Prevention Strategies for Pediatric Headaches

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Disclosures

Support – grants, contracts, honoraria

NIH, CHRF research foundation, Curelator

NIH – Advisory Board, Common Data Elements

Migraine Research Foundation – Advisory Board

Assoc Ed – Headache, Cephalalgia, The Journal of Headache Pain

Advisory Board – Alder, Amgen, Curelator, Depomed, Impax, Lilly, Teva

Objectives

- To understand the latest update on prevention of headaches in children and adolescents
- To develop a treatment strategy for prevention of headaches in children and adolescents.

Classification of Headache

International Classification of Headache Disorders – 3rd Edition (beta version), Cephalalgia, 2013

- **Migraine without aura**
- **Migraine with aura**
  - Migraine with typical aura
  - Migraine with brainstem aura
  - Hemiplegic migraine
  - Retinal migraine
- **Chronic migraine**
- **Complications of migraine**
  - Status migrainosus
  - Persistent aura without infarction
  - Migrainous infarction
  - Migraine aura-triggered seizure
- **Probable migraine**
  - Without aura
  - With aura
- **Episodic syndromes that may be associated with migraine**
  - Recurrent gastrointestinal disturbance
    - Cyclical vomiting syndrome
    - Abdominal migraine
  - Benign paroxysmal vertigo
  - Benign paroxysmal torticollis

Why Migraine

- Migraine prevalence
  - 4 % of young children
  - Up to 10.5% of children age 5-15
  - Up to 28% age 15-19
  - Adults 12% (17.1% women, 5.6% men)
- Migraine pathophysiology
  - Migraine as a genetic disease
  - Early intervention may have lifetime implications

- Migraine Impact
  - Up to 200,000 lost school days in US
  - $17 billion (1998) direct and $17 billion indirect cost
  - Individual cost (2006)
    - Direct $127 to $7089
    - Indirect $709 to $4453
  - Chronic Mig vs Episodic Mig (2016)
    - CM – Direct ($4943), Indirect ($3300)
    - EM – Direct ($1705), Indirect ($943)
    - Pharma – CM ($3925), EM ($1196)
  - Potential progression to refractory headaches if not treated

Why Migraine – Global Burden of Disease

GBD 2015 Disease and Injury Incidence and Prevalence Collaborators, Lancet, Oct 8, 2016

	1	2	3	4	5	6	7	8	9	10
Early neonatal	Iron	NN sepsis	PEM	Haemog	Other inf	Diarrhoea	NN preterm	Congenital	Endocrine	NN enceph
Late neonatal	Iron	PEM	Diarrhoea	Congenital	Haemog	NN preterm	Other nutr	NN enceph	Other inf	Epilepsy
Post neonatal	Iron	Diarrhoea	PEM	Haemog	Skin	Other NTD	Congenital	Other inf	NN preterm	Endocrine
1–4 years	Iron	Skin	PEM	Diarrhoea	Sense	Asthma	Haemog	Other NTD	Congenital	Otitis
5–9 years	Iron	Skin	Asthma	Sense	Haemog	Other NTD	Conduct	Malaria	ASD	Anxiety
10–14 years	Iron	Skin	Conduct	Anxiety	Asthma	Migraine	Sense	Depression	Back & neck	Haemog
15–19 years	Skin	Depression	Iron	Back & neck	Migraine	Anxiety	Sense	Conduct	Other MSK	Asthma
20–24 years	Depression	Back & neck	Skin	Migraine	Iron	Other MSK	Anxiety	Sense	Other mental	Drugs
25–29 years	Back & neck	Depression	Migraine	Skin	Iron	Other MSK	Anxiety	Sense	Drugs	Schiz
30–34 years	Back & neck	Depression	Migraine	Skin	Iron	Sense	Other MSK	Anxiety	Schiz	Gynae
35–39 years	Back & neck	Depression	Migraine	Sense	Other MSK	Skin	Iron	Anxiety	Diabetes	Schiz
40–44 years	Back & neck	Depression	Sense	Migraine	Other MSK	Diabetes	Skin	Iron	Anxiety	Schiz
45–49 years	Back & neck	Depression	Sense	Diabetes	Other MSK	Migraine	Skin	Iron	Anxiety	Schiz
50–54 years	Back & neck	Sense	Depression	Diabetes	Other MSK	Migraine	Skin	Osteoarth	Anxiety	Schiz
55–59 years	Back & neck	Sense	Diabetes	Depression	Other MSK	Migraine	Osteoarth	Skin	Oral	Anxiety
60–64 years	Back & neck	Sense	Diabetes	Depression	Other MSK	Osteoarth	Oral	Skin	Migraine	COPD
65–69 years	Sense	Back & neck	Diabetes	Depression	Other MSK	Osteoarth	Oral	COPD	Skin	IHD
70–74 years	Sense	Back & neck	Diabetes	Depression	Oral	Other MSK	Osteoarth	COPD	IHD	Skin
75–79 years	Sense	Back & neck	Diabetes	Alzheimer's	Depression	Oral	Osteoarth	Other MSK	COPD	IHD
≥80 years	Sense	Alzheimer's	Back & neck	Diabetes	Falls	IHD	Osteoarth	Depression	COPD	Oral

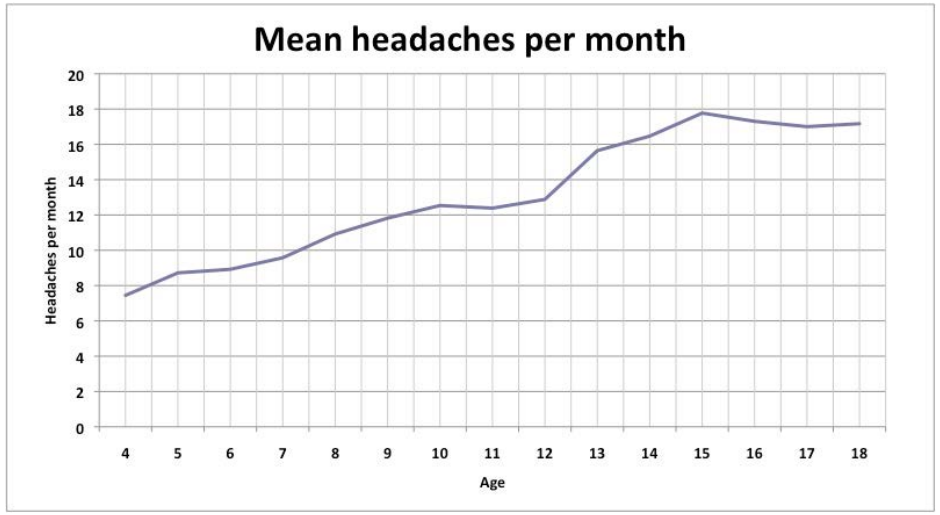
Rate of change 2005–15

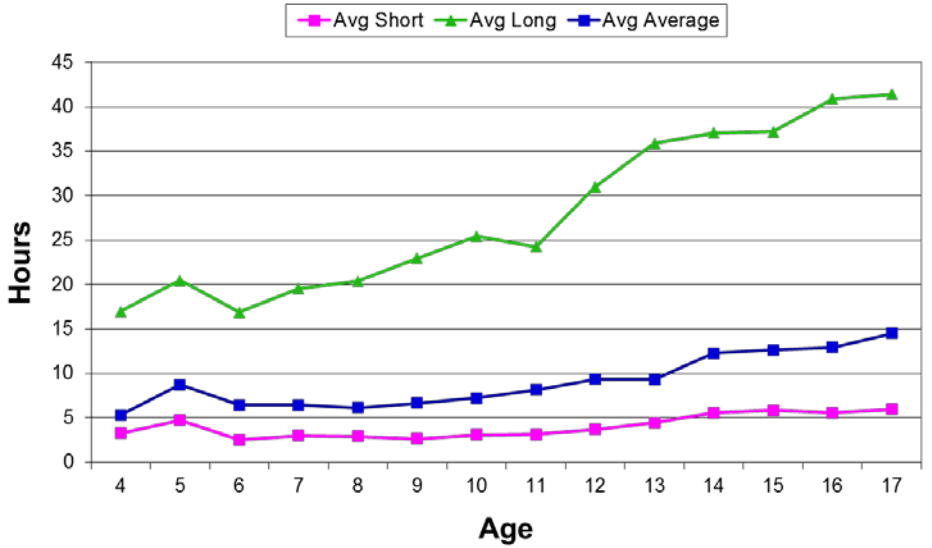
−0·19 to −0·03 | −0·03 to 0·01 | 0·01 to 0·06 | 0·06 to 0·09 | 0·09 to 0·15

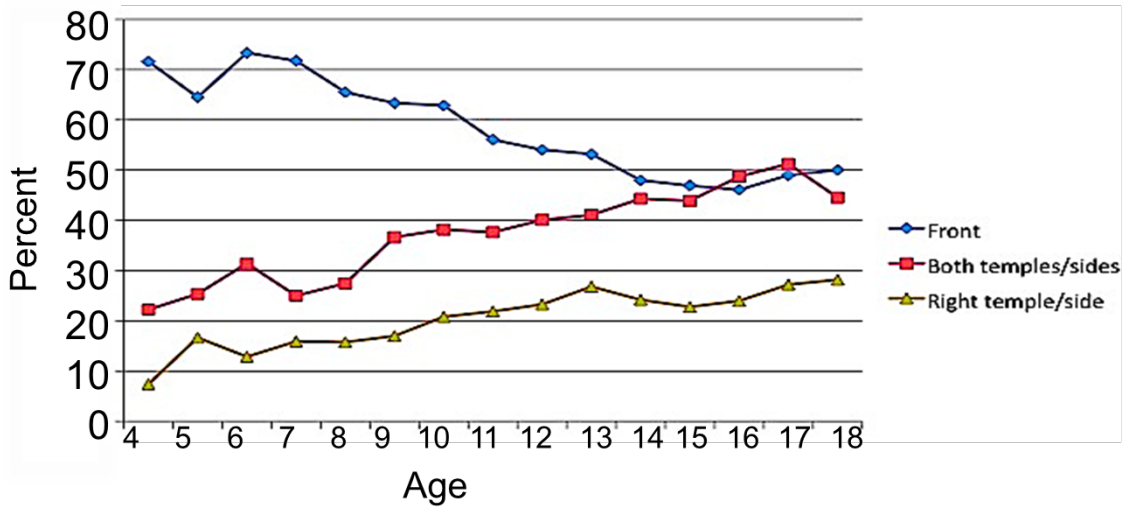
0·15 to 0·19 | 0·19 to 0·24 | 0·24 to 0·29 | 0·29 to 0·42 | 0·42 to 0·63

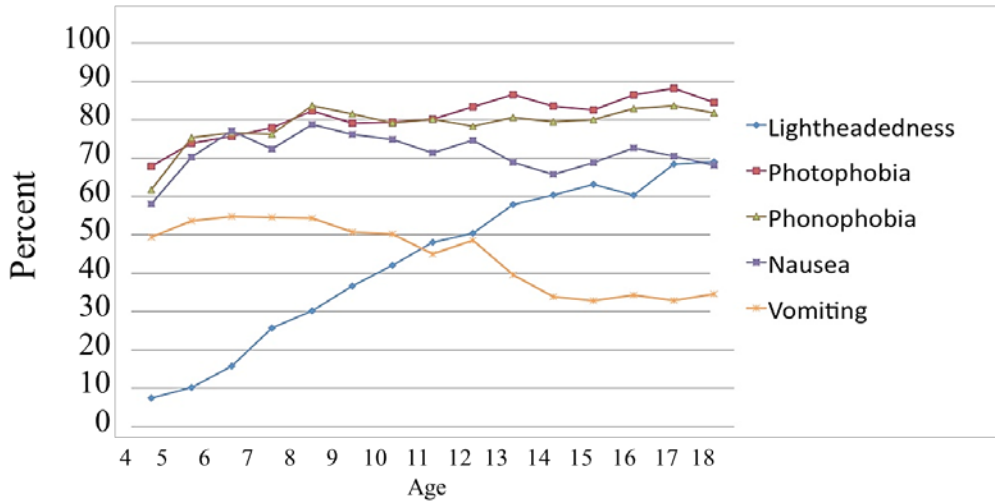
Changes in Character with Age

- 5659 patients headache characteristics compared
- Age 4 to 18, mean 11.95 ± 3.53
- Analysis of diagnostic criteria across the developmental ages
- McKenzie Miller, summer student


Mean headaches per month
Headaches per month
Age

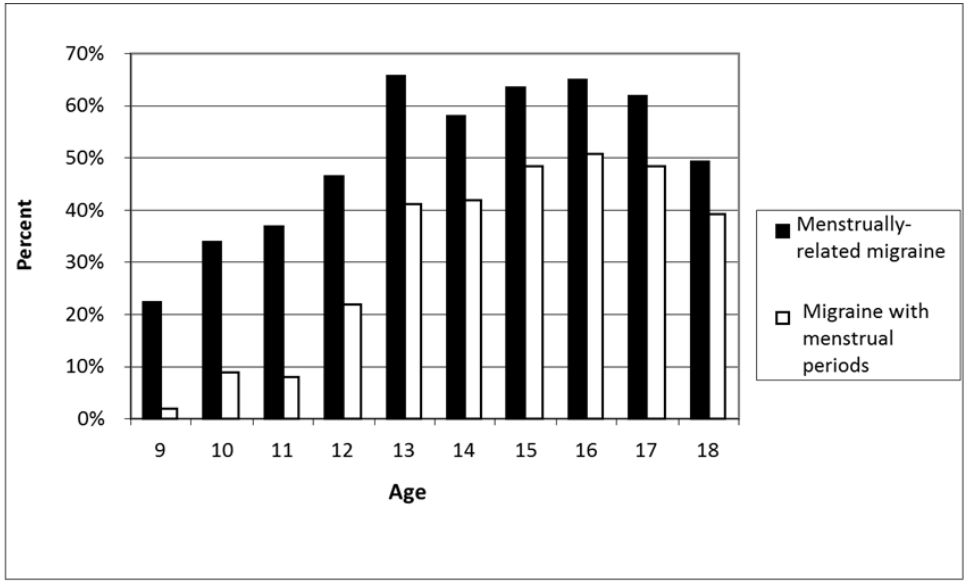

Avg Short
Avg Long
Avg Average
Hours
Age

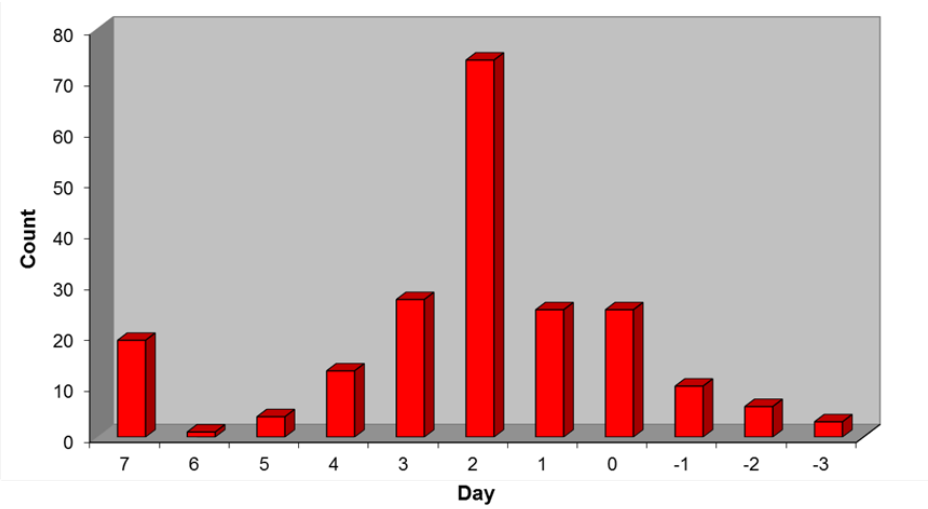

Percent
Front
Both temples/sides
Right temple/side
Age


Percent
Lightheadedness
Photophobia
Phonophobia
Nausea
Vomiting
Age

Menstrual Effects

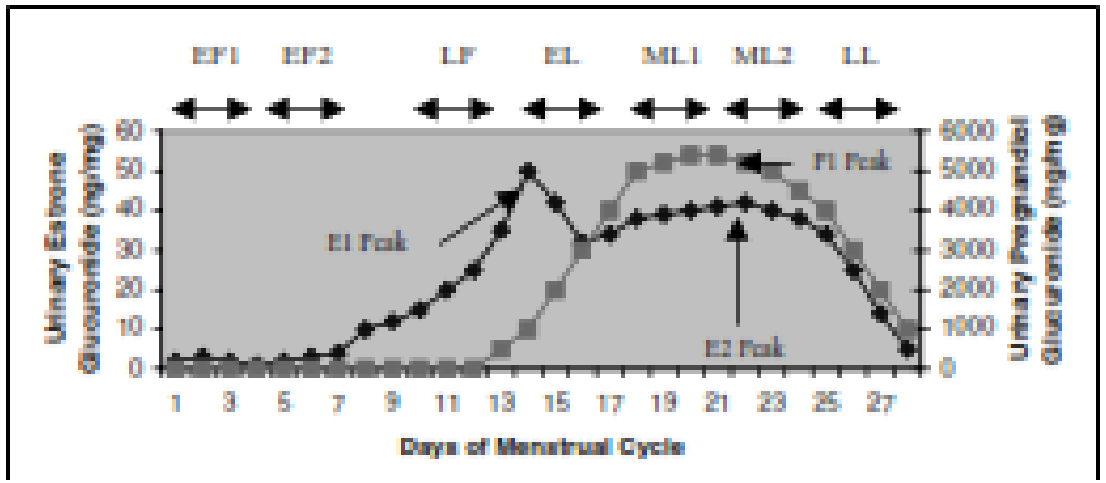
- Is Puberty the Reason?
- Reviewed Headache Center Database
  - 896 girls, age 9 to 18
  - Clinically asked
    - Had first period
    - Headaches worsen with periods
    - Monthly pattern of worsening headaches





Urinary Hormone Effect (Adults)

Martin et al, Headache, 2005



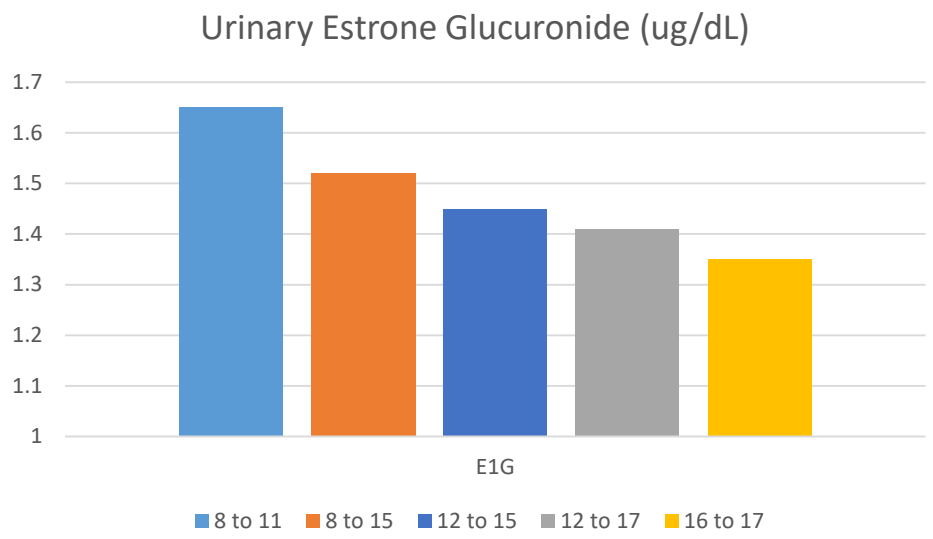
AUCs/Interval†	Cycle 1‡	Cycle 2‡	Cycle 3‡
AUC E1 peak vs.			
E1 peak interval	−.250	−.178	−.036
EL interval	−.213	−.170	−.060
AUC E2 peak vs.			
E2 peak interval	−.130	−.211	−.150
EF1 (next cycle)	−.071	−.202	.005
AUC P1 peak vs.			
P1 peak interval	.461 (.036)§	.481 (.027)§	.400 (.070)
EF1 (next cycle)	.226	.189	.486 (.026)
PdG/ E1G ratio of P1 peak vs.			
P1 peak interval	.460 (.036)	.553 (.0093)	.285
EF1 (next cycle)	.165	.189	.206

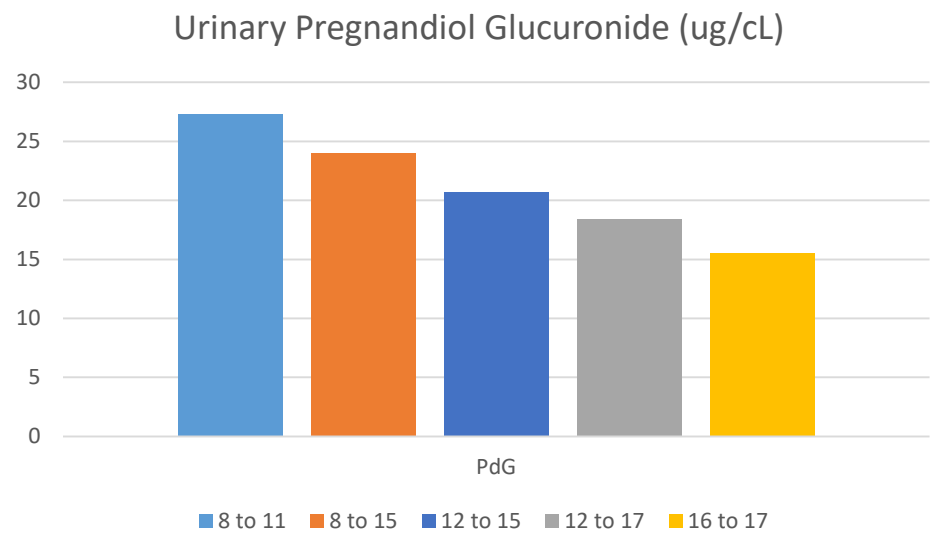
Urinary Hormone Effect

Martin et al, Cephalalgia, 2017

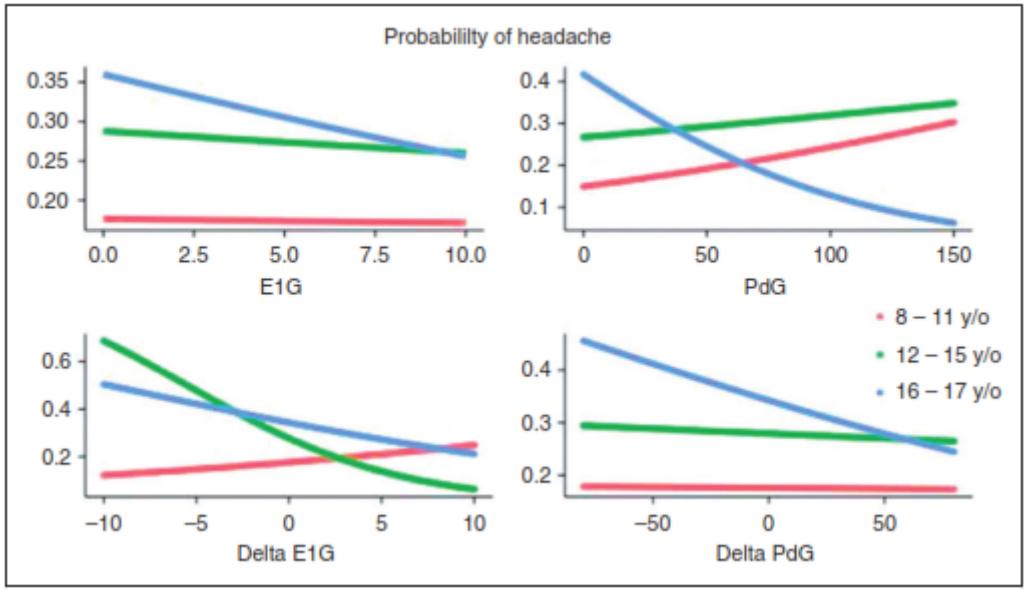
- Adult studies revealed hormonal fluctuations could predict headache
- What role does development have in this influence
- Stratification across 3 ages
  - 8-11 years old
  - 12-15 years old
  - 16-17 years old
- Daily urine samples
  - Estrone glucuronide (ElG), pregnandiol glucuronide (PdG)
  - 96.2% of days with sample collection
- Diary of headache characteristics and presentation

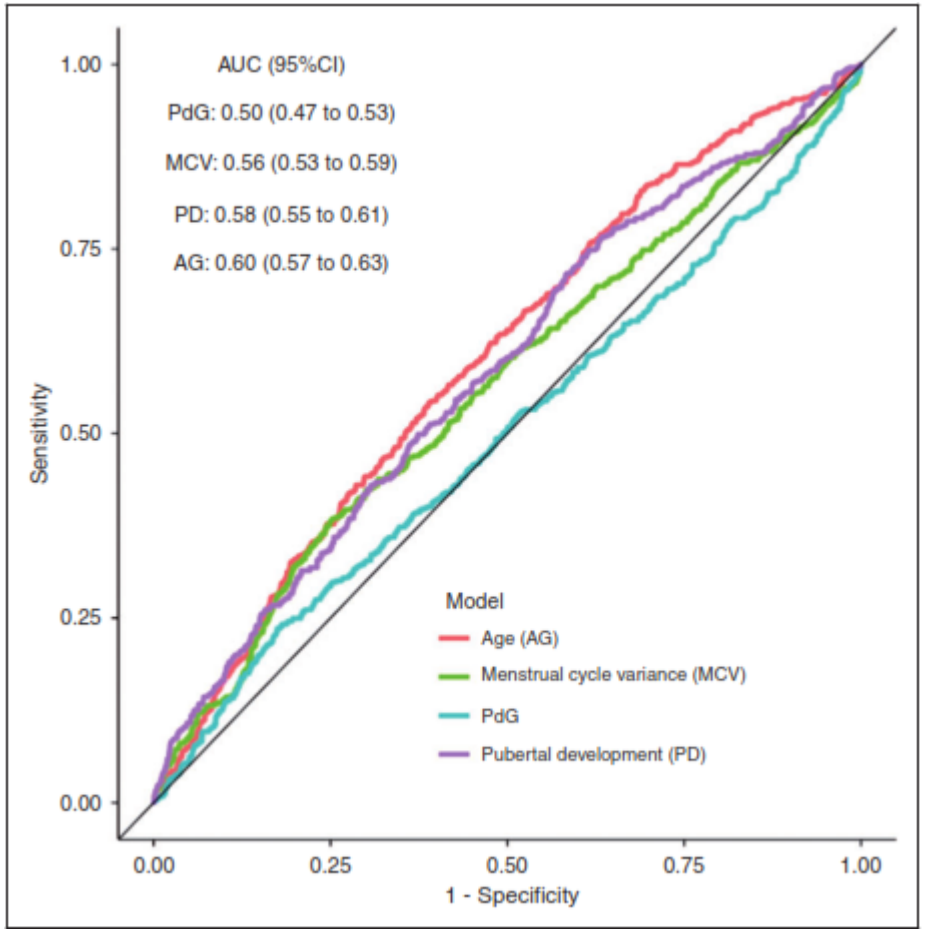
Pubertal Urinary Menstrual Level Changes



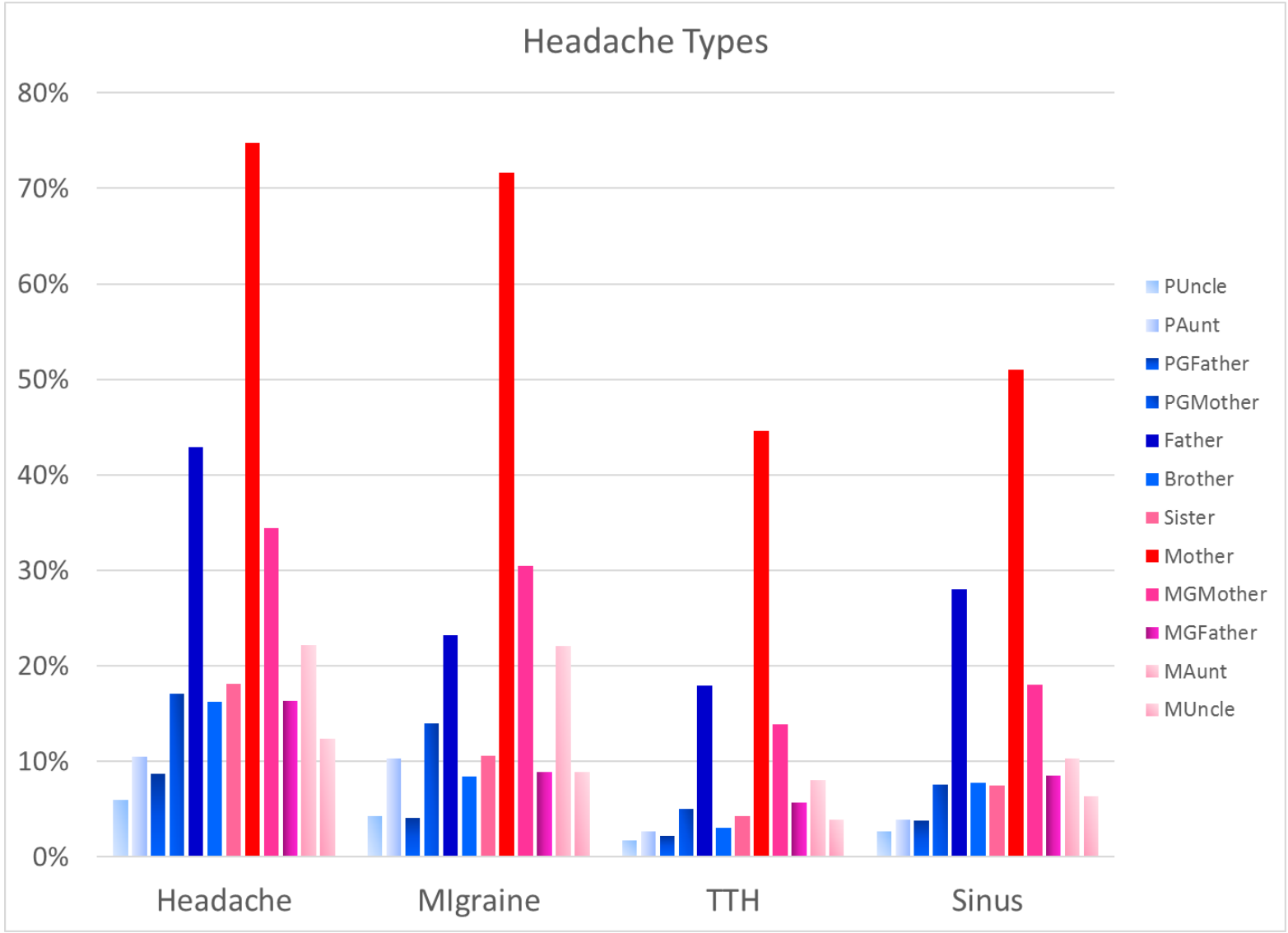


Urinary Hormone Effect (Children and Adolescents)





Family History



Migraine Twin Children

Svensson et al, *Cephalalgia* 1999

- 1480 Swedish twins
  - Born between Apr 1985 and Dec 1986
  - 8 to 9 year olds
  - Clinical Dx based on ICHD-I

	N	Twin pairs		
		−/−	+/−	+/+
MZ Boys	178	146	21	11
DZ Boys	183	142	36	5
MZ Girls	164	127	24	13
DZ Girls	200	155	38	7
DZ Us	314	227	80	7
Total	1039	797	199	43

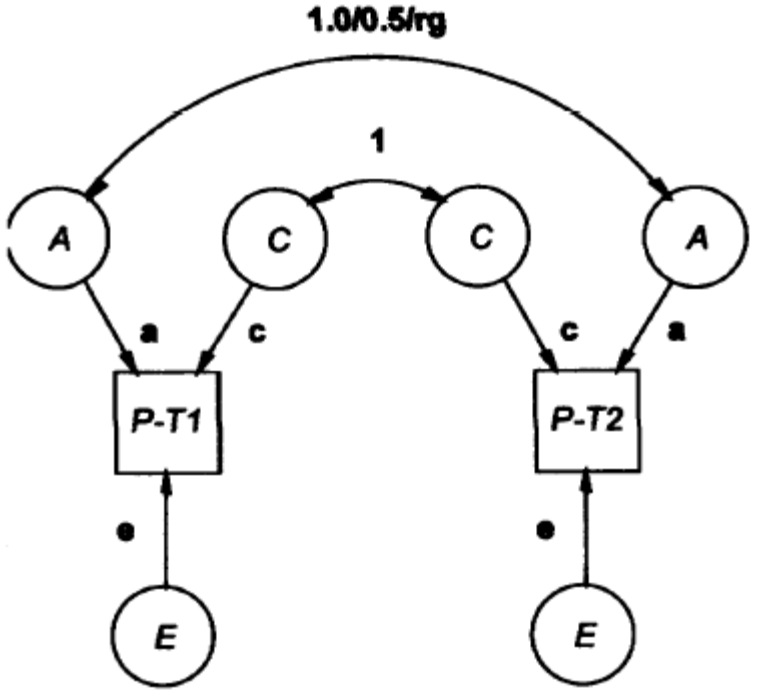


Table 5. Estimates of components of variance in 8 to 9-year-old boys and girls.

	a^2	c^2	e^2
Estimate	0.70	0	0.30
95% CI	0.54–0.82	-	0.18–0.46

a^2 = Additive genetic effects (heritability); c^2 = shared environmental effects; e^2 = nonshared environmental effects.

Migraine Gene Candidates

Persico et al, Neurogenetics 2015

- Examined by groupings
  - Neurological Candidates
  - Vascular Candidates
  - Hormonal Candidates
  - Inflammatory Candidates

Migraine Gene Candidates

Persico et al, Neurogenetics 2015

Table 3 Positive association findings with neurological candidate genes

Gene	Locus	Cases	Controls	Ethnicity	n. SNPs analyzed	Associated SNPs/VNTRs	*P* value	Refs
5-HT-related genes								
DDC	7p12.2	528 (308 MO, 220 MA)	528	Spanish	15	rs2329340 rs11974297 rs2044859 rs11761683	0.0019 (MA)	[77]
MAOA	Xp11.3	528	523	Spanish	2	rs3027400G rs2072743C	0.006 (MO)	[77]
HTR2B	2q37.1	528	523	Spanish	23	rs16827801 rs10194776	0.0017 (MO)	[77]
		91	119	Japanese	1	rs6323	<0.05	[78]
SLC6A4	17q11.2	154 (92MO, 52MA)	105	Italian	–	5-HTTLPR S/S	<0.05 (MA)	[79]
		251	192	German	2	rs1979572	<0.05 (MA)	[80]
Dopamine-related genes								
DBH	9q34	177	182	Australian	1	rs7239728	0.019	[81]
		275	275	Australian	2	rs7239728	0.003 (MA)	[82]
		200 300	200 300	Australian	2	rs1611115 rs1611115	0.012 0.031	[83]
		650	2937	German/Br	1	rs2097629	5.57×10^{-4}	[84]
		263	274	Spanish	11	rs1611131	0.04	[85]
		301 (99MA, 202MO)	202	Indian	1	rs72393728	0.027	[86]
		208, 127 (II)	200	Indian	2	rs7239728	<0.05	[87]
SLC6A3	5p15.3	650	2937	German/Br	1	rs40184	6.36×10^{-7}	[84]
DRD2	11q23	650	650	German	1	rs7131056	0.034	[84]
DRD3	3q13.3	263	274	Spanish	10	rs12363125	0.03	[85]
DRD4	11p15.5	194 (93MA, 101MO)	117	Italian	1	rs22832265	0.008	[88]
Glutamate receptors								
GRIA1	5q31.1	250	260	Italian	6	rs2195450	0.00002 (MA)	[89]
GRIA3	Xq25	250	260	Italian	8	rs548294 rs3761555	0.0003 (MO) 0.0001 (MA)	[89]
		472	472	Australian	1	rs3761555	0.008 (MA)	[90]

Migraine Gene Candidates

Persico et al, Neurogenetics 2015

Table 4 Positive association findings with vascular candidate genes

Gene	Locus	Cases	Controls	Ethnicity	n. SNPs analyzed	Associated SNPs/polymorphisms	*P* value	Refs
ACE	17q23.3	191	201	Italian	1	rs4646994	<0.05	[91]
		176	248	Japanese	1	rs4646994	<0.01 (MA)	[92]
		150	150	Indian	1	rs4646994	0.04 (MA)	[93]
MTHFR	1p36.3	74	261	Japanese	1	rs1801133	<0.01	[94]
		102	136	Turkish	2	rs1801133	0.015	[95]
		78MA,152MO	204	Spanish	1	rs1801133	0.006 (MA vs MO)	[96]
		270	270	Australian	1	rs1801133	0.017 (MA)	[97]
		91	119	Japanese	1	rs1801133	<0.05	[78]
		124	1725	British	1	rs1801133	<0.05 (MA)	[98]
		151	137	Chinese	1	rs1801133	0.003 (MO)	[99]
		150	107	Turkish	1	rs1801133	<0.001	[100]
NOTCH3	19p13.12	97	97	German	2	rs1043994	0.005	[101]
		275	275	Australian	2	rs3815188	0.002 (MO)	[102]
		300 (II)	300 (II)		2	rs1043994 rs3815188 rs1043994	0.001 (MA) 0.06 (MO) 0.003 (MA)	
EDNRA	4q31.22	850	890	Finnish	13	rs2048894	0.015 (MA)	[103]
		648 (II)	651 (II)	German	1	rs2048894	0.010 (MA)	
		217+179TTH	217	Indian	1	rs2048894	0.002 (MA/MO)	[104]
		77MA; 111MO	287	Portuguese	3	rs702757-rs5333	<0.05	[105]
		140		French	5	c.-231A>G		[106]
NOS2	17q11.2	504	512	Chinese	2	PNRP	0.007	[107]
		200 (52MA, 148MO)	142	Brazilian	1	rs2779249 rs2297518	<0.05	[108]
NOS3	12q14	156	125	Italian	1	rs1799983	<0.05 (MA)	[109]

Migraine Gene Candidates

Persico et al, Neurogenetics 2015

Table 5 Positive association findings with hormonal candidate genes

Gene	Locus	Cases	Controls	Ethnicity	n. SNPs analyzed	Associated SNPs/polymorphisms	*P* value	Refs.
ESR1	6q25.1	224 260 (II)	224 260 (II)	Australian	1	rs2228480	0.003 8×10^{-6}	131
		240	160	Spanish	1	rs1801132	0.008 (females)	132
		356 (198MA, 158MO)	374	Spanish	1	rs1801132	0.004	133
		217MA, 179TTH	217	Indian	1	rs2234693	0.002 MA	134
		207 127 (II)	200	Indian	4	rs2234693	P_{corr}0.01	135
ESR2		356 (198MA, 158MO)	374	Spanish	1	rs4986938	0.004	133
FSHR	2p21-p16	356 (198MA, 158MO)	374	Spanish	1	rs6166	0.004 MA (females)	133
CYP19A1	15q21	207 127 (II)	200	Indian	1	rs10046	p_{corr}0.01	135
PGR	11q22	275 300 (II)	275 300	Australian	1 1	PGR PROGIN insert	0.002 0.003	136

Migraine Gene Candidates

Persico et al, Neurogenetics 2015

Table 6 Positive association findings with inflammatory candidate genes

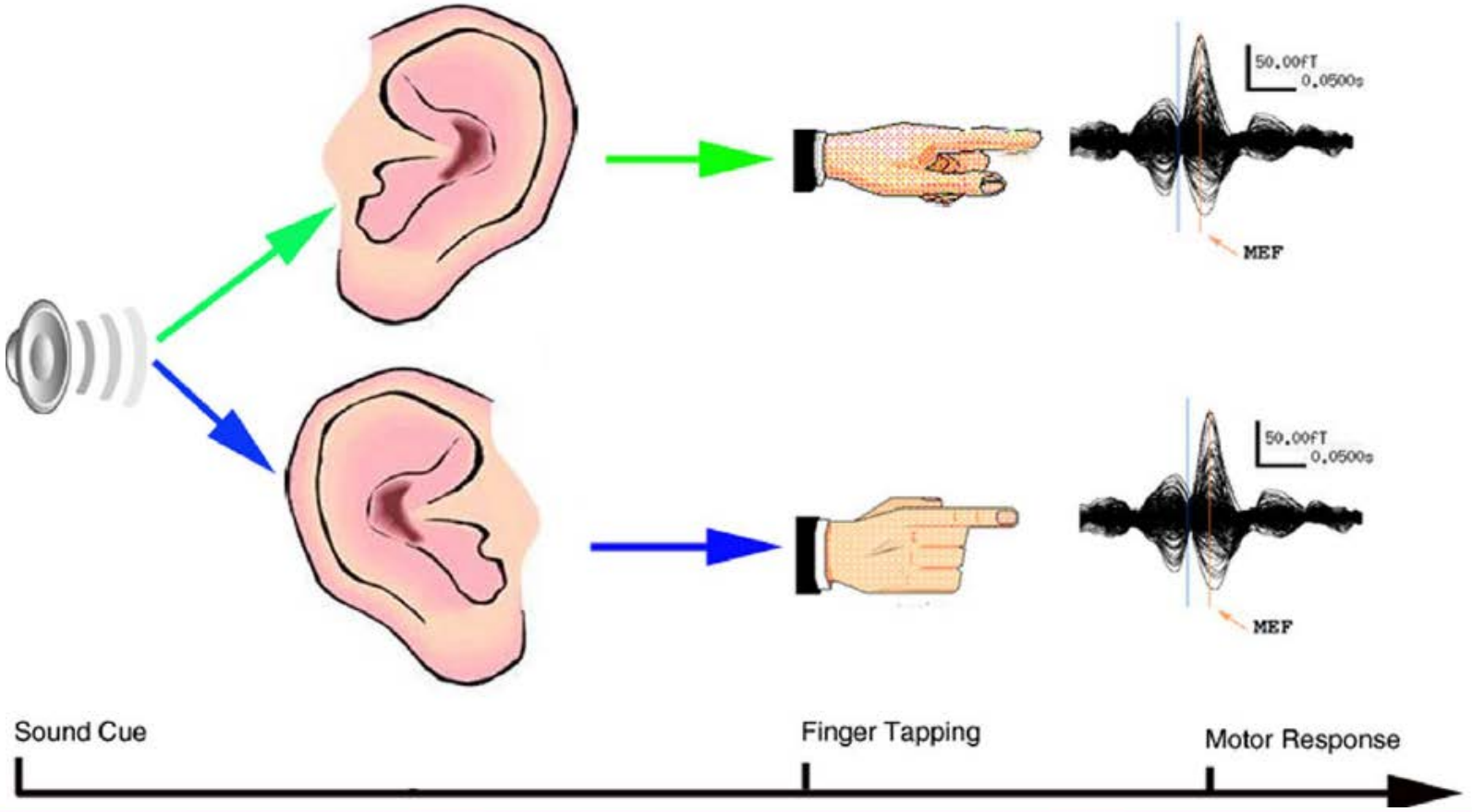
Gene	Locus	Cases	Controls	Ethnicity	n. SNPs analyzed	Associated SNPs/polymorphisms	*P* value	Refs
TNFA	6p21.3	299	306	Italian	1	rs1800629	<0.001 (MO)	[110]
		221 (MO)	183	Iranian	1	rs1800629	<0.0001	[111]
		216	216	Indian	1	rs1800629	<0.006 (MA)	[112]
		67 (MO)	96	Turkish	1	rs1800629	0.004 (MO)	[113]
		203	202	Turkish	1	rs1800629	<0.0001	[114]
TNFB/LTA	6p21.3	79 (47MO+32MA)	101	Italian	1	TNFB*2al.	0.004 (MO)	[115]
		439	382	South Korea	15	LTA-294C	0.005	[116]
		299	278	Italian (Sardinian)	1	rs909253	0.018	[117]
		91	119	Japanese	1	rs909253	<0.05	[78]
TNFRSF1B	1p36.22	416	415	Chinese Han	1	rs5745946	0.004	[118]
HLA-DRB1	6p21.3	255 (41MA, 214MO)	325	Italian	–	DRB1*16al.	0.043 (MO)	[119]
IL1 β	2q14	67 (MO)	96	Turkish	1	rs1143634	0.004	[113]
COX-2	1q25.2	144	123	Turkish	2	rs20417	0.0001	[120]

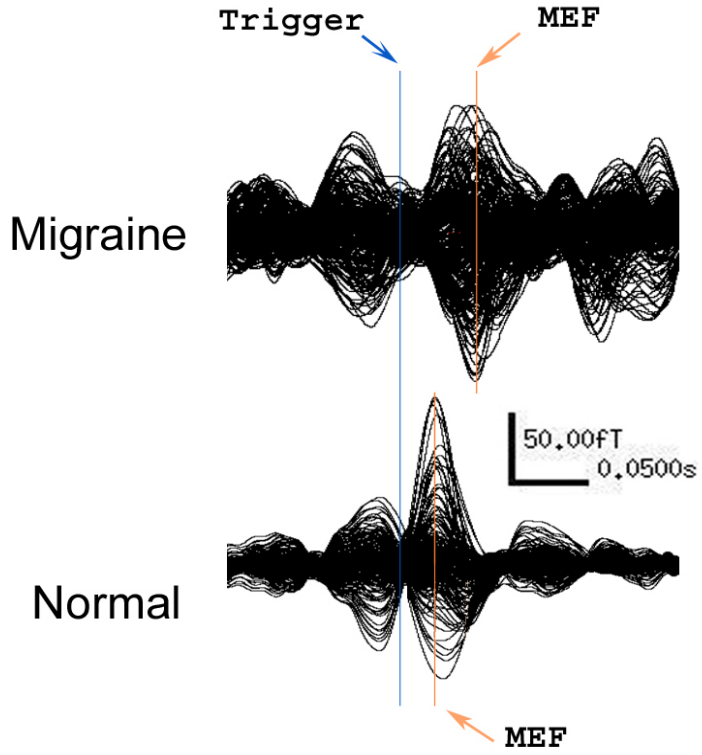
MEG

- Migraineurs frequently note that it is hard to think during an acute attack
- MEG can measure cortical function
  - Finger tapping (200 trials, randomly presented clicks in right or left ear to tap fingers)
  - Mis-matched negativity
- Compared subjects with acute migraine seen in the acute headache unit vs. controls

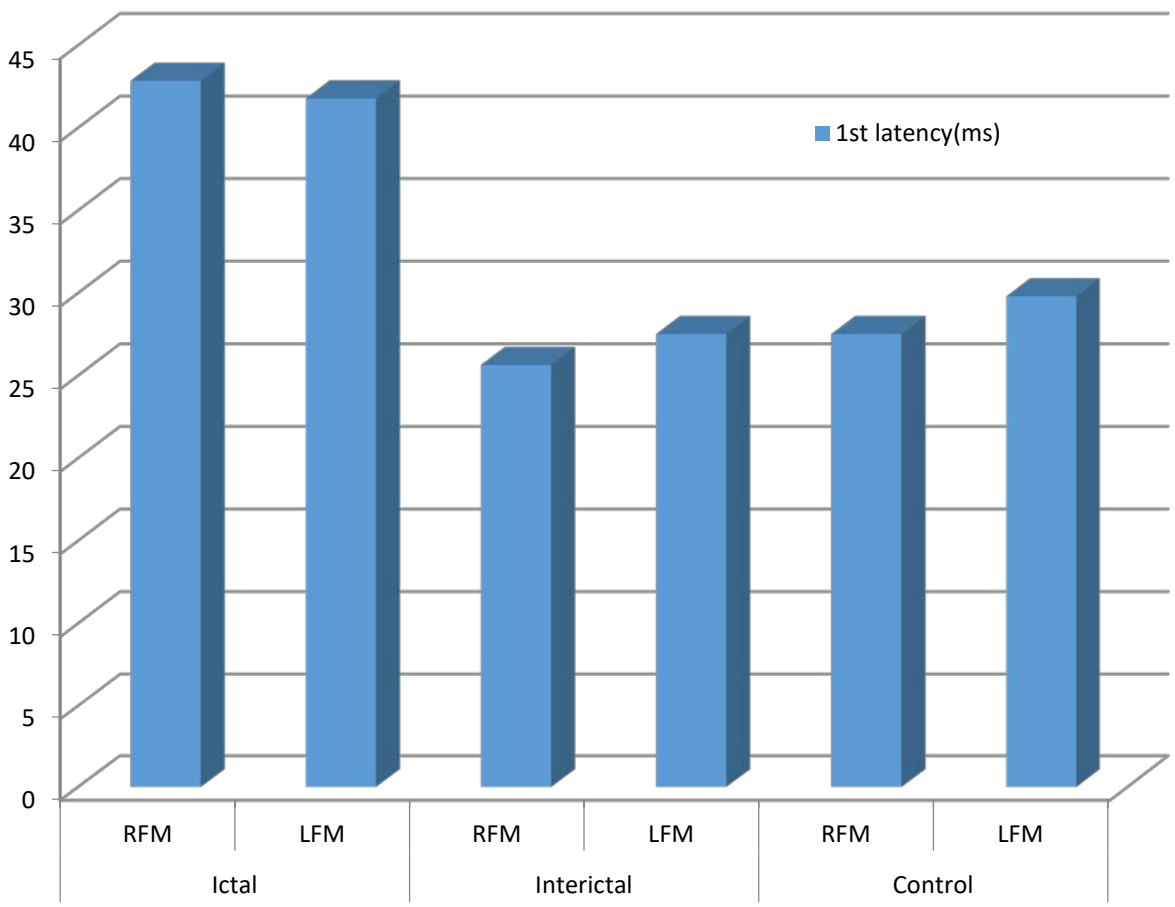
MEG Methodology

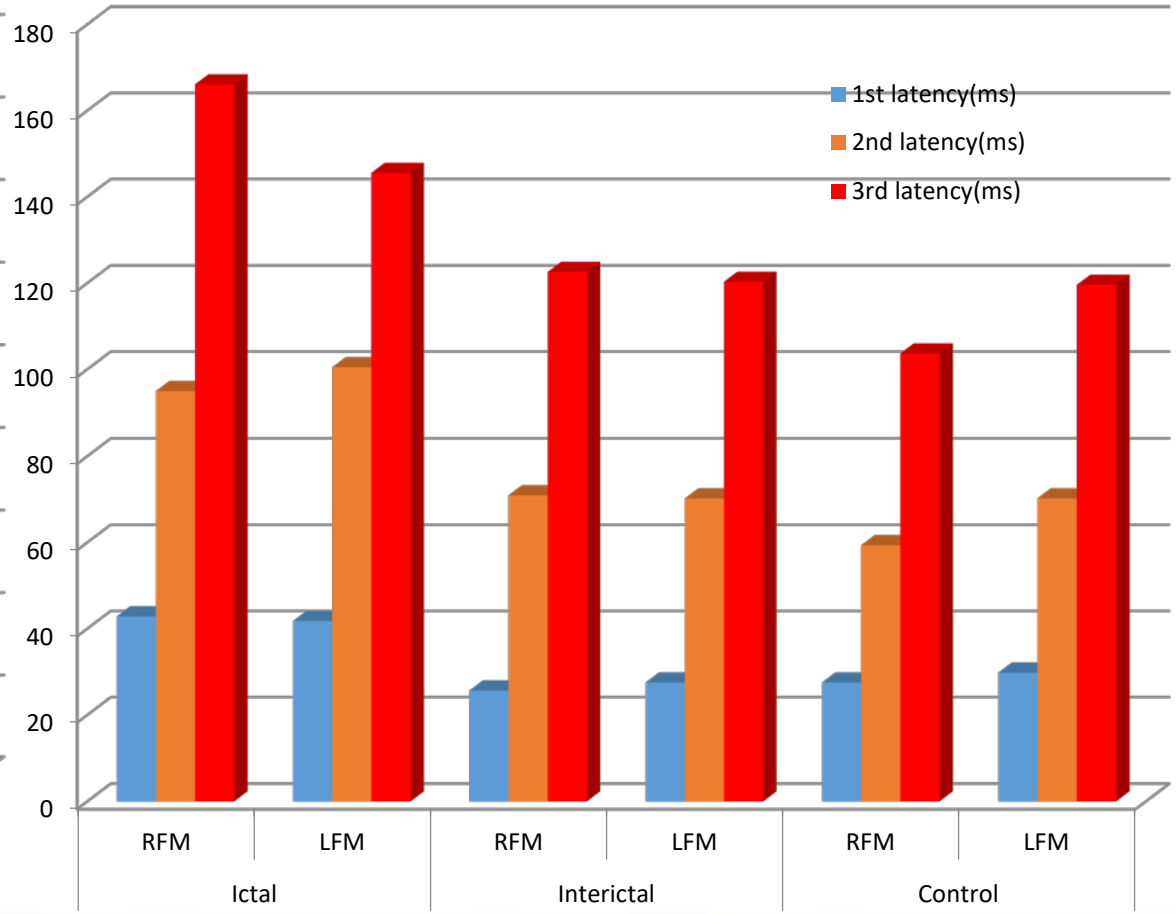
Guo et al, PLoS ONE 2012



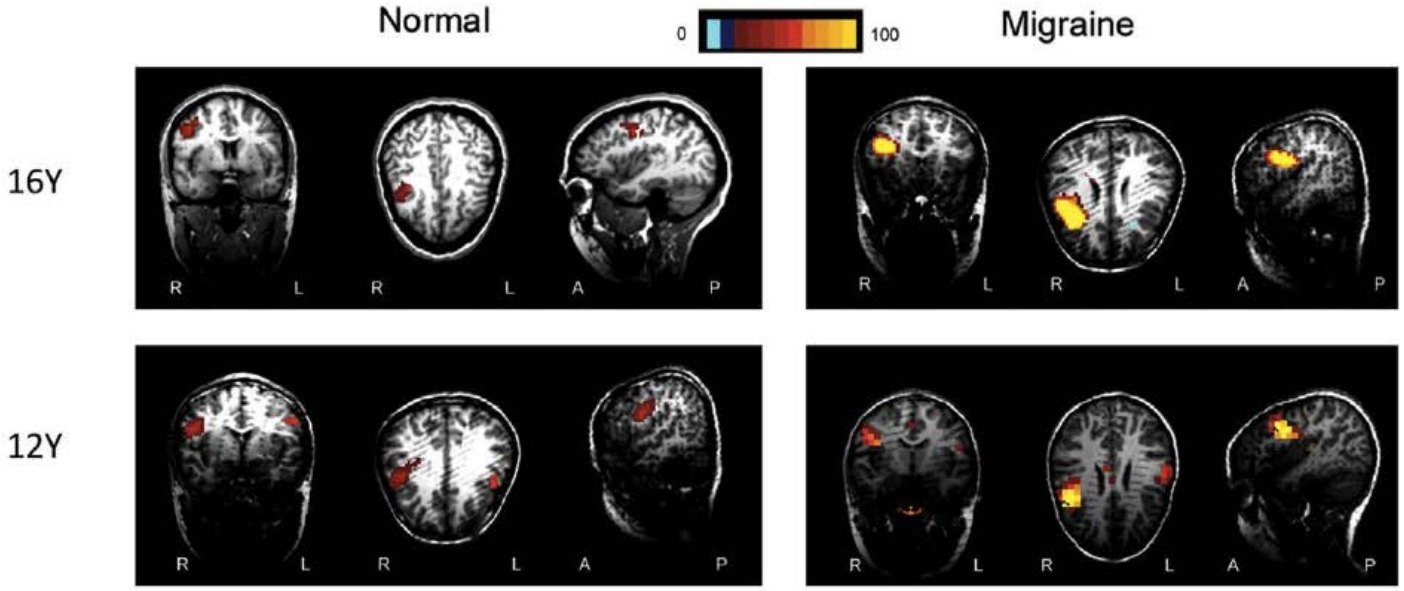


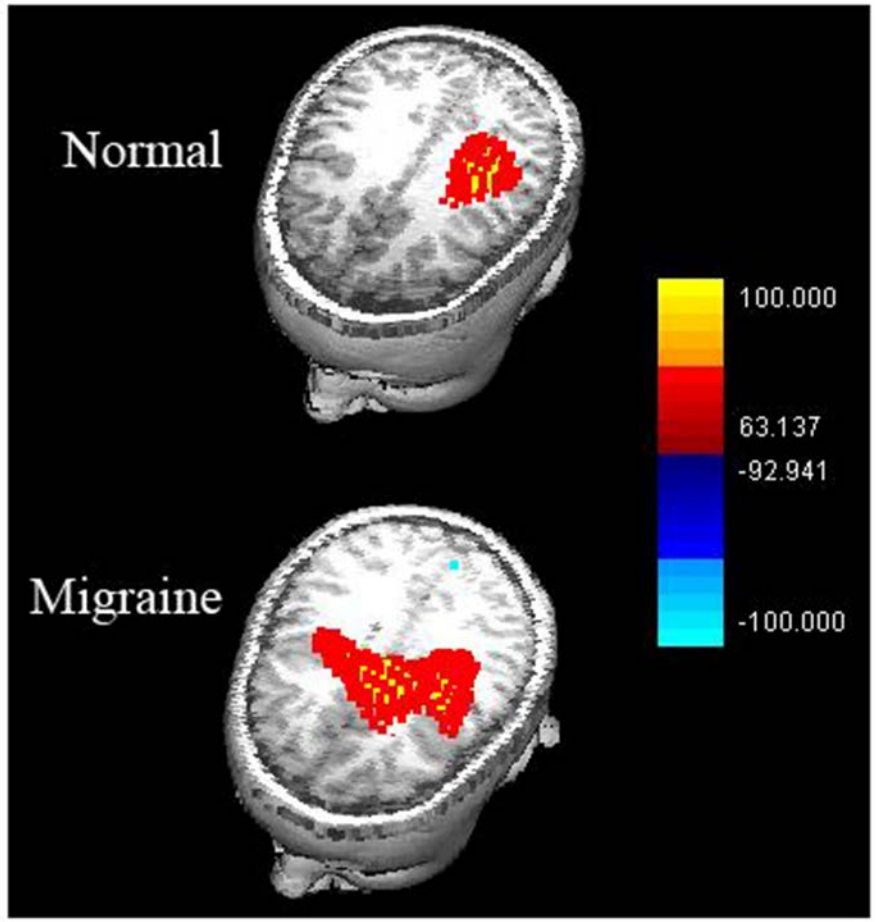
Delayed Movement-evoked Response in migraine





Movement-evoked Magnetic Fields (MEFs) in Children with Migraine (left)





Preventive Treatment

Pathophysiology to direct strategies

- Changing Characteristics
- Menstrual development
- Genetic basis
  - Neuronal
  - Vascular
  - Hormonal
  - Inflammatory
- Hypersensitive nervous system

Preventative Treatment Barriers

- What works best
- Need to reduce to <1/week
- May require 8-10 weeks to achieve dose
- Up to 16 weeks to reach full response
- Adherence

Treatment of Migraine

Preventive

Reviewed by Igarashi et al., 1992, Welch 1993

- Anticonvulsants
  - Phenobarbital
  - Phenytoin
  - Carbamazepine
  - **Valproic acid**
- Antiserotonergic
  - Methysergide
  - **Cyproheptadine**
- Antidepressants
  - **Amitriptyline**
  - Imipramine
  - Phenelzine
  - SSRIs
- NSAIDs
  - Aspirin
  - Naproxen
  - Indomethacin
  - Ketoprofen
- Beta-blockers
  - **Propranolol**, metoprolol, timolol nadolol, atenolol
  - Not alprenolol, osprenolol , acebutolol
- **Ca-channel blockers**
- **Vitamin B_2 (riboflavin)**
- **Biofeedback**

Gaps in Prevention

- Very limited number of studies in pediatric and adolescent headaches
- Translation from adults studies may be problematic
  - Are they really generalizable
- Prevention does not only mean medication

Termiine et al, J Headache Pain, 2011

Table 3 Prophylactic drugs for migraine management evaluated in placebo-controlled and open clinical trials

References	Drug	Daily dose	Age in (years)	Number of patients	Study design	Evidence level	% responders or *p* values (*)
Antihypertensive drugs							
Ludvigsson [50]	Propranolol	60–120 mg	7–16	28	RCT	C	82 vs. 14%
Forsythe et al. [51]	Propranolol	80 mg	9–15	39	RCT		NS
Olness et al. [52]	Propranolol	3 mg/kg	6–12	28	RCT		NS
Sillanpää [53]	Clonidine	25–50 μg	≤15	57	RCT	C	NS
Sills et al. [54]	Clonidine	0.07–0.1 mg	7–14	43	RCT		NS
Calcium channel blockers							
Guideti et al. [55]	Flunarizine	5 mg	10–13	12	OT	A	66%
Sorge et al. [56]	Flunarizine	5 mg	5–11	63	RCT		$p < 0.001$ (HA frequency) $p < 0.01$ (HA duration)
Visudtibhan et al. [57]	Flunarizine	5–10 mg	7–15	21	OT		%66
Battistella et al. [58]	Nimodipine	10–20 mg	7–18	37	RCT	C	NS
Serotonergic drugs							
Gillies et al. [59]	Pizotifen	1–1.5 mg	7–14	47	RCT	C	NS
Lewis et al. [60]	Cyproheptadine	2–8 mg	3–12	30	OT	C	83%
Antidepressants							
Battistella et al. [61]	Trazodone	1 mg/kg	7–18	35	RCT	C	NS
Hershey et al. [62]	Amitriptyline	1 mg/kg	9–15	192	OT	C	80%
Lewis et al. [60]	Amitriptyline	10 mg	3–12	73	OT		89%
Anticonvulsants							
Caruso et al. [63]	Divalproex sodium	15–45 mg/kg	7–16	42	OT	B	76%
Sedaroglu et al. [64]	Divalproex sodium	500–1,000 mg	9–17	10	OT		$p = 0.000$ (HA severity) $p = 0.002$ (HA frequency) $p = 0.001$ (HAduration)
Hershey et al. [65]	Topiramate	1.4 ± 0.7 mg/kg	8–15	75	OT	A	$p < 0.001$ (HA frequency)
Winner et al. [66]	Topiramate	2–3 mg/kg	6–15	162	RCT		NS
Lewis et al. [67]	Topiramate	100 mg	12–17	103	RCT		72%
Miller [68]	Levetiracetam	250–1,500 mg	3–17	19	OT	B	$p < 0.0001$ (HA frequency)
Pakalnis et al. [69]	Levetiracetam	250–1,500 mg	6–17	20	OT		$p < 0.0001$ (HA frequency)
Belman et al. [70]	Gabapentin	15 mg/kg	6–17	18	OT	C	80%
Pakalnis and Kring [71]	Zonisamide	5.8 mg/kg	10–17	12	OT	C	66%

AEDs for Migraine

Wheller, 2000

- GABAergic Agents
  - Valproate
  - Gabapentin
  - Tiagabine
  - Vigabatrin
- Other compounds
  - Topiramate
  - Levetiracetam
  - Zonisamide
  - Pregabalin
  - Oxcarbazepine
  - Lamotrigine

Treatment of Migraine - Prophylactic

- Amitriptyline
  - Non-specific re-uptake inhibitor
  - Effects on
    - Serotonergic receptors
    - Adrenergic receptors
    - Cholinergic receptors
    - Histaminergic receptors

CHAMP Study Design

Real World Approach

- **Subjects to reflect patients seen in typical headache, neurological and pediatric practice**
- **Subjects are children and adolescents, ages 8 to 17 years old**
- **Consistent headache frequency that indicates need for prophylaxis (>4 headaches per month)**
- **Standardized dosing of most commonly used preventative medication**
  - **AMI 1 mg/kg/day**
  - **TPM 2 mg/kg/day**

Study Design

Primary and Secondary Outcomes

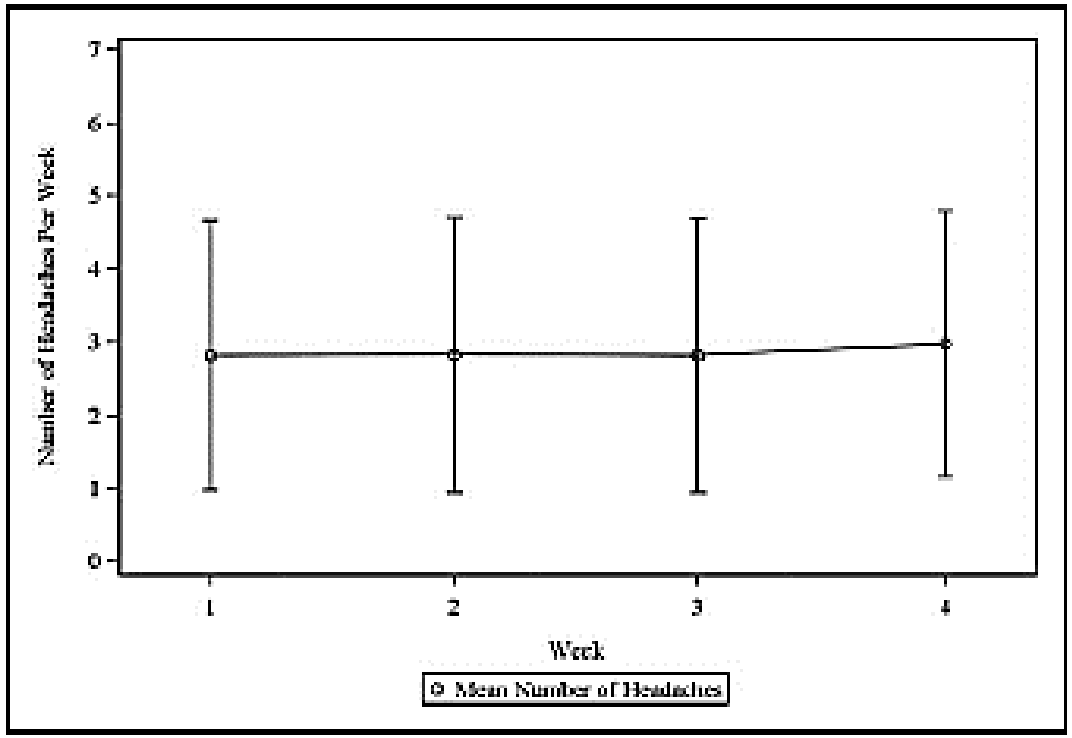
- **Greater than 50% reduction in migraine frequency**
- **Absolute reduction in monthly migraine frequency**
- **Reduction in migraine disability**
- **Tolerability of drug therapies**

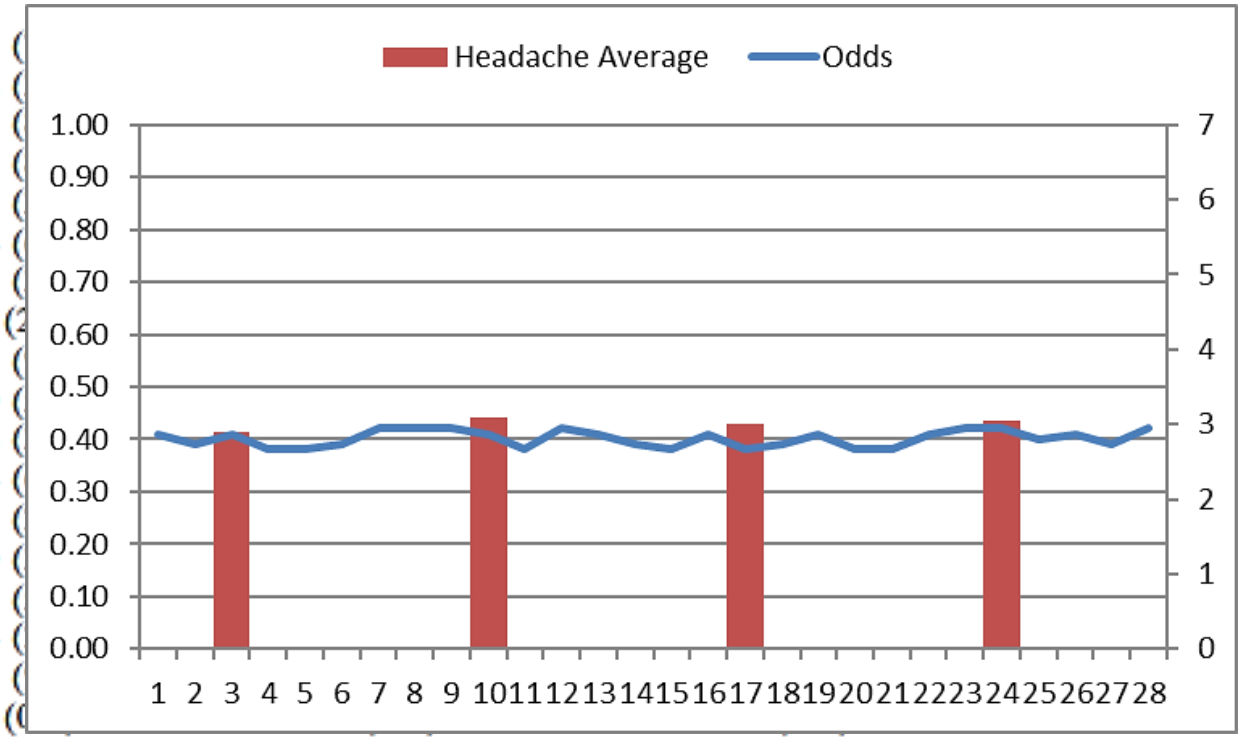
Definitions

- Headache Frequency
  - Headache Day – any headache in 24 hour period midnight to midnight
  - Headache Episode – any headache, start to headache free
  - Migraine Day – any headache with ICHD Migraine characteristics in 24 hour period
  - Migraine Episode – any migraine from start to headache free

Baseline Results

Table 2.—History of Headache Characteristics at Screening Visit†





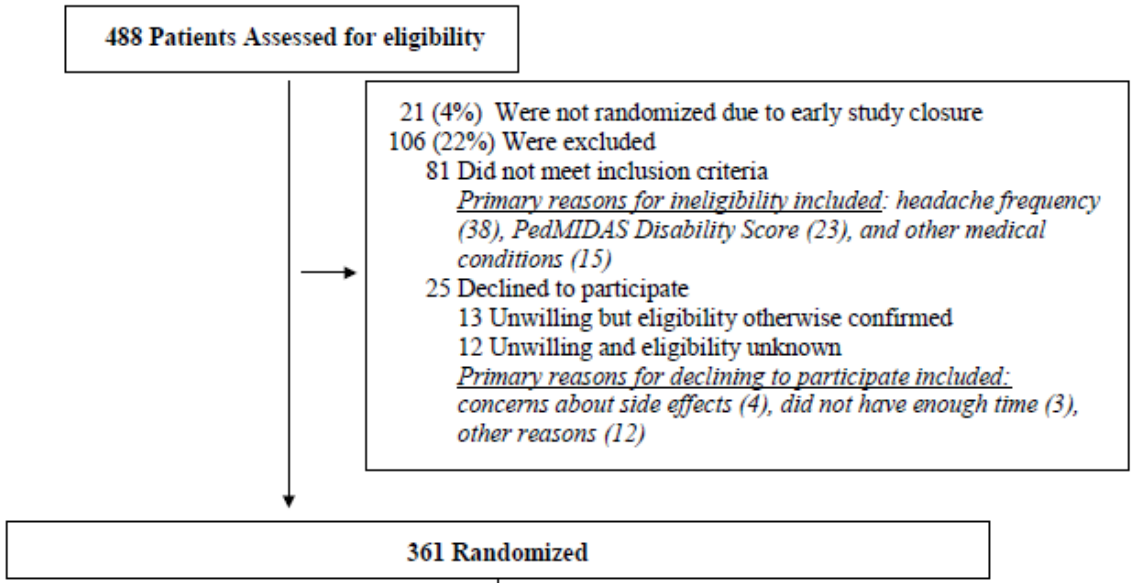
Headache changes activity level	423 (89%)	321 (89%)	102 (89%)
Activity or play made headache worse*	413 (87%)	307 (85%)	106 (93%)

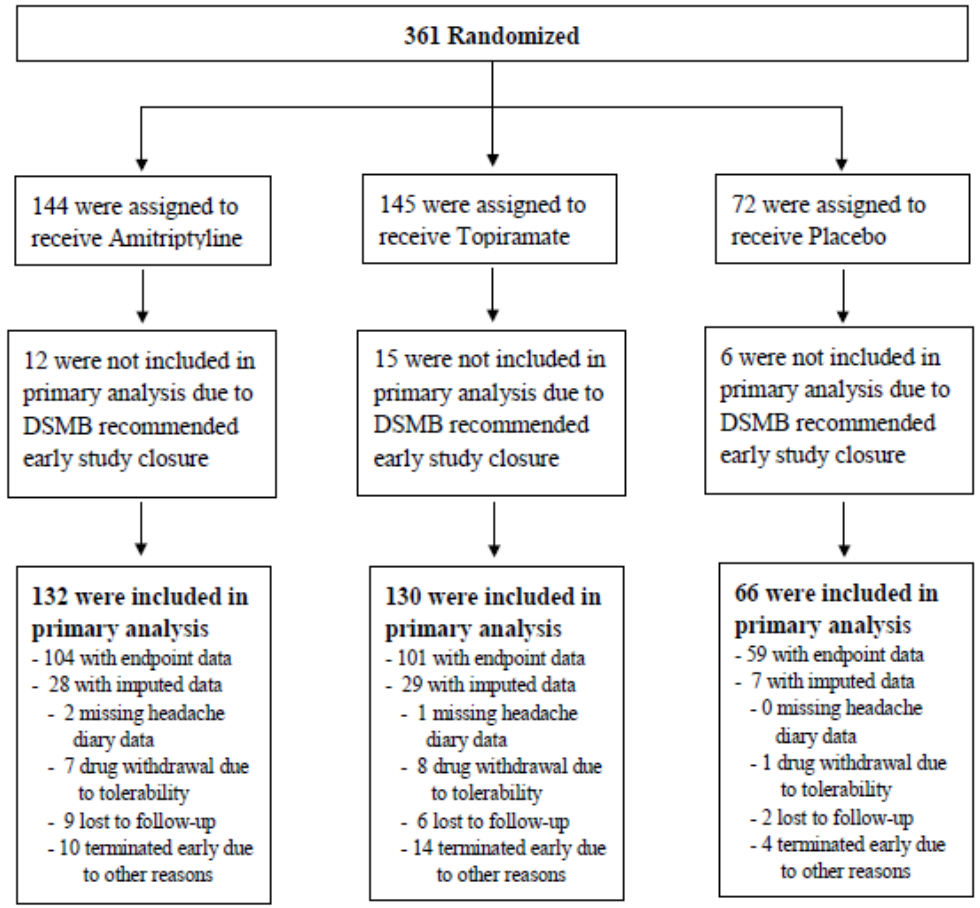
Protocol - Powers, et al, Headache 2016

CHAMP results

- Primary - ≥ 50% reduction in headache frequency (day)
  - 28 days prior to randomization vs 28 days prior to end of treatment phase
- Secondary
  - Headache Disability – PedMIDAS; compare randomization to end of treatment
  - Tolerability – whether or not subject completed entire 24 weeks
- Additional Secondary
  - Absolute reduction in headache frequency
  - Side effects

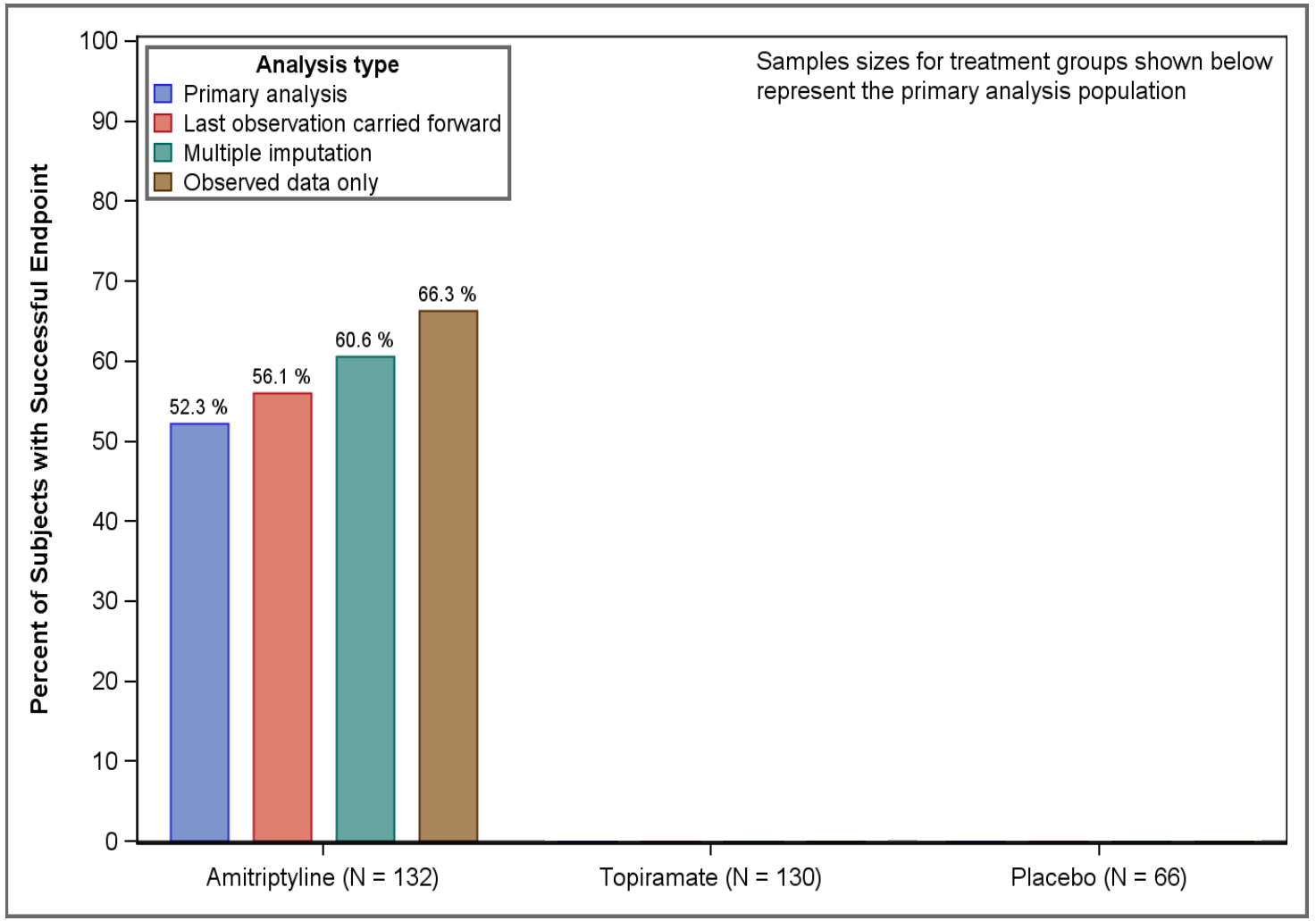
CHAMP results – Consort



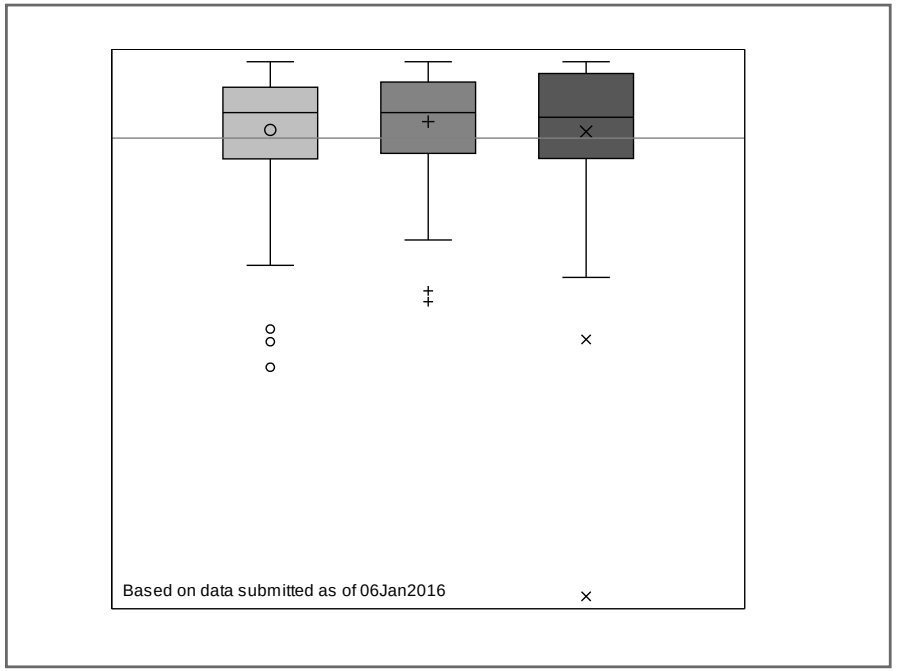


Primary (>50%)

- Primary – all subjects without data considered failures
- Last Observation Carried Forward – most recent visit with 28 day calendar
- Multiple Imputation – methods with multiple chains
- Observed data – all subjects with baseline and last 28 days



Primary (>50% distribution)



Neutriceuticals

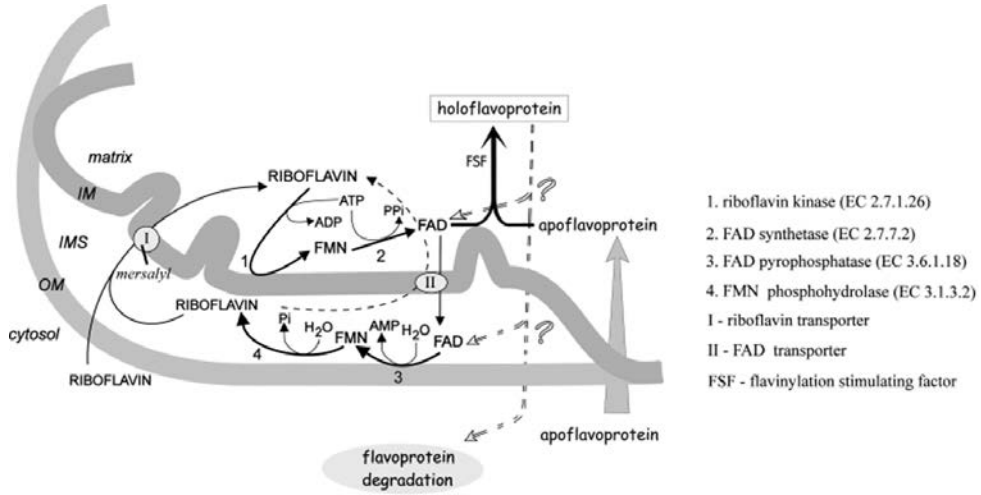
Neuronal Theory of Migraine

- **Cortical hyperexcitability**
  - Mitochondrial Association
    - Riboflavin
    - CoEnzyme Q10
    - Carnitine
    - Mitochondrial disorders

Riboflavin

- Involved in initial stages of electron transport
- Deficient in some migraineers
- Prophylactic response similar to VPA

- Barile, Eur J Biochem 267:4888 2000



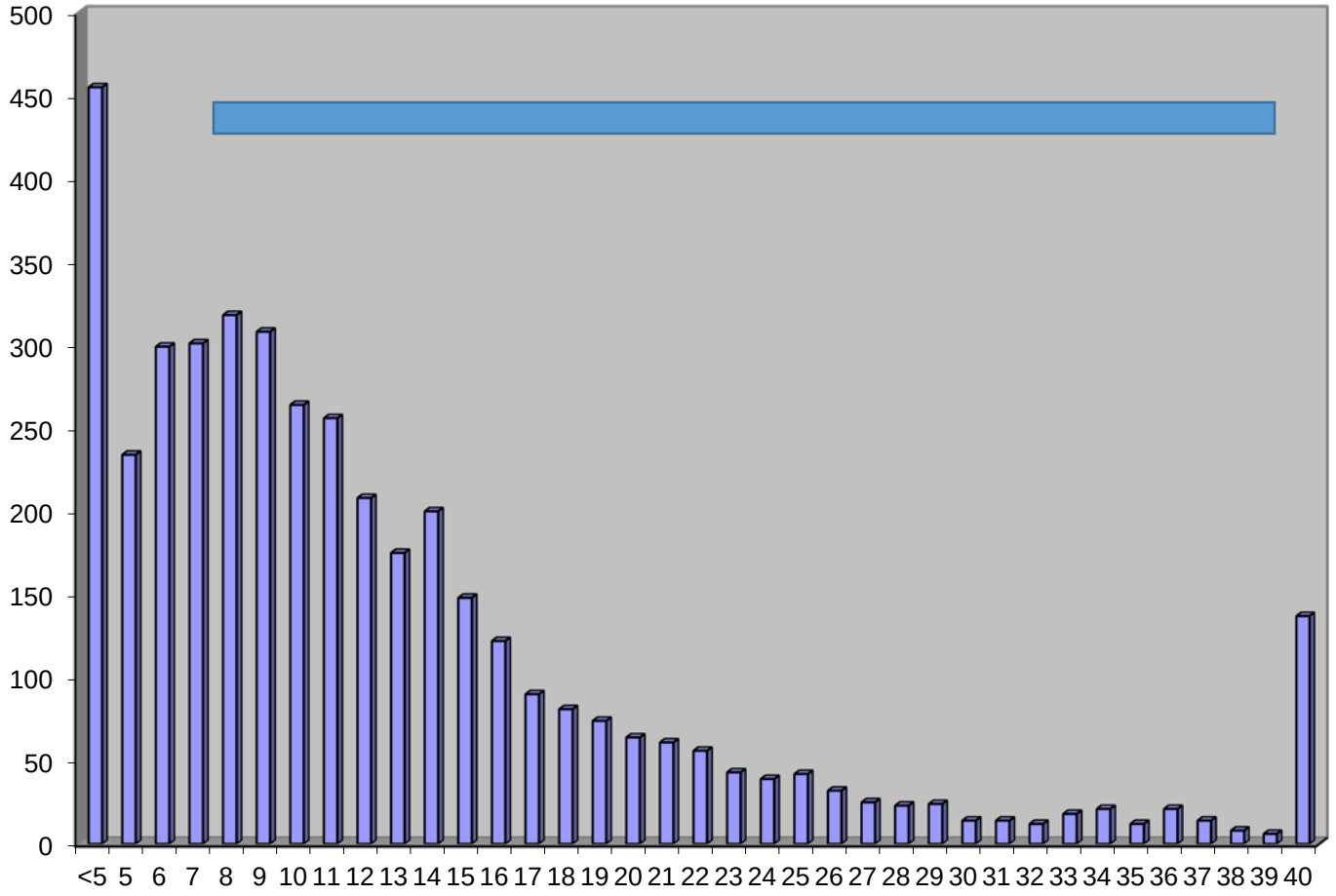
Riboflavin

Schoenen et al., 1998

- 54 patients in Belgium and Luxemburg
- Double-blinded, randomized placebo-controlled trial
- Reduction in HA frequency and headache days

- 50% “responders”
  - Riboflavin 59%
  - placebo 15%
- Number needed to treat
  - 2.3 (for adverse events 33.3)
  - vs Divalproex - 1.6 (for adverse events 2.4)
- ? Increases complex I and II, ∴ mitochondrial

Riboflavin


500
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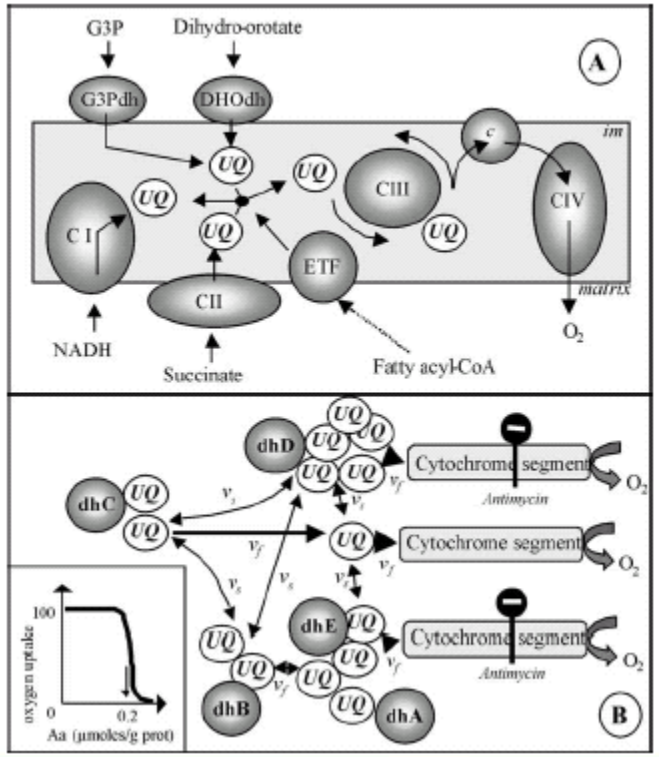
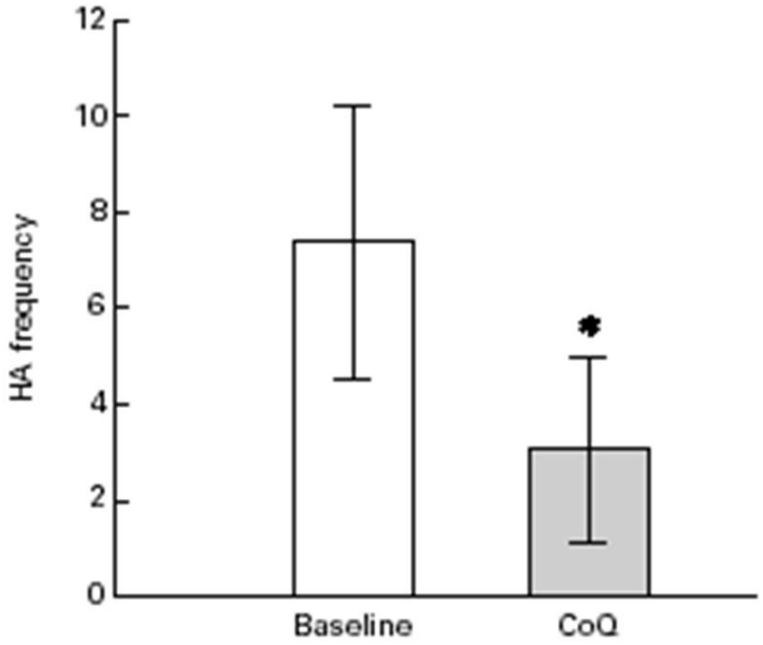
<5 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40

CoEnzyme Q10

- Geromel et al, 2002

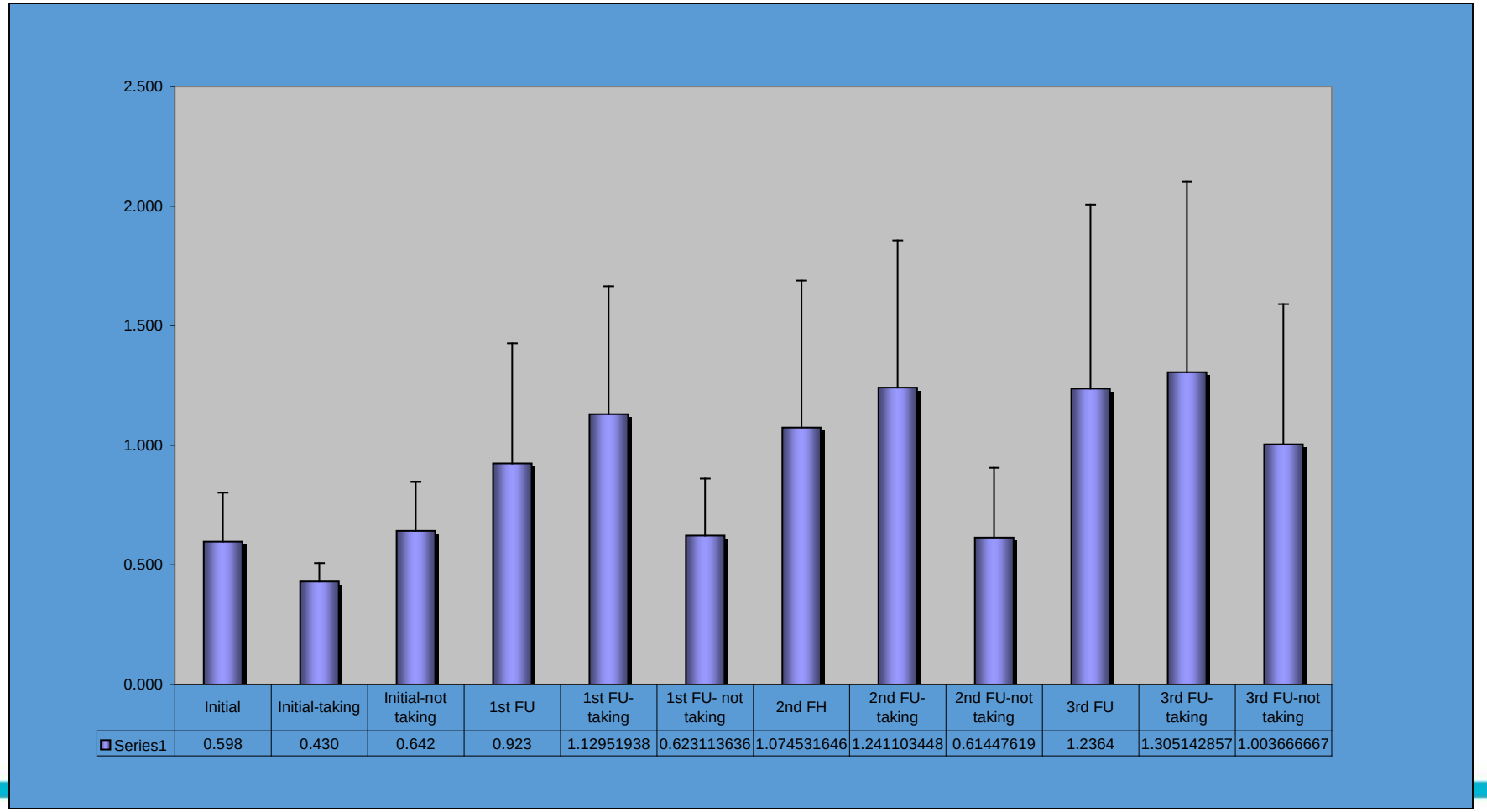


- Rozen et al, 2002 *Cephalalgia*



Q10 and CCHMC

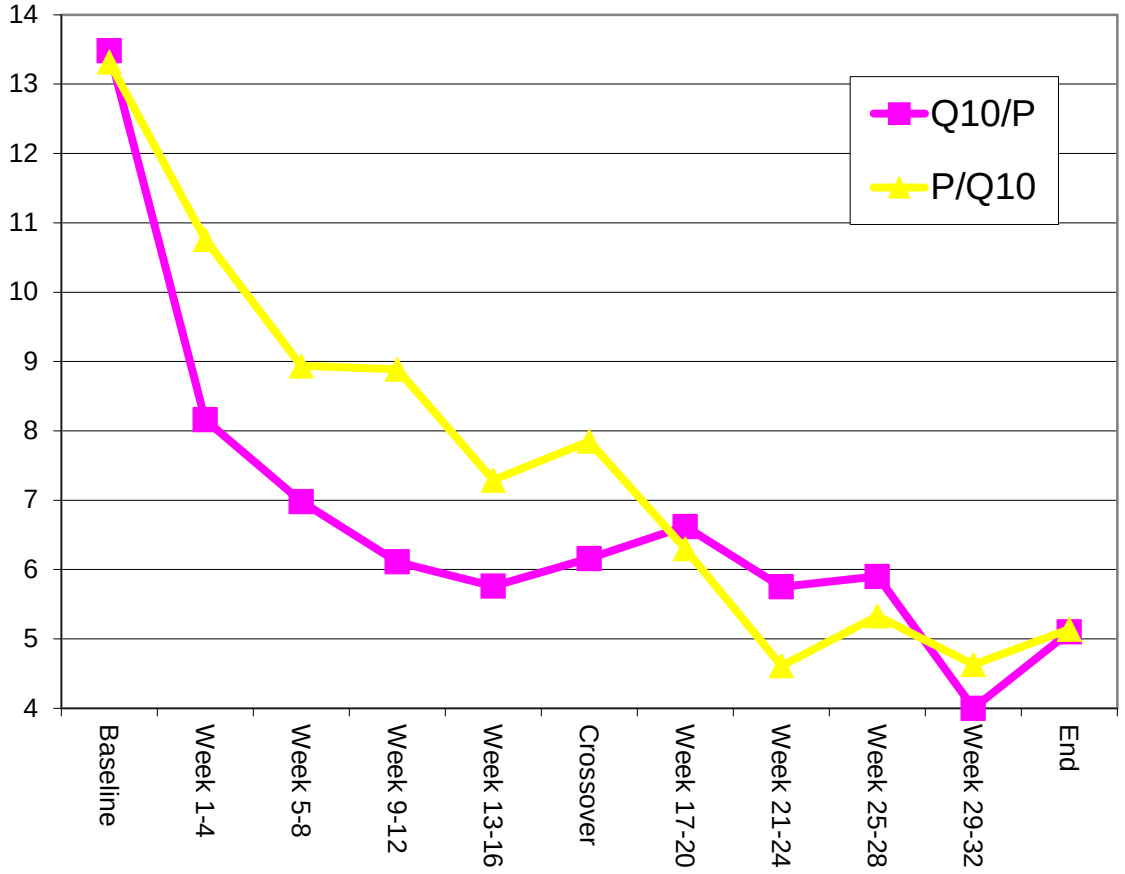
Hershey et al, Headache 2007

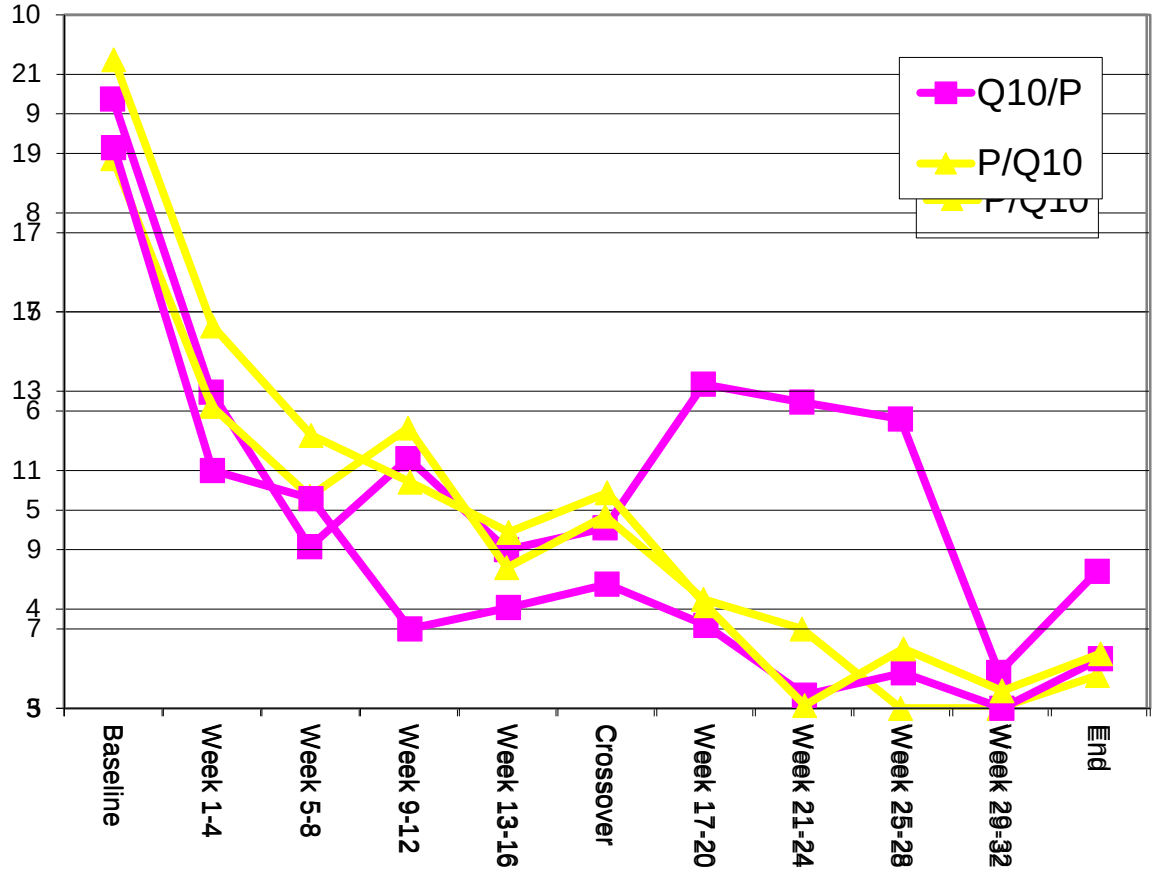


	Initial	Initial-taking	Initial-not taking	1st FU	1st FU-taking	1st FU- not taking	2nd FH	2nd FU-taking	2nd FU-not taking	3rd FU	3rd FU-taking	3rd FU-not taking
Series1	0.598	0.430	0.642	0.923	1.12951938	0.623113636	1.074531646	1.241103448	0.61447619	1.2364	1.305142857	1.003666667

Q10 and CCHMC

Slater et al, Headache 2011





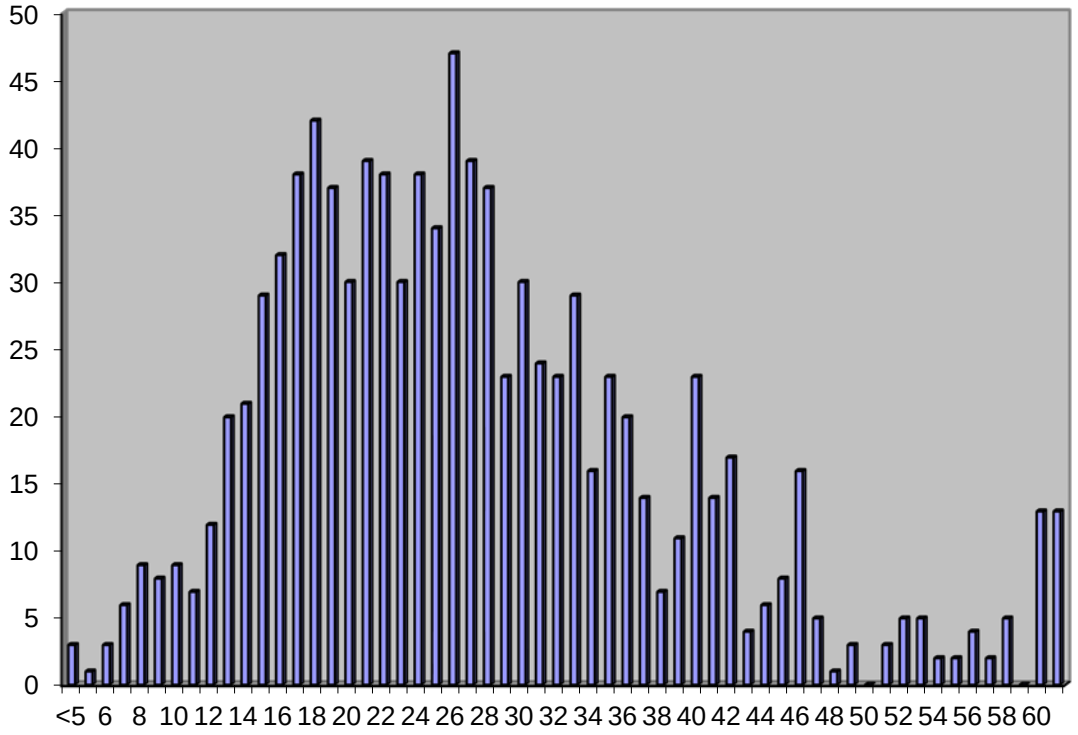
Vitamin D

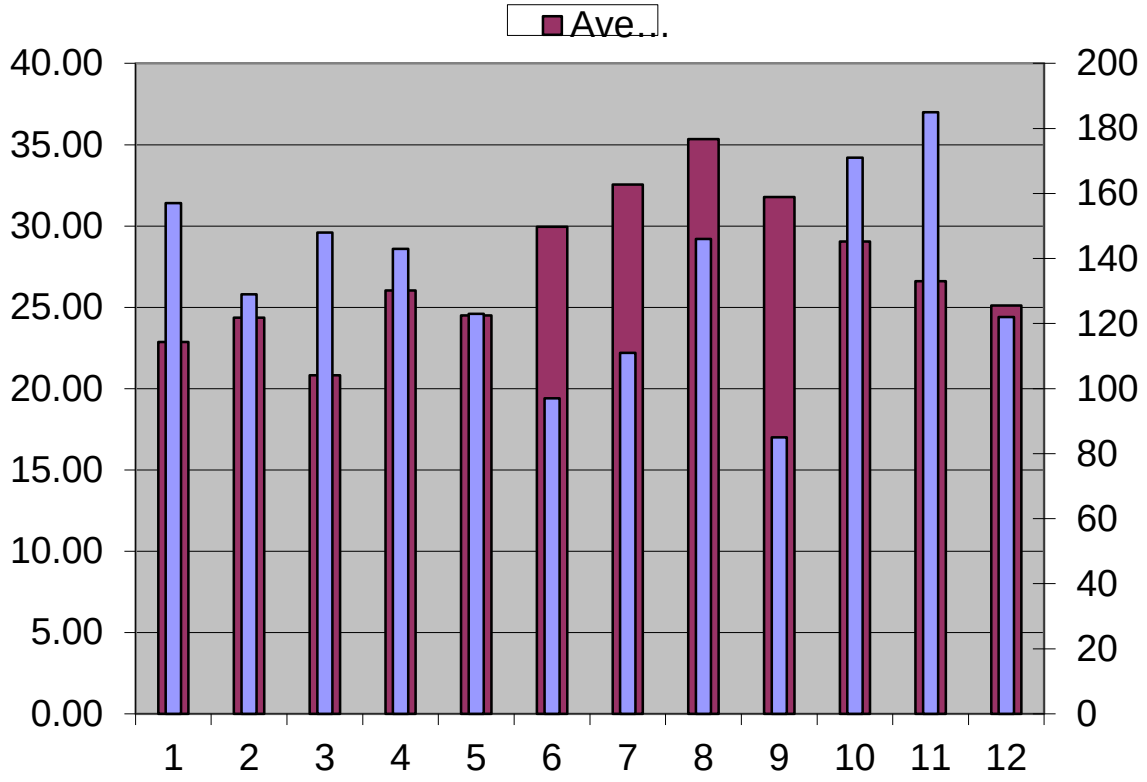
Vitamin D

- Neurological implications of Vitamin D
  - Association with Multiple Sclerosis
  - Association with early dementia
  - Association with chronic pain conditions
- Increasing incidence of Vitamin D deficiency

Vitamin D

Initial

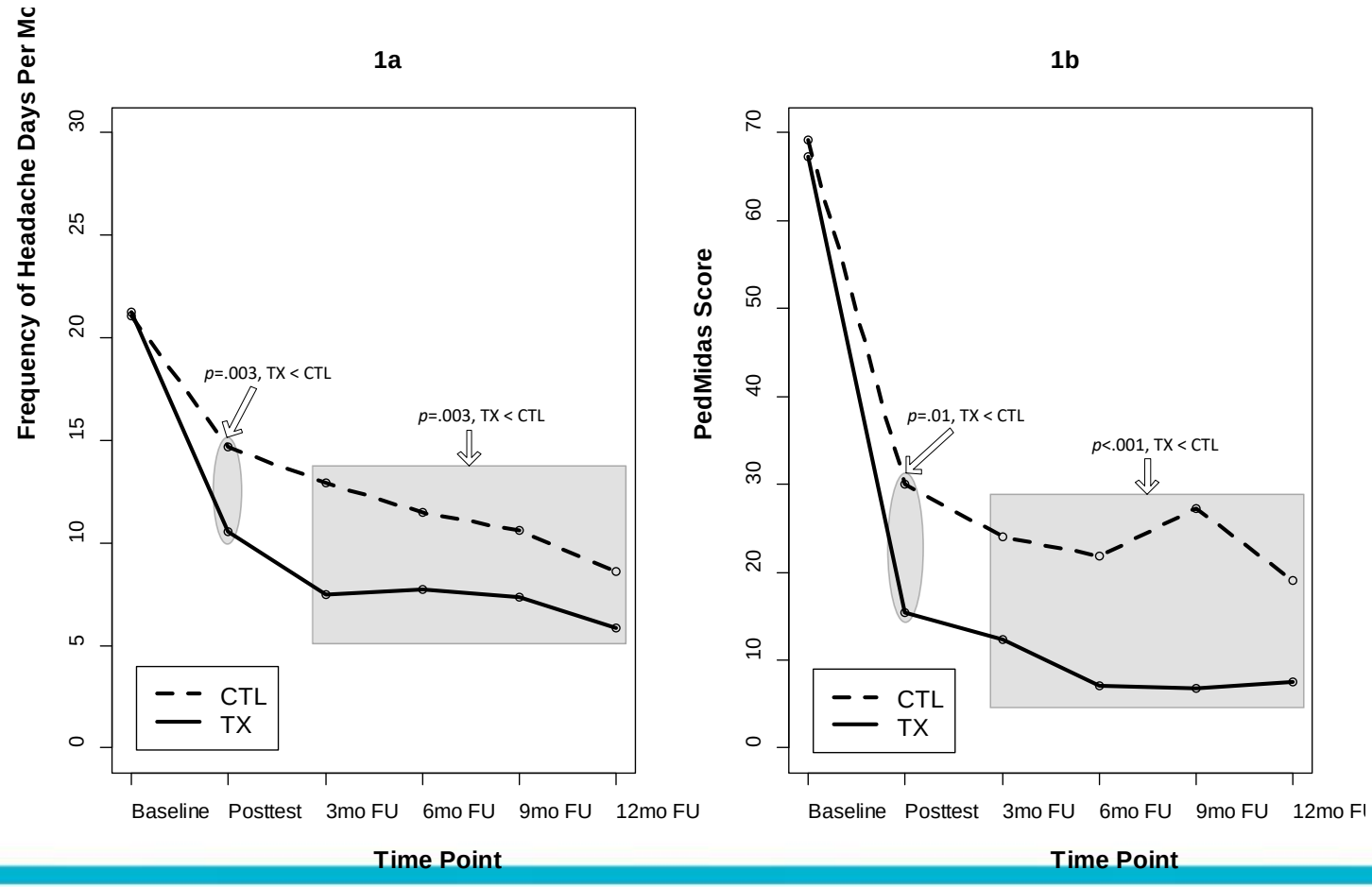




Coping Skills in Chronic Migraine

- NIH/NINDS
- Chronic Migraine (>15 days per month)
- PedMIDAS restriction (>20 and <140)
- No Medication Overuse
- Randomized to Coping Skills vs. Education Control
- 8 year treatment, 20 week treatment phase, 12 month follow-up
- Enrollment and Treatment phase complete, 12 month follow-up pending

Coping Skills in Chronic Migraine

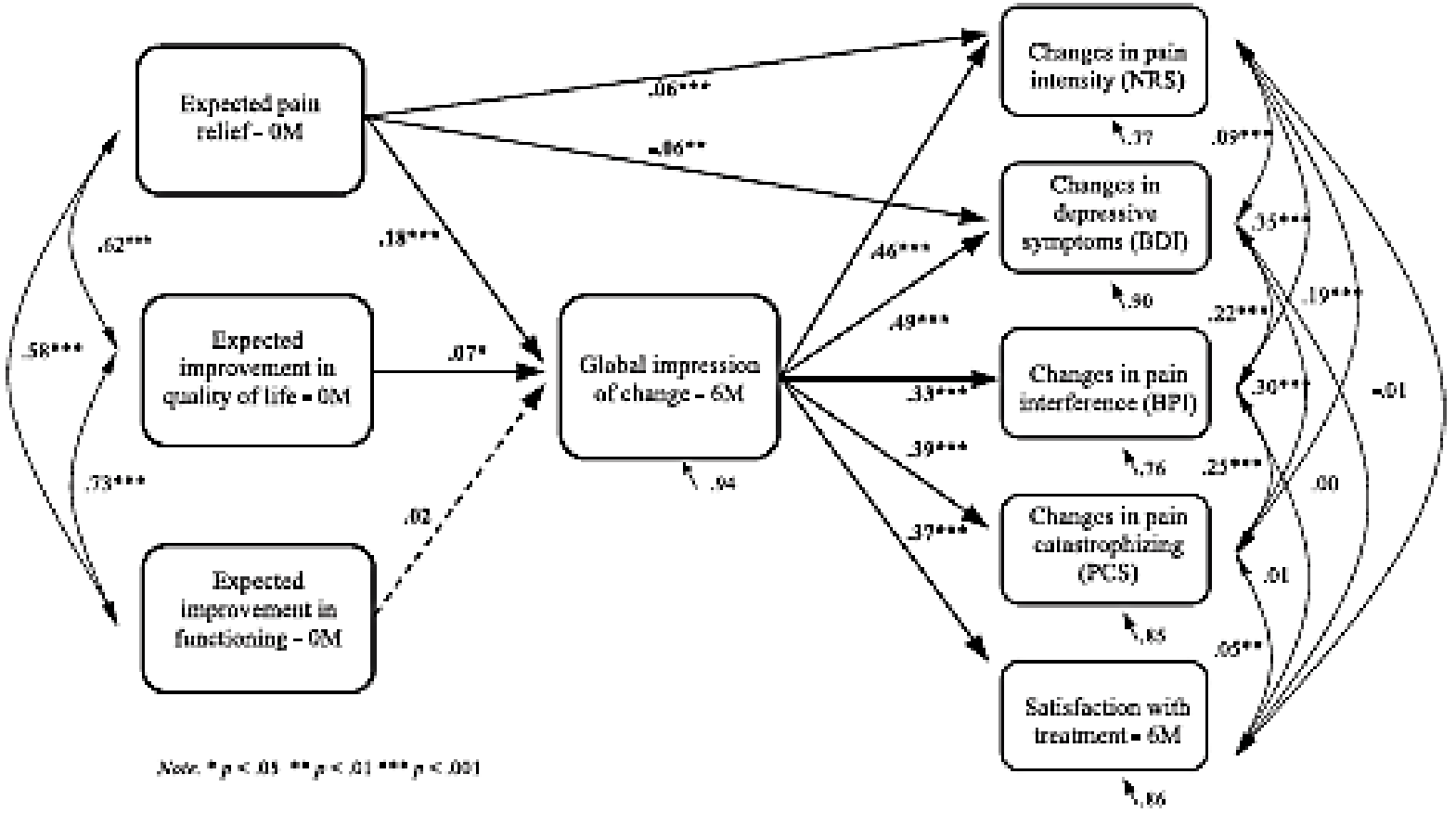


Where do we go from here?

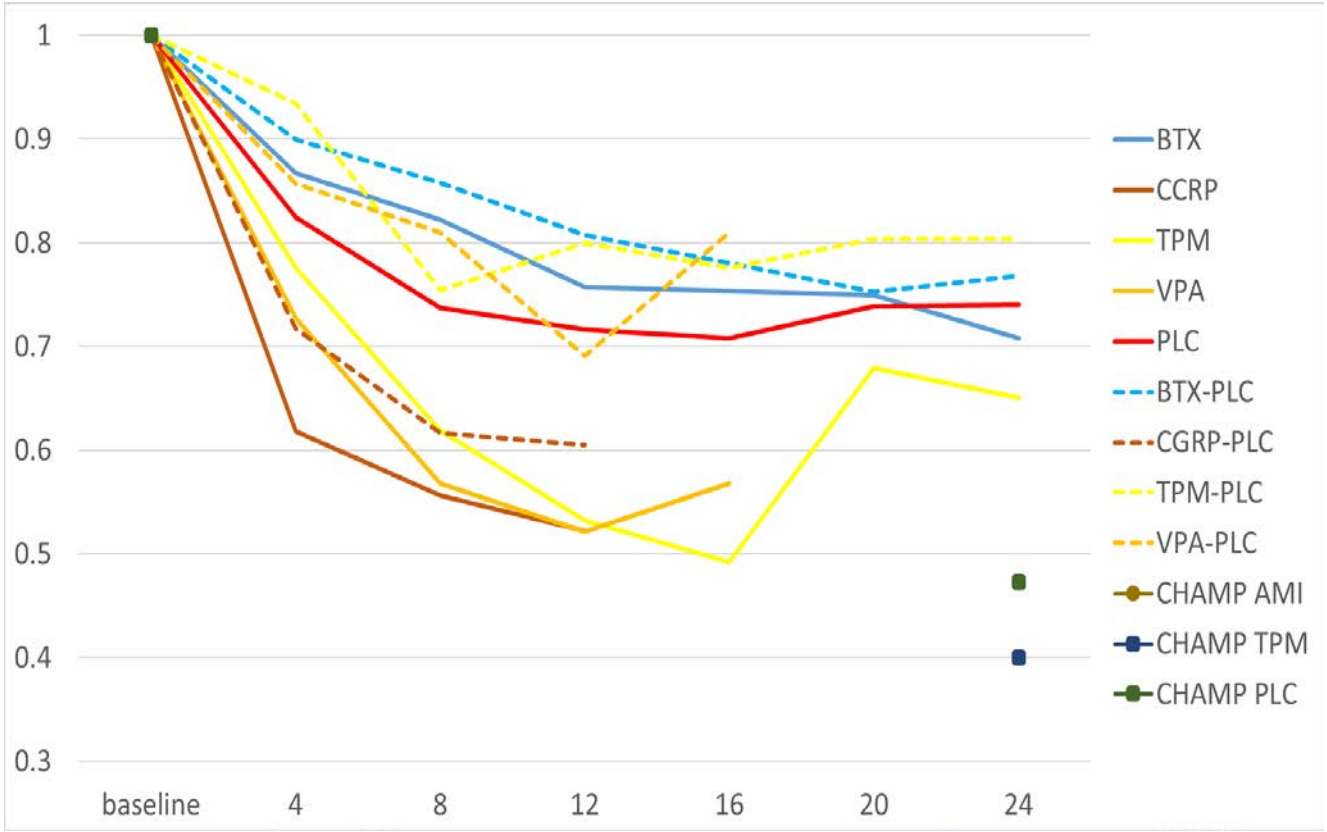
- Children and adolescents with real world migraine get better
  - 50 to 70% with a >50% reduction in headache frequency
  - Mean frequency at end down to almost 1 per week
  - Thus, multidisciplinary care works
- Biochemical effect of medication is not the reason
- Is the reason expectation of response?
- What do we do with the 30-40% that don’t get better?

Expectation of Response

Cormier et al, Pain 2016



Trajectory Response



Putting it all together – a treatment strategy

- Patients and parents present because headaches are impacting their lives “Need to do something”
- Baseline of CHAMP shows that just because you diagnosis, provide acute treatment, and introduce healthy habits, it’s not enough
- Expectation of response is needed
  - Pharmaceutical expectation
  - Cognitive Behavioral Therapy
  - Wait and see
  - “The Expert Effect”

Strategies

- Migraine in pediatrics and adolescents can be diagnosed with standardized criteria
- The “why” of migraine is multifactorial, but likely a genetic basis with environmental factors
- A multidisciplinary treatment plan is ideal
- Plan must include education of the patient and addressing barriers while enhancing expectation
- SMART and MOST designs may be the next way to go

Thank you

Thank you

- Headache Center
  - Scott Powers, PhD, FAHS
  - Marielle Kabbouche, MD, FAHS
  - Hope O'Brien, MD
  - Joanne Kacperski, MD
  - Susan LeCates, FNP
  - Shannon White, DNP
  - Jessica Weberding, PNP
  - Mimi Miller, FNP
  - Shawna Hess, PNP
  - Ann Segers, RN
  - Paula Manning, RN
  - Judy Bush, RN
  - Anne Jordan-Lynch, PhD
  - Shalonda Slater, PhD
  - Antoinette Green
  - Janelle Allen
- Collaborators
  - AMI/TPM Comp Effectiveness
    - Chris Coffey, PhD
    - Dixie Ecklund
    - Linda Porter, PhD
    - Deborah Hirtz, MD
  - Genomics
    - Frank Sharp, MD
    - Yang Tang, MD, PhD
    - Paul Horn, PhD
  - Allodynia
    - Rami Burstein, MD, PhD
    - Paul Winner, DO
  - MEG
    - Jing Xiang, MD, PhD
    - Milena Korostenskaja, PhD
  - Menstrual Hormonal Levels
    - Vince Martin, MD
    - Timothy Houle, PhD