biofeedback (44%)</td>
</tr>
<tr>
<td>Yoga (20%)</td>
<td>Chiropractic (23%)</td>
</tr>
<tr>
<td>Prayer (16%)</td>
<td>Yoga (20%)</td>
</tr>
<tr>
<td>Acupuncture (10%)</td>
<td>Deep Breathing (24%)</td>
</tr>
<tr>
<td>Energy/Med (10%)</td>
<td>Guided Imagery (12%)</td>
</tr>
<tr>
<td>Medication (10%)</td>
<td>Chinese Medicine (3%)</td>
</tr>
<tr>
<td>Deep Breathing (7%)</td>
<td>Energy/Med (10%)</td>
</tr>
<tr>
<td>Other (10%)</td>
<td>Chinese Medicine (3%)</td>
</tr>
<tr>
<td>Treatments, other (39%)</td>
<td>Chinese Medicine (3%)</td>
</tr>
</tbody>
</table>

Table 3. MEDICATION & SUPPLEMENT OVERVIEW

<table>
<thead>
<tr>
<th>Medications at baseline* (% of subjects) (n=38)</th>
<th>Supplements at baseline (% of subjects) (n=38)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preventatives (53%)</td>
<td>Vitamin D (42%)</td>
</tr>
<tr>
<td>Anti-depressants (23%)</td>
<td>Omega-3 (32%)</td>
</tr>
<tr>
<td>NAC/CoQ (23%)</td>
<td>Magnesium (21%)</td>
</tr>
<tr>
<td>Tryptophan (27%)</td>
<td>Other (70%)</td>
</tr>
<tr>
<td>Opioid (63%)</td>
<td></td>
</tr>
<tr>
<td>Nutraceuticals (40%)</td>
<td></td>
</tr>
<tr>
<td>Antioxidant (32%)</td>
<td></td>
</tr>
</tbody>
</table>

Table 4. Covariates with ability to predict MIDAS

<table>
<thead>
<tr>
<th>Covariate (onset)</th>
<th>Coefficient</th>
<th>Standard Error</th>
<th>t-value</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BFID 1</td>
<td>-0.016</td>
<td>0.08</td>
<td>-2.03</td>
<td>0.04</td>
</tr>
<tr>
<td>BFID 2</td>
<td>-0.009</td>
<td>0.04</td>
<td>-2.27</td>
<td>0.02</td>
</tr>
<tr>
<td>BFID 3</td>
<td>0.017</td>
<td>0.06</td>
<td>0.31</td>
<td>0.76</td>
</tr>
</tbody>
</table>

CONCLUSIONS

- Headache outcomes evaluated at an integrative medicine facility appear to have a significant burden of disease based on MIDAS and CES scores as well as reported co-morbidities.

DISCUSSION & RECOMMENDATIONS

- Further research should evaluate integrative therapies for headache versus a control group in a larger, multi-center design.
- Further evaluation of predictors of improvement including compliance, desire for and combination of certain treatments should be investigated.

ACKNOWLEDGEMENTS

We are thankful to the subjects and their families as well as the research support provided by the BraveNet Practice Based Research Network. Corresponding Author: Bonakdar.Robert@scripps.org

REFERENCES

- 58% clinically depressed (CES)
- >50% insufficient vitamin D
- 45% reduced migraine severity by I or II MIDAS levels
Conclusion: Integrative Approach

- By the time of diagnosis, migraine patients have or are expecting a large burden of disease...
- Individualized integrative therapies:
  - Based on areas of current / future need (*mood, muscle, mitochondria*), and
  - Focused on lifestyle approaches and active coping strategies (diet, exercise, stress management)
- Work synergistically with conventional care
- Demonstrate improvement in QOL & Self Efficacy
Integrative Approaches to Headache Management

BY ROBERT BONAKDAR, MD, FAAFP, and CHRISTY JACKSON, MD
Scripps Integrative Headache Guidelines Part II
The Role of Integrative Therapies

Robert A. Bonakdar, MD FAAFP
Director of Pain Management
Scripps Center for Integrative Medicine

Christy Jackson MD FAAN
Director, Dalessio Headache Center
Division of Neurology
Snap out of afternoon Drowsy Time

You yawn. You're tired...
And you lag in your work.

Take a minute for an ice-cold Coca-Cola, and bounce back to normal. An ice-cold Coca-Cola is more than just a drink. It's a very particular kind of drink—combining those pleasant wholesome substances which foremost scientists say do most in restoring you to your normal self. Really delicious, it invites a pause—the pause that refreshes.

Refresh yourself
Bounce back to normal
Scripps Integrative Headache Guidelines Part II
The Role of Integrative Therapies

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