Agenda

- Case presentation
- Primary and Secondary Headache
- Primer on Pain

Agenda

- Migraine Morphology
  - Premonitory Phase
  - Aura
  - Headache
  - Postdromic Phase
- Medication Overuse Headache

Case Presentation

RT is a 25 year old woman with daily headache

- Global HA for past 6 months
- Formerly occasional HA beginning with wavy visual distortion for 20 minutes
- Then nausea & unilateral HA throbbing for 4+ hours

Case Presentation

RT is a 25 year old woman with daily headache

- Typically resolved after sleeping
- Some benefit from ibuprofen 600 mg
- HA daily 1 week before menses
- Frequency increasing until now HA every day

Case Resolution

RT is a 25 year old woman with daily headache

- ✓ Addressed triggers including sleep changes, OCP; stressful events; eat breakfast; decrease caffeine
- ✓ Amitriptyline 10 mg at bedtime
- ✓ No other analgesic for 2 weeks
- ✓ Breakthrough HA: 100% respond to zolmitriptan

Truths about Headaches (1980)

- Most headaches were muscle-tension headaches
- Migraines (and cluster) were vascular headaches
- Migraine aura was due to vasospasm
- Drugs were aspirin/caffeine, aspirin/butalbital/caffeine, caffeine/ergotamine, or acetaminophen/dichloralphenazone/isometheptene

Truths about Headaches (2018)

- ~~Most headaches were muscle-tension headaches~~
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International Headache Society Classification of Migraine

Necessary	At least 2	At least 1
Episodic 4-36 hours	Unilateral	Photophobia
	Throbbing	Phonophobia
	Aggravated by movement	Nausea or vomiting
	Severe	

Headache Nomenclature

Primary	Secondary
Paroxysmal	Chronic

Primary Paroxysmal Headache

Synonyms	Not Migraine Headaches
Common migraine	Cluster
Migraine without aura	Paroxysmal hemicrania
Migraine with aura	Orgasmic
Muscle tension	
Tension-type	

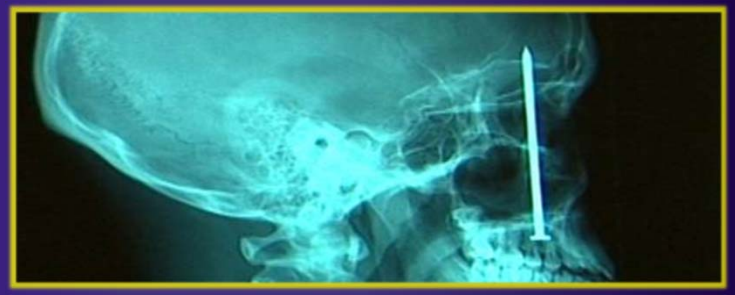
Primary Chronic Headache

Medication Overuse Headache
Transformed migraine
Chronic migraine
Chronic daily headache

Secondary Headache

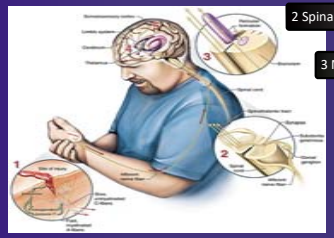
Meningeal irritation	Brain tumor
Temporal arteritis	Subdural hematoma
Post-concussion	Intracranial hypertension
Cocaine	Subarachnoid hemorrhage
Pituitary apoplexy	Normal pressure hydrocephalus
Cervical artery dissection	Call-Fleming Syndrome (diffuse cerebral vasculopathy)
Facial pain (sinusitis, etc.)	Many medical illnesses

Secondary Headache



Primer on Pain

Pain Pathway



1 Nociceptor stimulation

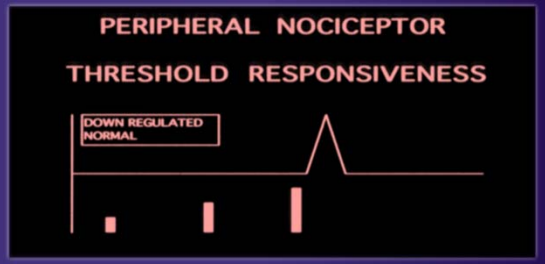
2 Spinal interneuron (Substance P)

3 Midbrain signal modulation

4 Thalamic synapse

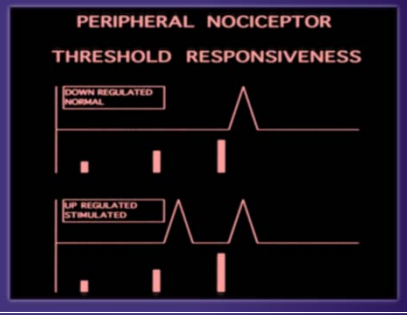
5 Parietal cortex

Nociceptor Threshold

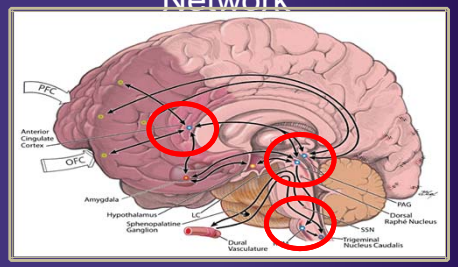


Thought Experiment

Nociceptor Threshold



Migraine as a Dysfunctional Neurolimbic Pain Network



Maizels M, Aurora S, Heinricher M. *Headache* (2012) 52;10:1553-65

Migraine Morphology

- Premonitory phase
- Aura
- Headache
- Postdromic phase

Premonitory Phase

Irritable

Fatigued

Mood changes

Difficulty concentrating

Nausea

Cravings

Premonitory Phase

Irritable

Fatigued

Mood changes

Difficulty concentrating

Nausea

Cravings

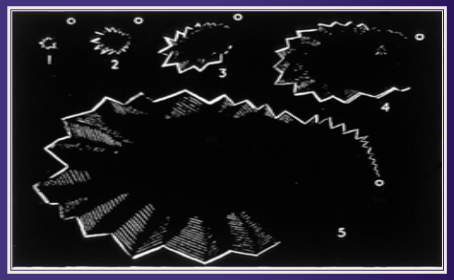
Triggers

- ✓ Sleep (too much or too little)
- ✓ Fasting
- ✓ Caffeine (too much or withdrawal)
- ✓ Alcohol
- ✓ Estrogen

Aura Provides a Clue

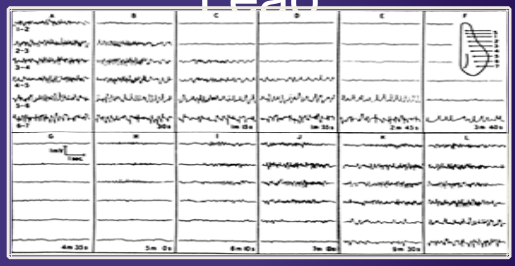
1. Lashley draws an aura
2. Leão describes spreading electrochemical depression
3. Lauritzen and Olesen measure regional cerebral blow flow (rCBF) of cortex

Visual Aura



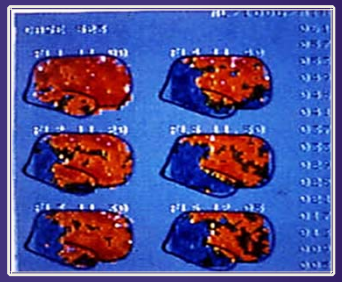
Olesen J in The Headaches Olesen J, Tfelt-Hansen P, Welch KMA editors (1993) Raven Press, New York;264

Spreading Depression of Leão



Teive H et al. Neurology 2005;65:1455-1459

rCBF During Aura



Lauritzen M, Olesen J. *Brain*.1984; 107: 447-461

Independent Characteristics of Aura

Observer	Velocity
Lashley Aura (1943)	2-3 mm/min
Leão Cortical Spreading Depression (1943)	3 mm/min
Olesen rCBF (1983)	3 mm/min

Sensory Associations

- ✓ Colic
- ✓ Motion sickness
- ✓ Ice pick-like head pain
- ✓ Freezer brain

Treatment

- Acute treatment
- Preventive treatment

Acute treatment (1)

- NSAID
- Acetaminophen
- Triptans (Serotonin receptor antagonists)
  - ✓ Choose route of administration
  - ✓ Choose formulary compliance
- DHE
- Metoclopramide

Triptans

Drug	PO	SC	IN	Transbuccal
Sumatriptan	✓	✓	✓	
Almotriptan	✓			
Eletriptan	✓			
Frovatriptan	✓			
Naratriptan	✓			
Rizatriptan	✓			✓
Zolmitriptan	✓		✓	✓

Acute treatment (2)

Directions For Triptans and DHE

- Take one dose at onset
- Repeat once if HA persists at 1-2 hours
- If HA remits, but then returns, repeat same dose at 8-10 hours
- Do not treat more than 3 HA events in a week

Barbiturate and Opiates Increase Transformation

	Women		Men		
	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	Overall Adjusted OR (95% CI)
Acetaminophen	1.0 (reference)	1.0 (reference)	1.0 (reference)	1.0 (reference)	1.0 (reference)
Prescribed medication + NSAIDs	0.88 (0.62-1.26)	0.97 (0.67-1.41)	0.85 (0.46-1.55)	0.93 (0.46-1.88)	0.96 (0.69-1.34)
Triptans	1.11 (0.76-1.63)	0.93 (0.62-1.40)	2.37 (1.20-4.71)	2.11 (0.97-4.63)	1.05 (0.73-1.50)
Barbiturate compounds	2.29 (1.44-3.64)	1.97 (1.21-3.23)	1.42 (0.43-4.72)	1.29 (0.38-4.37)	1.73 (1.10-2.73)
Opiates	1.74 (1.15-2.63)	1.28 (0.81-1.97)	3.48 (1.74-6.96)	2.76 (1.20-6.38)	1.44 (1.10-2.08)
Isomethoptene compounds	0.94 (0.41-2.16)	0.85 (0.36-2.02)	1.64 (0.38-7.09)	1.60 (0.34-7.54)	0.93 (0.44-1.98)

CM = chronic migraine; OR = odds ratio; CI = confidence interval; NSAID = nonsteroidal anti-inflammatory drug.

Lipton RB. *Neurology* (2009). 72;5: Supplement 1S3-S7

Cost of Transformation from Episodic to Chronic

	CM	EM
Missed work or school, d	2.4	0.54
≥50% Reduced productivity at work or school, d	10.4	1.7
Incomplete household work or chores, d	21.4	3.5
≥50% Reduced productivity in household work or chores, d	18.7	2.6
Missed time with family, social, or leisure activities, d	10.5	1.7
Total	63.4	10.0

Lipton RB. *Neurology* (2009) 72;5: Supplement 1S3-S7

Preventive Treatment (1)

Good Evidence

- Low dose tricyclic
- Topiramate and Divalproex
- Nadolol, metoprolol, timolol, propranolol

Pringsheim T, Davenport WJ, Becker WJ. *CMAJ.* (2010) 182;7: E269-E276

Preventive Treatment (2)

Inconclusive Evidence

- Gabapentin
- Venlafaxine

Pringsheim T, Davenport WJ, Becker WJ. *CMAJ.* (2010) 182;7: E269-E276

Preventive Treatment (3)

Good Evidence *Against*

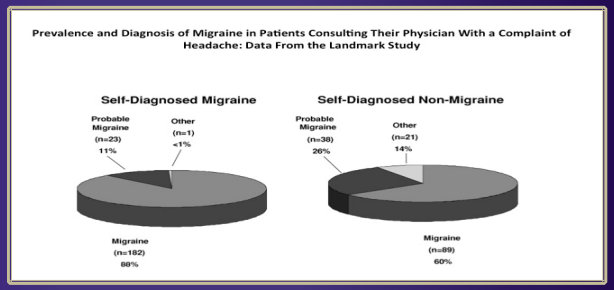
- Pregabalin, Duloxetine
- Lamotrigine
- SSRI - *ALL*

Pringsheim T, Davenport WJ, Becker WJ. *CMAJ.* (2010) 182;7: E269-E276

Special Considerations

Hypertension CVD	Nadolol, Propranolol, ACEi (?)
Initial insomnia	Amitriptyline
Mood disorder	Amitriptyline, Venlafaxine
Epilepsy	Topiramate, Divalproex, Gabapentin
Obese	Topiramate
Intolerance of side effects	Riboflavin, Coenzyme Q10, Butterbur
Pregnant or Trying to Conceive	*Contraindicated* Divalproex
Oral Contraceptives	*Contraindicated* Topiramate

Self Diagnosis of Headaches



Tepper SJ, et al. *Headache* (2004) 44:856-64

Self Diagnosis of Headaches

When patients see a doctor for headache, if they say…

"I think I have a migraine."	They are almost always right.
"I think I have a headache that is not a migraine."	They are almost always wrong.

Tepper SJ, et al. *Headache* (2004) 44:856-64