

Trying to Understand Headache

(Models, Concepts and Ideas)



Dr Paul Davies
Maastricht 2011

Amount of research interest in rare and common neurological conditions: bibliometric study

Rustam Al-Shahi, Robert G Will, Charles P Warlow

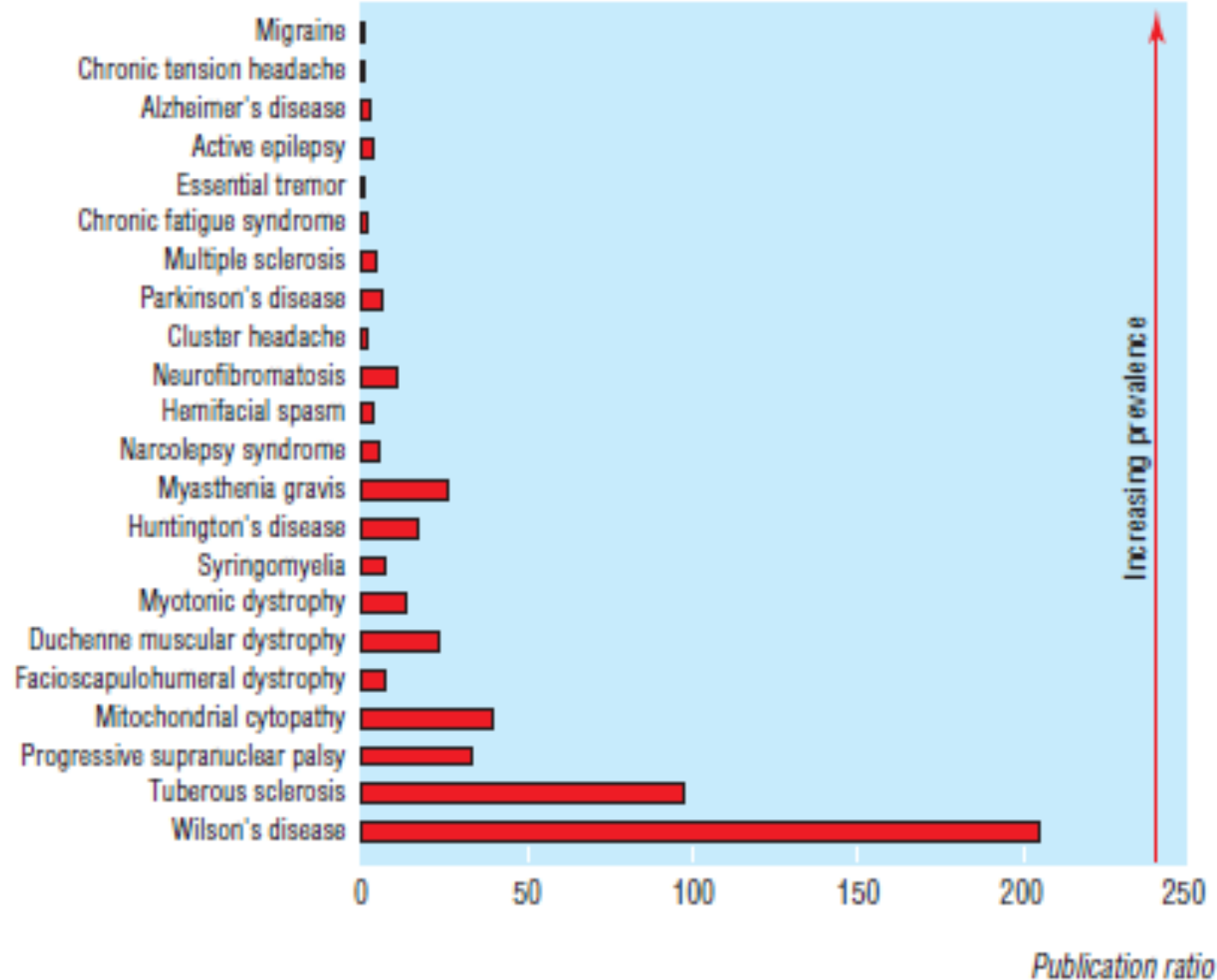
Neurologists are often accused of being interested in only rare incurable diseases. Although this may have been true in the past, today's neurologists claim to be more concerned with common disorders—but are they really?

death, economic hardship, and loss of quality of life. It is recognised that funding for research into a disease should be proportional to that disease's burden on society²; however, conditions that account for 90% of the global burden of disease receive less than one tenth of the world's health budget.³

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BMJ 2001;323:1461-2

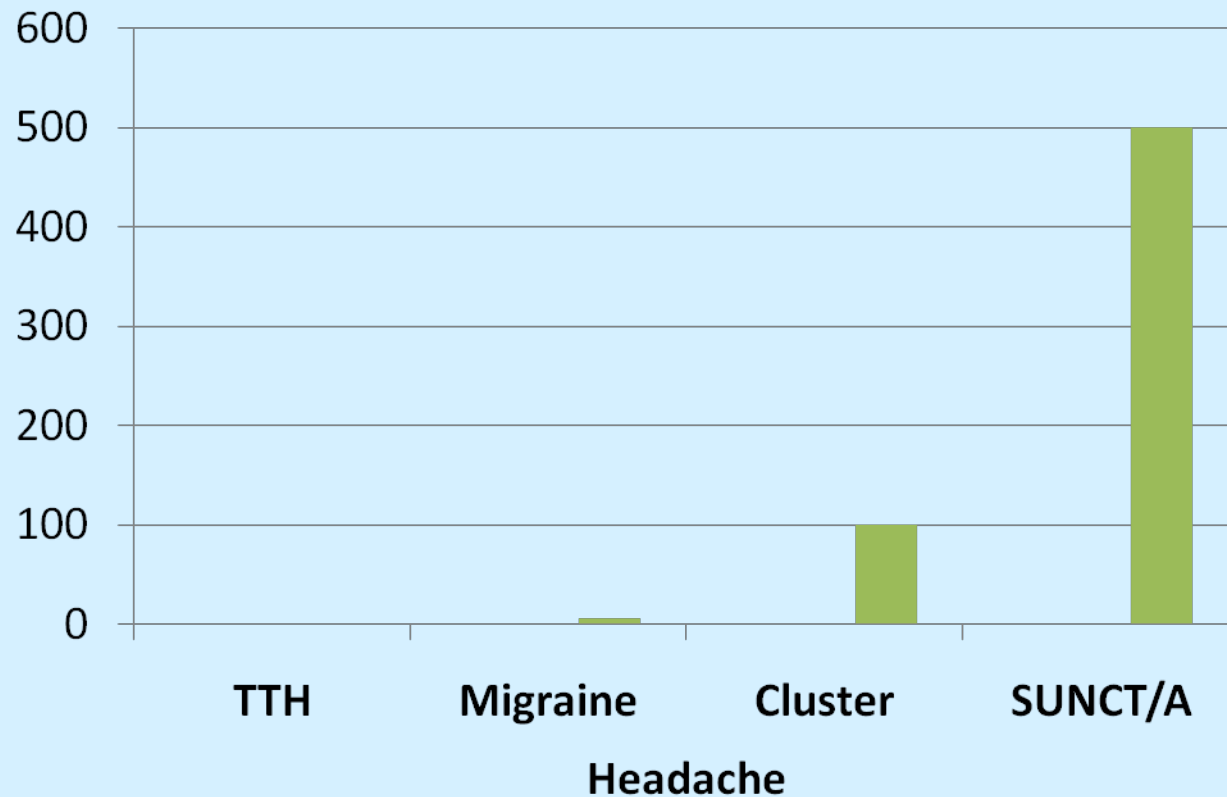


Publications Per Prevalence (Google Scholar 2010)

In a population of 100,000

	Sufferers	Publications	Ratio
TTH	30,000	7,540	0.25
Migraine	15,000	91,200	6
Cluster	200	19,600	100
SUNCT/A	6.6	3,410	500

Google Scholar (2010) Publications per Prevalence Ratios



doi:10.1111/j.1468-2982.2009.01846.x

Local field potentials reveal a distinctive neural signature of cluster headache in the hypothalamus

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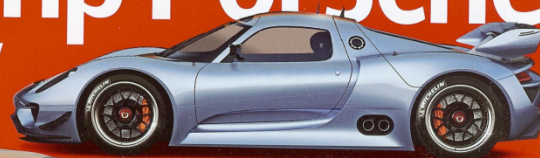
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Our Audi A8: final report plus Big Alfas for a song

p65



TACs and Lamborghini



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Episodic Migraine



Transformed Migraine



Tension-type Headache



Tension-type Headache



Table 4. Lifetime prevalence of all primary and secondary headaches and 95% confidence limits in parentheses (46).

PRIMARY HEADACHES

1.1	Migraine without aura	9% (7-11)
1.2	Migraine with aura	6% (5-8)
2.1	Episodic tension-type headache	66% (62-69)
2.2	Chronic tension-type headache	3%(2-5)
3.1	Cluster headache	0.1% (0-1)
4.1	Idiopathic stabbing headache	2% (1-4)
4.2	External compression headache	4% (3-6)
4.3	Cold stimulus headache	15% (11-17)
4.4	Benign cough headache	1% (0-2)
4.5	Benign exertional headache	1% (0-2)
4.6	Headache associated with sexual activity	1% (0-2)

SECONDARY HEADACHES

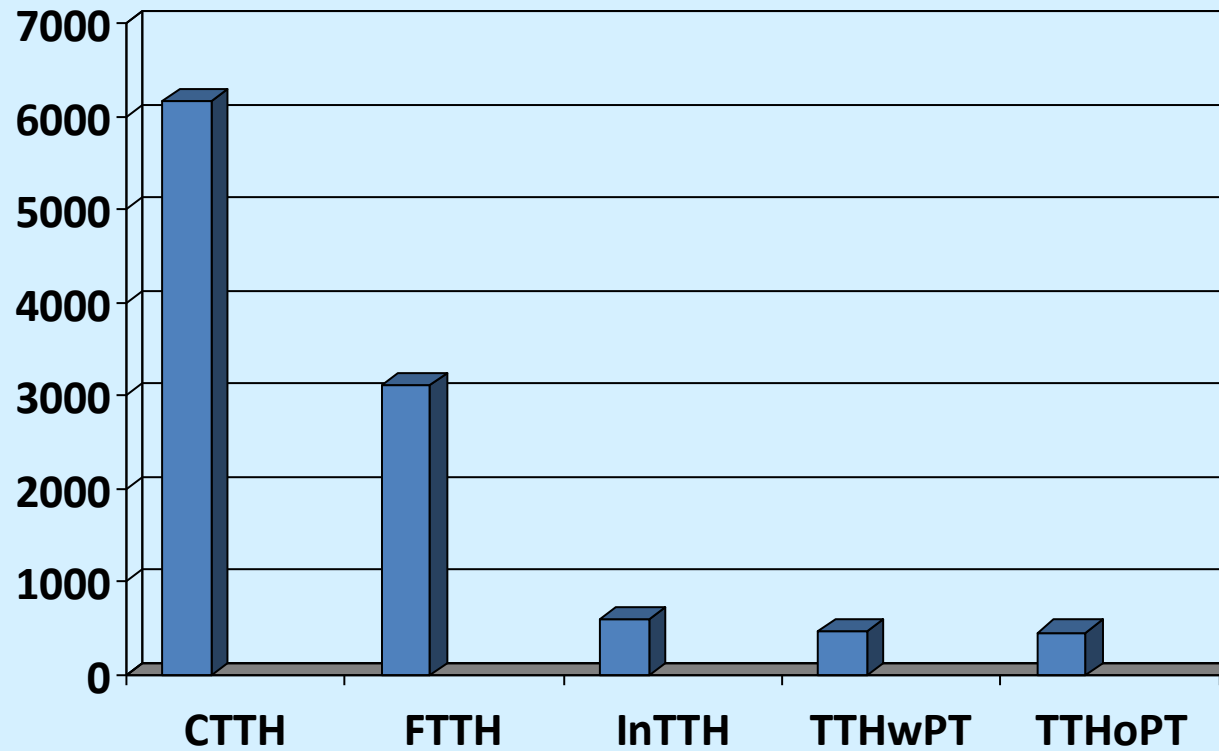
Headache associated with:

5.	Head trauma	4% (2-5)
6.	Vascular disorders	1% (0-2)
7.	Non-vascular intracranial disorders	0.5% (0-1)
8.	Substances or their withdrawal (excl. hangover)	3% (2-4)
8.1.4	Hangover	72% (68-75)
9.	Fever headache	63% (59-66)
10.	Metabolic disorders	22% (19-25)
11.2	Disorders of the neck	1% (0-2)
11.3	Disorders of the eyes	3% (2-4)
11.4	Disorders of the ears	0.5% (0-1)
11.5	Disorders of nose or sinuses	15% (12-17)
12.	Cranial neuralgias	0.5% (0-1)
13.	Headache not classifiable	0.3% (0-1)

Google Scholar Publications 2010

Tension-type headache (all)	7540
Chronic TTH	6170
Frequent TTH	3110
Infrequent TTH	598
TTH with pericranial tenderness	476
TTH without pericranial tenderness	461

Google Scholar 2010 TTH PPP



What is Tension-type Headache?

What is Migraine?

What is Chronic tension-type headache?

What is Chronic Migraine?

Are they interconnected?

How different are they?

Tension-type Headache

Tension-type headache is the most common headache subtype in the world.

It is defined as a headache that is bilateral, pressing or tightening in quality, mild to moderate in severity, with possible light or sound sensitivity, but not both. It is not aggravated by physical activity, nor associated with vomiting.

Lifetime prevalence of TTH is 69% in men and 88% in women...

Ailani J 2010

ICH-2

This is the most common type of primary headache: its lifetime prevalence in the general population ranges in different studies from 30 to 78%.

At the same time, it is the least studied of the primary headache disorders, despite the fact that it has the highest socio-economic impact.

IHS	Diagnosis	ICD-10
2	TENSION-TYPE HEADACHE (TTH)	G44.2
Previously used terms	Tension headache, muscle contraction headache, psychomyogenic headache, stress headache, ordinary headache, essential headache, idiopathic headache and psychogenic headache	
Coded elsewhere	Tension-type-like headache attributed to another disorder is coded to that disorder.	

Frequent TTH

Diagnostic criteria:

At least 10 episodes occurring on ≥ 1 but < 15 days per month for at least 3 months (≥ 12 and < 180 days per year) and fulfilling criteria B-D

Headache lasting from 30 minutes to 7 days

Headache has at least two of the following characteristics:

bilateral location

pressing/tightening (non-pulsating) quality

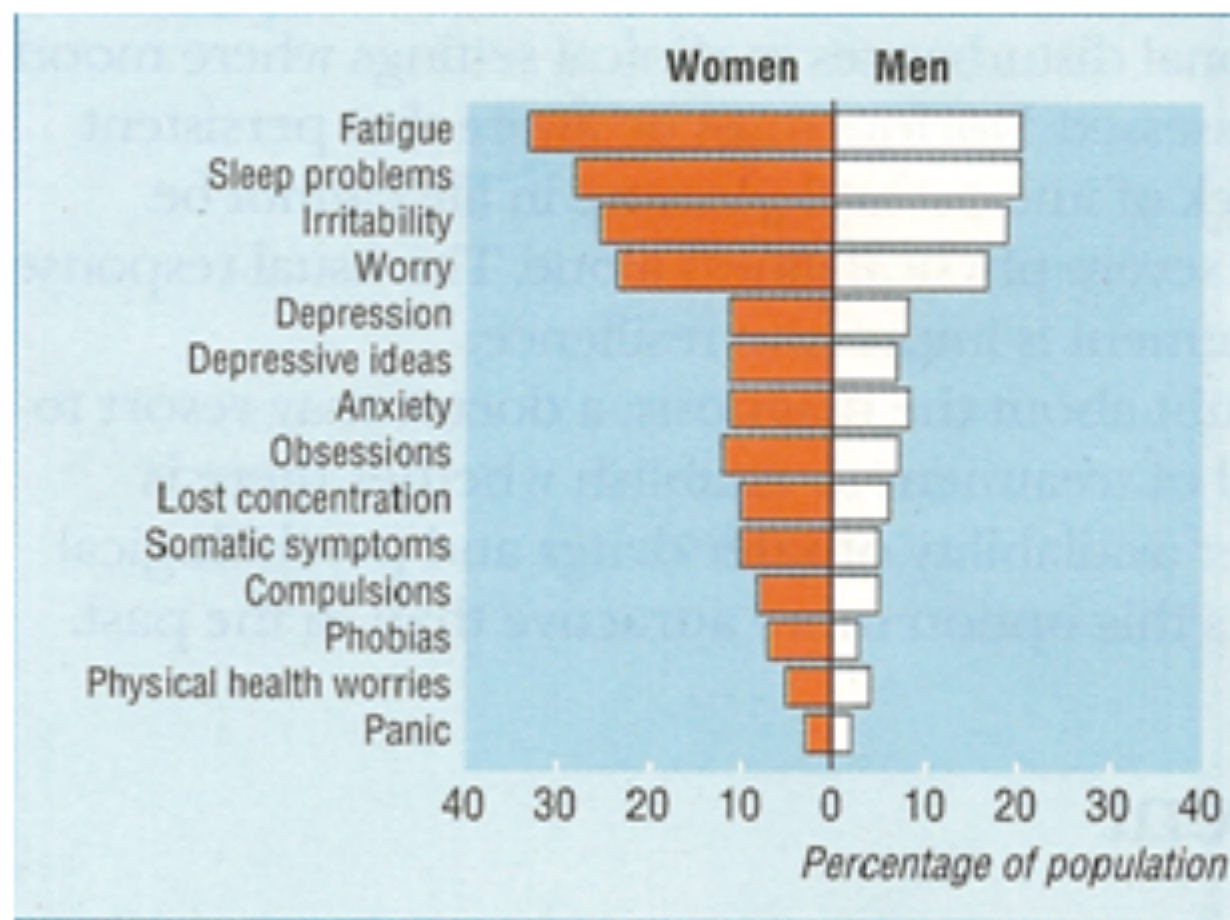
mild or moderate intensity

not aggravated by routine physical activity such as walking or climbing stairs

Both of the following:

no nausea or vomiting (anorexia may occur)

no more than one of photophobia or phonophobia



“Neurotic” symptoms, including depression, are continuously distributed in the UK population

Tension-type-like Headaches

Fatigue (not in IHS-2)

Hunger (headache attributed to fasting, 10.5)

**Hormonal (oestrogen withdrawal headache
8.4.3)**

**Alcohol (immediate alcohol-induced headache
8.1.4.1)**

Dehydration

Environmental (eg fumes, sun over-exposure)

Fasting Headache

Paola Torelli • Gian Camillo Manzoni

ache Disorders (“Headache attributed to disorder of homeostasis”). A study conducted in Denmark’s general population found a lifetime prevalence rate of 4.1% for fasting headache. Fasting headache is usually diffuse or

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The only certain evidence is that fasting appears to be an important precipitating factor for headache attacks and that individuals who fast may very likely develop fasting headache. However, much remains to be clarified on this topic.

Frequent ETTH versus Headache attributed to Fasting

- A. At least 10 episodes occurring on ≥ 1 but < 15 days per month for at least 3 months (≥ 12 and < 180 days per year) and fulfilling criteria B-D
- B Headache lasting from 30 minutes to 7 days
- C Headache has at least two of the following characteristics:
 - 1. bilateral location**
 - 2. pressing/tightening (non-pulsating) quality**
 - 3. mild or moderate intensity**
 - 4. not aggravated by routine physical activity such as walking or climbing stairs**
- D Both of the following:
 - no nausea or vomiting (anorexia may occur)
 - no more than one of photophobia or phonophobia

- A Headache with at least one of the following characteristics and fulfilling criteria C and D:

- 1. frontal location**
- 2. diffuse pain**
- 3. non-pulsating quality**
- 4. mild or moderate intensity**

- B The patient has fasted for > 16 hours
- C Headache develops during fasting
- D Headache resolves within 72 hours after resumption of food intake

Comments:

Headache with fasting is significantly more common in individuals with a prior history of headache. In those individuals with a prior history of migraine, the headache may resemble 1.1 Migraine without aura.

Benign featureless headache: Conclusions

There are many causes and many names for episodic benign rather featureless headache.

There are similar causes but less names for a featureful type of headache called migraine.

How does the featureless link to the featureful?

What is Migraine?

Migraine

“An intermittent, complex, unpleasant cerebral response, constitutionally and genetically determined, occurring in response to lifestyle and environmental changes which sometimes are of a noxious nature.”

What is/are the fundamental migraine feature(s)?

- 1. Pain severity?**
- 2. Aura?**
- 3. Premonitory symptoms?**
- 4. Unilaterality?**
- 5. Impaired sensory control?**

Trigger factors in migraine with aura

Cephalalgia
30(3) 346–353
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DOI: 10.1111/j.1468-2982.2009.01930.x
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AW Hauge, M Kirchmann and J Olesen

Hauge et al.

351

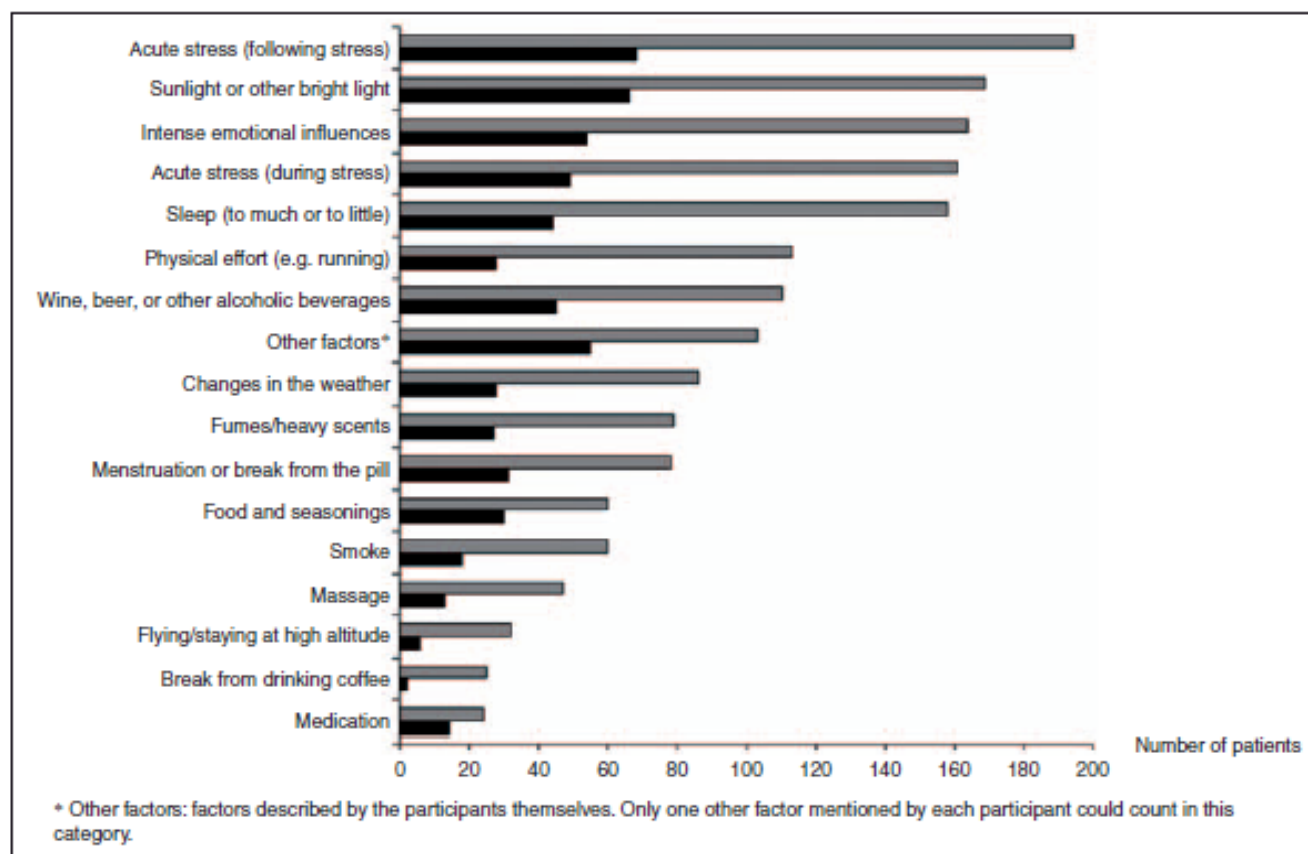
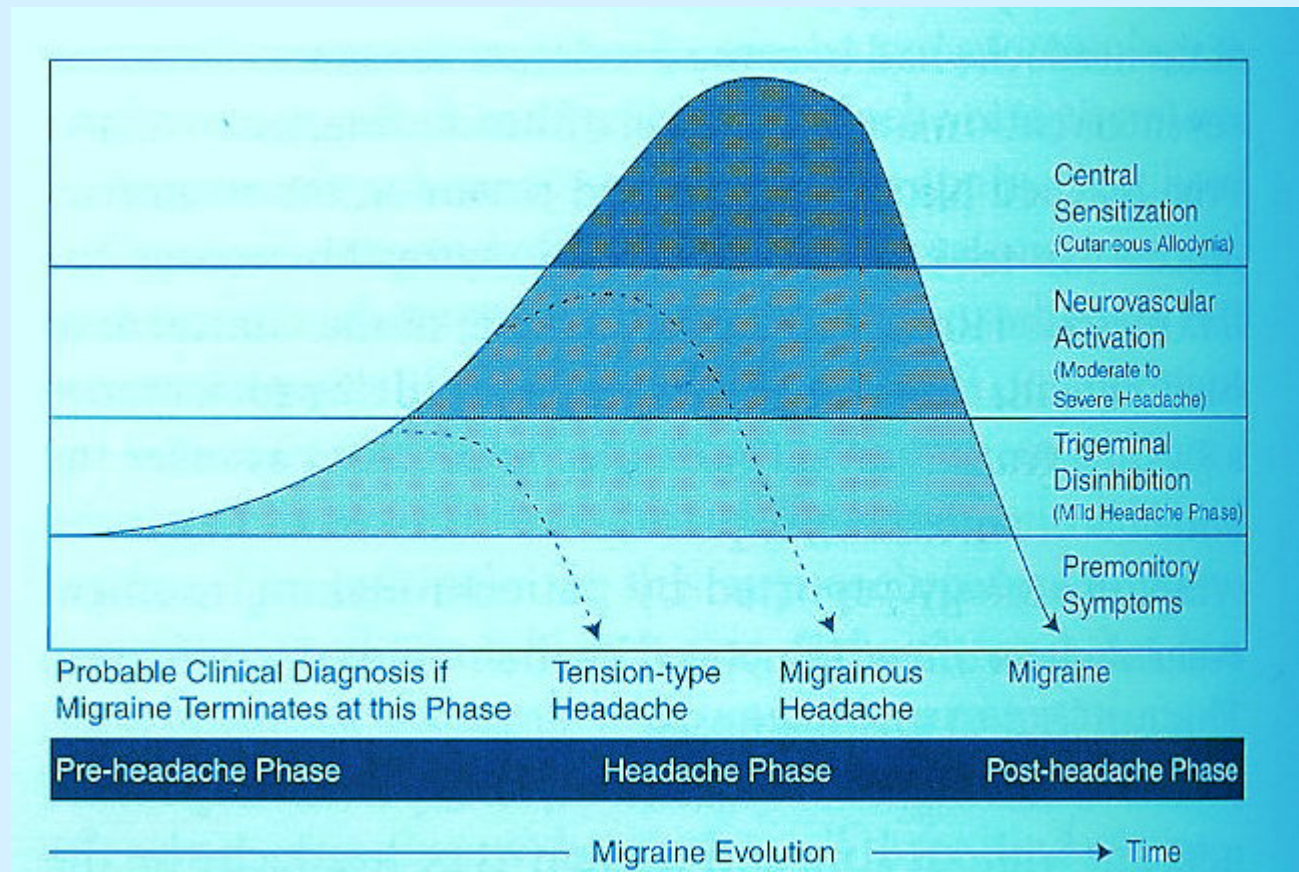


Figure 5. Number of patients reporting each individual trigger factor ($n = 278$). Grey bars indicate the total number of patients who have reported the individual trigger. Black bars indicate the number of patients who have indicated that the specific trigger factor often or always triggers an attack.

Migraine: A Neurobiological process that can be terminated at any phase of its Evolution?



Curr Pain Headache Rep (2010) 14:465–469

DOI 10.1007/s11916-010-0147-1

Pure Tension-type Headache Versus Tension-type Headache in the Migraineur

Andrew Blumenfeld • Jack Schim • Jessica Brower

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Pure TTH versus TTH in the migraineur

- 1. Could the tension-type features in migraineurs be a manifestation of associated comorbid conditions?**
- 2. Could the tension-type features in migraineurs be a manifestation of mild migraine?**
- 3. Could the tension-type features in migraineurs be a manifestation of the chronification of migraine?**
- 4. Are TTH and migraine part of the same disorder, with patients at one end of the spectrum having predominantly migraine features and those at the other end having predominantly TTH features?**

The prevalence of migraine in neurologists

Randolph W. Evans, MD; Richard B. Lipton, MD; and
Stephen D. Silberstein, MD

Abstract—To assess the prevalence of migraine among neurologists and neurologist headache specialists, the authors performed a survey of neurologists who attended a headache review course. The 1-year and lifetime prevalences of migraine in the 220 respondents were as follows:

male neurologists, 34.7%, 46.6%;
male headache specialists, 59.3%, 71.9%;
female neurologists, 58.1%, 62.8%; and
female headache specialists, 74.1%, 81.5%.

Migraine is much more prevalent among neurologists than in the general population.

NEUROLOGY 2003;61:1271–1272

Types of Pain

Acute pain is pain of sudden onset, lasting for hours to days and disappears once the underlying cause is treated. Acute pain has a clear cause.

Chronic pain is the pain that starts as an acute pain and continues beyond the normal time expected for resolution of the problem or persists or recurs for various other reasons. It is not therapeutically beneficial to the patient.

Chronic pain can be Nociceptive or Neuropathic

Nociceptive pain arises from damage to tissues other than nerve fibers.

Neuropathic pain is caused by the lesion in the nervous system when they are structurally or functionally damaged.

Nociceptive and neuropathic pain can co-exist in the same patient

Other pain types: allodynia, hyperalgesia, phantom limb pain, psychogenic pain

HISTORY

Chronic migraine and medication-overuse headache through the ages

CJ Boes¹ & DJ Capobianco²

Department of Neurology, Mayo Clinic College of Medicine, ¹Rochester, MN and ²Jacksonville, FL, USA

Cephalalgia

Boes CJ & Capobianco DJ. Chronic migraine and medication-overuse headache through the ages. *Cephalalgia* 2005; 25:378–390. London. ISSN 0333-1024

We set out to review early descriptions of chronic migraine and medication-overuse headache. The International Headache Society (IHS) recently gave criteria for chronic migraine and medication-overuse headache. Chronic migraine was absent from the 1988 IHS criteria. Peters and Horton described ergotamine-overuse headache in 1951. In the 1980s it was more fully appreciated that overuse of other acute headache medications could increase headache frequency. We reviewed published English-language papers and book chapters. Willis (1672), Oppenheim (1900), Collier (1922), Balyeat (1933), and von Storch (1937) all described chronic migraine. Lennox (1934), O'Sullivan (1936), Silfverskiöld (1947), Graham (1955), Friedman (1955), and Lippman (1955) wrote about ergotamine-overuse headache. Graham (1955), Friedman (1955), Lippman (1955), and Horton and Peters (1963) outlined withdrawal protocols. Chronic migraine has been mentioned in the literature for centuries, while medication-overuse headache has been written about for decades. Graham, Friedman, and Lippman deserve credit for separately reporting the first ergotamine withdrawal programmes. □ *Analgesic-overuse headache, chronic migraine, ergotamine-overuse headache, medication-overuse headache, transformed migraine*

James Collier (1870–1935) (Fig. 3) was ‘a [Queen Square] clinical neurologist of superlative ability’ (24). His contemporaries at Queen Square included Gordon Holmes and S. A. Kinnier Wilson (24). Collier, J. S. Risien Russell, and Frederick Batten were credited with the first serious description of subacute combined degeneration of the spinal cord (24, 25).

In 1922 a new textbook of medicine was issued, edited by Dr Frederick Price. Collier and Dr W. J. Adie wrote the section on neurology, which was a ‘dazzling contribution based largely on personal experience’ (24). In the chapter on migraine, Collier commented that there were migraine cases ‘in which the headache lasts for weeks, or becomes continuous’ (26). He (26) also stated:

‘In some cases of long standing [migraine], the attacks become less severe towards middle life, and a persistent aggravating headache may develop between the attacks. When such a persis-

tent headache is complained of alone, it is very important to inquire about preceding migraine, for the same treatment is applicable to the two conditions’ (p. 1504)

Theodore J. C. von Storch (1905–1965) (Fig. 4) received his MD from Johns Hopkins in 1931. He trained in neurology at Boston City Hospital. In subsequent years he worked at Harvard Medical School and Boston City Hospital, and at the Albany and Montefiore Hospitals in New York. He eventually became a Clinical Professor of Neurology at Columbia. He finished his career as a Lecturer in Neurology at the University of Miami. He was a member of the American Neurological Association.

Dr von Storch (27) supported Collier’s view on chronic migraine, noting in 1937 that

‘There are . . . exceptions to the invariable inclusion of recurrent headaches in the migraine syndrome. The first occurs when recurrent headaches

The Chronification of Headache

Risk Factors for Headache Chronification

Ann I. Scher, PhD; Lynn A. Midgette, MPH; Richard B. Lipton, MD

About 4% of the adult population and about 1% to 2% of children experience chronic attacks on a daily or near daily basis. While there is uncertainty about the biological mechanisms that lead to headache “chronification,” the epidemiologic literature has provided some insight into modifiable and nonmodifiable factors that appear to influence risk of headache progression. This review summarizes the evidence from population-based studies related to the chronic daily headache phenotype, natural history, and risk factors that may influence incidence, prevalence, or prognosis.

Key words: chronic daily headache, epidemiology, risk factors

(Headache 2008;48:16-25)

Headache Chronification

What makes a pain chronic?

Are the factors the same for migraine pain?

Why is Cluster Headache different?

In what way does acute (episodic) pain differ from chronic pain?

Risk factors for Headache Chronification (CDH)

Non-modifiable

Age

Gender F:M = 2

**Socio-economic status
(low at greater risk)**

Married (lower risk)

Potentially modifiable risk factors for CDH

**Include obesity, snoring
and sleep problems,
comorbid pain
conditions, head or
neck injury, major life
events, smoking, and
possibly caffeine
intake.**

Frequent ETTH versus CTTH

ETTH

- A. At least 10 episodes occurring on ≥ 1 but < 15 days per month for at least 3 months (≥ 12 and < 180 days per year) and fulfilling criteria B-D
- B Headache lasting from 30 minutes to 7 days
- C **Headache has at least two of the following characteristics:**
 - bilateral location**
 - pressing/tightening (non-pulsating) quality**
 - mild or moderate intensity**
 - not aggravated by routine physical activity such as walking or climbing stairs**
- D **Both of the following:**
 - 1. no nausea or vomiting (anorexia may occur)**
 - 2. no more than one of photophobia or phonophobia**

CTTH

- A. Headache occurring on ≥ 15 days per month on average for > 3 months (≥ 180 days per year)¹ and fulfilling criteria B-D
 - B. Headache lasts hours or may be continuous
 - C. **Headache has at least two of the following characteristics:**
 - bilateral location**
 - pressing/tightening (non-pulsating) quality**
 - mild or moderate intensity**
 - not aggravated by routine physical activity such as walking or climbing stairs**
- Both of the following:**
- 1. no more than one of photophobia, phonophobia or mild nausea**
 - 2. neither moderate or severe nausea nor vomiting**

Chronic Migraine (2004, 2006)

Chronic Migraine (original): ICHD-2

Migraine headache occurring on 15 or more days per month in the absence of medication overuse

A. Headache fulfilling criteria C and D for migraine without aura on ≥ 15 days per month for >3 mo

B. Not attributed to another disorder

Note:

1. History and physical and neurological examination do not suggest any of the disorders listed in groups 5–12; or history and/or physical and/or neurological examinations do suggest such disorder but it is not ruled out by appropriate investigations; or such disorder is present but headache does not occur for the first time in close temporal relation to the disorder.
2. When medication overuse is present and fulfills criterion B for any of the subforms of 8.2 (medication-overuse headache), it is uncertain whether criterion B for 1.5.1 (chronic migraine) is fulfilled until 2 months after medication has been withdrawn without improvement.

Chronic Migraine (revised): ICHD-2

Frequently occurring headache (≥ 15 days per month) with at least 8 days of migraine or probable migraine per month in the absence of medication overuse

A. Headache (tension-type and/or migraine) on 15 or more days per month for at least 3 months

B. Occurring in a patient who has had at least five attacks fulfilling criteria 1.1 (migraine without aura)

C. On 8 or more days per month for at least 3 months, headache has fulfilled C.1 and/or C.2 below; that is, has fulfilled criteria for pain and associated symptoms of migraine without aura:

1. Has at least two of a–d:
 - a. Unilateral location
 - b. Pulsating quality
 - c. Moderate or severe pain intensity
 - d. Aggravation by or causing avoidance of routine physical activity (eg, walking or climbing stairs)

And at least one of a or b below:

- a. Nausea and/or vomiting
 - b. Photophobia and phonophobia
2. Treated and relieved by triptan(s) or ergot before the expected development of C.1 above
- D. No medication overuse and not attributed to another causative disorder**

Migraine or TTH?

Episodic or Chronic?

What if chronic TTH and 1 migraine a month? Are you a migraineur or a CTTH sufferer?

Migraine: Why not 3 types – infrequent, frequent and chronic?

Scenario:

You have 2 migraines a month (each lasting 2 days respond poorly to paracetamol) and 7 days of non-descript headache (stress/fatigue) responds to paracetamol.

4 days of migraine and 7 headache days = 11 days a month = Episodic migraine

See GP! Discover triptans (big improvement in acute therapy) - Migraine triptan rebound 2 days to 4 days and so 8 triptan doses a month and 7 non-descript days = 15 days 8 of which are with migraine = Chronic migraine

Review Article

The Evolution of Chronic Migraine: Classification and Nomenclature

Aubrey Manack, PhD; Catherine Turkel, PharmD, PhD; Stephen Silberstein, MD, FACP

After nearly 3 decades of debate, the headache community still lacks globally accepted criteria for *chronic migraine*. This review summarizes the evolution of *chronic migraine* nomenclature and criteria. We concluded that although there are discrepancies in the currently proposed criteria, there is a significant amount of overlap with previously used classifications such that they all appear to describe the same subset of highly burdened migraine patients. In order to continue to understand the natural history of *chronic migraine*, address the unmet medical need, and develop effective therapies, field experts and physicians must have a classification that is well understood and accepted by the broader clinical community. It is our view that of the currently established classifications, the Silberstein and Lipton revised criteria for *transformed migraine* are the most applicable to daily clinical practice and field research.

Key words: chronic migraine, headache, classification, epidemiology, nomenclature, evolution

Abbreviations: ICHD International Classification of Headache Disorders, IHCC International Headache Classification Committee, IHS International Headache Society, MOH medication overuse headache

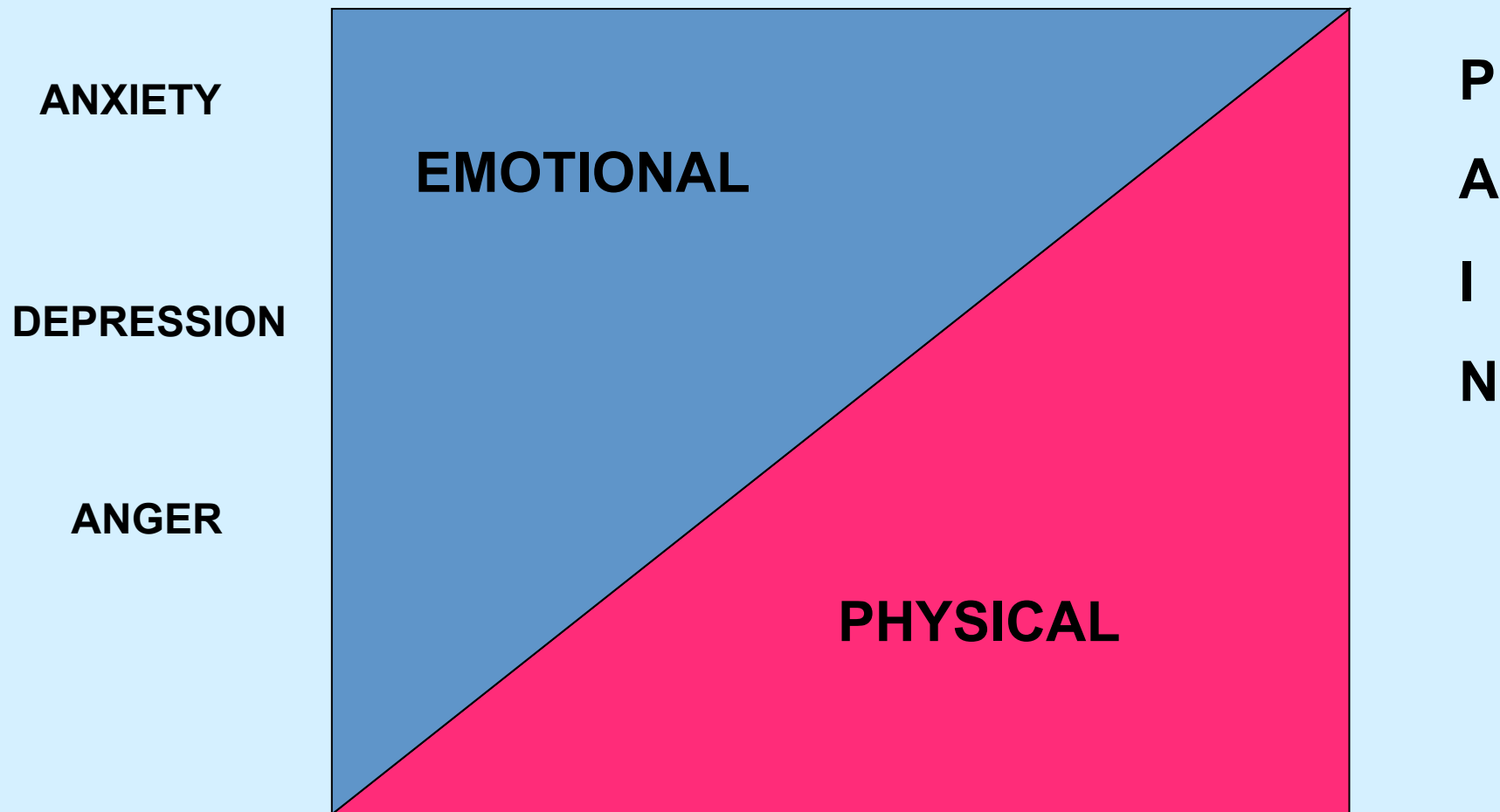
(*Headache* 2009;49:1206-1213)

Mechanism of Chronic Migraine

**Sheena K. Aurora • Arun Kulthia •
Patricia M. Barrodale**

Published online: 4 January 2011
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Emotional versus Physical Factors in Pain Causation



Can neuroimaging studies identify pain endophenotypes in humans?

Irene Tracey

Abstract | Pain is a complex, multidimensional experience that has defied our understanding for centuries. Through the advent of noninvasive neuroimaging techniques, we have been able to examine the human brain and its response to nociceptive inputs. As a result, our knowledge of which brain regions are critical for generating an acute pain experience has grown, as has our understanding of how cognitive, emotional, contextual and various physiological factors influence the pain experience. Furthermore, we have been able to identify key processes within the brain that underpin the transition to and maintenance of chronic pain states, as well as highlight the dramatic consequences of chronic pain on the brain's structure and neurochemistry. Building upon this knowledge, we are now in a position to consider whether any of these brain imaging 'phenotypes' of acute or chronic pain should be considered as useful endophenotypes; thereby enabling us to relate the complex genetics that underpin everyday pain sensitivity or chronic pain states to intermediate biomarkers. This endophenotypic approach—the focus of this Review—simplifies the connection between genes and behavior and is needed for complex disorders like chronic pain.

Tracey, I. *Nat. Rev. Neurol.* 7, 173–181 (2011); published online 8 February 2011; [doi:10.1038/nrneurol.2011.4](https://doi.org/10.1038/nrneurol.2011.4)



HYPOTHESIS

Modular headache theory

WB Young, MFP Peres & TD Rozen

Jefferson Headache Center, Thomas Jefferson University Hospital, Philadelphia, Pennsylvania, USA

Cephalalgia

Young WB, Peres MFP & Rozen TD. Modular headache theory. *Cephalalgia* 2001; 21:842–849. London. ISSN 0333-1024

Table 3 Modules that may be involved in primary headaches

Proposed module	Most typically involved headache	Other headaches that may recruit module
Throbbing vascular pain	Migraine	Some TTH, cluster migraine, cluster, HC
Nonthrobbing pain	Tension-type	Migraine, ?HH?, ?HC
Cervical muscle tenderness and pain	Cervicogenic (not a primary headache)	TTH, migraine, cluster
Allodynia	Migraine	?
Eye pain	Cluster	SUNCT, CPH, EPH, migraine
Stabbing pain	Idiopathic stabbing	HC, migraine, cluster
Tic-like pain	Trigeminal neuralgia	Cluster tic
Nausea/vomiting	Migraine	Cluster, HC
Photo- phono-osmophobia	Migraine	Cluster, CPH, HC
Ptosis (miosis)	Cluster	CPH, EPH, SUNCT
Lacrimation/nasal congestion	Cluster	CPH, EPH, SUNCT
Prodrome	Migraine	Cluster (24)
Aura	Migraine	Cluster, HC
Lysis (termination)	Migraine	?
Timer-diurnal	Cluster	HH, migraine
Timer-seasonal	Cluster	Cyclic migraine, EPH
Unilateral/suppressor (5)	Cluster	HC, CPH, EPH, migraine, etc.
Postdrome	Migraine	Cluster

CPH, chronic paroxysmal hemicrania; EPH, episodic paroxysmal hemicrania; HC, hemicrania continua; HH, hypnic headache; SUNCT, short-lasting unilateral neuralgiform headache with conjunctival injection and tearing; TTH, tension-type headache.

