Epilepsy 101

Conflict of Interest Declaration

Nothing to Disclose

Presenter: Dr. O. Carter Snead III, M.D. FRCP(C)

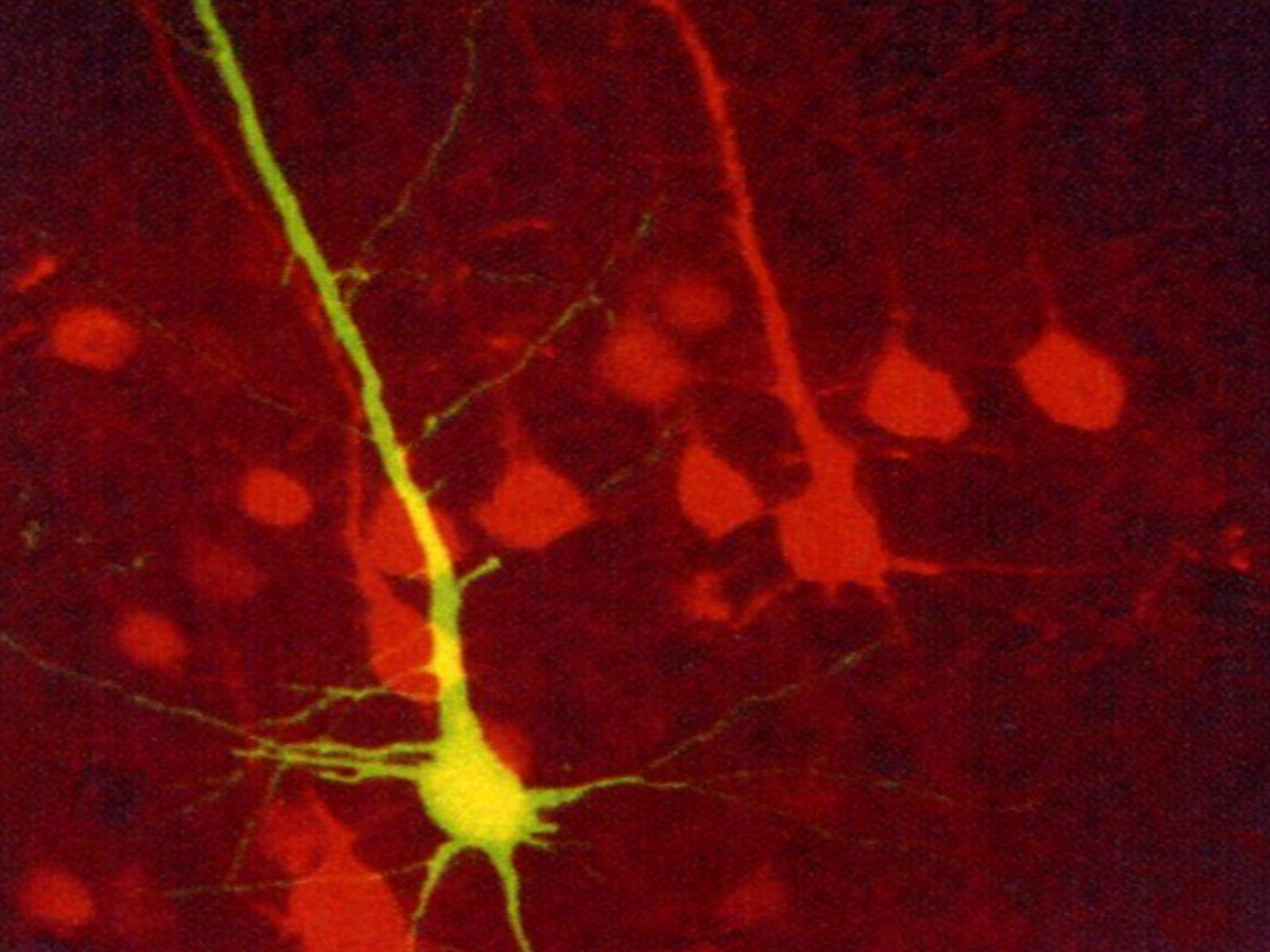
Title of Presentation Epilepsy 101

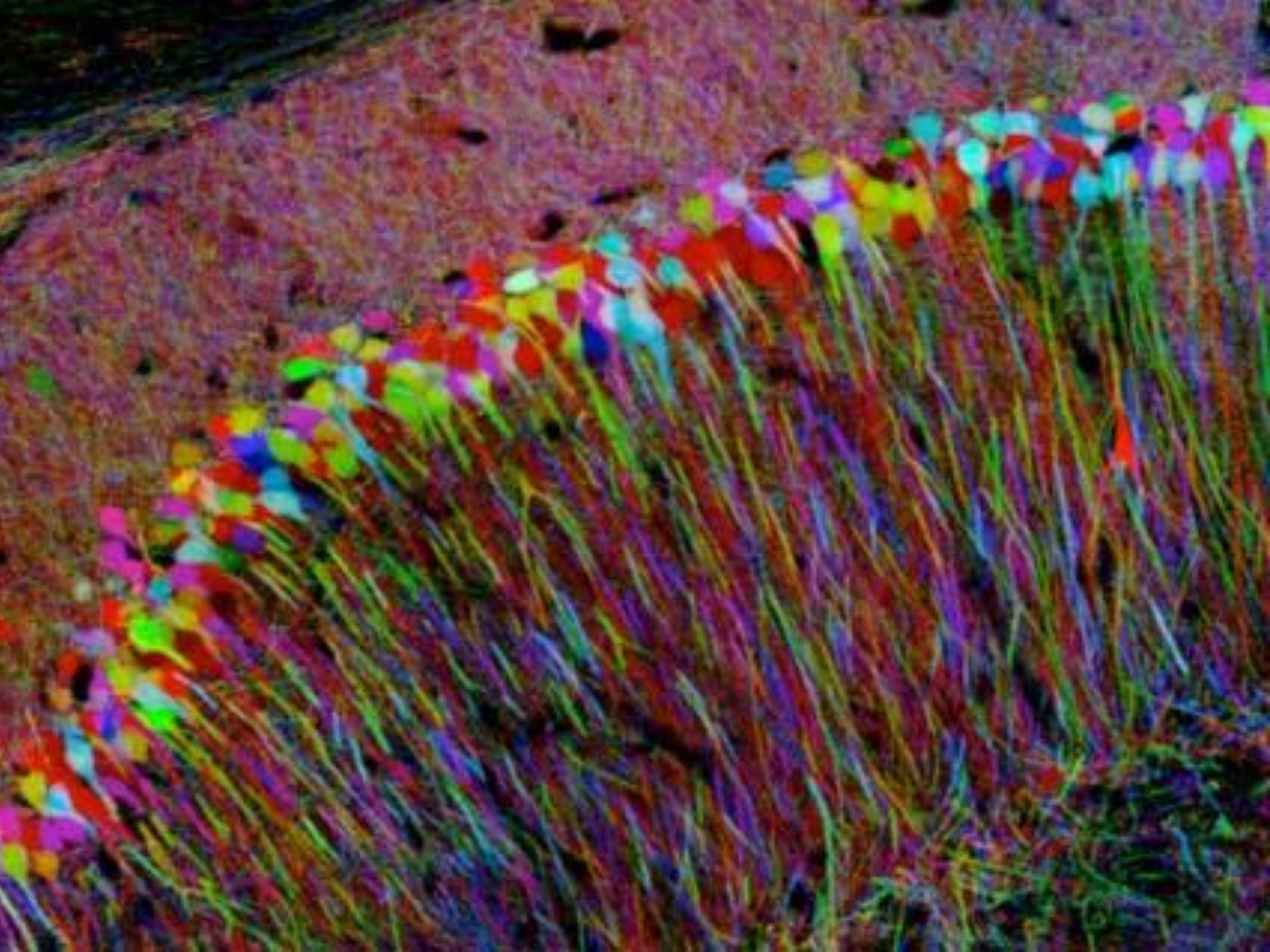
I have no financial or personal relationship related to this presentation to disclose

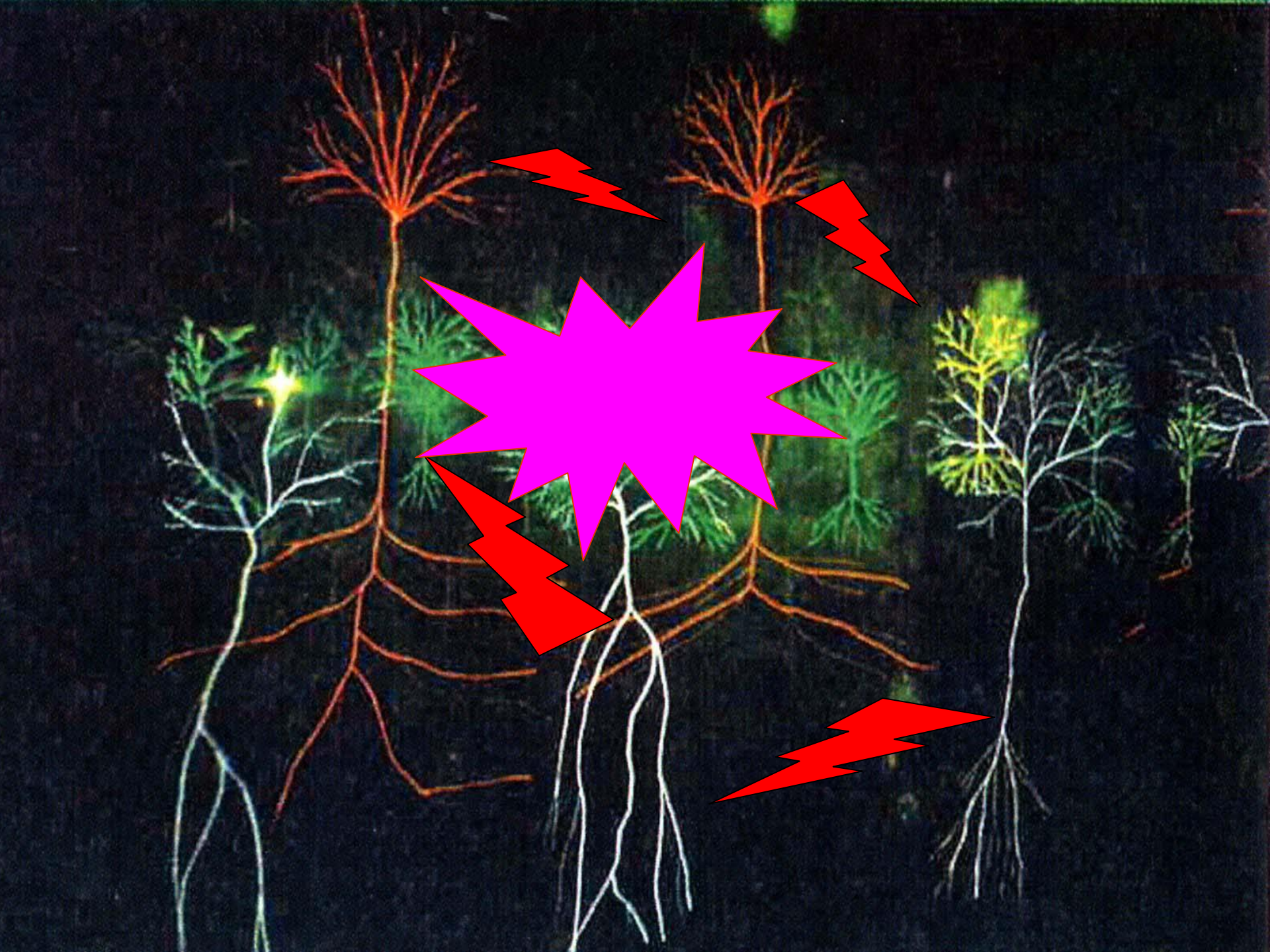
Learning Objectives – To answer the Following

1. The basics: What is a seizure? what is epilepsy?
2. How do I approach a new seizure patient? How do I work them up?
3. What on earth does this EEG interpretation mean? Does everyone with a seizure need a CT scan or MRI?
4. When do I treat a seizure and with what?
5. The seizures are not controlled and they want to try CBD. What to do?
6. What about driving?
7. When should I refer and to whom? What is Project ECHO?

What is a seizure?







What is a Seizure?

Official definition:

- An **epileptic seizure is a transient occurrence** of signs and/or symptoms due to **abnormal excessive or synchronous neuronal activity** in the brain

Source: https://www.ilae.org/guidelines/definition-and-classification/the-2014-definition-of-epilepsy-a-perspective-for-patients-and-caregivers

What is Epilepsy?

Epilepsy is a disease characterized by an enduring predisposition to generate epileptic seizures and by the neurobiological, cognitive, psychological, and social consequences of this condition

1. Spontaneous recurrent seizures
2. Seizure occurs as part of an epilepsy syndrome
    1. e.g. Tuberous sclerosis syndrome
3. There is >60% chance of recurrence after a single seizure
    1. Focal seizures
    2. Abnormal EEG
    3. Family history in a first degree relative
    4. Structural lesion on neuroimaging
    5. Nocturnal seizure

Source: https://www.ilae.org/guidelines/definition-and-classification/the-2014-definition-of-epilepsy-a-perspective-for-patients-and-caregivers

Seizures and Epilepsy

User-friendly definitions

Seizure: An episodic behavioral event caused by a paroxysmal discharge of neurons

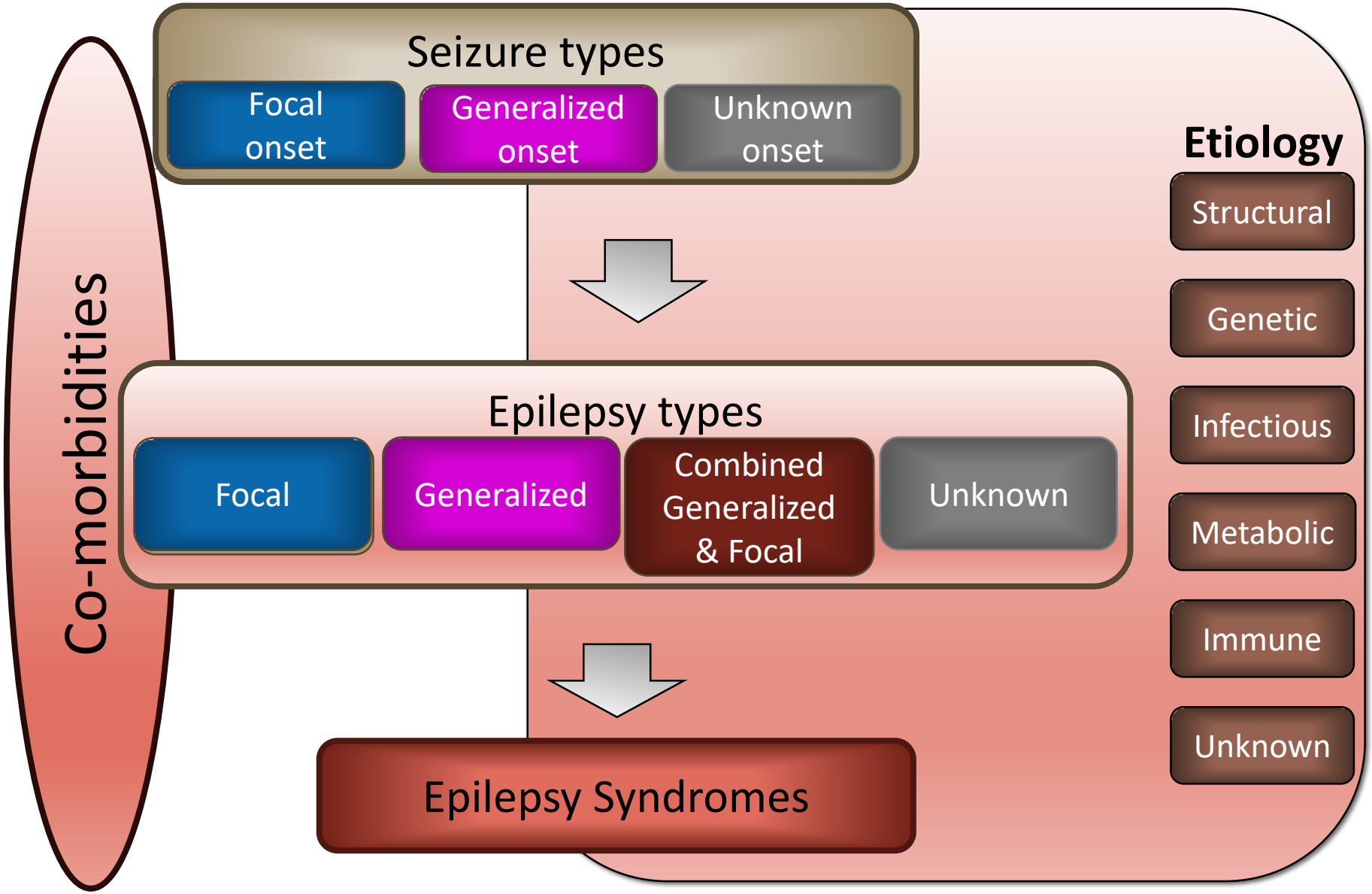
Epilepsy: A disorder [disease] characterized by spontaneous recurrent seizures

Do Seizures mean the same thing as epilepsy?

NO

- seizure and epilepsy are not the same.
- seizure is an event and epilepsy is the disease involving recurrent unprovoked seizures

Source: https://www.ilae.org/guidelines/definition-and-classification/the-2014-definition-of-epilepsy-a-perspective-for-patients-and-caregivers



Scheffer et al. Epilepsia 2017; 58 (4): 512-521

How do I approach the patient with a seizure?

- Detailed history of Event
  - ? Aura, ? Postictal confusion
- Past and Recent Medical History
  - Identify risk factors – Trauma, ingestion, drugs, etc.
- Family History
  - Key
- General Physical Examination
  - Dysmorphisms, Skin, back, hips, heart
- Neurological Examination
  - Focality

What caused the seizure?

The answer often is age-specific

- Adults – neoplastic, toxic-metabolic,,vascular, traumatic, neuroinflammatory, genetic, infectious
- Children -Genetic, congenital anomalies of brain, toxic-metabolic, vascular, infectious, neuro-inflammatory, neoplastic, traumatic,

Source: http://pediatriccare.solutions.aap.org/content.aspx?resultClick=1&gbosid=165567#sec_59043243

How do I work up my seizure patient?

- Laboratory tests always should be driven by clinical circumstances
- Toxicology screening should be considered across the entire age range if there is any relevant history.

Ontario Provincial Guidelines for Management of Epilepsy in Adults and Children
http://ontarioepilepsyguidelines.ca/)

When do I order an EEG in a patient who has had a seizure?

Virtually always

- A critical part of the neurodiagnostic evaluation of the adult and child with an apparent unprovoked first seizure
- May indicate diagnosis, prognosis and have treatment implications
- Can be done electively

Source :http://ontarioepilepsyguidelines.ca/

How do I deal with an EEG interpretation when I don't have a clue?

A few hints;

- Be aware of who is reading the EEG. It may be an adult neurologist unfamiliar with developmental features of the EEG in a child
- Be aware of the limitations of EEG
- Be aware of the buzz words to look for in an EEG report

What are the limitations of an EEG in a seizure work up?

Records field electrical potential of 10^7 neurons out of 10^{11} neurons in brain

- Records 45 minutes out of a 24 hour day so many things can be missed
- Recording the tiny electrical signal from the brain requires amplification and thus creates possibilities for artifacts which limit interpretation

HOWEVER, EEG REMAINS THE MOST IMPORTANT DIAGNOSTIC TEST DONE IN EPILEPSY WORKUP

WHAT SHOULD I FOCUS UPON IN TRYING TO INTEPRET THE FORMAL EEG INTERPRETATION?

BUZZWORDS TO LOOK FOR AND ACT UPON

- Description of *background activity* as slow or normal – this is non-specific abnormality which may mean nothing

WHAT SHOULD I FOCUS UPON IN TRYING TO INTEPRET THE FORMAL EEG INTERPRETATION?

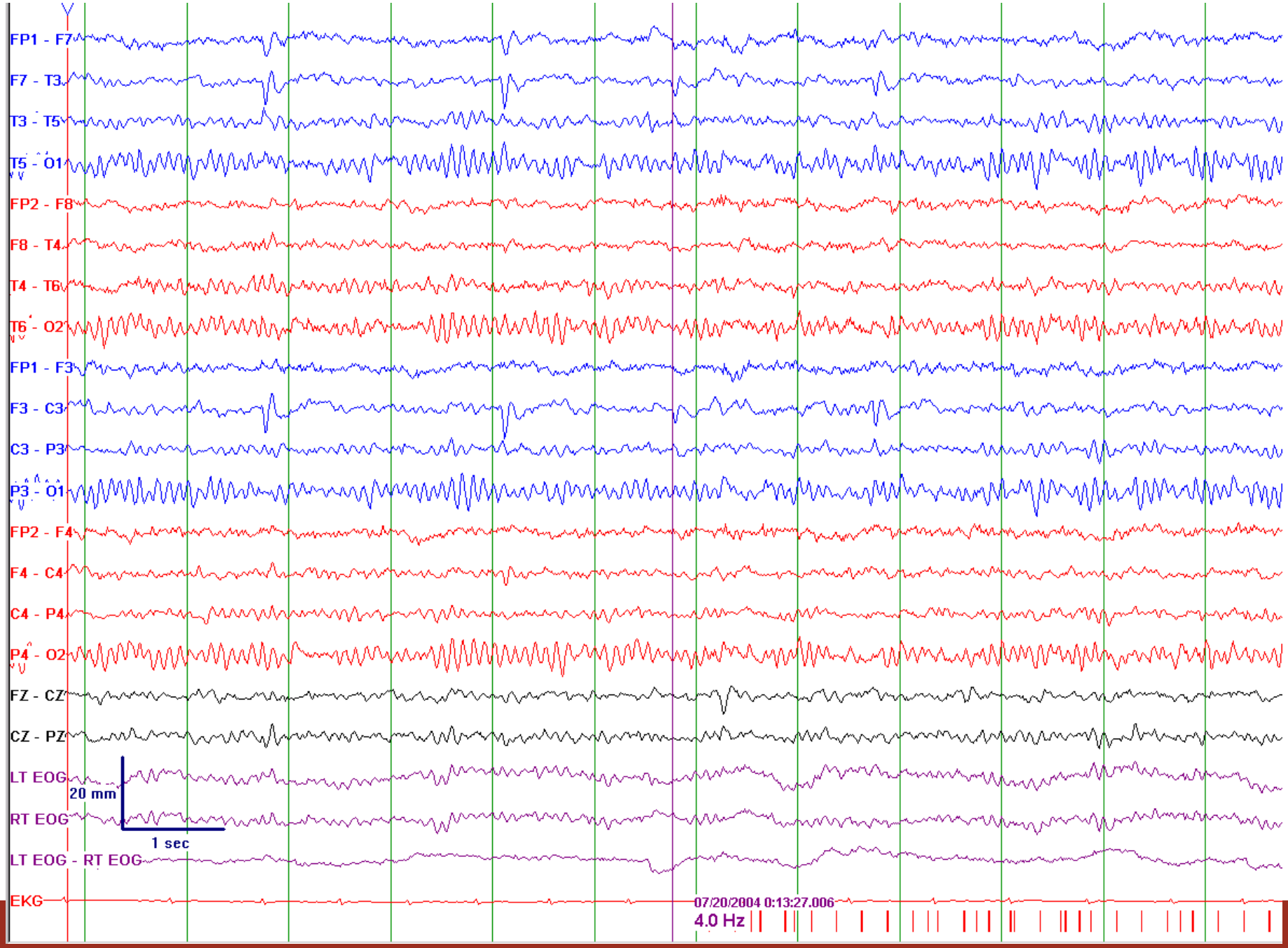
BUZZWORDS TO LOOK FOR

- Description of *focal slowing* on one side or side to side asymmetry – this is significant and raises possibility of structural lesion underlying the side where slow wave activity is described. If you see any reference to focality, you should order an MRI scan of the brain

WHAT SHOULD I FOCUS UPON IN TRYING TO INTEPRET THE FORMAL EEG INTERPRETATION?

BUZZWORDS TO LOOK FOR

- Description of *epileptiform activity, ie. spike, spike wave, sharp waves* – all wave forms that appear and disappear quickly. This finding is suggestive, but not diagnostic of a seizure disorder. It has to be interpreted in light of clinical history and findings.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T4 - T6
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C3 - P3
P3 - O1
FP2 - F4
F4 - C4
C4 - P4
P4 - O2
FZ - CZ
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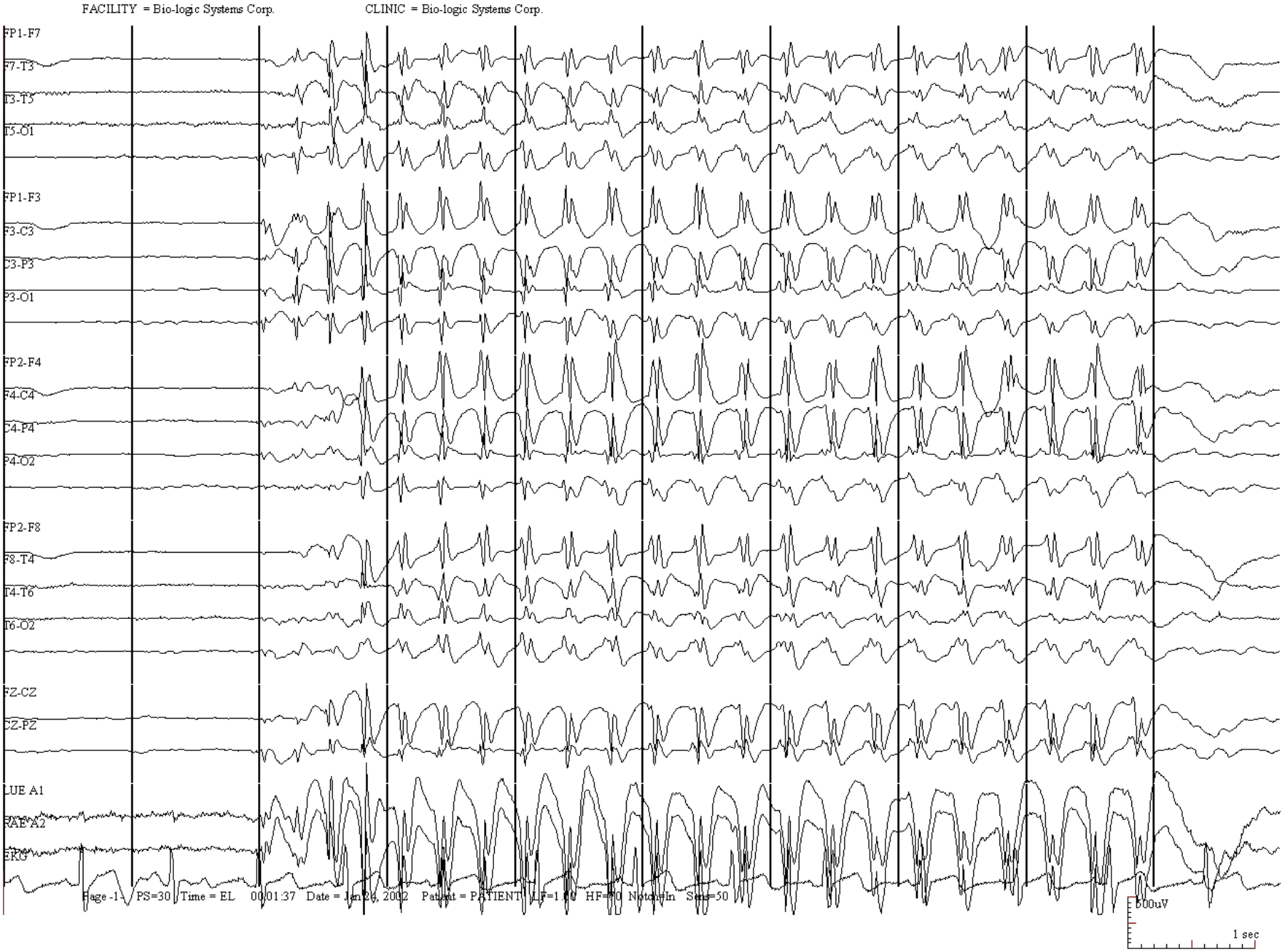
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What do I do with an abnormal EEG result?

An EEG abnormality by itself is not sufficient to make a diagnosis that an epileptic seizure occurred, nor can its absence rule out a seizure

Source: http://ontarioepilepsyguidelines.ca/

When do I consider neuroimaging in investigation of seizures?

- For children with first seizure, neuroimaging is reserved for those with focal seizures, focal neurological abnormalities associated with the seizure, a pre-existing neurological disorder, or seizures that cannot be controlled.
- Neuroimaging is always indicated in new onset seizures in anyone 15 years or older
- CT is limited – MR always procedure of choice

http://epilepsyontario.org/wp-content/uploads/2015/03/Provincial-Guidelines-for-the-Management-of-Epilepsy-in-Adults-and-Children_Janurary-20151.pdf https://ontarioepilepsyguidelines.ca/;

Seizure - Workup

Guideline for Other Tests

- Seizure-like attacks with a cardiovascular cause may be misdiagnosed as epilepsy.
- A 12-lead electrocardiography (ECG) should be performed in adults with suspected epilepsy.
- In children and young people, a 12-lead ECG should be considered in cases of diagnostic uncertainty where syncope is an issue.

Source:https://www.criticalcareontario.ca/EN/Epilepsy%20Guideline%20Series/Provincial%20Guidelines%20for%20Management%20of%20Epilepsy%20in%20Adults%20and%20Children_January%202015.pdf

When do I treat?

DECISION IS BASED UPON RISK OF RECURRENCE

- Single Seizure = 50% chance next 5 years
- TWO Seizures = 80% chance next 5 years
- Single Seizure PLUS Abnormal EEG OR Imaging = >80% chance of recurrence
- Nocturnal seizure = > 50% chance next 5 years

Treatment recommended following 2 unprovoked seizures OR after a single unprovoked seizure with abnormal EEG or CT/MRI

Krumholz et al. Neurology 2015;84:1705-1713

When should I *not* treat?

Clear provoked seizures with *reversible* or *avoidable* causes

- Drug/alcohol intoxication-withdrawal
  - opiates
  - high doses of-βlactam antibiotics
  - quinolones
  - antidepressants (welbutrin)
  - antipsychotics (clozapine, olanzapine)
- Metabolic derangement
- Systemic illness
- Febrile seizures in children under 6

Seizure mimics

- Vasovagal syncope
- Cardiac or autonomic cause
- Non-epileptic seizure

Uncertainty of diagnosis

What should I treat with?

Initiating the first trial of anticonvulsant treatment

Seizure Type	Drug of Choice
Focal Onset	Carbamazepine/Oxcarbazepine [Non-Asian Descent) Clobazam Levetiracetam [Alternate]
General Onset – Absence	Ethosuximide Valproic Acid
General Onset – Motor	Valproic Acid Lamotrigine Leviteracetam
Unknown Onset	Valproic Acid

http://epilepsyontario.org/wp-content/uploads/2015/03/Provincial-Guidelines-for-the-Management-of-Epilepsy-in-Adults-and-Children_Janurary-20151.pdf

What co-morbidities can I expect?

- Social stigma
- Psychiatric co-morbidity
- Poor school performance, peer relationships
- Higher unemployment
- Inability to drive
- Marriage and family less likely
- Lower educational status
- Higher mortality

http://epilepsyontario.org/wp-content/uploads/2015/03/Provincial-Guidelines-for-the-Management-of-Epilepsy-in-Adults-and-Children_Janurary-20151.pdf

What can I tell my patient about prognosis?

- 70 % of patients with epilepsy can have the seizures controlled with medications

- 30 % continue to have medically refractory epilepsy, i.e. frequent, severe seizures in spite of treatment with antiepileptic drugs
- Drug resistant epilepsy is when seizures fail to respond to 2 AEDs that are indicated for seizure type in appropriate doses.

What about CBD?

ANNALS of Clinical and Translational Neurology
Open Access
ANA American Neurological Association

:2

RESEARCH ARTICLE

A prospective open-label trial of a CBD/THC cannabis oil in dravet syndrome

Bláthnaid McCoy[1,2], Laura Wang[3], Maria Zak[1], Sameer Al-Mehmadi[1], Nadia Kabir[1], Kenda Alhadid[1], Kyla McDonald[4], Grace Zhang[4], Rohit Sharma[1], Robyn Whitney[1,2], Katia Sinopoli[4] & O. Carter Snead III[1]

[1]Division of Neurology, the Hospital for Sick Children, Toronto, Canada
[2]Department of Pediatrics, University of Toronto, Toronto, Canada
[3]Department of Pharmacy, Hospital for Sick Children, Toronto, Canada
[4]Department of Psychology, the Hospital for Sick Children, Toronto, Ontario, Canada

What about CBD? Bottom line

Effective in the pediatric population

High-level evidence required for adults

CBD appears to be effective for LGS and Dravet Syndrome

- Other conditions: CDKL5 Deficiency, Aicardi, Dup15q, Doose Syndrome

48.5% effective reducing seizures by 50%

Seizure-freedom in 8.5%

As safe as current anti-epileptic drugs

CBD-only and CBD + THC preparations have both demonstrated efficacy

Legitimate 3rd line drug

*STOCKINGS ET AL (2018): EVIDENCE FOR CANNABIS AND CANNABINOIDS FOR EPILEPSY:
A SYSTEMATIC REVIEW OF CONTROLLED AND OBSERVATIONAL EVIDENCE

What about driving?

As of July 2018, under Section 203 of the Highway Traffic Act,

- MANDATORY reporting of CERTAIN high risk medical conditions, vision conditions, or functional impairments (described in Ontario Regulation 340/94) that could make it dangerous for a person to drive
  - This applies to
    - Physicians
    - Optometrists
    - Nurse practitioners
- Discretionary reporting of conditions that in the opinion of the healthcare practitioner make it dangerous to drive, but not in the list of certain high risk conditions

	CCMTA		CMA	
	Non-commercial driver	Commercial driver	Non-commercial	Commercial
Provoked sz, brain abnormality	6 months	Same		
Provoked sz, no brain abnormality	No waiting period	Same		
Alcohol withdrawal	6 months, treatment program	Same	6 months sz free Alcohol free, treatment program	
Single unprovoked sz	No specific # of months Normal evaluation complete (MRI & EEG normal)	12 months Normal evaluation	3 months Neurological assessment	12 months Neurological assessment
Epilepsy	6 months	5 years	6 months	5 years
Epilepsy with sz ONLY in sleep or upon awakening	6 months OR Stable pattern x >1year	Stable pattern for >5 years	1 year from initial seizure If drug level levels are therapeutic	5 years
Epilepsy with Simple Partial Sz	6 months OR Stable pattern x >1 year No head/eye deviation, LOC	5 years OR Stable pattern x >3 years	Stable pattern for >1 year No generalized seizures No head/eye deviation, LOC	3 years
Surgery for epilepsy	12 months after surgery	5 years (can be reduced to 3)	12 months after surgery on AEDs	5 years (can be reduced to 3)
Epilepsy with med change	3 months since med change OR 3 months after sz due to med change and resumption of previous effective regimen	6 months since med change OR 6 months after sz due to med change, and resumption of previous effective regimen	3 months after med changed or stopped OR 3 months after sz recurrence (presumably after resuming appropriate meds)	6 months since med change OR 6 months sz free after recurrence

What about driving?

https://joulecma.ca/evidence/CMA-drivers-guide

https://epilepsyontario.org/living-with-epilepsy/epilepsy-and-driving-in-ontario/

http://ccmta.ca/images/publications/pdf//Determining-Driver-Fitness-In-Canada-Final.pdf

*STOCKINGS ET AL (2018): EVIDENCE FOR CANNABIS AND CANNABINOIDS FOR EPILEPSY:
A SYSTEMATIC REVIEW OF CONTROLLED AND OBSERVATIONAL EVIDENCE

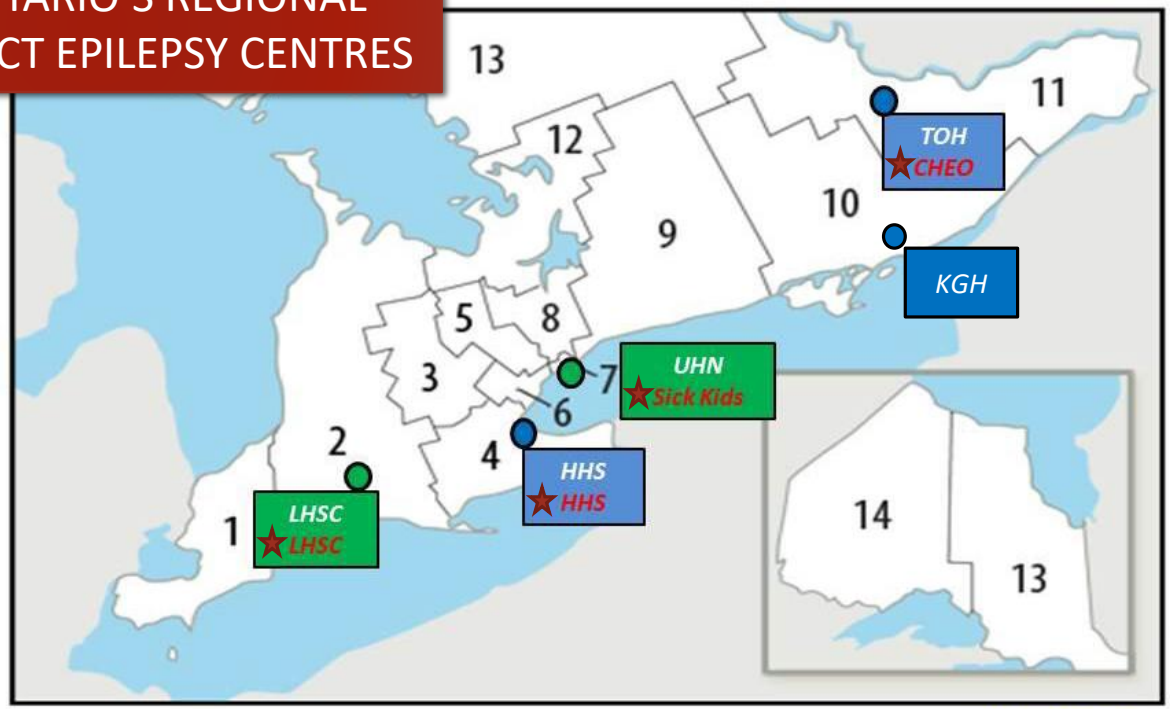
When should I refer my patient with epilepsy?

- Drug resistant
- Potential surgical candidates
  - Never a treatment of last resort – can be curative
  - Always consider in any focal seizure, focal epilepsy, or structural lesion on MRI
- Requirement for diet therapy for epilepsy
- **Any discomfort you have** based on clinical judgment, even if the epilepsy is not drug resistant
  - Adverse drug effects
  - Psychosocial co-morbidities

Source:https://www.criticalcareontario.ca/EN/Epilepsy%20Guideline%20Series/Provincial%20Guidelines%20for%20Management%20of%20Epilepsy%20in%20Adults%20and%20Children_January%202015.pdf

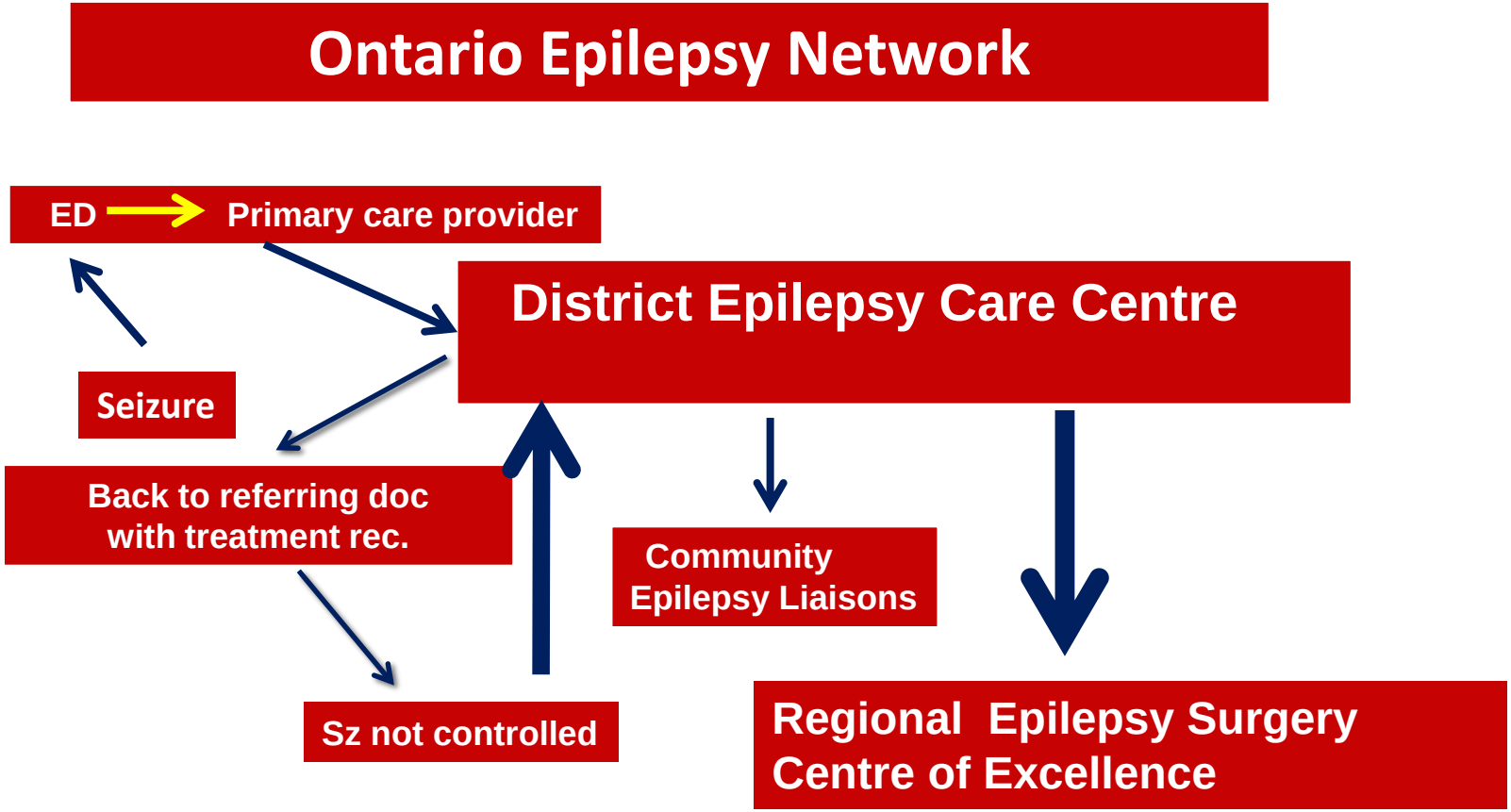
Where should I refer?

MAP OF ONTARIO'S REGIONAL AND DISTRICT EPILEPSY CENTRES



https://www.criticalcareontario.ca/EN/Library/Epilepsy%20Guideline%20Series/Pages/default.aspx

How Do I refer?



Ontario Epilepsy Network

District Epilepsy Centres

Resource for community health providers

Evaluate medically refractory patients for medical and surgical treatment

COMPREHENSIVE EPILEPSY PROGRAM

- **Epileptologist**
- **EEG + EEG video**
- **MRI w/standardized epilepsy imaging protocols**
- **Neuropsychology**
- **Social Work**
- **Dietitian**
- **Community Epilepsy Liaison**

Ontario Epilepsy Network

Regional Epilepsy Surgery Centres of Excellence

DEC for Catchment Area

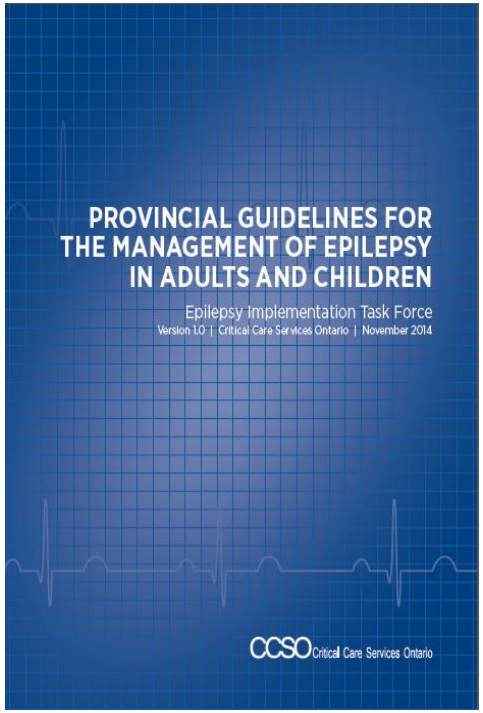
Evaluate Referrals from DEC for surgery

Comprehensive Epilepsy Program + sophisticated neuroimaging beyond MRI

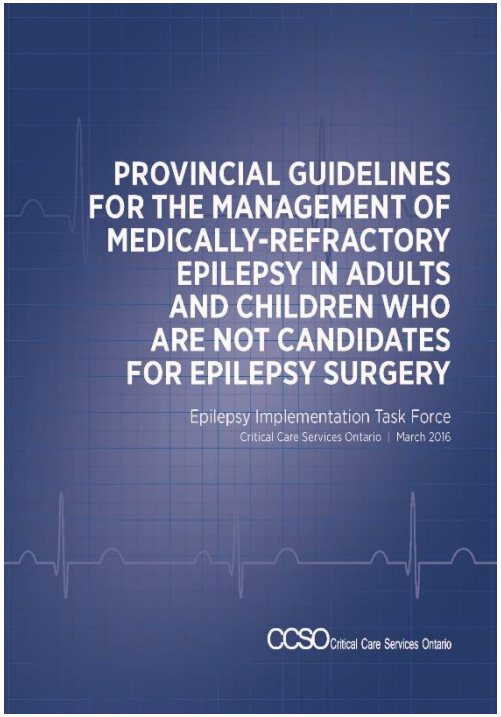
Capability for Epilepsy Surgery

Ontario Epilepsy Network

Provincial Epilepsy Guidelines



2015



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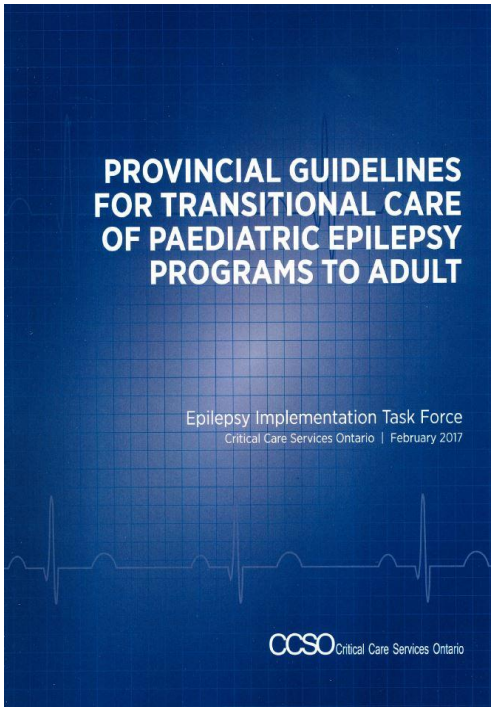


2017

Andrade D, et al. Epilepsia 2017;59:1502-17

Knowledge Translation

How can I provide better care for my epilepsy patient with fewer referrals, shorter wait times, and improved patient satisfaction?

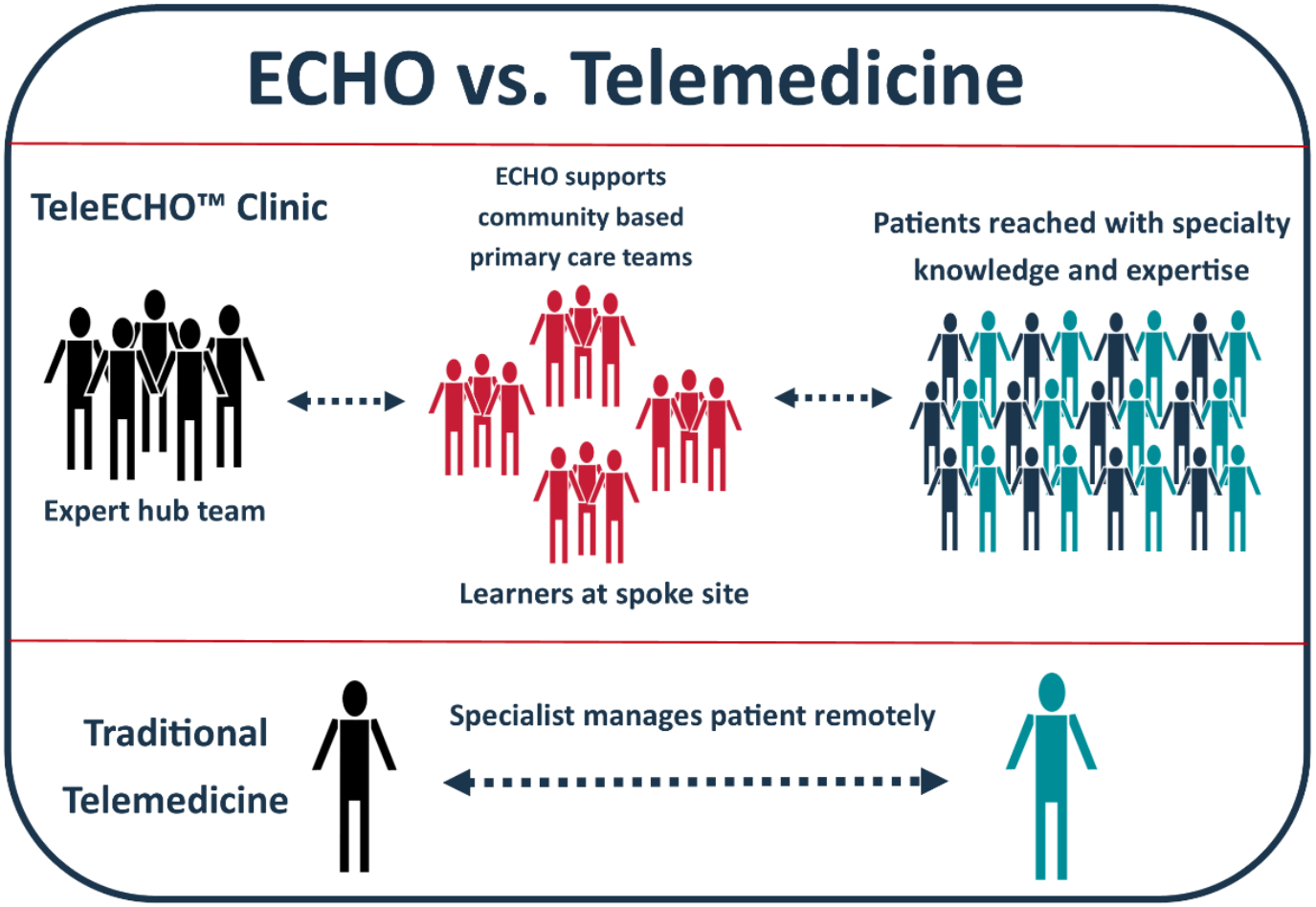
Sanjeev Arora

EXTENDING COMMUNITY HEALTH CARE OUTCOMES

Case-based continuing profession education designed for primary healthcare providers

Delivered through one-to-many videoconferencing [ZOOM]

ECHO vs. Telemedicine



ALL TEACH, ALL LEARN

Project ECHO®

IT WORKS!

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Outcomes of Treatment for Hepatitis C Virus Infection by Primary Care Providers

Sanjeev Arora, M.D., Karla Thornton, M.D., Glen Murata, M.D., Paulina Deming, Pharm.D., Summers Kalishman, Ph.D., Denise Dion, Ph.D., Brooke Parish, M.D., Thomas Burke, B.S., Wesley Pak, M.B.A., Jeffrey Dunkelberg, M.D., Martin Kistin, M.D., John Brown, M.A., Steven Jenkusky, M.D., Miriam Komaromy, M.D., and Clifford Qualls, Ph.D.

RESULTS

A total of 57.5% of the patients treated at the UNM HCV clinic (84 of 146 patients) and 58.2% of those treated at ECHO sites (152 of 261 patients) had a sustained viral response (difference in rates between sites, 0.7 percentage points; 95% confidence interval, −9.2 to 10.7; P=0.89). Among patients with HCV genotype 1 infection, the rate of sustained viral response was 45.8% (38 of 83 patients) at the UNM HCV clinic and 49.7% (73 of 147 patients) at ECHO sites (P=0.57). Serious adverse events occurred in 13.7% of the patients at the UNM HCV clinic and in 6.9% of the patients at ECHO sites.

N Engl J Med. 2011;364:2199–2207

Project ECHO®

Ontario Epilepsy Network
Canada

Epilepsy across the Life Span

-
  - London Health Sciences Centre
  - University Health Network
  - Hamilton Health Sciences Centre
  - The Ottawa Hospital
  - Kingston General Hospital
  - Thunder Bay

Decentralized hub approach

- Dedicated Paediatric Programs
  - SickKids
  - McMaster Children's Hospital (Hamilton)
  - Children's Hospital – London Health Sciences Centre
  - Children's Hospital of Eastern Ontario

Project ECHO®
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Canada

Program Structure

Inter-professional team for each Hub

- **Epileptologist**
- **Nurse Practitioner**
- **Pharmacist**
- **Social Worker**
- **Community Epilepsy Liaison**

Spokes can attend any session offered by any Centre

- **Staggered "cycles" to provide more options for spokes to cover all the didactic learning**

Case presentations by spokes to be made to the local Hub so that appropriate local resource supports can be identified for patients

CME-accredited curricula for Epilepsy in Child and Youth and Epilepsy in Adults

Project ECHO®

Ontario Epilepsy Network
Canada

TeleECHO Sessions

CME accrredited – Short Didactic [Clinical Pearls]

Objective: to enhance self-efficacy re epilepsy management among primary care providers to start first line [and sometime second line] AEDs and co-manage epilepsy patients with academic interprofessional teams

How do I register for Project ECHO Epilepsy Across the Life Span?

https://oen.echoontario.ca/register-for-an-echo/

Epilepsy 101 – Bringing it all together

A case of drug resistant focal motor epilepsy who is referred for potential epilepsy surgery

15 year old boy with life-long seizures since age 4 years

Focal sensory -> focal motor involving left arm and hand
Secondary generalization
Classification: Focal Epilepsy - motor

Unresponsive to 5 different antiepileptic drugs
Drug Resistant Epilepsy

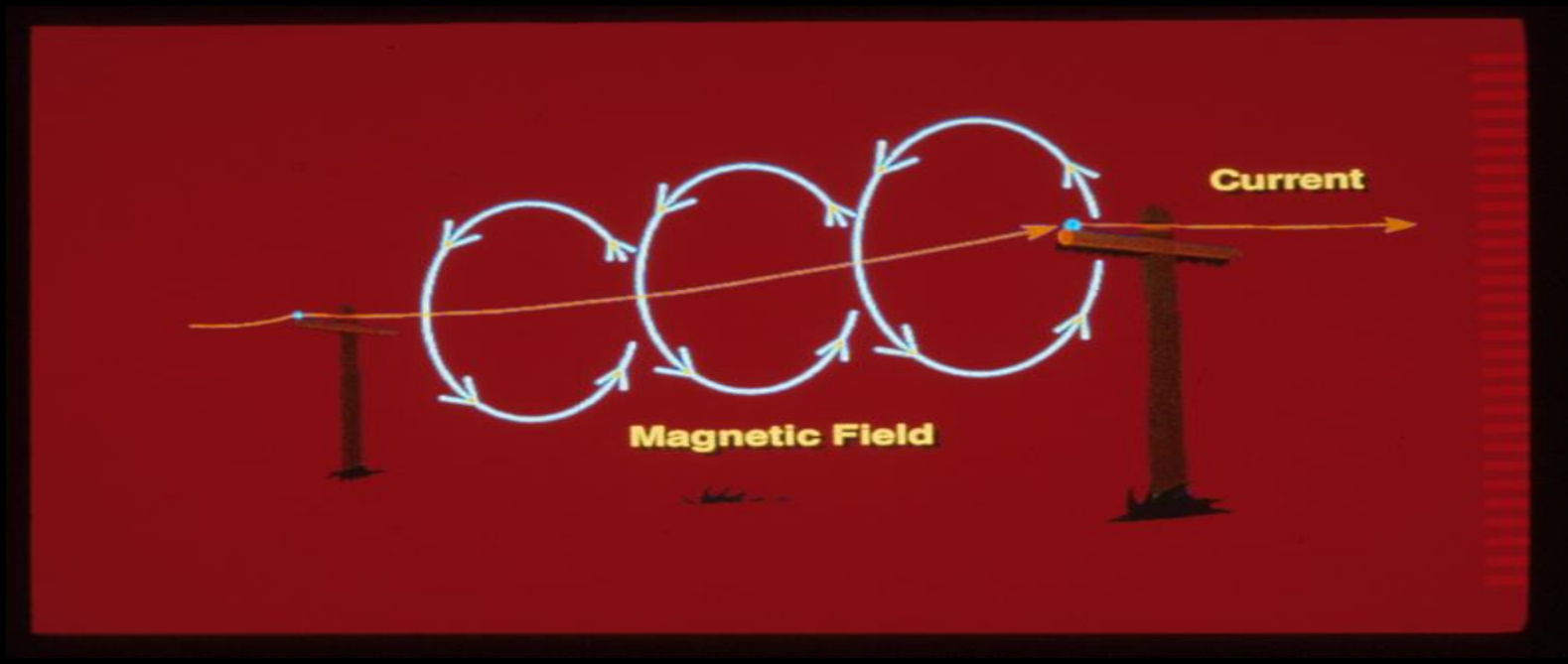
Depressed, anxious, bullied in school
Co-morbidities

Referred to Regional Epilepsy Surgery Centre of Excellence at SickKids
When and where to refer

Investigations

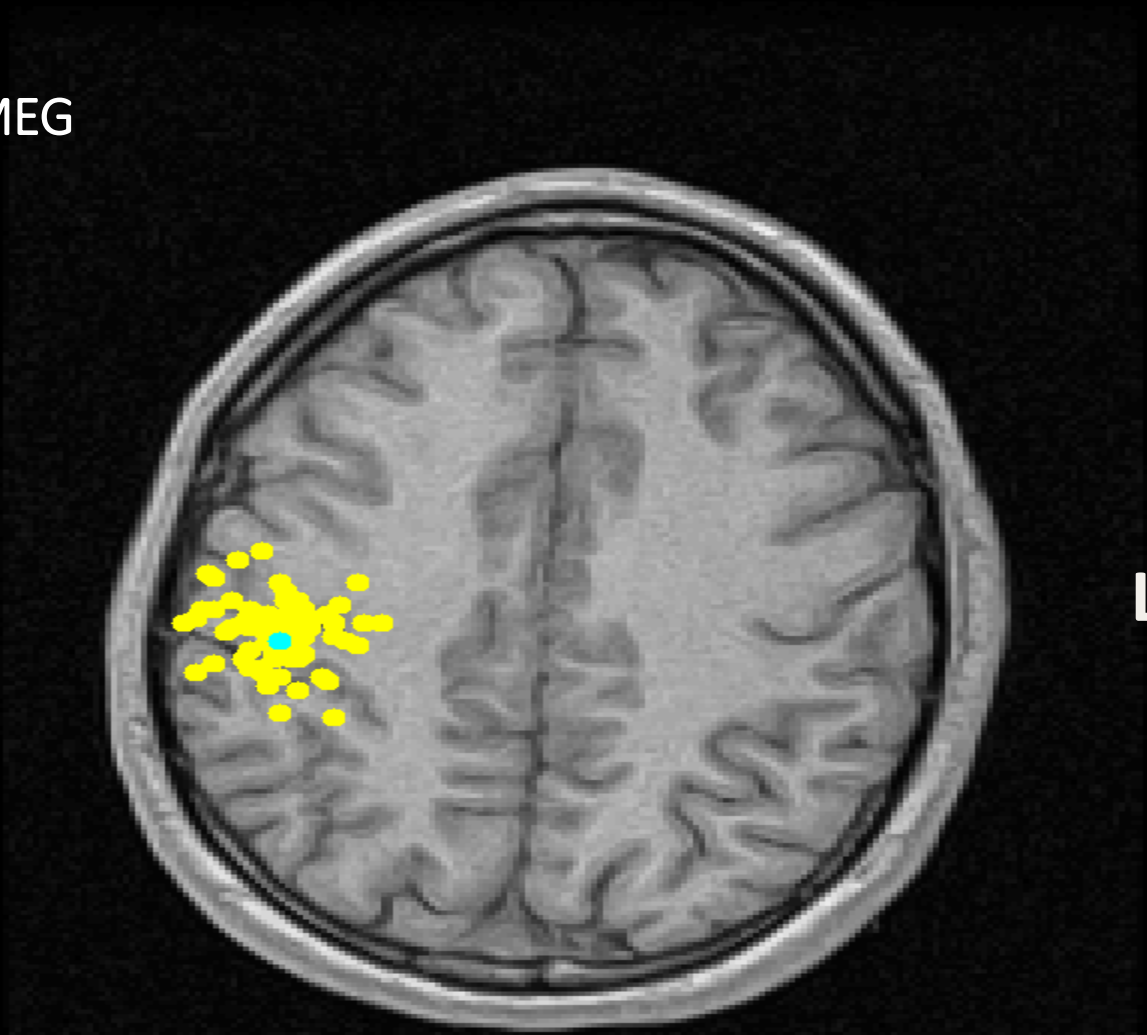
History & Physical	Seizure history as noted; Exam normal
EEG	Sharp waves/spikes on right - ***epileptiform***
Video EEG	Seizure captured; comes from R brain
3T MRI	Normal
fMRI	Language on the left
Neuropsychology	Normal
Psychiatry	Depressed & Anxious
MEG	Dipole cluster – right sensory cortex

MEG - PRINCIPLE

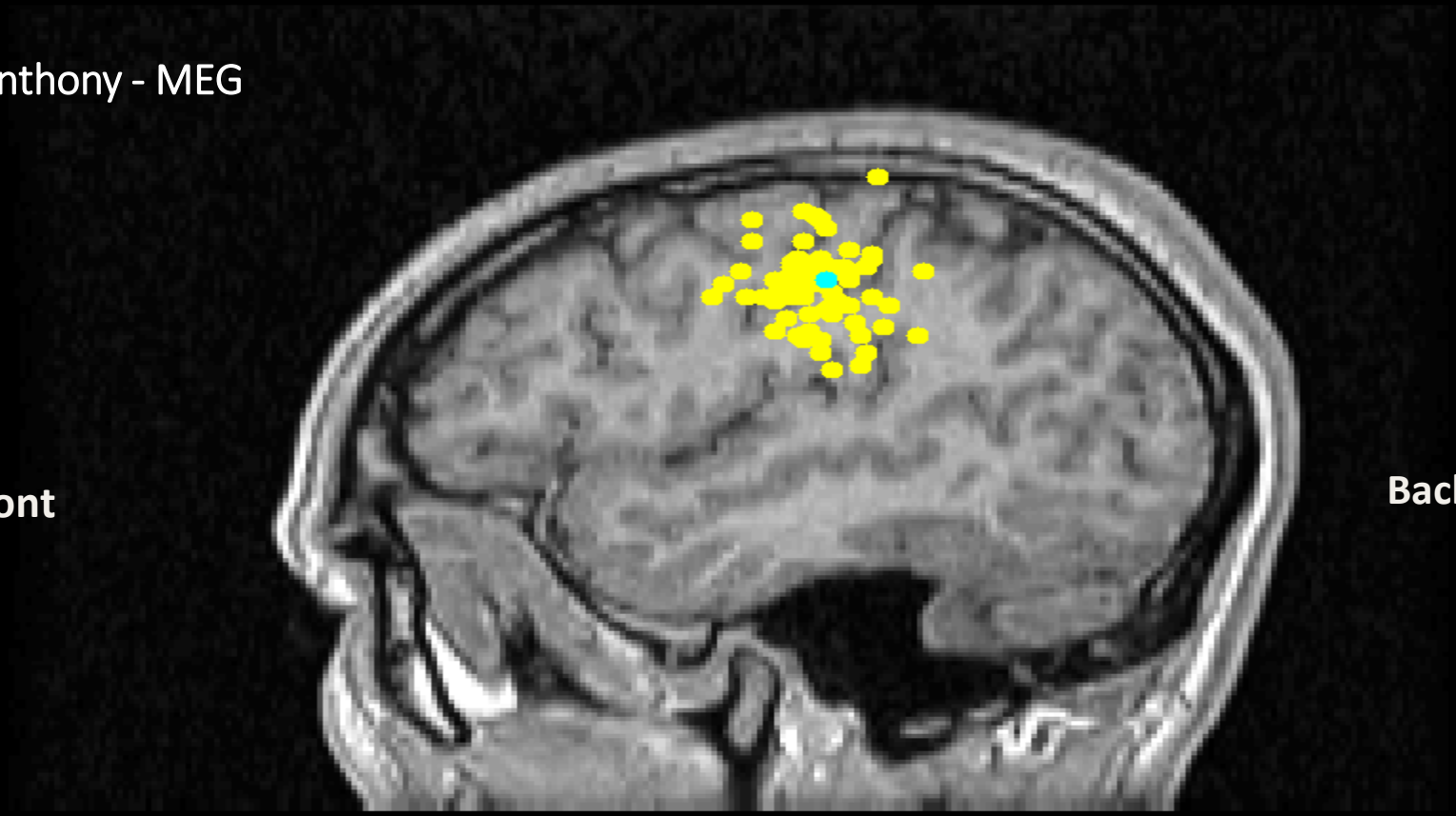


MEG - PRINCIPLE

Anthony - MEG



Anthony - MEG



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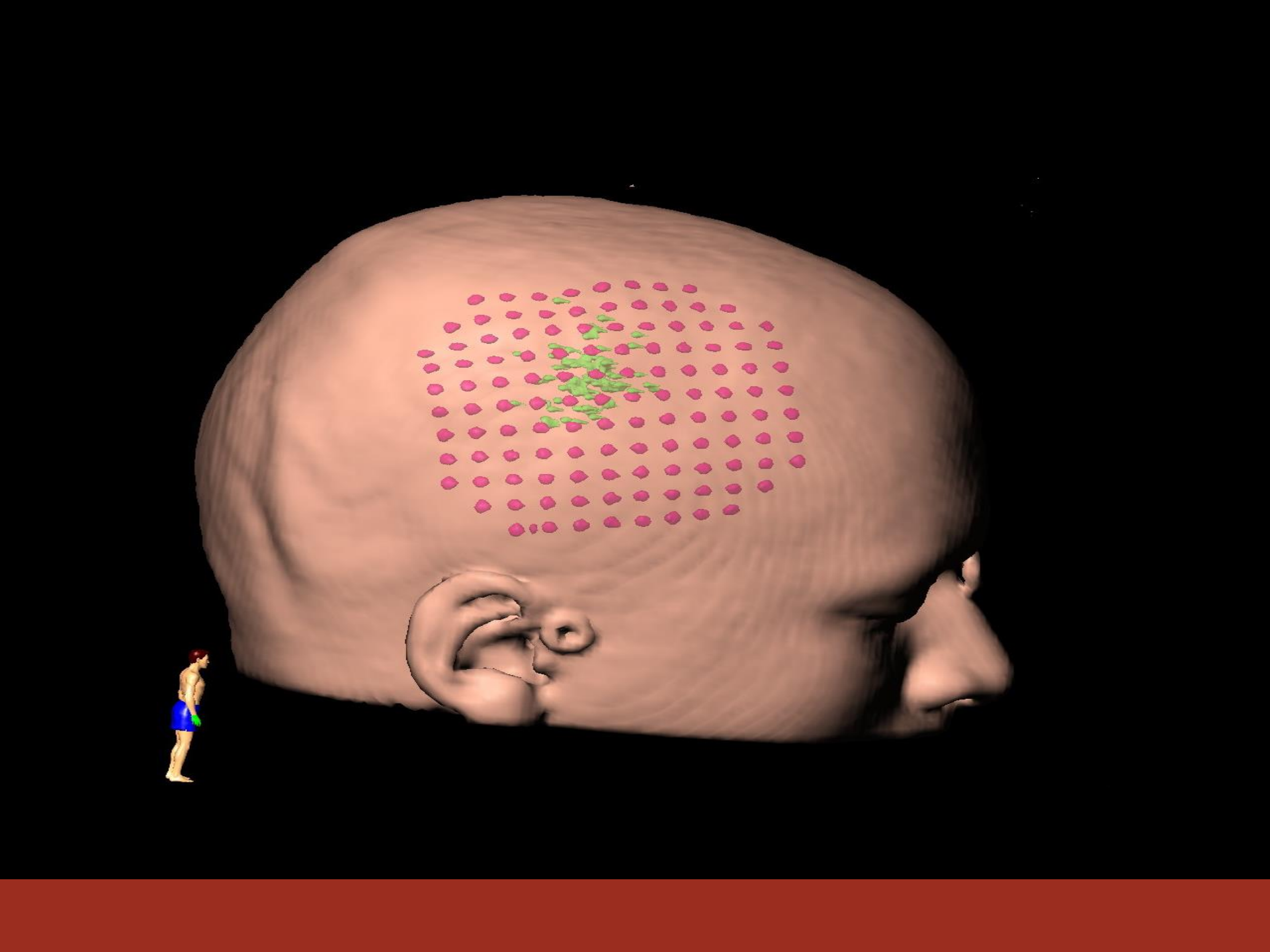

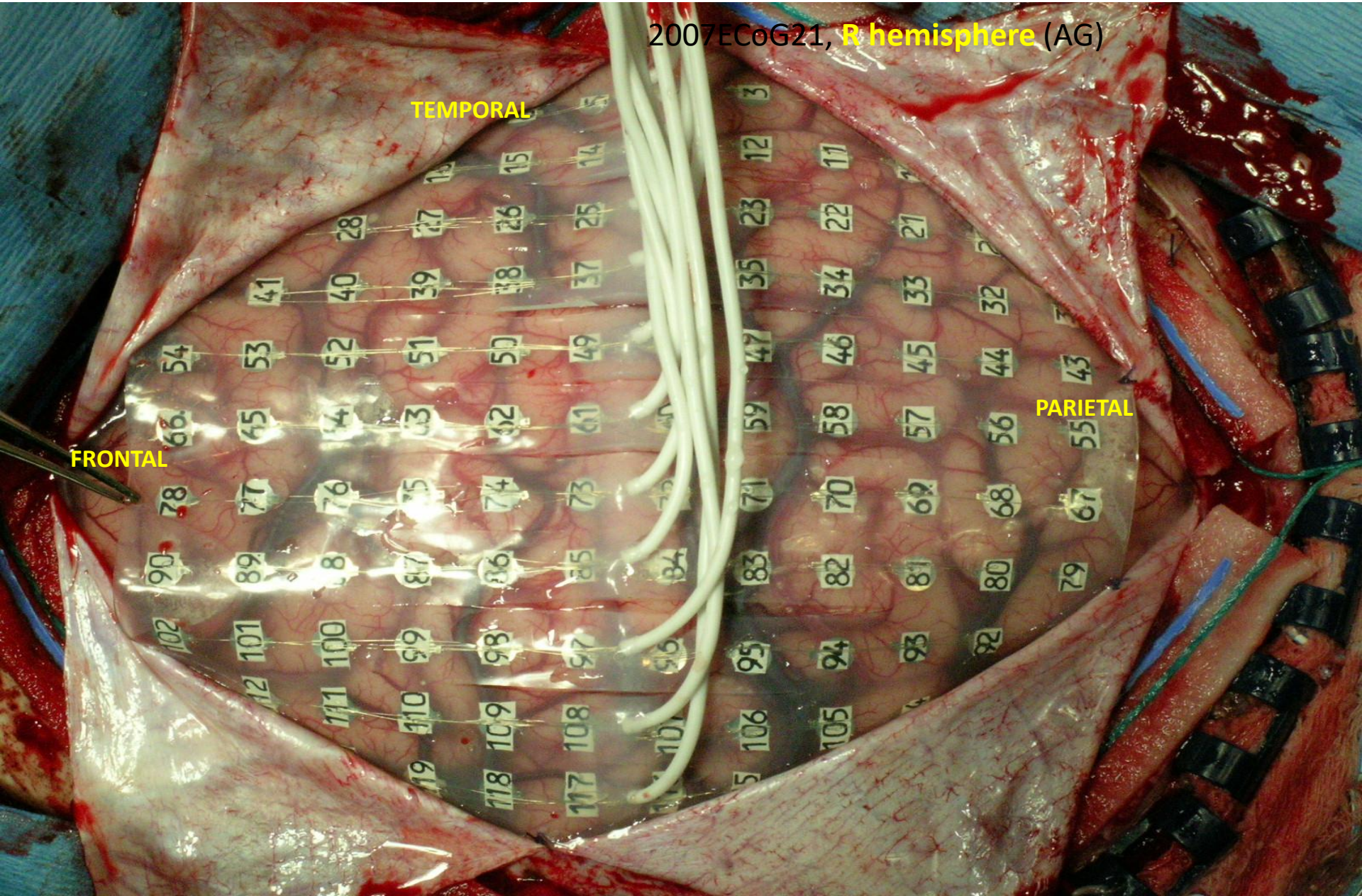
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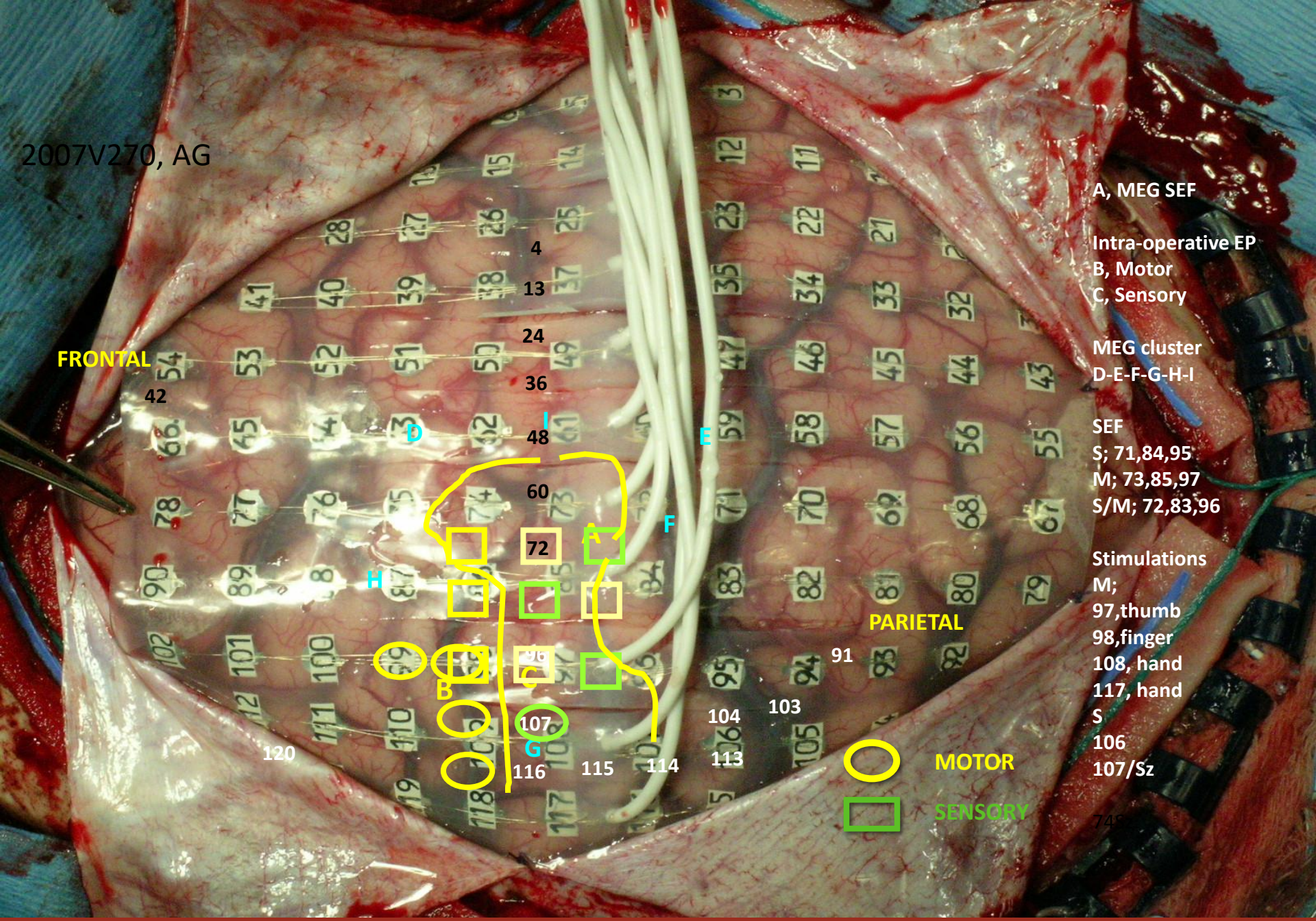
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FRONTAL
PARIETAL
A, MEG SEF
Intra-operative EP
B, Motor
C, Sensory
MEG cluster
D-E-F-G-H-I
SEF
S; 71,84,95
M; 73,85,97
S/M; 72,83,96
Stimulations
M;
97,thumb
98,finger
108, hand
117, hand
S
106
107/Sz
MOTOR
SENSORY
A
B
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D
E
F
G
H
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4
13
24
36
42
48
60
72
91
96
103
104
106
107
113
114
115
116
120

Outcome

seizure free for ten years

drives

plays the guitar

finished University

married w/one child

Chartered Accountant

What would the outcome have been without surgery?

Continued daily seizures on chronic AEDs

Living at home; ± finish high school

Chronic anxiety and depression

Unable to drive or work

Unable to go to University

Remain unmarried and socially isolated
for all his life

at risk for SUDEP

TAKE HOME MESSAGES

Epilepsy surgery is NEVER a treatment of last resort

You should ALWAYS think of epilepsy surgery in any patient with drug resistant focal epilepsy

Project ECHO
Epilepsy Across the Life Span

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Ontario's Comprehensive Epilepsy Program Model