Epilepsy & Migraine: Clinical and Epidemiological Aspects

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Epilepsy & Migraine

are linked by their

• symptom profiles
• comorbidity
• treatment
Migraine
Recurrent headache in attacks of 4-72 hours

Typical characteristics:

- Unilateral
- Pulsating
- Moderate/severe
- Aggravation by physical activity
- Nausea and/or vomiting
- Photo-and phonophobia

-without aura
-with aura

IHS 2004
Epilepsy
Recurrent spontaneous epileptic seizures

Epileptic seizure
A clinical manifestation resulting from an excessive discharge of a set of neurons in the brain

ILAE 1993
Epilepsy & Migraine

- Pathophysiology
- Symptomatology
- Epidemiology
- Pharmacology
Epilepsy & Migraine

- Pathophysiology
- Symptomatology
- Epidemiology
- Pharmacology
Migraine aura: Spreading depression

“Trigger wave”: Spreading depression

Process which spreads anteriorly by diffusion
(volume transmission: $K^+$, glutamate?)
Pathophysiology of Epilepsy

Excitatory Fiber

Glutamate

Inhibitory Fiber

GABA

Postsynaptic Neuron

Excessive synaptic action potentials

EPSP

IPSP

Summated Potential

Threshold
Hyperexcitability

Non-synaptic

Spreading depression

Synaptic

Neuronal hypersynchrony

MIGRAINE

EPILEPSY
Hyperexcitability

Triggers

Non-synaptic

Spreading depression

Neuronal hypersynchrony

Synaptic

MIGRAINE

EPILEPSY

Triggers
Hyperexcitability

SLOW

Non-synaptic volume transmission

Spreading depression

Synaptic transmission

Neuronal hypersynchrony

Propagation

MIGRAINE

BRIEF

EPILEPSY
Epilepsy & Migraine

- Pathophysiology
- Symptomatology
- Epidemiology
- Pharmacology
The What and Where pathways

Both cortical pathways are crucial for the visual function
• the ventral pathway for object vision
• the dorsal pathway for spatial vision
Visual aura

• **Epilepsy**
  Round, coloured patterns
  Complex pseudohallucinations,
  sometimes related to past events

• **Migraine**
  Illusions
  Monochromatic mosaics
  Positive and negative symptoms
Visual aura

• **Epilepsy**
  Round, coloured patterns
  Complex pseudohallucinations,
  sometimes related to past events

• **Migraine**
  Illusions
  Positive and negative elements
  Monochromatic mosaics
Migraine aura

- Duration: 20-30 min (<1h), but may develop within 5 min
- Mix of excitatory and inhibitory phenomena symptoms
- Typically visual and/or sensory and/or speech symptoms
Migraine aura

Complex disturbances of visual perception:

- Metamorphopsia,
- Macro-, Micropsia (Lilliput hallucinations)
- Zoom vision
- Mosaic vision
- Alice in Wonderland syndrome
Alice’s Adventures in Wonderland

By

Lewis Carroll

Oxford 1862
“Curiouser and curiouser!” cried Alice (she was so much surprised, that for the moment she quite forgot how to speak good English).

“Now I’m opening up like the largest telescope that ever was! Goodbye feet” (for when she looked down at her feet, they seemed to be almost out of sight, they were getting so far off).
Picasso
La femme qui pleure
Epileptic vs. migraine aura

• Epilepsy
  Synaptic transmission
  Rapid onset and brief
  Frequent attacks, clustering
  Often evolving to temporal lobe symptoms

• Migraine
  Volume transmission (by diffusion)
  Gradual development >5 min.
  Duration 5-60 min
  From occipital to parietal cortex
Hyperexcitability

MIGRAINE

Spreading depression

EPILEPSY

Non-synaptic

Neuronal hypersynchrony

Migralepsy

Synaptic
Migralepsy
(migraine-triggered seizure)

An epileptic attack occurring during or within one hour after migraine aura

ICHD, 2nd edition, 2004
Postictal headache

- Common after GTCs
- Often with migraine-like features
- Related to occipital lobe epilepsy
Postictal headache

• Develops within 3 h following the seizure

• Resolves within 72 h after the seizure

ICHĐ, 2nd edition, 2004
Syvertsen M, Helde G, Stovner LJ, Brodtkorb E

**Headaches add to the burden of epilepsy**

Postictal headaches in 109 patients with active epilepsy 44 %

Migraine-like postictal headaches 17 %

Interictal migraine in patients with postictal migraine-like headaches 74 %

*J Headache Pain 2007;8:224-30*
Hyperexcitability

Hemiplegic migraine

Hyperexcitability

Childhood occipital epilepsies

MIGRAINE

Spreading depression

Neuronal hypersynchrony

EPILEPSY

Non-synaptic

Synaptic

Synaptic
Childhood occipital epilepsies

- **Early onset** (Panayiotopoulos syndrome)
  - Autonomic symptoms with vomiting
  - Deviation of eyes
  - Impaired consciousness
    - non-convulsive status

- **Late onset** (Gastaut type)
  - Brief visual seizures
  - Postictal headache
Hemiplegic migraine
-one-sided motor weakness during the aura phase

• Sporadic

• Familial
Hemiplegic migraine
-one-sided motor weakness during the aura phase

- Sporadic
- Familial
  - CACNA1A
  - ATP1A2
  - SCN1A
Hyperexcitability

Mutations

CACNA1A
ATP1A2
SCN1A

HEMIPLEGIC MIGRAINE

Spreading depression

Neuronal hypersynchrony

EPILEPSY
Epilepsy & Migraine

- Background and definitions
- Pathophysiology
- Symptomatology
- Epidemiology
- Pharmacology
Comorbidity of migraine and epilepsy

Telephone interviews with 1.948 adult probands with epilepsy and 1.411 of their siblings and parents.

Cumulative incidence of migraine was
  • 24 % in probands with epilepsy
  • 23 % in relatives with epilepsy
  • 12 % in relatives without epilepsy

Conclusion: Risk of migraine is 2.4 higher in persons with epilepsy than without

Neurology 1994;44:2105-10
Epilepsy

Migraine

Gene B
Gene C

Gene A

Separate genetic influences

Shared genetic influences

?
Is the comorbidity of epilepsy and migraine due to a shared genetic susceptibility?

• Equal risk of migraine in genetic vs. non-genetic epilepsy

• Risk of epilepsy in relatives was not associated with proband’s history of migraine

Conclusion: The overall comorbidity is not explained by genes predisposing to both disorders.

Neurology 1996;47:918-24
The Vågå Study of Headache Epidemiology
(Ottar Sjaastad)

Structured headache interview of 1838 inhabitants aged 18-65
(89% of target population was accessed)

- Have you ever had convulsions, epileptic fits or other epileptic symptoms?
The Vågå Study

Prevalence rates

• Migraine without aura 23%
• Migraine with aura 9.7%
• Epilepsy 1.2%
  (cases under treatment)
Comorbidity of migraine and epilepsy in a Norwegian community

Active epilepsy (seizures within last 5 years)
In migraine (5/524) 1.0 %
In migraine with aura (3/168) 1.8 %
Without migraine (6/1132) 0.5 %

Migraine
In active epilepsy (5/11) 45%
In epilepsy in remission (4/28) 14 %  (p =0.09)

Seizure 2008;15:1421-3
Does epilepsy render the brain susceptible to migraine?

Does migraine cause epilepsy?
- by reducing seizure threshold?
- by vascular factors?
Migraine with aura is a risk factor for unprovoked seizures in children

METHODS: Migraine symptoms were evaluated in all incident epilepsy and in matched controls.

RESULTS: Migraine with aura was associated with a fourfold increased risk for developing epilepsy.

*Ann Neurol* 2006;59:210-3
The impact of migraine on epilepsy: a prospective prognosis study

METHOD: 59 patients were diagnosed with both epilepsy and migraine and were compared with controls with epilepsy only during 10 years follow-up.

CONCLUSION: Comorbid migraine had a negative effect on the prognosis of epilepsy

*Cephalalgia 2005;25:528-35*
Hyperexcitability

Spreading depression

Neuronal hypersynchrony

MIGRAINE

EPILEPSY

Genes

Special syndromes

Non-synaptic

Synaptic
Epilepsy & Migraine

- Background and definitions
- Pathophysiology
- Symptomatology
- Epidemiology
- Pharmacology
Anticonvulsants in migraine prophylaxis: a Cochrane review

Valproate and topiramate were better than placebo, whereas acetazolamide, clonazepam, lamotrigine and vigabatrin were not; gabapentin, in particular, needs further evaluation.
Migraine is common in active epilepsy
The association may be bidirectional
Headaches may add to the burden of seizures
Comorbidity may influence the drug choice
Epilepsy & Migraine: Epidemiology

Prevalence of migraine

Prevalence of epilepsy

Leniger T, Diener HC, Hufnagel A. Nervenarzt 2003;74:869-74
## Therapeutic activity of AEDs in pain

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- ● controlled trial/general acceptance
- ● less extensive evidence

*From Rogawski & Loscher, Nat Med 2004;10:685-92*
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Does migraine cause epilepsy?
- by vascular factors?
- by reducing seizure threshold?
Migraine & Epilepsy
Prevalence

Migraine
Nord-Trøndelag 1997

Epilepsy
Iceland 1993
Incidence of Epilepsy
Highest in the young and the elderly
MELAS Syndrome: characteristic migrainous and epileptic features and maternal transmission

Severe prolonged migrainous symptoms and prolonged partial status epilepticus are characteristic features of the MELAS syndrome (mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes).

Maternal transmission, previously found in MERRF, is suggested in this disorder as well.

*Neurology* 1988;38:751-4
Some patients with cerebral AVMs suffer migrainous attacks which meet criteria for migraine

Correlation for
- side of unilateral headache
- lateralized auras

Haas DC
Headache 1991;31:509-13
Classic migraine in epilepsy:

In all with Epilepsy Hx: \( \frac{5}{40} = 12.5\% \)
In those still treated: \( \frac{4}{21} = 19.0\% \)
In active epilepsy: \( \frac{2}{11} = 18.2\% \)
The Vågå Study of Headache Epidemiology
Migraine & Epilepsy
are linked by

♦ symptom profiles
♦ cortical hyperexcitability
♦ comorbidity
♦ the efficacy of “antimigraine antiepileptics”
Epilepsy & Migraine: Clinical and Epidemiological Aspects
Epileptic vs. migraine postdrome phase

- **Epilepsy**
  - Somnolence, sleep
  - Headache, nausea
  - Focal neurological deficits

- **Migraine**
  - Tired, irritable, impaired concentration
  - Some: refreshed, euphoric
The epileptic aura: Simple partial seizure

The ictal symptoms are determined by the function of the seizure-generating cortical area
The Detailed History of the Ictal Event

1. Precipitating factor / situation
2. What did the patient experience?
3. What did eye witnesses observe? 
   onset - progression - end
4. Duration
5. Postictal/ Postdromal phase
Pathophysiology of Migraine
Concept of neuronal hyperexcitability

Triggers → Neuroelectric event (spreading depression)

↑

Ion channels

↑

Genes

Brain stem pathways/
Trigeminovascular system

CGRP

Vascular changes
Epilepsy & Migraine: Pathophysiology

Propagation of the attack

• Epilepsy
  Synaptic transmission

• Migraine
  Volume transmission via diffusion ("spreading depression")
Hyperexcitability

MIGRAINE

Spreading depression

Neuronal hypersynchrony

EPILEPSY

Non-synaptic

Synaptic
## Association between migraine and seizure disorders

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<tr>
<th>Seizure disorders</th>
<th>Combined MwA / MwoA</th>
<th>Migraine total</th>
<th>Controls</th>
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<tbody>
<tr>
<td></td>
<td>MwoA n=356</td>
<td>MwA n=112</td>
<td></td>
</tr>
<tr>
<td>Active epilepsy</td>
<td>2 (0.6%)</td>
<td>1 (0.9%)</td>
<td>2 (3.6%)</td>
</tr>
<tr>
<td>Epilepsy in remission with treatment</td>
<td>0</td>
<td>1 (0.9%)</td>
<td>0</td>
</tr>
<tr>
<td>Epilepsy in remission without treatment</td>
<td>2 (0.6%)</td>
<td>1 (0.9%)</td>
<td>3 (0.6%)</td>
</tr>
<tr>
<td>Single or situation-related seizures</td>
<td>6 (1.7%)</td>
<td>1 (0.9%)</td>
<td>3 (5.4%)</td>
</tr>
<tr>
<td>All</td>
<td>10 (2.8%)</td>
<td>4 (3.6%)</td>
<td>5 (8.9%)</td>
</tr>
</tbody>
</table>
Picasso
Portrait de Dora Maar
Vågå mountains
The ictal event

- Prodrome
- Aura
- Ictus
- Postictal phase

Interictal period

Epilepsy