Treatment of Migraine Associated Vertigo

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Migraine Pathophysiology

- Baseline sensory hyperexcitability (thicker sensitive brains)
- Environmental events push past a threshold leading to:
  - Electrical changes (cortical spreading depression -- CSD) occurs in brain.
  - Causes aura (aura is no longer attributed to vasospasm)

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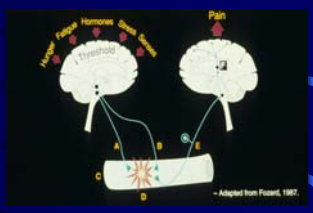
(Schreiber,2006).

The "new" migraine process

- CSD →
  - Trigeminal nucleus caudalis (TNC) stimulation
  - Release of inflammatory neuropeptides (CGRP)
- CGRP ->
  - Vasodilation
  - "sensitization" (allodynia) in trigeminal circuit
- Pain and sensitization leads to positive feedback.



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(Schreiber,2006).

Treatments for Migraine

- Abortive agents
  - Triptans, Ergots
- Symptom agents
  - Analgesics
  - Antiemetics
- Prevention
  - Interrupt the feedback loop

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Abortive medications
Triptans bind to serotonin 5-HT_{1B} and 5-HT_{1D} receptors

- Reduce pain by blocking TNC and reduce secondary sensitization
- Usually very effective for headache phase
- Can block some sensory triggers and prodrome (e.g. nausea) if taken prophylactically

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Available Abortive Agents

- Pre-triptan era – agents little used now
  - DHE, Ergotamine, Isomethptene (Midrin)
- Triptans – first was sumatriptan (now generic)
- Common features of triptans:
  - Highly effective, minimal side effects
  - Highly expensive, highly marketed
  - Can be addictive

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Triptans – pharmacokinetics

- Rapid/powerful agents
  - rizatriptan (Maxalt), eletriptan (Relpax)
- Moderate
  - Sumitriptan (Immitrex), zolmitriptan (Zomig)
- Weak/slow
  - Naratriptan (Amerge), frovatriptan (frova)

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Prophylaxis is more important

- Unpredictable vertigo spells may prevent driving or be dangerous
- Migrainous vertigo rarely responds to vestibular suppressant medications
- Often helps to treat underlying sensory amplifications

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Prophylaxis of Migraine – 2008

Mechanism of most of these is not well understood, but they all work about 75% of the time. They all take weeks-months to work.

- CSD blockers
  - Anticonvulsants
- Mysterious mechanism agents
  - Beta blockers
  - L-channel calcium channel blockers
- Neurochemical modulators
  - Antidepressants

Sanchez-Del-Rio et al. (2006).

Anticonvulsants – probably raise threshold for CSD

- **Topirimate (Topamax)**
- Gabapentin (Neurontin)
- Sodium Valproate (Depakote)
- Levetiracetam (Keppra)

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Anticonvulsants: Topiramate (Topamax)

- Very effective – about 75%
- Dose: 25 mg to 150 mg, Start with 25, increase weekly
- Associated with weight loss !
  - Large doses – speech disturbance
  - Tingling in hands and feet too
  - Expensive -- $1/dose.

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Beta Blockers

- Very effective - -75%
- Mechanism – not entirely clear --
- Any beta blocker works (not just central ones)
  - **Propranolol 60 LA (category C)**
  - Metoprolol 50 XL (category C)
  - Atenolol 50-100/day (Category D)
- Side effects
  - Fatigue, Slow pulse, Hypotension, impotence
- 1 month to work

Sanchez-Del-Rio et al. (2006)

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L-channel Calcium Channel Blockers -- Verapamil

- Very effective (75%)
- Mechanism – not well understood
  - Perhaps block TNC (Akerman, 2003)
  - Perhaps relates to genetics (calcium channel gene)
- **Verapamil dose 120-240 SR.**
- Takes 2 weeks to work
- Constipation main side effect – increase dose if not constipated after 2 weeks.

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Antidepressants Venlafaxine (Effexor) 80% effective

- Mechanism – not very clear -- Dual SNRI and SSRI
- Very useful in managing the sensory amplifications seen in migraine.
- Cheap and very effective (Bulut, Berilgen et al. 2004)
- Start with 12.5 mg, increase slowly to maximum of 75 mg
- Side effects are minor, high doses have withdrawal syndrome

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Antidepressants – less used amitriptyline/nortriptyline

- Tricyclic group
- Messy agents
  - Central antihistamine, antihistamine, norepinephrine, serotonin
  - Accumulate in body
  - Weight gain – 25 lbs – not unusual

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Summary

- The migraine process is complex and includes electrical, vascular and neurochemical processes and a positive feedback loop
- Migraine can be effectively treated with agents that interrupt this loop.