Migralepsy: Definition, Cases, Work-up and Management

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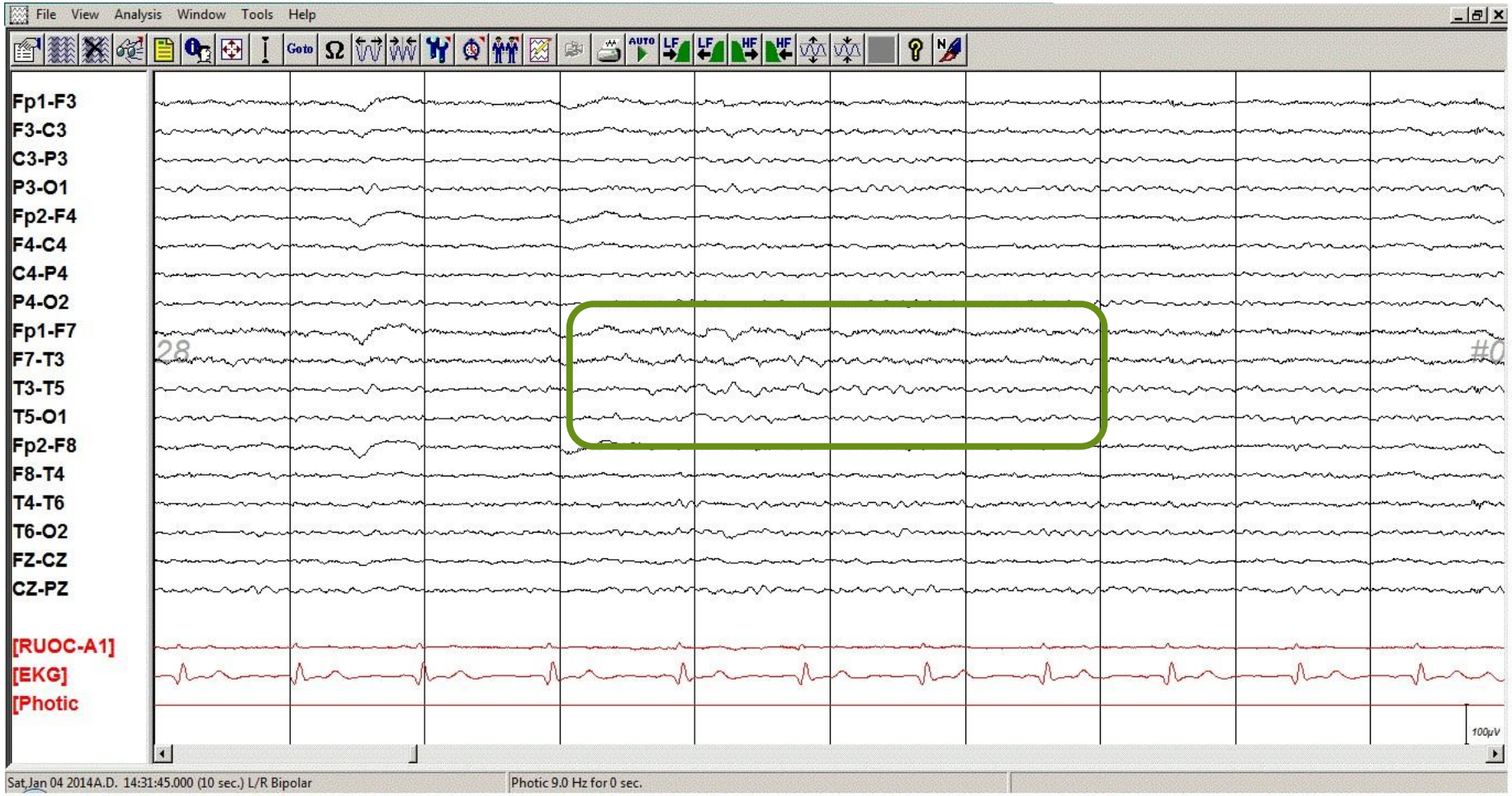
Disclosures

- None

Objectives

- Using the ICHD3 Beta to define the cross section between migraine an epilepsy (1.2.3.1 Familial hemiplegic migraine, 1.4.4 Migraine aura-triggered seizure, 7.6 Headache attributed to epileptic seizure, 7.6.1 Hemicrania epileptic, 7.6.2 Post-ictal headache)
- Review the common clinical features of migraine, aura and epilepsy
- Review possible mechanisms and current research on the intersection of migraine and epilepsy
- Critical evaluation of the differential diagnosis and workup in this patient population
- Treatment guidance for patients that present with migralepsy

MT is a 26 y/o male

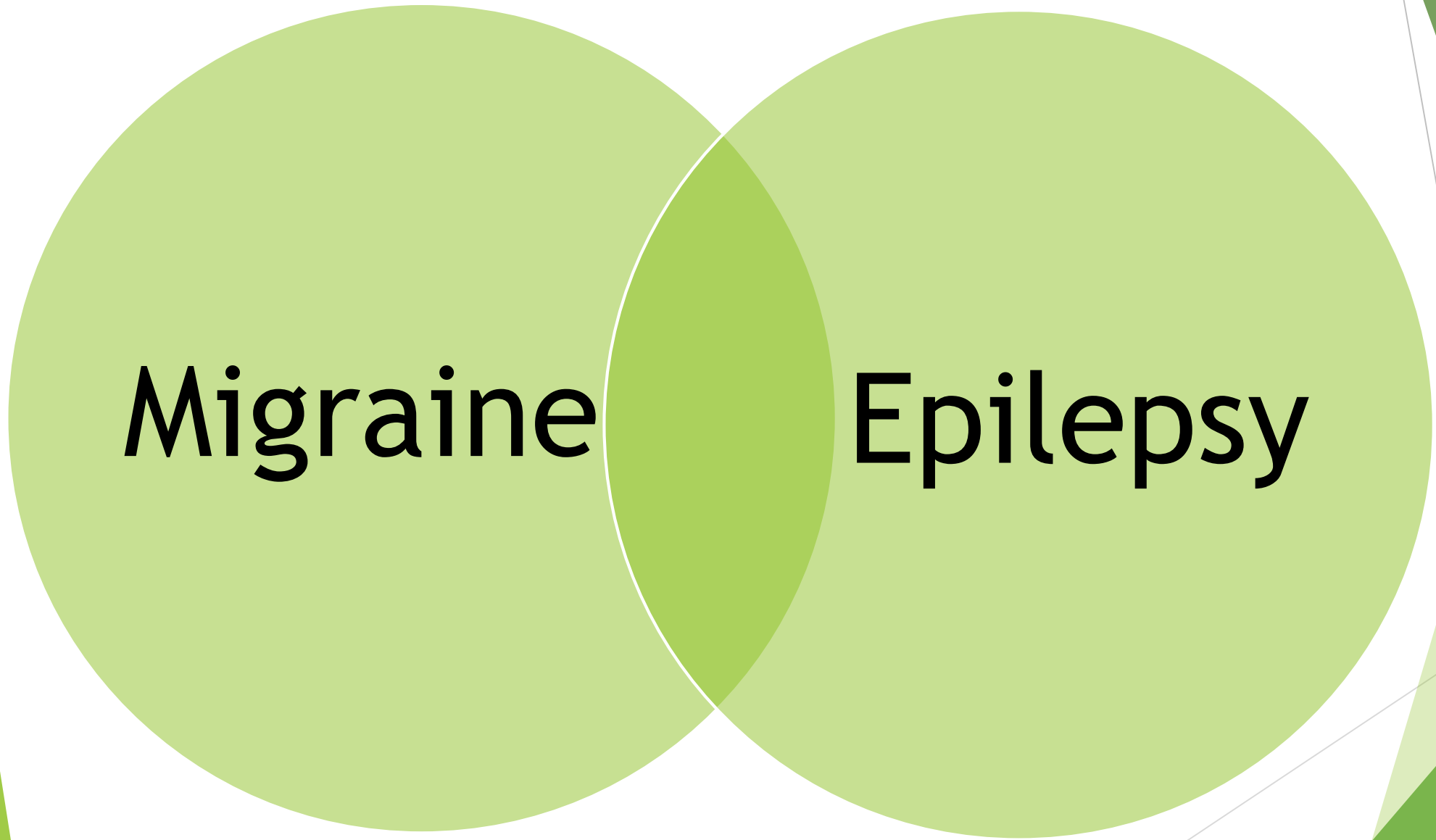


MT is a 26 y/o male

- RH male presented to the ED for evaluation of right sided weakness and dysarthria. He was accompanied by his girlfriend who gives the initial hx:

- They were walking in a local mall at 6pm when patient reported feeling that his RLE went to sleep the sensation ascended to involve the right arm and right side of the face over the course of an hour. This progressed to answering questions with a “weird combination of words”. He had a holocephalic throbbing headache at the time.

- PMH: Migraine without aura - tx with OTC medications

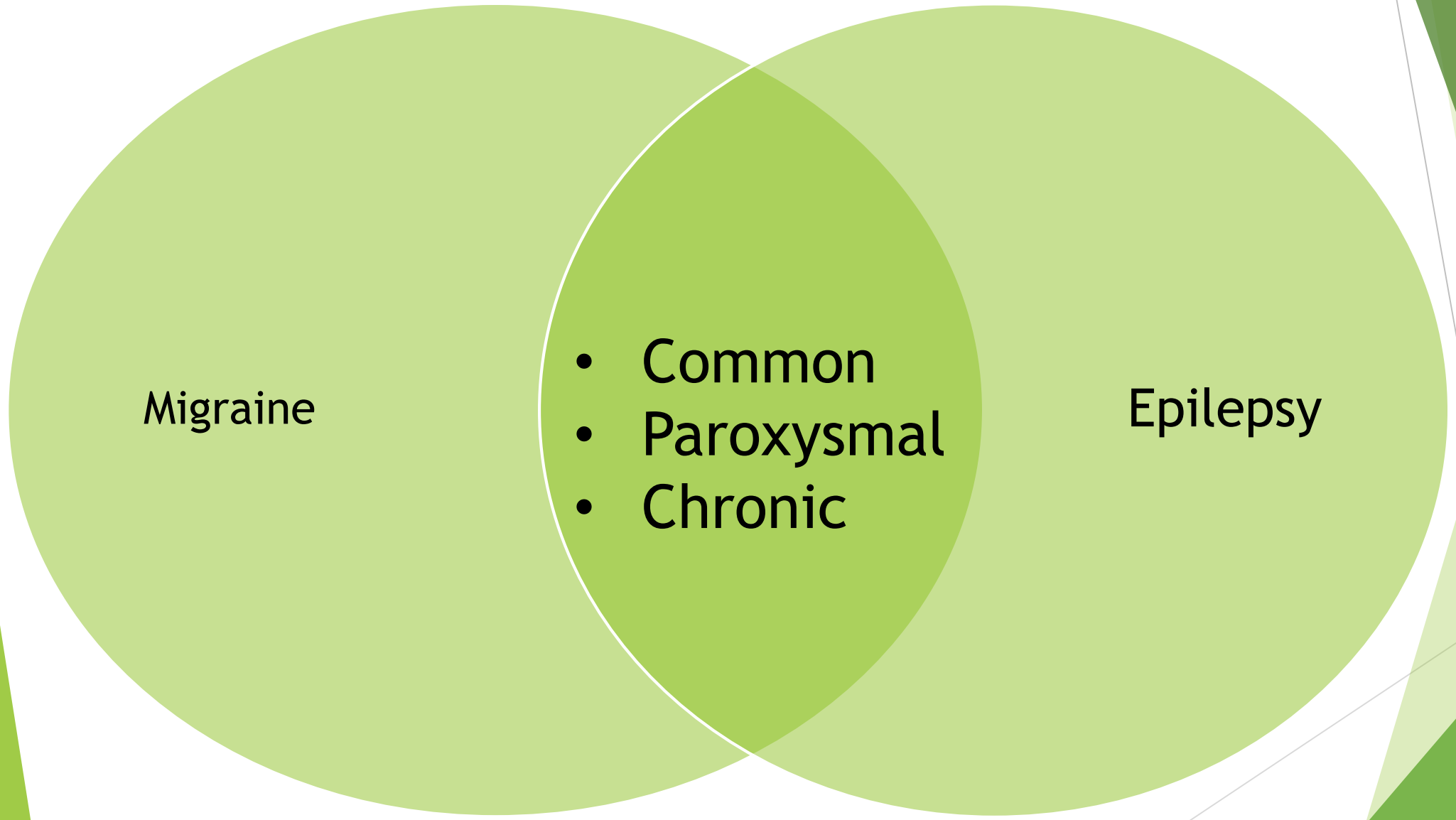

Migraine
Epilepsy

Migralepsy

- First described by William Lennox

  Syndrome of migraine with aura where migraine is almost immediately followed by an epileptic seizure in a way that gives rise to the suspicion that one triggers the other
- The headache can follow a seizure as well
- Both can be relieved with use of Triptan medications

Lennox WG, Lennox-Buchthal MA. Epilepsy and Related Disorders. Boston, MA: Little, Brown; 1960.
Sances G, Guaschino E, Perucca P, et al. Migralepsy: A call for a revision of the definition. *Epilepsia*.2009;**50**:2487-2496.
Perucca P, Terzaghi M, Manni R. Status epilepticus migrainosus: Clinical, electrophysiologic, and imaging characteristics. *Neurology*. 2010;**75**:373-374.
Striano P, Belcastro V, Parisi P, et al. Status epilepticus migrainosus: Clinical, electrophysiologic, and imaging characteristics. *Neurology*. 2011;**76**:761. author reply 761.
Jacob J, Goadsby PJ, Duncan JS. Use of sumatriptan in post-ictal migraine headache. *Neurology*. 1996;**47**:1104.


Migraine
• Common
• Paroxysmal
• Chronic
Epilepsy

Common: Incidence

Migraine

- 12% of the general population
- 2% Chronic Migraine
- W>M

Epilepsy

- 4% life time prevalence of epilepsy
- No gender dominance

Lipton RB, Bigal ME. Migraine: Epidemiology, impact, and risk factors for progression. *Headache*.2005;**45**(Suppl. 1):S3-S13.
Schwedt TJ. Chronic migraine. *BMJ*. 2014;**348**:g1416.
Oakley C, Kossoff E. Migraine and epilepsy in the pediatric population. *Curr Pain Headache Rep*. 2014;**18**:1-12.

Paroxysmal: Premonition, Aura, Ictal, Post Ictal

	Premonition	Aura	Ictal	Postictal
Migraine	Days or hours before attack	Visual is most common 5-60 minutes duration	Headache	
	Fatigue, nausea, neck stiffness, yawning, pallor, photophobia, phonophobia	Visual Olfactory Motor Sensory		Fatigue lethargy, exhaustion
Epilepsy	10 min to 3 days	Seconds to minutes in duration	Focal or GTC activity	

Amery WK, Waelkens J, Vandenbergh V. Migraine warnings. *Headache*. 1986;**26**:60-66.
Giffin NJ, Ruggiero L, Lipton RB, et al. Premonitory symptoms in migraine: an electronic diary study.*Neurology*. 2003;**60**:935-940.
Hughes J, Devinsky O, Feldmann E, et al. Premonitory symptoms in epilepsy. *Seizure*. 1993;**2**:201-203.

Chronic

- Migraine
  - Starts in teens to 20s
  - May resolve premenopausal for women
- Epilepsy
  - Medications required for better management
  - Consideration for surgery
  - Quality of life

RS is a 36 y/o

- Reports a h/o headaches that started in her 20s, originally intermittent having headaches monthly that were severe with associated photophobia, photophobia nausea and vomiting. She would have to take the day off to sleep and take medications.
- She has an aura of scotoma off the right that will grow in size to obscure her vision over the course of 15 minutes and can last 20 min at a time then the headache will start.

- She reports additional hx of spells that can occur with headache

  Occurs yearly, there is no triggering event, she will get a rising heat sensation that starts in the abdomen, followed by difficulty with concentration and orientation. She develops a holocephalic headache. She has never fallen. Episodes last only a few minutes, but then she feels whipped for the rest of the day. She denies any GTC movement, urinary incontinence or tongue biting.

Evaluation of Our Patients

MT

- ED evaluation
  - Looking for life threatening and reversible cause of the patient's sx
  - You are on a time line
- Differential dx
  - Stroke
  - Migraine
  - Seizure
  - Meningitis/Encephalitis
- Work up
  - Imaging
  - Labs

1.2.3 Hemiplegic Migraine

- Diagnostic criteria:
  A. At least two attacks fulfilling criteria B and C
  B. Aura consisting of both of the following:
     1. fully reversible motor weakness
     2. fully reversible visual, sensory and/or speech/ language symptoms
  C. At least two of the following four characteristics:
     1. at least one aura symptom spreads gradually over 5 minutes, and/or two or more symptoms occur in succession
     2. each individual non-motor aura symptom lasts 5–60 minutes, and motor symptoms last 5–60 minutes, and motor symptoms last
     3. at least one aura symptom is unilateral
     4. the aura is accompanied, or followed within 60 minutes, by headache
  D. Not better accounted for by another ICHD-3 diagnosis, and transient ischaemic attack and stroke have been excluded.

Headache Classification Committee of the International Headache Society (HIS). The International Classification of Headache Disorders, 3rd edition (beta version). *Cephalalgia*. 2013;**33**:629-808

1.2.3.1 Familial hemiplegic migraine

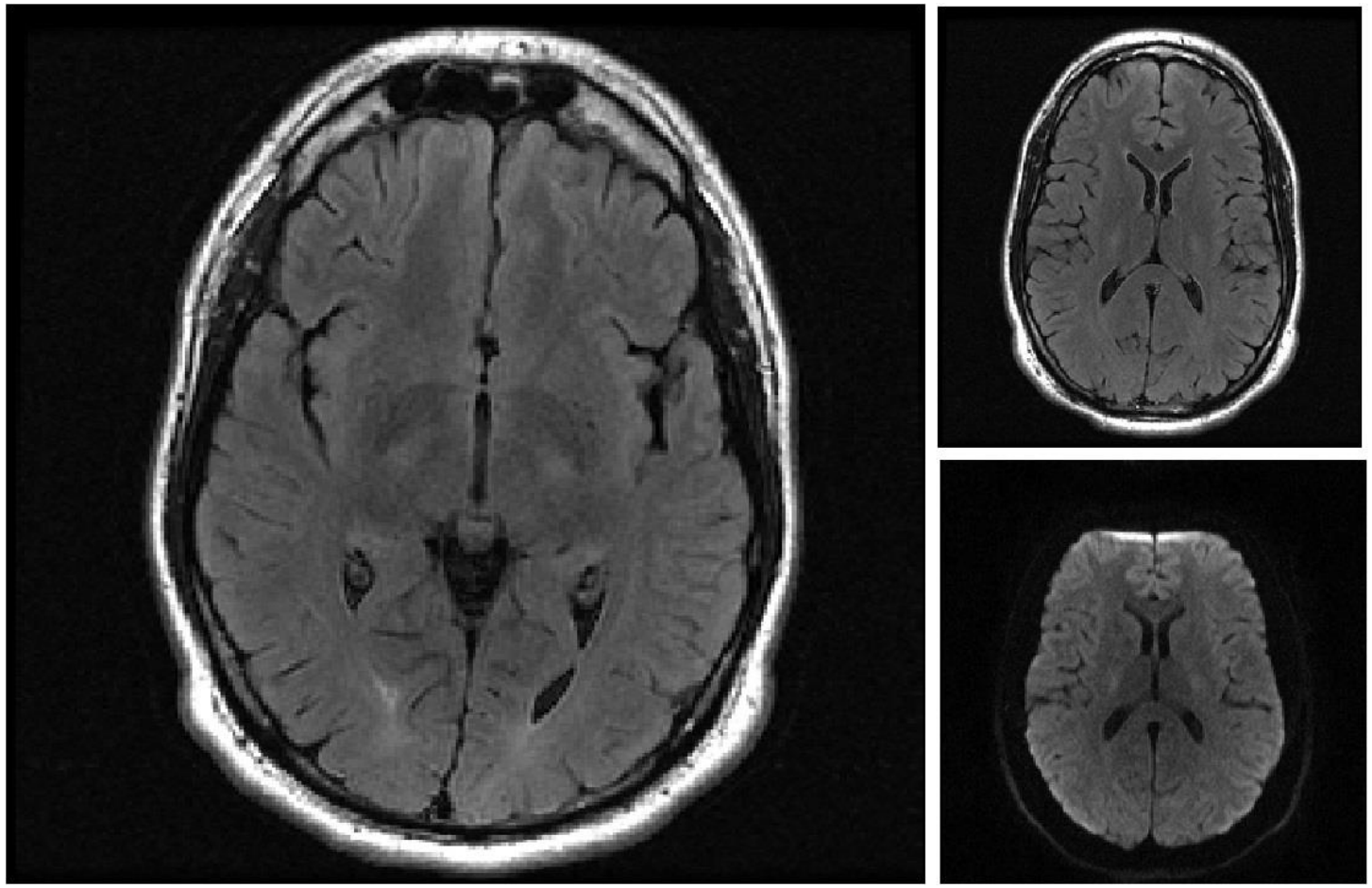
- Description: Migraine with aura including motor weakness, and at least one first- or second-degree relative has migraine aura including motor weakness.
- Diagnostic criteria:
  A. Fulfils criteria for 1.2.3 Hemiplegic migraine
  B. At least one first- or second-degree relative has had attacks fulfilling criteria for 1.2.3 Hemiplegic migraine.

Headache Classification Committee of the International Headache Society (HIS). The International Classification of Headache Disorders, 3rd edition (beta version). *Cephalalgia*. 2013;**33**:629-808

MT

- Patient was evaluated by the stroke team, he was with in the window for TPA and received IV TPA for the management of his sx.

MRI Brain



MT is a 26 y/o

- Patient recovered back to his baseline over night
- Additional history
  - A shorter event, lasting 15 minutes, occurred during a New Year's Celebration (3 days prior to this presentation). The sensory sx were left sided with associated headache. He had consumed EtOH. Due to the short duration he did not seek medical attention at that time.

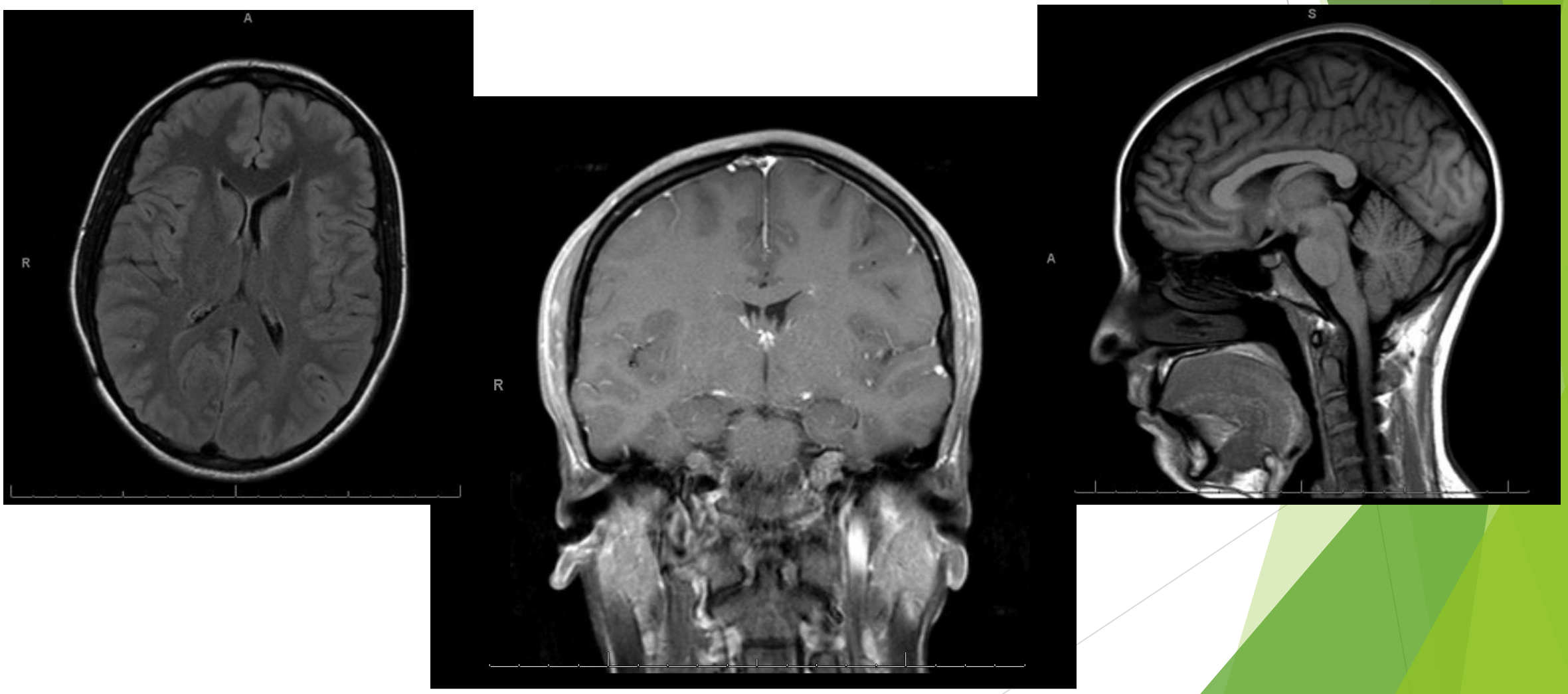
RS

- Clinical Patient evaluation
- Differential Dx:
  - Migraine
  - Epilepsy
  - Migrolepsy
- Evaluation
  - Imaging
  - EEG
    - VEEG vs 30 minute with provoking maneuvers

RS

- She has no h/o meningitis or encephalitis
- She has no h/o febrile seizures
- There is a maternal cousin with epilepsy

MRI brain



RS

- Normal MRI brain
- Normal labs
- Normal 30 min EEG, sleep deprived

1.4.4 Migraine aura-triggered seizure

- Description: A seizure triggered by an attack of migraine with aura.
- Diagnostic criteria:
  A. A seizure fulfilling diagnostic criteria for one type of epileptic attack, and criterion B below
  B. Occurring in a patient with 1.2 Migraine with aura, and during, or within 1 hour after, an attack of migraine with aura
  C. Not better accounted for by another diagnosis

Headache Classification Committee of the International Headache Society (HIS). The International Classification of Headache Disorders, 3rd edition (beta version). *Cephalalgia*. 2013;**33**:629-808

7.6 Headache attributed to epileptic seizure

- Description: Headache caused by an epileptic seizure, occurring during and/or after the seizure and remitting spontaneously within hours or up to 3 days.
- Diagnostic criteria:
  A. Any headache fulfilling criterion C
  B. The patient is having or has recently had an epileptic seizure
  C. Evidence of causation demonstrated by both of the following:
     1. headache has developed simultaneously with onset of the seizure
     2. headache has resolved spontaneously after the seizure has terminated
  D. Not better accounted for by another ICHD-3 diagnosis.

Headache Classification Committee of the International Headache Society (HIS). The International Classification of Headache Disorders, 3rd edition (beta version). *Cephalalgia*. 2013;**33**:629-808

7.6.1 Hemicrania epileptic

- Description: Headache occurring during a partial epileptic seizure, ipsilateral to the epileptic discharge, and remitting immediately or soon after the seizure has terminated.
- Diagnostic criteria:
  A. Any headache fulfilling criterion C
  B. The patient is having a partial epileptic seizure
  C. Evidence of causation demonstrated by both of the following:
     1. headache has developed simultaneously with onset of the partial seizure
     2. either or both of the following:
        a) headache has significantly improved immediately after the partial seizure has terminated
        b) headache is ipsilateral to the ictal discharge
  D. Not better accounted for by another ICHD-3 diagnosis

Headache Classification Committee of the International Headache Society (HIS). The International Classification of Headache Disorders, 3rd edition (beta version). *Cephalalgia*. 2013;**33**:629-808

7.6.2 Post-ictal headache

- Description: Headache caused by and occurring within 3 hours after an epileptic seizure, and remitting spontaneously within 72 hours after seizure termination.
- Diagnostic criteria:
  A. Any headache fulfilling criterion C
  B. The patient has recently had a partial or generalized epileptic seizure
  C. Evidence of causation demonstrated by both of the following:
     1. headache has developed within 3 hours after the epileptic seizure has terminated
     2. headache has resolved within 72 hours after the epileptic seizure has terminated
  D. Not better accounted for by another ICHD-3 diagnosis.

Headache Classification Committee of the International Headache Society (HIS). The International Classification of Headache Disorders, 3rd edition (beta version). *Cephalalgia*. 2013;**33**:629-808

Mechanisms

- Fundamental differences:
  - Migraine: burst of abnormal electrical activity results in SUPRESSION of neuronal activity and release of inflammatory substances
  - Epilepsy: abnormal interictal low frequency firing of small groups of neurons entrain larger groups that then produce a high-frequency discharge that constitutes the epileptic seizures

Mechanisms

- Vasodilation and oligemia
  - Neuro inflammatory marker release
- Excitatory brain network
  - Cortical spreading depression
  - Excess glutamate
    - Alterations in the NMDA receptors
  - Voltage gated Na channel abnormalities
  - Variations in GABA receptor

Mechanisms

- Genetics
  - Both are highly hereditary disorders
    - Migraine with aura > migraine without aura
  - Epilepsy Phenome/Genome Project
    - Patients with epilepsy who have 2 or more 1' relatives with epilepsy have a 2 fold increase risk of having Migraine with aura
    - Patients with migraine were at heightened risk of epilepsy

Ludvigsson P, Hesdorffer D, Olafsson E, et al. Migraine with aura is a risk factor for unprovoked seizures in children. *Ann Neurol*. 2006;**59**:210-213.
Winawer MR, Connors R. Evidence for a shared genetic susceptibility to migraine and epilepsy. *Epilepsia*.2013;**54**:288-295.

Shared Genetics

- CACNIA gene mutations - P/Q Calcium Channel (medicating serotonin and glutamate release)
  - Hemiplegic migraine
  - Hemiplegic migraine with complex partial and secondary generalized seizures
  - Episodic ataxia with vermian atrophy
- ATP1A2 gene mutations – alpha2 subunit of Na+/K+ pump (causes increased K+ and glutamate in the extracellular space)
  - Hemiplegic migraine isolated or with Infantile convulsions and mental retardation
- **SCN1A gene mutations – alpha1 subunit of the voltage gated Na+ Channel**
  - Hemiplegic migraine
  - Generalized convulsions
- MELAS syndrome

Ducros A, Denier C, Joutel A, et al. The clinical spectrum of familial hemiplegic migraine associated with mutations in a neuronal calcium channel. *N Engl J Med*. 2001;**345**:17-24.
Eikermann-Haerter K, Dilekoz E, Kudo C, et al. Genetic and hormonal factors modulate spreading depression and transient hemiparesis in mouse models of familial hemiplegic migraine type 1. *J Clin Invest*. 2009;**119**:99-109.
Kurth T, Chabriat H, Bousser MG. Migraine and stroke: a complex association with clinical implications. Lancet Neurol. 2012;**11**:92-100.
Eikermann-Haerter K, Lee JH, Yuzawa I, et al. Migraine mutations increase stroke vulnerability by facilitating ischemic depolarizations. *Circulation*. 2012;**125**:335-345.
De Fusco M, Marconi R, Silvestri L, et al. Haploinsufficiency of ATP1A2 encoding the Na+/K+ pump alpha2 subunit associated with familial hemiplegic migraine type 2. *Nat Genet*. 2003;**33**:192-196.
Dichgans M, Freilinger T, Eckstein G, et al. Mutation in the neuronal voltage-gated sodium channel SCN1A in familial hemiplegic migraine. *Lancet*. 2005;**366**:371-377.
Castro MJ, Stam AH, Lemos C, et al. First mutation in the voltage-gated Nav1.1 subunit gene SCN1A with co-occurring familial hemiplegic migraine and epilepsy. *Cephalalgia*. 2009;**29**:308-313.

Management and Patient outcomes

MT

- Placed on prophylactic medication management with Topiramate
- Naproxen sodium and vsitaril PRN
- Triptan was NOT give due to hemiplegic episode

- Considerations:
  - Use of medications with NMDA receptor action
    - Magnesium
    - Namenda
    - Ketamine
  - Calcium Channel Blockers
  - Genetic Testing

RS

- Placed on ADE for prevention of both headache and seizures - Topiramate
- Naproxen sodium and vistaril PRN
- Ativan 2mg PO PRN
- Sumatriptan 100mg PO PRN

- Considerations:
  - Medications
    - Avoiding medications that lower seizure threshold in this patient
    - Choosing medications for duel purpose
  - Driving

Thank you for your attention