Recent Advances in Pediatric Epilepsy Management: From Diagnosis to Therapy

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و چهل و ششمین بزرگداشت
استاد دکتر محمد قریب

Annual congress of Iranian
Society of Pediatrics &
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Professor Mohammad Gharib

June 12_15, 2025 ۲۲ الی ۲۵ خرداد ۱۴۰۴

دارای حداکثر ۲۰ امتیاز بازآموزی برای متخصصین و
فوق تخصص های کودکان و پزشکان عمومی

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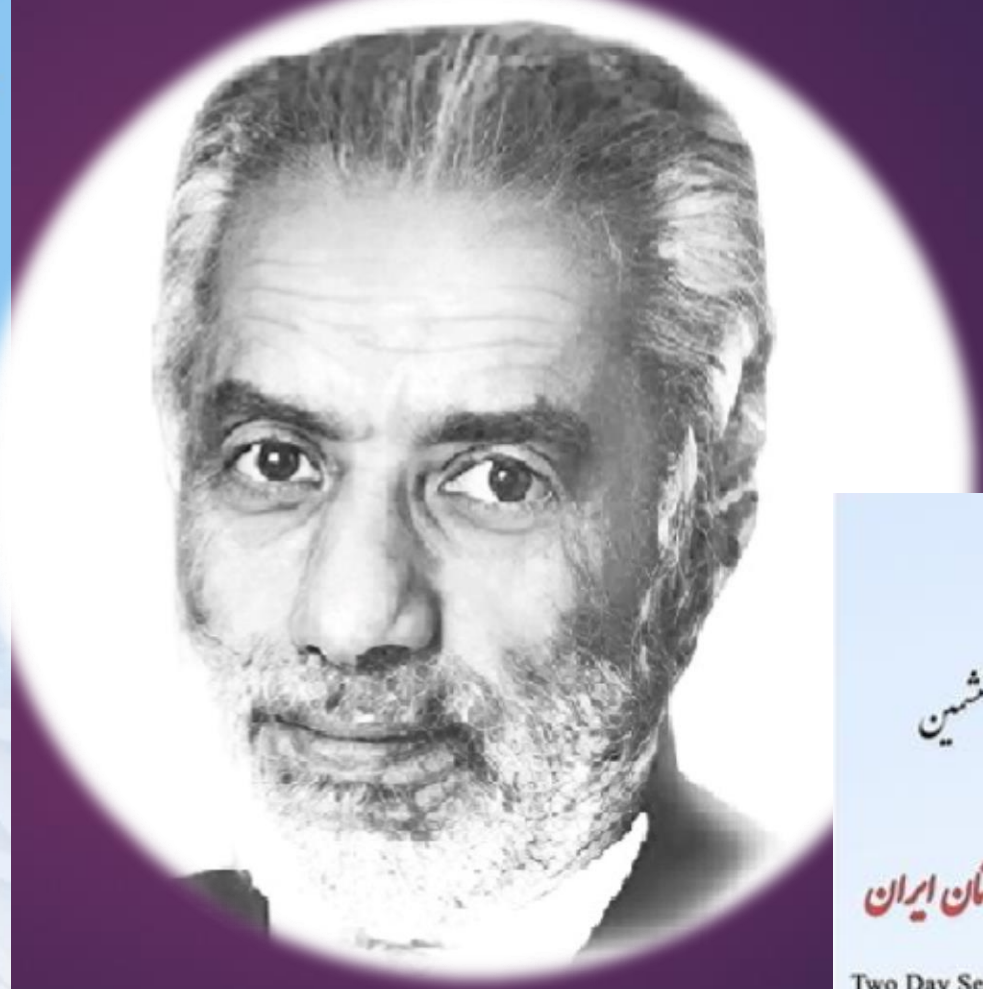
رئیس همایش: دکتر علی ربانی

دبیر علمی: دکتر محمدرضا بلورساز



همایش سالیانه جامعه پزشکان کودکان ایران و چهل و ششمین
بزرگداشت استاد دکتر محمد قریب و

سمینار دو روزه انجمن مغز و اعصاب کودکان و نوجوانان ایران

Two Day Seminar Iranian Child & Adolescent Neurology Society

June 14_15, 2025 ۲۴ الی ۲۵ خرداد ۱۴۰۴

Outlines

- Updated ILAE Classification
- Diagnostic Innovations
- Therapeutic Advances

ILAE POSITION PAPER

Operational classification of seizure types by the International League Against Epilepsy: Position Paper of the ILAE Commission for Classification and Terminology

*Robert S. Fisher, †J. Helen Cross, ‡Jacqueline A. French, §Norimichi Higurashi, ¶Edouard Hirsch, #Floor E. Jansen, **Lieven Lagae, ††Solomon L. Moshé, ‡‡Jukka Peltola, §§Eliane Roulet Perez, ¶¶Ingrid E. Scheffer, and ##***Sameer M. Zuberi

Epilepsia, 58(4):522–530, 2017
doi: 10.1111/epi.13670

ILAE 2017 Classification of Seizure Types Expanded Version

Focal Onset

Aware | Impaired Awareness

Motor Onset
- automatisms
- atonic [2]
- clonic
- epileptic spasms [2]
- hyperkinetic
- myoclonic
- tonic

Nonmotor Onset
- autonomic
- behavior arrest
- cognitive
- emotional
- sensory

focal to bilateral tonic–clonic

Generalized Onset

Motor
- tonic–clonic
- clonic
- tonic
- myoclonic
- myoclonic–tonic–clonic
- myoclonic–atonic
- atonic
- epileptic spasms

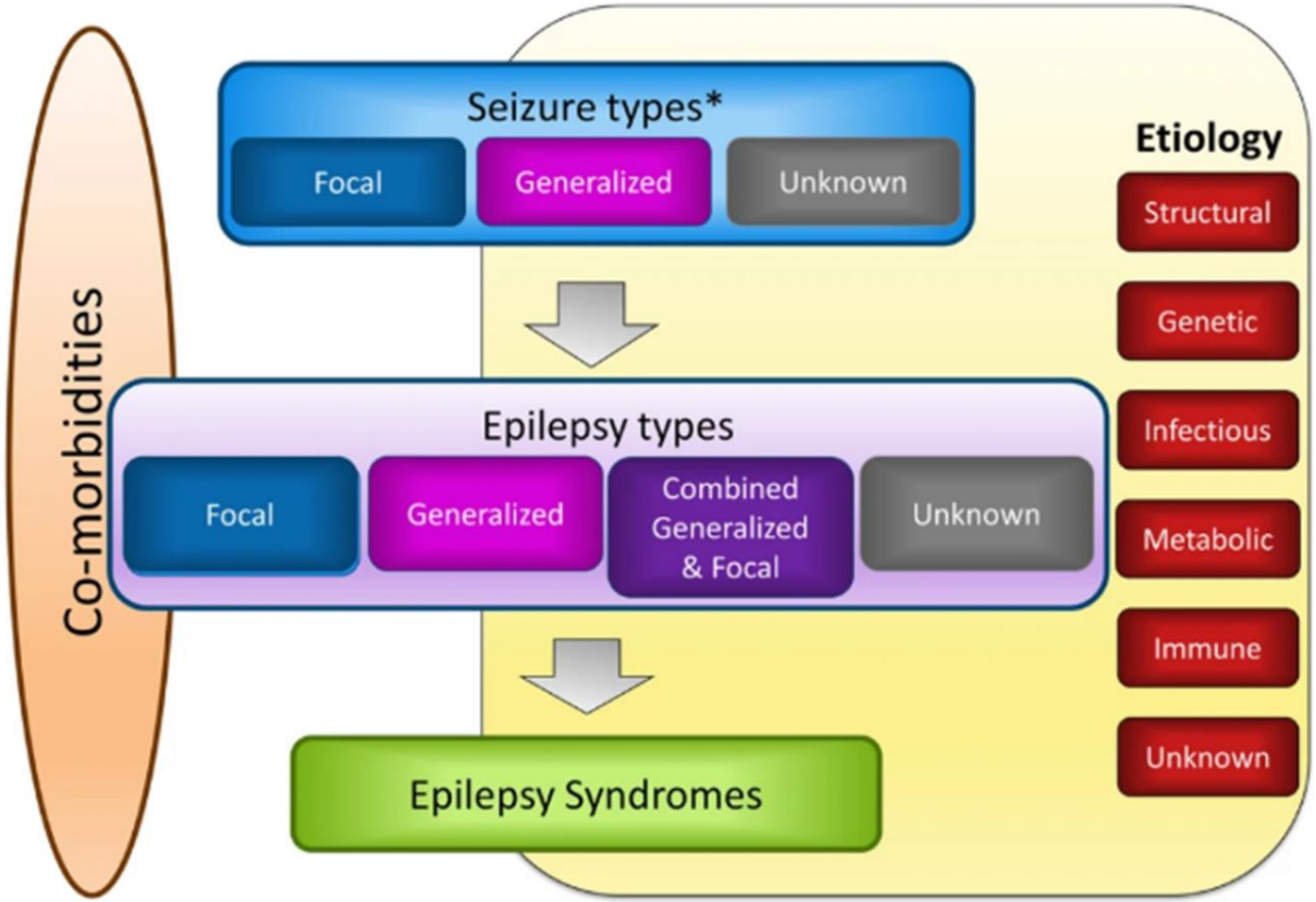
Nonmotor (absence)
- typical
- atypical
- myoclonic
- eyelid myoclonia

Unknown Onset

Motor
- tonic–clonic
- epileptic spasms

Nonmotor
- behavior arrest

Unclassified [3]



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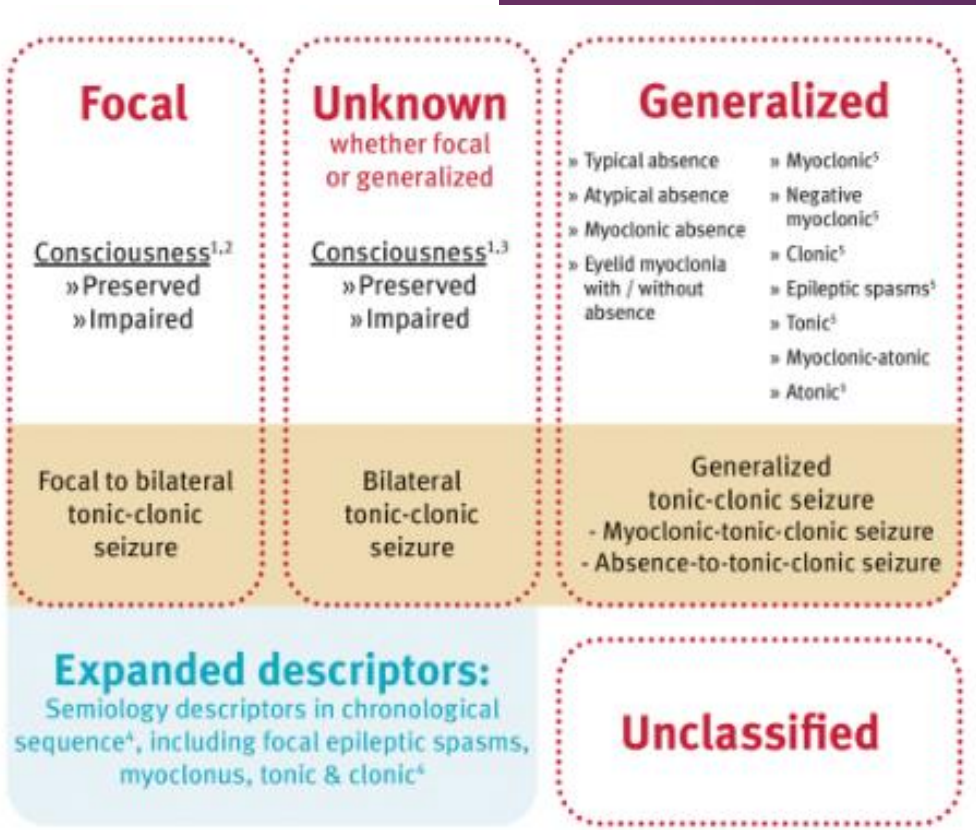
DOI: 10.1111/epi.18338

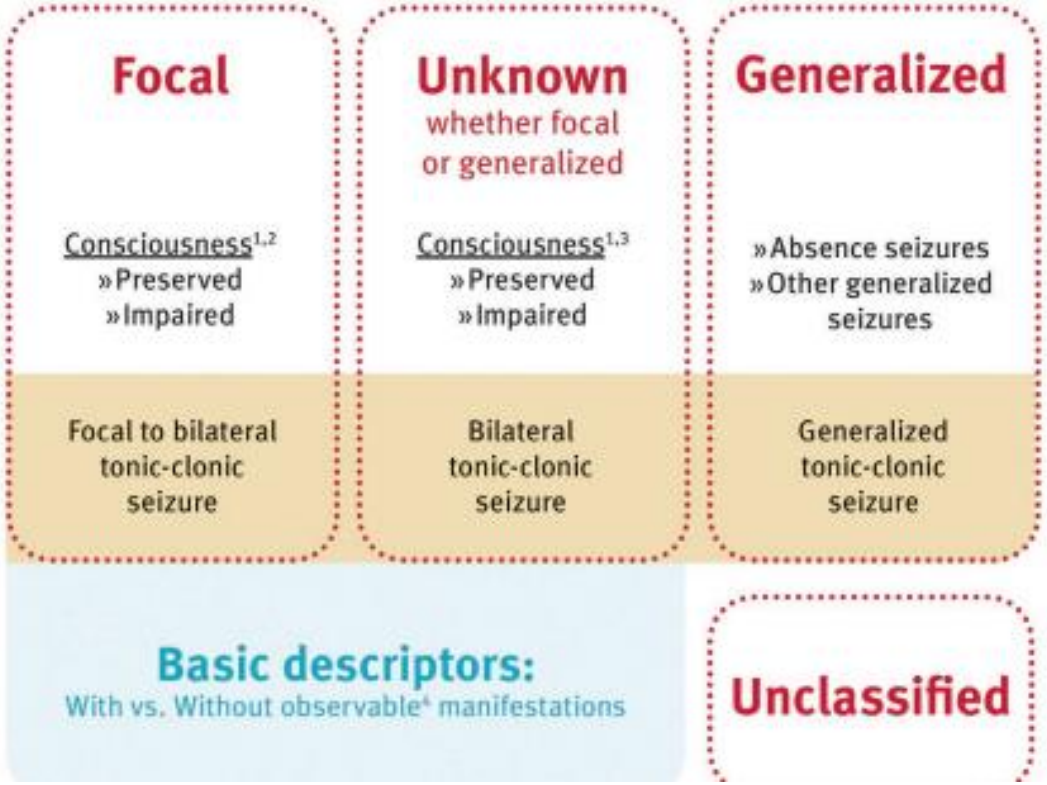
Epilepsia

SPECIAL REPORT

Updated classification of epileptic seizures: Position paper of the International League Against Epilepsy

Sándor Beniczky[1,2,3] | Eugen Trinka[4,5,6]
Raidah Al Baradie[9] | Mario Alonso Vai
Mamta Bhushan Singh[14] | Hal Blumen
Roberto Caraballo[17] | Mar Carreno[18,19]
Augustina Charway[22] | Mark Cook[23] |
Birgit Frauscher[28,29] | Jacqueline Frenc
Norimichi Higurashi[33] | Akio Ikeda[34]
Philippe Kahane[37] | Nirmeen Kishk[38]
Kollencheri Puthenveettil Vinayan[42] | Li
Angelica Lizcano[45,46] | Aileen McGoni
Katerina Tanya Perez-Gosiengfiao[48,49,50] |
Michael R. Sperling[53] | Hermann Stefa
Manjari Tripathi[56] | Elza Márcia Yacubia
Jo Wilmshurst[59] | Dong Zhou[60] | J.





Diagnostic Innovations

Telemedicine

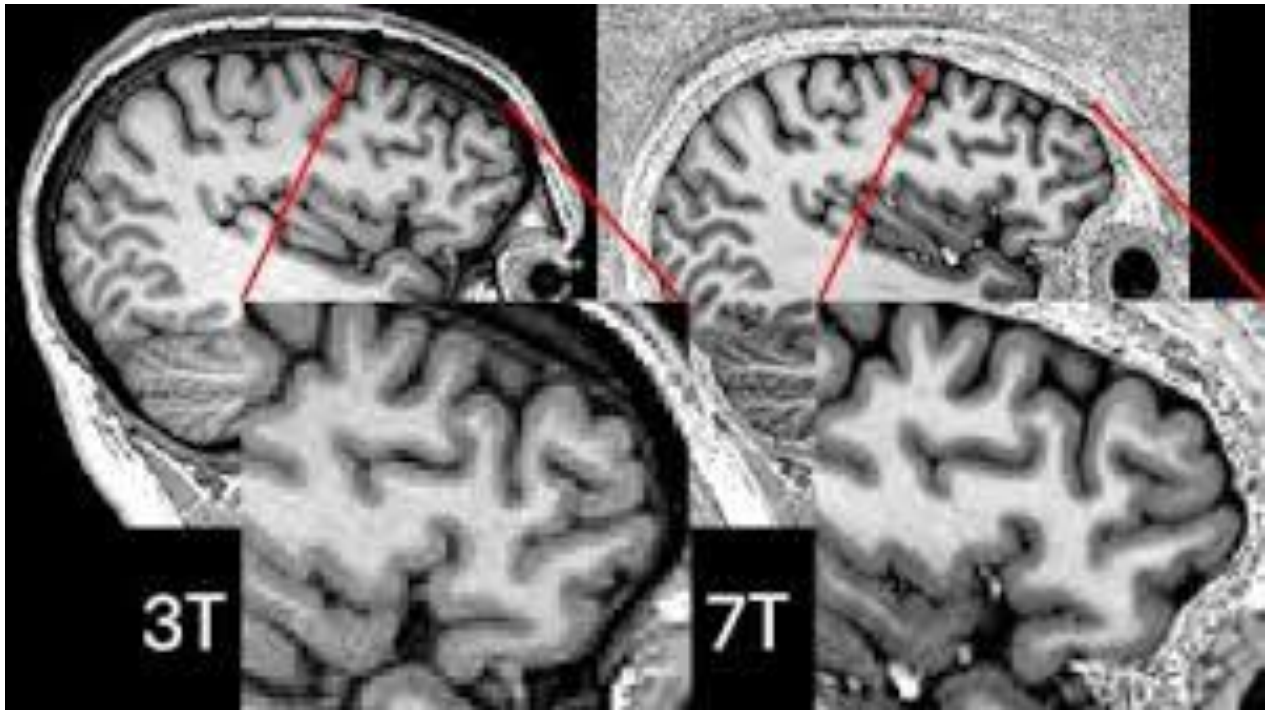
Artificial Intelligence

High Field MRI

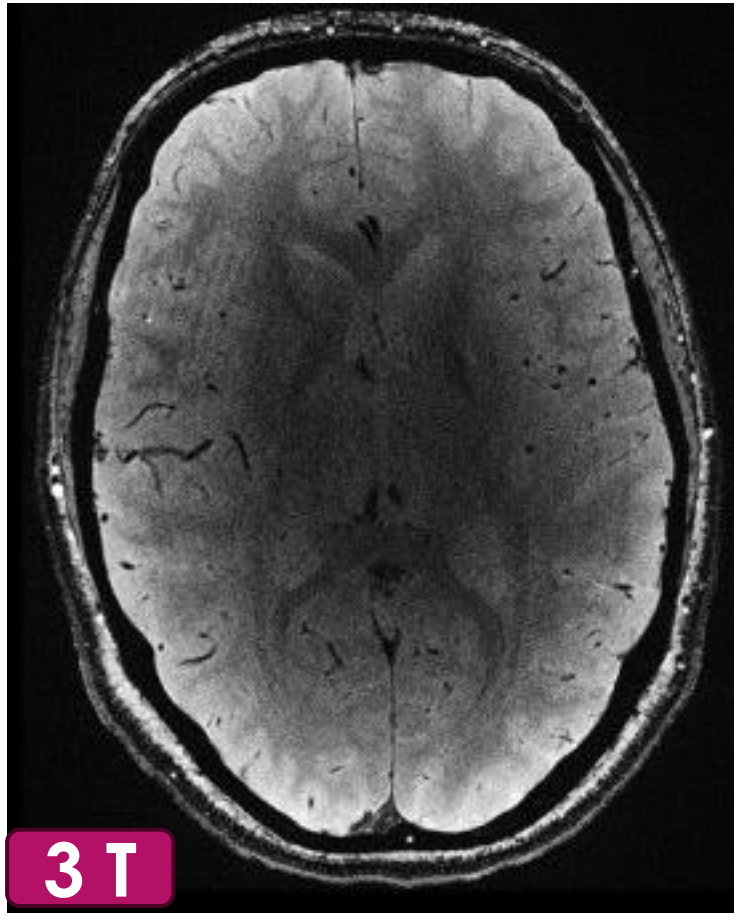
Brain MRI

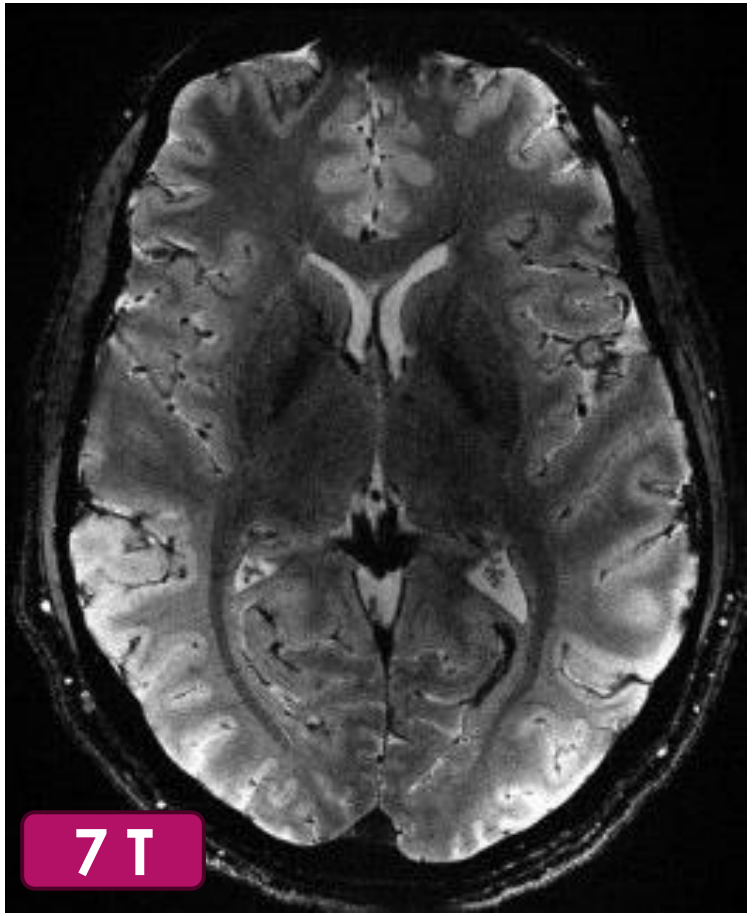
1.5 T

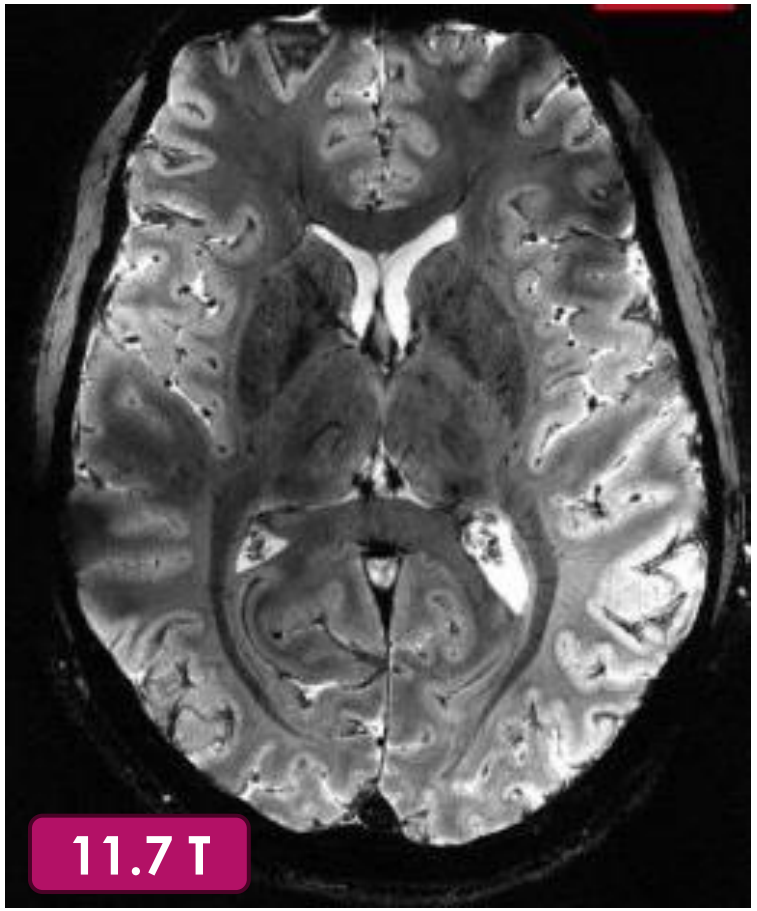
3 T



Brain MRI







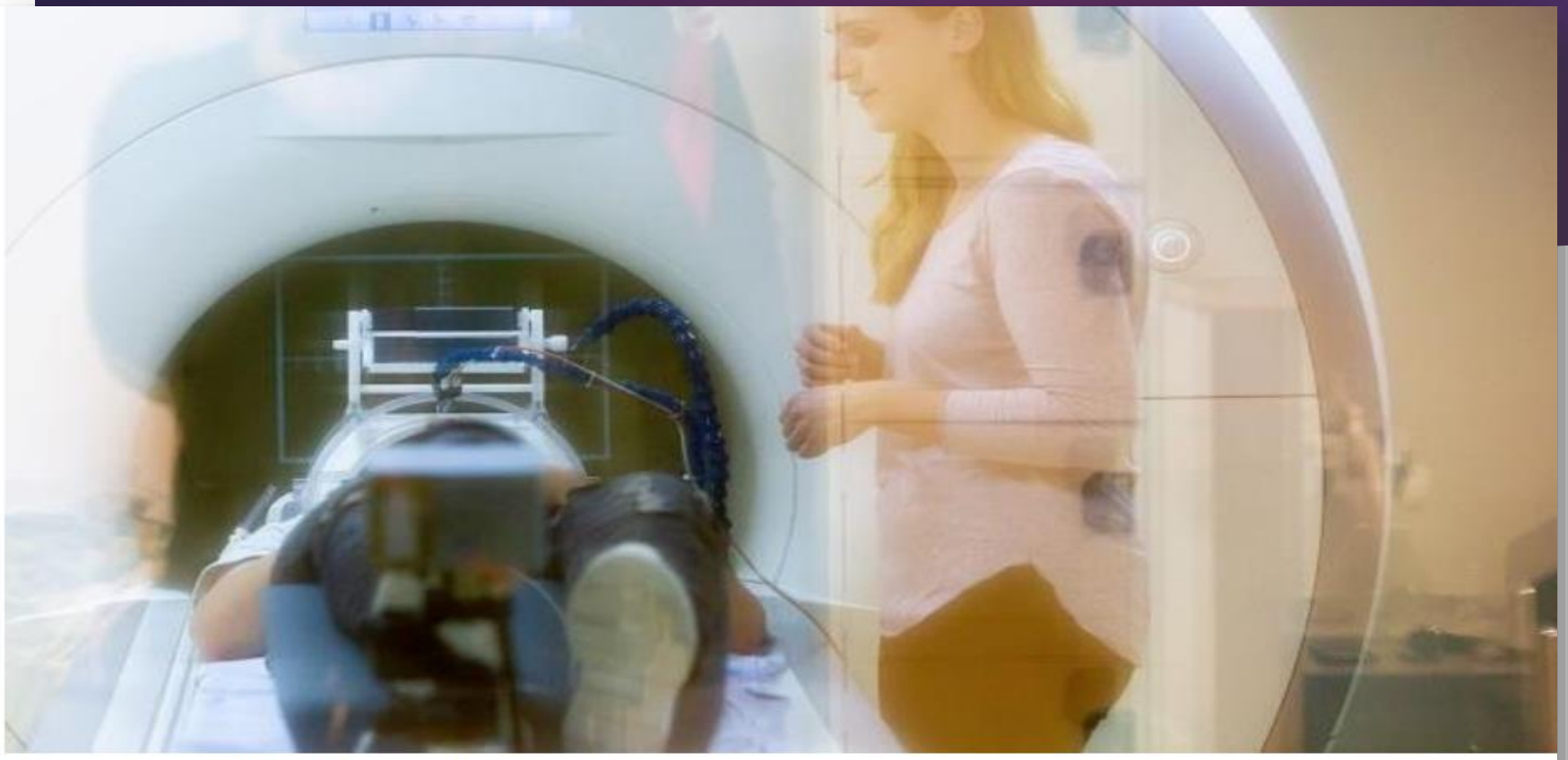


Image source: Radboud University

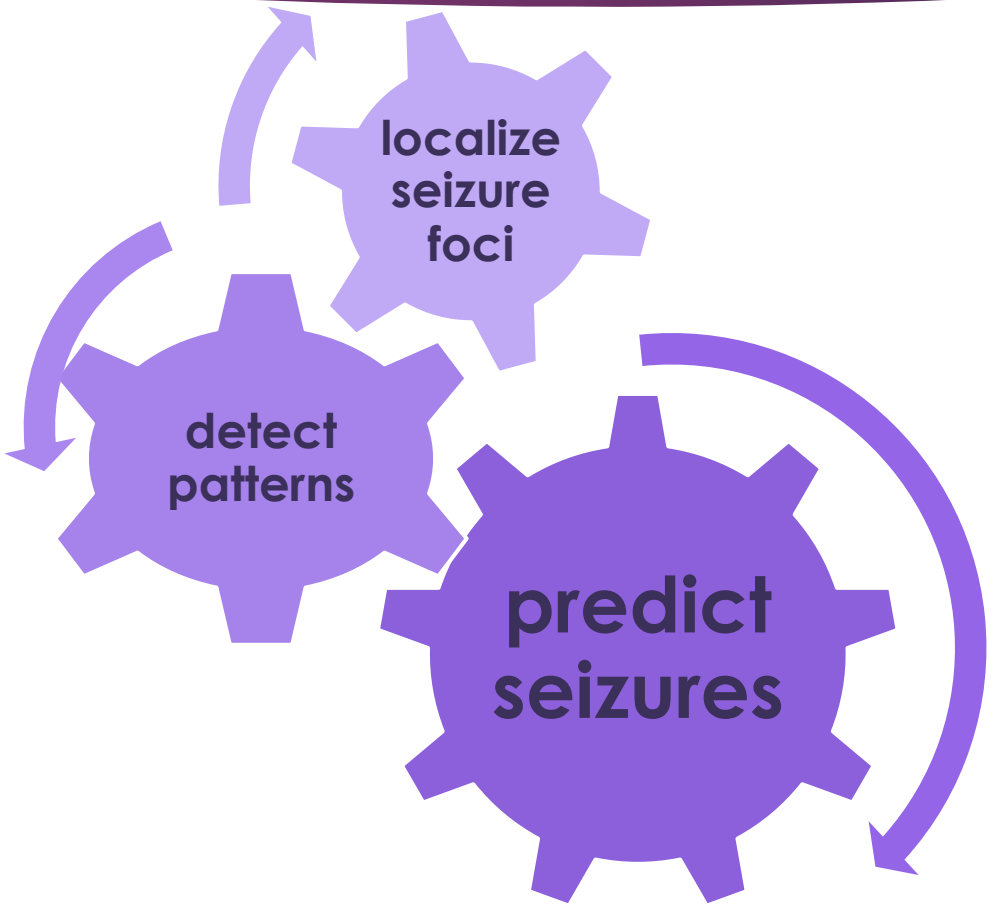
News • Ultrahigh field strength

14 Tesla: Researchers to build world's strongest MRI scanner

Diagnostic Innovations
AI in EEG interpretation and seizure prediction

- EEG is essential, but
  - time-consuming
  - pediatric EEG specialists
  - more artifacts and age-related variability in pediatric EEG

Clinical decision-making



Core Applications of AI in EEG

1. Automated Seizure Detection

- ICU monitoring (non-convulsive seizures)
- Ambulatory/home EEG (detect unobserved events)
- Real-time seizure alarm
- Example: Persyst, Nihon Kohden systems

Core Applications of AI in EEG

2. **Interictal Epileptiform Discharge (IED) Detection**
   - Screening speed improvement
   - Reduces the burden on EEG technicians and neurologists

Core Applications of AI in EEG

3. Seizure Onset Zone Localization

- AI combined with high-density EEG (HD-EEG) or MEG helps:

  Predict focal regions

- Improve surgical candidacy evaluation

Summary

- It is not a replacement for expert review—**AI supports**, **doesn't replace!**
- **Risk of false positives/negatives**, especially with motion artifacts!
- **Regulatory approval** is still limited for certain pediatric-specific models
- **Ethical concerns** with autonomous decision-making!

AI helps us see patterns faster — but it's our job to interpret the story

Diagnostic Innovations
Telemedicine in epilepsy care continuity

- Why Telemedicine?
  - Pediatric epilepsy is chronic-→ requires frequent follow-up
  - Many families live far from epilepsy centers
  - During the pandemic, telehealth proved effective --→ and it's here to stay!

Key Benefits in Seizure Control

- Regular virtual visits, tighter follow-up (after changes)
- Monitoring side effects, comorbidities
- Improved monitoring → leads to better adherence
- Uploading videos of seizure events or digital diaries
- Parental Empowerment
- Easier access improves parent education, satisfaction, and involvement

Real-World Implementation

- Project ECHO Epilepsy (New Mexico & beyond)
- Children's Hospital of Philadelphia (CHOP)
- NIMHANS Epilepsy Center, Bengaluru

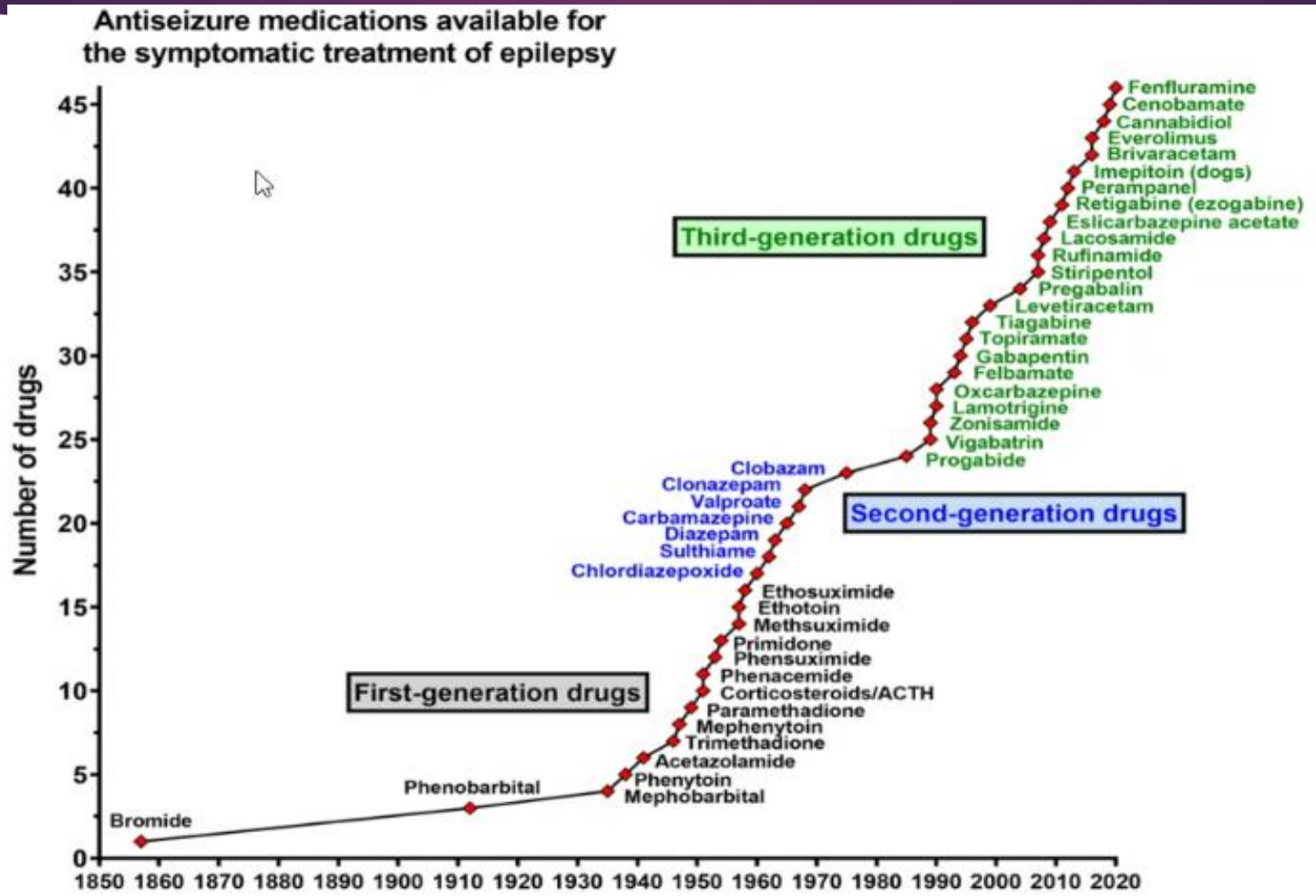
Summary

- Telemedicine is safe and effective
- Improves access and adherence
- Useful for ongoing management, not first-time seizures
- Strong parental satisfaction and reduced travel burden

Therapeutic Advances

Therapeutic Advances

New Anti-Seizure Medications (ASMs)



Approved after 2020

1. Cenobamate
2. Perampanel
3. Fenfluramine (Fintepla)
4. Brivaracetam (Briviact)
5. Soticlestat (Daybue)
6. Canabidiol

Review > Nat Rev Drug Discov. 2024 Sep;23(9):682-708. doi: 10.1038/s41573-024-00981-w. Epub 2024 Jul 22.

New epilepsy therapies in development

Drug	Companies	Mechanism of action	Indication	Status
PAMs at $GABA_A$ receptors (GABAkines)				
Darigabat (formerly PF-06372865 and CVL-865)	Cerevel Therapeutics	α_1-Sparing, $\alpha_2/\alpha_3/\alpha_5$-selective	Adult focal epilepsy	Phase II
ENX-101	Engrail Therapeutics	$\alpha_2/\alpha_3/\alpha_5$-Selective, α_1-blocking	Focal-onset seizures	Phase I
SAN-2219	Saniona	$\alpha_2/\alpha_3/\alpha_5$-Selective	Epilepsy	Preclinical
KRM-II-81	RespireRx Pharmaceuticals	α_2/α_3-Selective	Epilepsy	Preclinical
BAER-101	Avenue Therapeutics	α_2/α_3-Selective	Focal epilepsy	Phase IIa
SAN-711	Saniona	α_3-Selective	Generalized seizures	Phase I
Alogabat (RG-7816)	Roche	α_5-Selective	Angelman syndrome	Phase II
Ganaxolone (allopregnanolone analogue)	Marinus Pharmaceuticals	Neurosteroid analogue PAM on synaptic and extrasynaptic $GABA_A$ receptors	Refractory SE and TSC	Phase II/III
Zuranolone (SAGE-217)	SAGE Therapeutics	Synthetic neurosteroid analogue PAM on synaptic and extrasynaptic $GABA_A$ receptors	Seizures	Phase I
SAGE-324 (BIIB-124)	SAGE Therapeutics	Synthetic neurosteroid analogue PAM on synaptic and extrasynaptic $GABA_A$ receptors	Epileptiform disorders	Phase I/II
SAGE-689	SAGE Therapeutics	Second-generation neuroactive steroid PAM on synaptic and extrasynaptic $GABA_A$ receptors	Resistant SE	Phase I
Gaboxadol (OV101; THIP)	Ovid/Healx	Orthosteric agonist of $GABA_A$ receptors with high affinity at extrasynaptic δ-subunit-containing receptors that mediate tonic inhibition	Angelman syndrome and FXS	Phase I/II
ETX-155	Eliem Therapeutics	Neuroactive steroid PAM on synaptic and extrasynaptic $GABA_A$ receptors	Focal-onset seizures	Phase Ib
CPT-021	Mercaptor Discoveries	$GABA_A$ receptor PAM	Epilepsy	Preclinical
GRX-917 (deuterated version of etifoxine)	GABA Therapeutics	$GABA_A$ receptor PAM and activator of TSPO (increases synthesis of endogenous neurosteroids)	Epilepsy	Phase I

Drug	Companies	Mechanism of action	Indication	Status
PAMs, NAMs or antagonists at glutamate receptors (continued)				
JBPOS-0101	Bio-Pharm Solutions	Antagonist of mGlu1, mGlu4 and mGlu7	DEEs, refractory SE	Phase II
JNJ-55511118	Janssen	NAM of AMPA receptors containing TARP-γ8	Epilepsy	Phase I
CERC-611 (LY3130481)	Eli Lilly/Cerecor/Avalo Therapeutics	NAM of AMPA receptors containing TARP-γ8	Focal seizures	Preclinical
Radiprodil	GRIN Therapeutics/UCB Pharma	NAM of NR2B-NMDA receptors	Gain-of-function variants of *GRIN2B*	Phase II
AV-101	Vistagen	Prodrug of 7-chloro-kynurenic acid, a selective antagonist of glycine co-agonist site of NMDA receptor	Epilepsy	Phase I
PAM of the glutamate transporter EAAT2 (GLT1)				
iQ-007	iQure	PAM of astrocytic glutamate transporter EAAT2	DRE	Preclinical
Serotonergic (5-HT) mechanisms				
EPX-100 (clemizole HCl)	Epygenix	Probably modulation of 5-HT receptors	Dravet syndrome	Phase II
EPX-300 (trazodone HCl)	Epygenix	SSRI	Dravet syndrome	Phase I
Lorcaserin (E2023)	Eisai	$5\text{-}HT_{2C}$ receptor agonist	Dravet syndrome	Phase III
Bexicaserin (LP352)	Longboard Pharmaceuticals	$5\text{-}HT_{2C}$ receptor agonist	DEEs	Phase Ib/IIa
BMB-101	Bright Minds Biosciences	$5\text{-}HT_{2C}$ receptor agonist	Dravet syndrome	Phase I
NLX-101	Neurolixis	$5\text{-}HT_{1A}$ receptor agonist	Rett syndrome and FXS	Phase I
Potassium channel modulators				
XEN1101	Xenon Pharmaceuticals	PAM of neuronal Kv7.2–7.5 (KCNQ2–5) channels	Adult focal epilepsy, adult primary generalized epilepsy	Phase III
Pynegabine (HN37)	Chinese Academy of Sciences/Hainan Haiyao Company	PAM of neuronal Kv7.2–7.5 (KCNQ2–5) channels	Epilepsy	Phase I
BHV-7000 (KB-3061; BNP-25203)	Knopp Biosciences/ Biohaven Pharmaceuticals	Kv7.2/7.3 modulator	Seizures associated with *KCNQ2* DEE; focal epilepsy, generalized epilepsy	Phase I–III
CB-003	Zhimeng Biopharma	Kv7.2/7.3 modulator	Epilepsy	Phase I
ZM-003	Protheragen	Kv7.2/7.3 modulator	Epilepsy	Preclinical
ETX-123	Eliem Therapeutics	Kv7.2/7.3 modulator	Epilepsy	Preclinical
AUT-00206	Autifony Therapeutics	Kv3.1/3.2 positive modulator	FXS	Phase II
AUT-00201	Autifony Therapeutics	Kv3.1/3.2 positive modulator	Orphan epilepsy syndromes	Phase I
PRAX-020	Praxis Precision Medicines/ UCB Pharma	Inhibitor of KCNT1 (T-type) channels	KCNT1-related DEE	Preclinical

Therapeutic Advances

Dietary Therapies

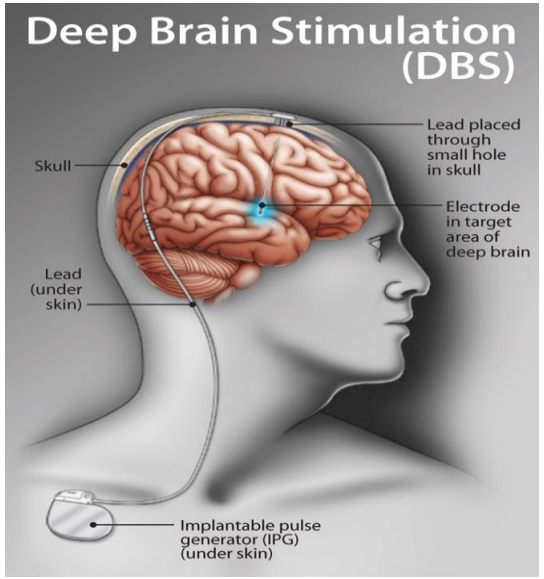
- Classic Ketogenic

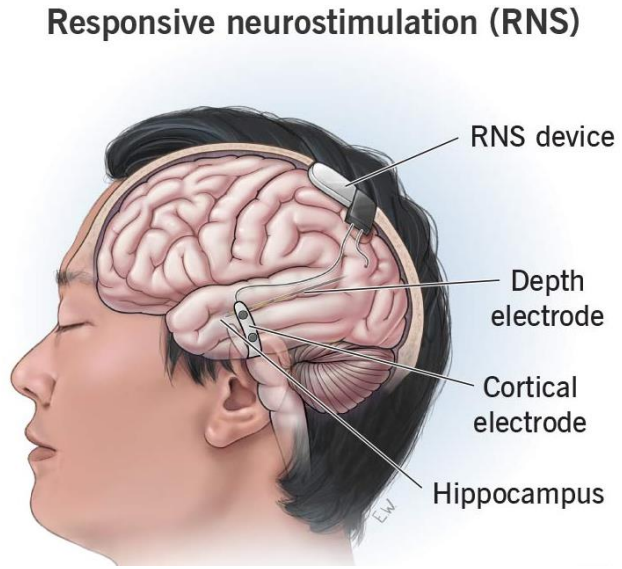
  Modified diets

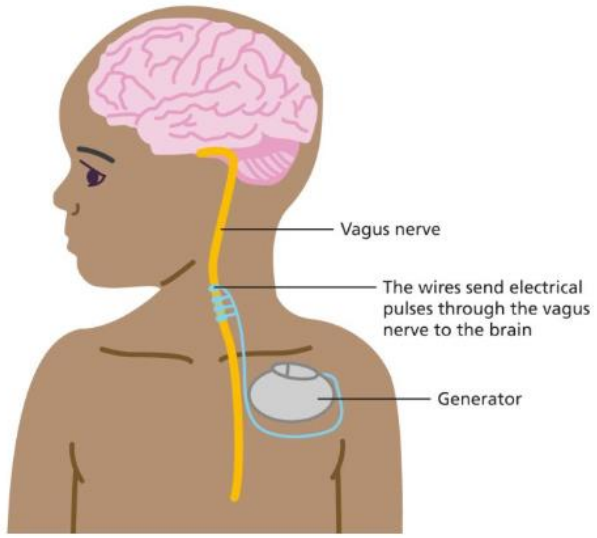
- Early initiation in refractory epilepsy
- First choice in some special epilepsy syndromes

Therapeutic Advances
Neuromodulation

- Vagus Nerve Stimulation (VNS): FDA-approved for children >4 years
- Responsive neurostimulation (RNS) : under investigation in peds
- Deep Brain Stimulation (DBS): under investigation in peds







Therapeutic Advances
Epilepsy Surgery

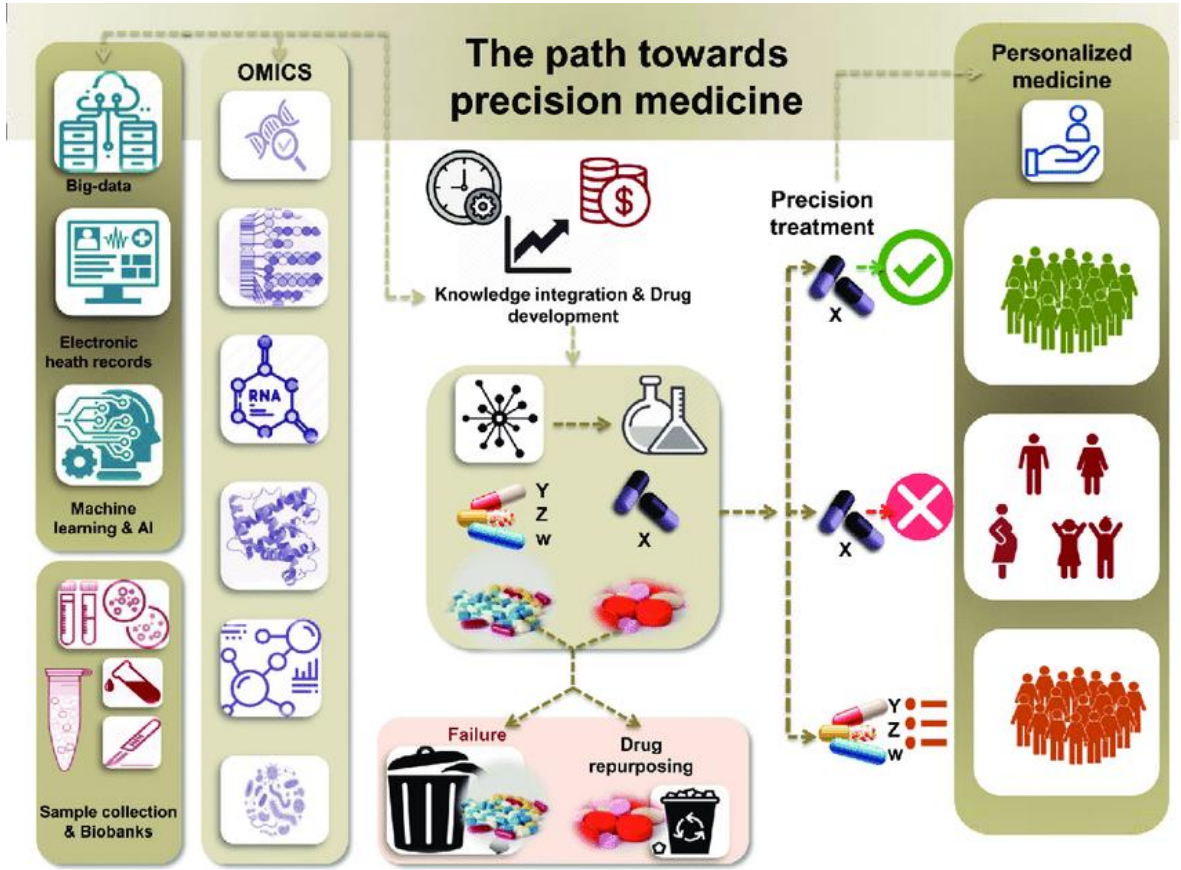
Resective epilepsy surgery

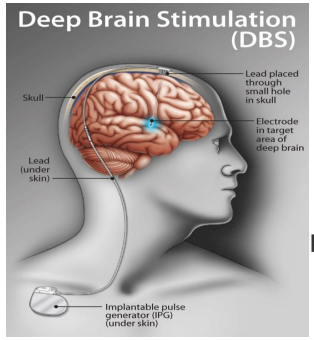
- **Hemispheric surgery**
- **lesionectomy/ lobar resection**
- **Multilobar resection**

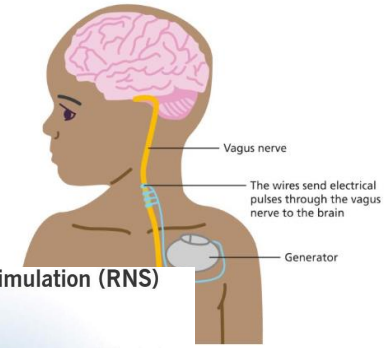
Palliative Methods

- Callosotomy
- Vagal Nerve Stimulation
- Multiple Subpial Transaction

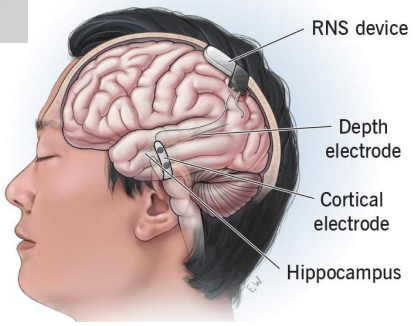
Therapeutic Advances
Precision Medicine







Responsive neurostimulation (RNS)




Thank You
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