Epilepsy highlight 2010

คณิตพงษ์ ปราบพาล

หน่วยประสาทวิทยา ภาควิชาอายุรศาสตร์

คณะแพทยศาสตร์ ม. สงขลานครินทร์

อ. หาดใหญ่ จ. สงขลา

HIGHLIGHT TOPIC

- Terminology, concepts and definition
- Epileptogenesis and drug development
- Gene and epilepsy
- Treatment related complication

TOPIC

- EEG, advance neuroimaging
- Antiepileptic drugs and non-pharmacological
- Neuropsychosocial quality of life and cognitive
- Epilepsy in special group
- Other

TERMINOLOGY AND CONCEPTS FOR ORGANIZATION OF SEIZURES AND EPILEPSIES

IF= 3.733

Revised terminology and concepts for organization of seizures and epilepsies: Report of the ILAE Commission on Classification and Terminology, 2005–2009

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Epilepsia 2010; 51: 676-685

MODE OF SEIZURE ONSET AND CLASSIFICATION OF SEIZURE

- **Generalized epileptic seizure are conceptualized as originating at some point within, and rapidly engaging, bilaterally distributed network.**

- **Focal epileptic seizures are conceptualized as originating within networks limited to one hemisphere.**

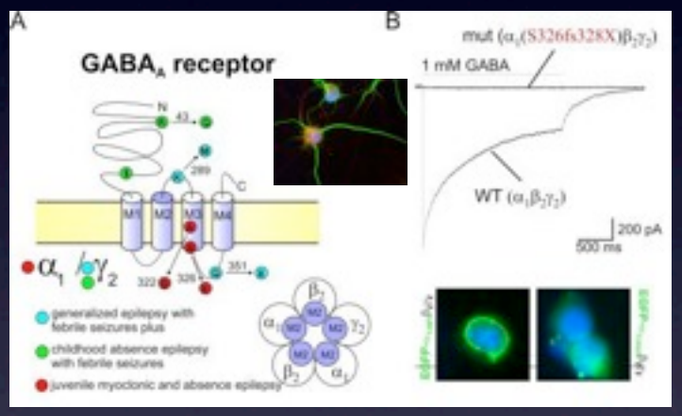
Epilepsia 2010; 51: 676-685

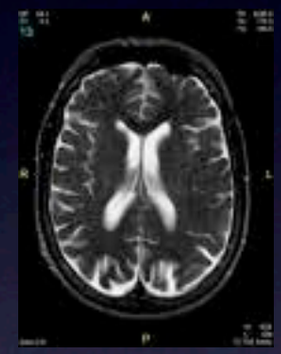
Epilepsy

1% of world's population

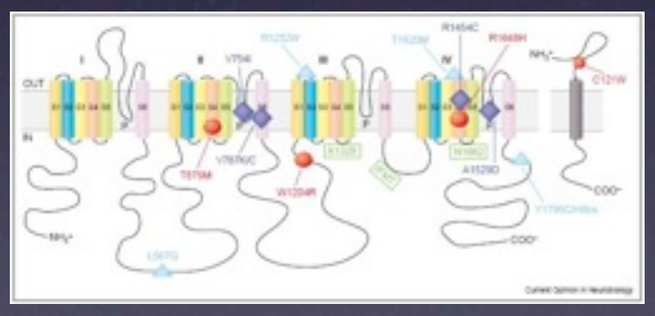
Genetics

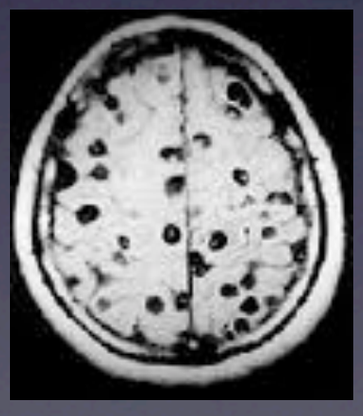
Unknown cause

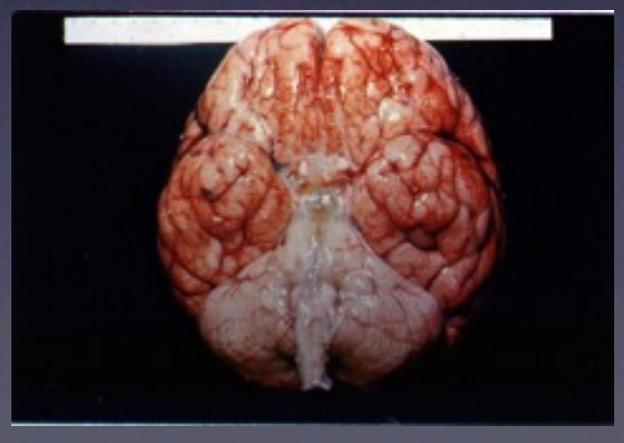




Structural and metabolic







Epilepsia 2010; 51: 676-685

Epilepsy

1% of world's population

Structural and metabolic

2009-2010

Traumatic brain

LONG-TERM RISK OF EPILEPSY AFTER TRAUMATIC BRAIN INJURY

IF= 28.409

- Population-based study cohort study of more than 1.5 million people
- 78572 of them had at least one head injury and 17470 were diagnosed with epilepsy, of whom 1017 had had a head injury before diagnosis.
- Overall, the relative risk of epilepsy 2.2 after mild head injury and 7.4 after a severe head injury
- The rate of development of epilepsy was greatest in few years
- The excess risk continued for 10 years after mild and severe brain injury
- Risk were greater in those with a family history of epilepsy (6 times in crease relative risk after mild head injury and 10 time for severe head injury)

Lancet 2009; 373: 1105-10.

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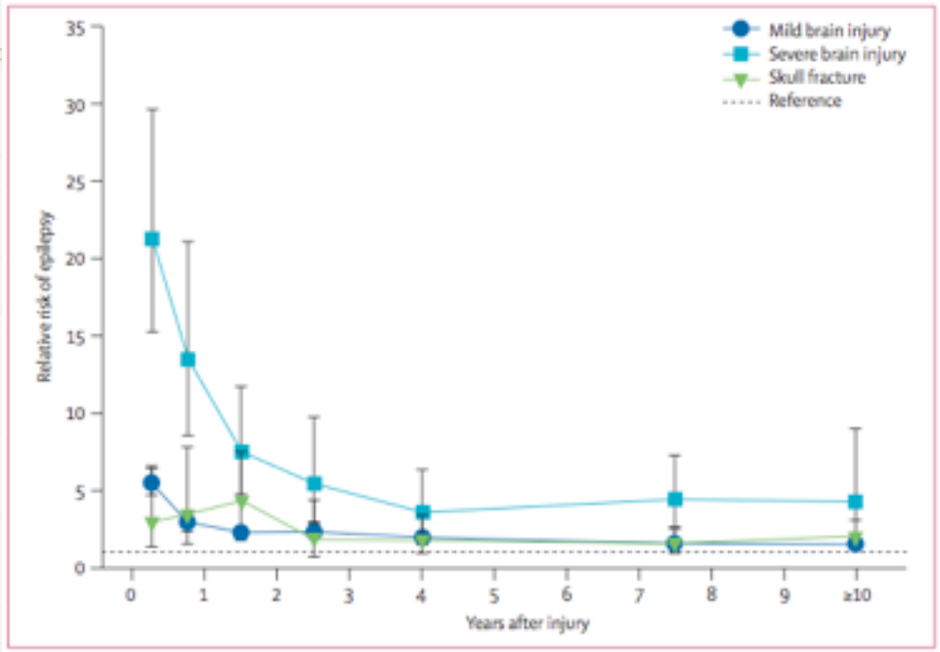

	No family history of epilepsy			Family history of epilepsy		
	Number of patients with epilepsy	Adjusted relative risk (95% CI)	p value	Number of patients with epilepsy	Adjusted relative risk (95% CI)	p value
Mild brain injury						
No	15511	1·00	..	1122	3·37 (3·17–3·58)	<0·0001
Yes	766	2·24 (2·08–2·41)	<0·0001	71	5·75 (4·56–7·27)	<0·0001
Severe brain injury						
No	16166	1·00	..	1188	3·35 (3·16–3·56)	<0·0001
Yes	11	7·81 (6·48–9·42)	<0·0001	5	10·09 (4·20–24·26)	<0·0001
Skull fracture						
No	16202	1·00	..	1190	3·35 (3·16–3·55)	<0·0001
Yes	75	2·28 (1·81–2·86)	<0·0001	3	2·71 (0·87–8·41)	0·0842
Any brain injury						
No	15338	1·00	..	1115	3·39 (3·19–3·61)	<0·0001
Yes	939	2·47 (2·31–2·65)	<0·0001	78	5·73 (4·58–7·16)	<0·0001

Patients might have been exposed to more than one type of brain injury at separate admissions/outpatient visits.
Relative risk adjusted for age and its interaction with sex and calendar year.

Table 4: Family history and relative risk of epilepsy after traumatic brain injury

GENE AND EPILEPSY

IF= 3.733

SPECIAL REPORT

Genetic testing in the epilepsies—Report of the ILAE Genetics Commission

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Epilepsia 2010; 51:655-670

Table 3. Genes identified in idiopathic epilepsy syndromes

	Locus	Gene	Product	References
Syndromes beginning in the first year of life				
Benign familial neonatal seizures	20q13.3	*KCNQ2*	$K_V7.2$ (K^+ channel)	(Biervert et al., 1998; Singh et al., 1998)
	8q24	*KCNQ3*	$K_V7.3$ (K^+ channel)	(Charlier et al., 1998)
Benign familial neonatal-infantile seizures	2q23-q24.3	*SCN2A*	$Na_V1.2$ (Na^+ channel)	(Heron et al., 2002; Berkovic et al., 2004; Striano et al., 2006; Herlenius et al., 2007)
Ohtahara syndrome	9q34.1	*STXBP1*	Syntaxin binding protein 1	(Saitsu et al., 2008)
	Xp22.13	*ARX*	Aristaless-related homeobox protein	(Kato et al., 2007; Fullston et al., 2009)
Early onset spasms	Xp22	*STK9/CDKL5*	cyclin-dependent kinase-like 5	(Kalscheuer et al., 2003)
X-linked infantile spasms	Xp22.13	*ARX*	Aristaless-related homeobox protein	(Stromme et al., 2002; Gecz et al., 2006)
Syndromes with prominent febrile seizures				
Dravet syndrome (severe myoclonic epilepsy of infancy)	2q24	*SCN1A*	$Na_V1.1$ (Na^+ channel)	(Claes et al., 2001; Nabbout et al., 2003; Wallace et al., 2003; Harkin et al., 2007)
Genetic (generalized) epilepsy with febrile seizures plus (GEFS+)	2q24	*SCN1A*	$Na_V1.1$ (Na^+ channel)	(Escayg et al., 2000b; Sugawara et al., 2001; Wallace et al., 2001b)
	19q13.1	*SCN1B*	β_1 subunit (Na^+ channel)	(Wallace et al., 1998, 2002; Audenaert et al., 2003; Scheffer et al., 2007)
	5q34	*GABRG2*	γ_2 subunit ($GABA_A$ receptor)	(Baulac et al., 2001; Harkin et al., 2002)
Childhood absence epilepsy with febrile seizures	5q34	*GABRG2*	γ_2 subunit ($GABA_A$ receptor)	(Wallace et al., 2001a; Kananura et al., 2002)
Epilepsy and mental retardation limited to females	Xq22	*PCDH19*	protocadherin	(Dibbens et al., 2008)
Idiopathic generalized epilepsies				
Early-onset absence epilepsy	1p35-p31.1	*SLC2A1*	GLUT1 (glucose transporter type 1)	(Suls et al., 2009)
Juvenile myoclonic epilepsy	5q34-q35	*GABRA1*	α_1 subunit ($GABA_A$ receptor)	(Cossette et al., 2002)
	6p12-p11	*EFHC1*	EF hand motif protein	(Suzuki et al., 2004)
Focal epilepsies				
Autosomal dominant nocturnal frontal lobe epilepsy	20q13.2-q13.3	*CHRNA4*	α_4 subunit (nACh receptor)	(Steinlein et al., 1995; Phillips et al., 2000)
	1q21	*CHRNB2*	β_2 subunit (nACh receptor)	(De Fusco et al., 2000; Phillips et al., 2001)
	8p21	*CHRNA2*	α_2 subunit (nACh receptor)	(Aridon et al., 2006)
Autosomal dominant partial epilepsy	10q24	*LGI1*	Leucine-rich repeat protein	(Gu et al., 2002; Kalachikov et al.,

Table 4. Examples of assessment of clinical validity and clinical utility for diagnostic testing in an affected individual[a]

	Gene(s)	Proportion of patients/families with mutations[b]	How accurate is a positive mutation test for confirming the diagnosis?	Clinical utility: In an affected individual, how useful is knowledge of mutation status for clinical management?
Syndromes beginning in first year of life				
Benign familial neonatal seizures	*KCNQ2* *KCNQ3*	>50% of families ~7% of families	Highly accurate in correct clinical context (but most cases have clear AD inheritance so diagnosis is usually clear without testing)	*Somewhat useful* Outcome usually benign (although severe outcome has been reported) Mutation status predicts favorable outcome; hence less aggressive management may be warranted De novo *KCNQ2* mutations reported in rare isolated cases. Finding of de novo mutation informs diagnosis and has management implications Genetic counseling implications
Benign familial neonatal-infantile seizures	*SCN2A*	unknown	Highly accurate in correct clinical context (but most cases have clear AD inheritance so diagnosis is usually clear without testing)	*Somewhat useful* Outcome is usually benign Mutation status predicts favorable outcome, hence less aggressive management may be warranted Genetic counseling implications
Ohtahara syndrome	*STXBP1* *ARX*	~35% of patients unknown	Highly accurate in correct clinical context	*Very useful* Establishes etiology so avoids further diagnostic test procedures Genetic counseling implications Usually de novo

Table 5. Examples of assessment of clinical validity and clinical utility for predictive testing in an unaffected relative of an affected individual who tests positive

	Gene(s)	How accurate is a positive mutation test for predicting occurrence of the syndrome?	Clinical utility: In an unaffected family member, how useful is knowledge of mutation status?
Syndromes beginning in first year of life			
Benign familial neonatal seizures	*KCNQ2* *KCNQ3*	Highly accurate because of high penetrance	*Not useful* Outcome usually benign Knowledge of mutation status before onset would usually not alter management decisions
Benign familial neonatal-infantile seizures	*SCN2A*	Not established	*Not useful* Outcome usually benign Knowledge of mutation status before onset would usually not alter management decisions
Ohtahara syndrome	*STXBP1* *ARX*	Not established	

Table 6. Genetic testing FAQs

1. What are the benefits of testing?

Test results can provide a sense of relief from uncertainty and help people make informed decisions about managing their health care. With diagnostic testing, a positive test result can confirm the diagnosis, save the patient and family from unnecessary diagnostic procedures, and may help in the selection of optimal therapy. With predictive testing, a negative result can provide relief, and a positive result can direct a person toward available monitoring and treatment options. Some test results can also help people make decisions about having children.

2. What are the risks or limitations of testing?

The primary risks of genetic testing relate to the emotional, social, or financial consequences of the test results. People may feel angry, depressed, anxious, or guilty about their results. Genetic testing may also affect family relationships because the results can reveal information about family members other than the person who is tested. The possibility of genetic discrimination in employment or insurance is also a concern.

3. What is the difference between clinical genetic testing and research genetic testing?

Clinical tests are performed for the purpose of diagnosis, prevention, or treatment in the care of individual patients, usually for a fee. The results are provided in writing to the provider or patient. In the United States, laboratories performing clinical tests must be CLIA approved. In contrast, research tests are performed for the purpose of increasing understanding of a disorder, or developing a clinical test. The cost of research testing is covered by the researcher, and test results are not generally given to patients or providers. Laboratories performing research testing are not subject to CLIA regulation.

4. How can I find out whether or not genetic testing is available for my patient and where it is performed?

Extensive information about the available clinical genetic tests for a wide array of syndromes may be found on the Gene Tests website (http://www.genetests.org), a publicly funded medical genetics information resource developed for physicians, other health care providers, and researchers. The site also contains authoritative reviews on the genetics of several epilepsy syndromes.

5. Should I offer a test to the patient?

For a diagnostic test, the first step is to arrive at an informed opinion about whether or not the patient is likely to have the disorder in question. This should involve a thorough clinical evaluation and careful family history. The next step is to evaluate the likely clinical utility of the test. Consider the following questions:

a. Is the test result likely to lead to a meaningful change in the procedures used for evaluation (e.g., repeated spinal tap or neuroimaging)?

b. Is the test result likely to lead to a change in the optimal treatment choice or prognosis?

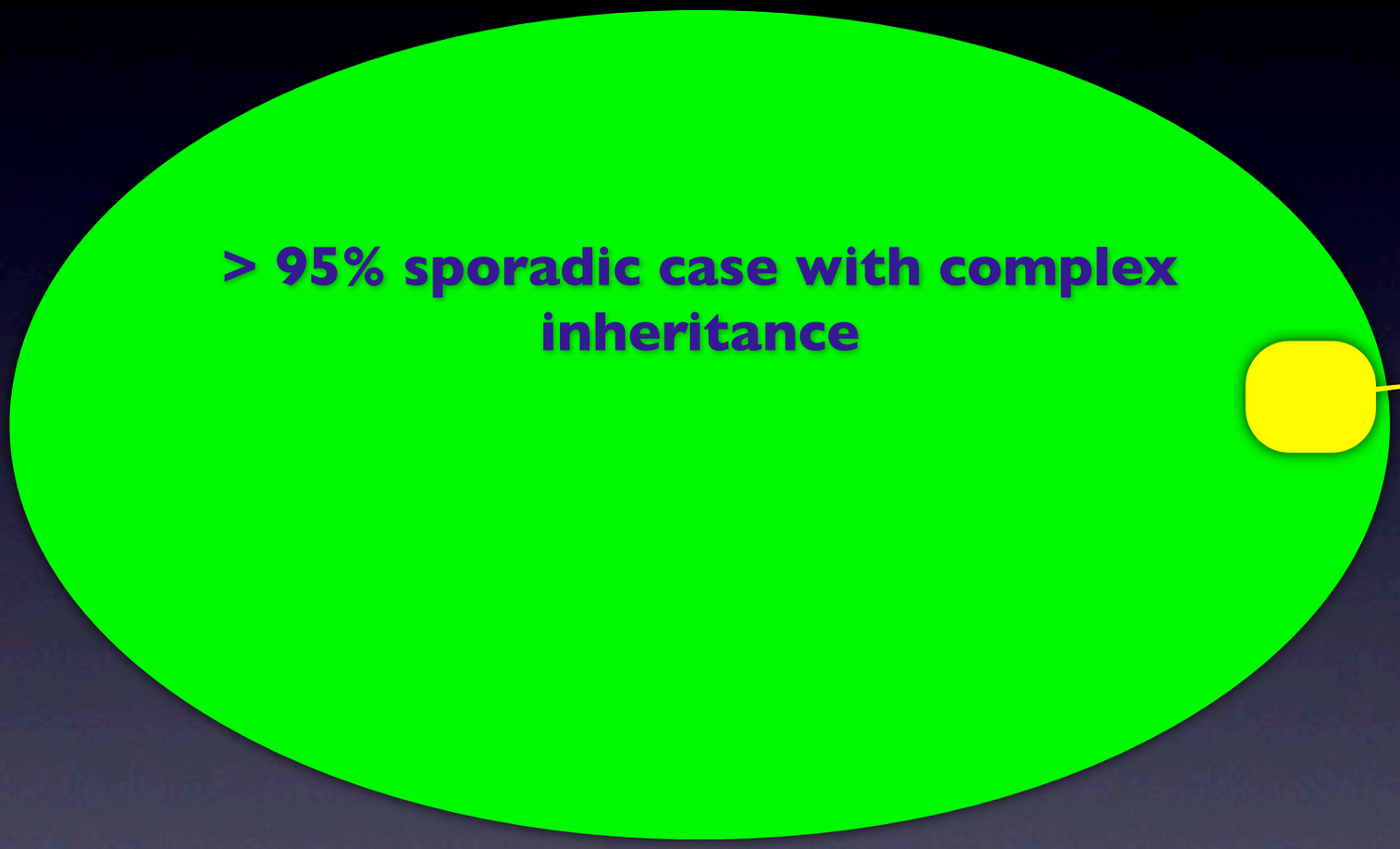
c. Is the test result likely to have any other positive or negative social or psychological effects? For example, is the patient likely to be relieved or disturbed by the knowledge that he or she carries a mutation?

d. Is the test result likely to influence the patient's decisions about reproduction?

6. I believe the test could provide important information—what are the next steps?

Epilepsia 2010; 51:655-670

Genetics



European congress of epileptology 2010

GENE AND EPILEPSY

IF= 30.259

BRIEF COMMUNICATIONS

nature genetics

15q13.3 microdeletions increase risk of idiopathic generalized epilepsy

Ingo Helbig[1], Heather C Mefford[2], Andrew J Sharp[3], Michel Guipponi[3], Marco Fichera[4], Andre Franke[1], Hiltrud Muhle[1], Carolien de Kovel[1], Carl Baker[2], Sarah von Spiczak[1], Katherine L Kron[1], Ines Steinich[1], Ailing A Kleefuß-Lie[1], Costin Leu[1], Verena Gaus[1], Bettina Schmitz[1], Karl M Klein[1], Philipp S Reif[1], Felix Rosenow[1], Yvonne Weber[1], Holger Lerche[1], Fritz Zimprich[1], Lydia Urak[1], Karoline Fuchs[1], Martha Feucht[1], Pierre Genton[5], Pierre Thomas[6], Frank Visscher[1], Gerrit-Jan de Haan[1], Rikke S Møller[1], Helle Hjalgrim[1], Daniela Luciano[4], Michael Wittig[1], Michael Nothnagel[1],

We identified 15q13.3 microdeletions encompassing the *CHRNA7* gene in 12 of 1,223 individuals with idiopathic generalized epilepsy (IGE), which were not detected in 3,699 controls (joint $P = 5.32 \times 10^{-8}$). Most deletion carriers showed common IGE syndromes without other features previously associated with 15q13.3 microdeletions, such as intellectual disability, autism or schizophrenia. Our results indicate that 15q13.3 microdeletions constitute the most prevalent risk factor for common epilepsies identified to date.

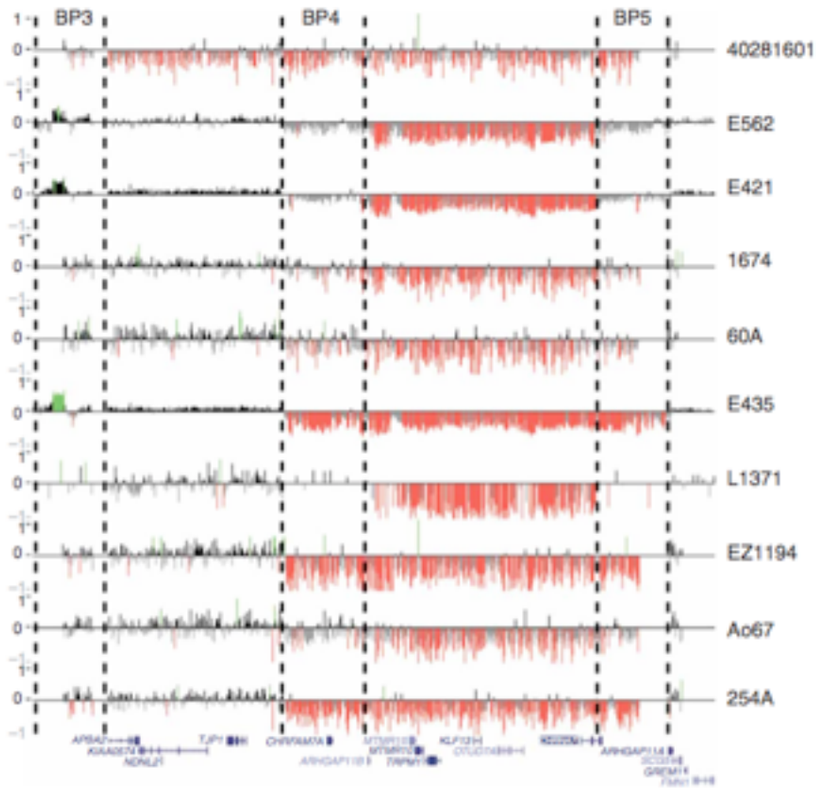


Figure 1 Confirmation of 15q13.3 microdeletions using custom array CGH. High-resolution oligonucleotide array mapping of the 15q12–q13.3 region in 10 of 12 IGE probands with 15q13.3 microdeletions. Probes with $\log_2$ ratios above or below a threshold of 1.5 s.d. are colored green (duplications) or red (deletions). Hashed lines indicate the breakpoint regions BP3–BP5.

Nature Genetics 2009; 41: 160-62

IF= 3.733

Epilepsia, **(*):1–9, 2010
doi: 10.1111/j.1528-1167.2010.02640.x

CRITICAL REVIEW AND INVITED COMMENTARY

Sodium channel *SCN1A* and epilepsy: Mutations and mechanisms

*Andrew Escayg and †Alan L. Goldin

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Summary

Mutations in a number of genes encoding voltage-gated sodium channels cause a variety of epilepsy syndromes in humans, including genetic (generalized) epilepsy with febrile seizures plus (GEFS+) and Dravet syndrome (DS, severe myoclonic epilepsy of infancy). Most of these mutations are in the *SCN1A* gene, and all are dominantly inherited. Most of the mutations that cause DS result in loss of function, whereas all of the known mutations that cause GEFS+ are missense, presumably altering channel activity. Family members with the same GEFS+ mutation often display a wide range of seizure types and severities, and at least part of this variability likely results from variation in other genes. Many different biophysical effects of *SCN1A*-GEFS+ mutations have been observed in heterologous expression systems, consistent with both gain and loss of channel activity. However, results from mouse models suggest that the primary effect of both GEFS+ and DS mutations is to decrease the activity of GABAergic inhibitory neurons. Decreased activity of the inhibitory circuitry is thus likely to be a major factor contributing to seizure generation in patients with GEFS+ and DS, and may be a general consequence of *SCN1A* mutations.

KEY WORDS: GEFS, Dravet syndrome, Genetics, Knock-in mice, Knockout mice.

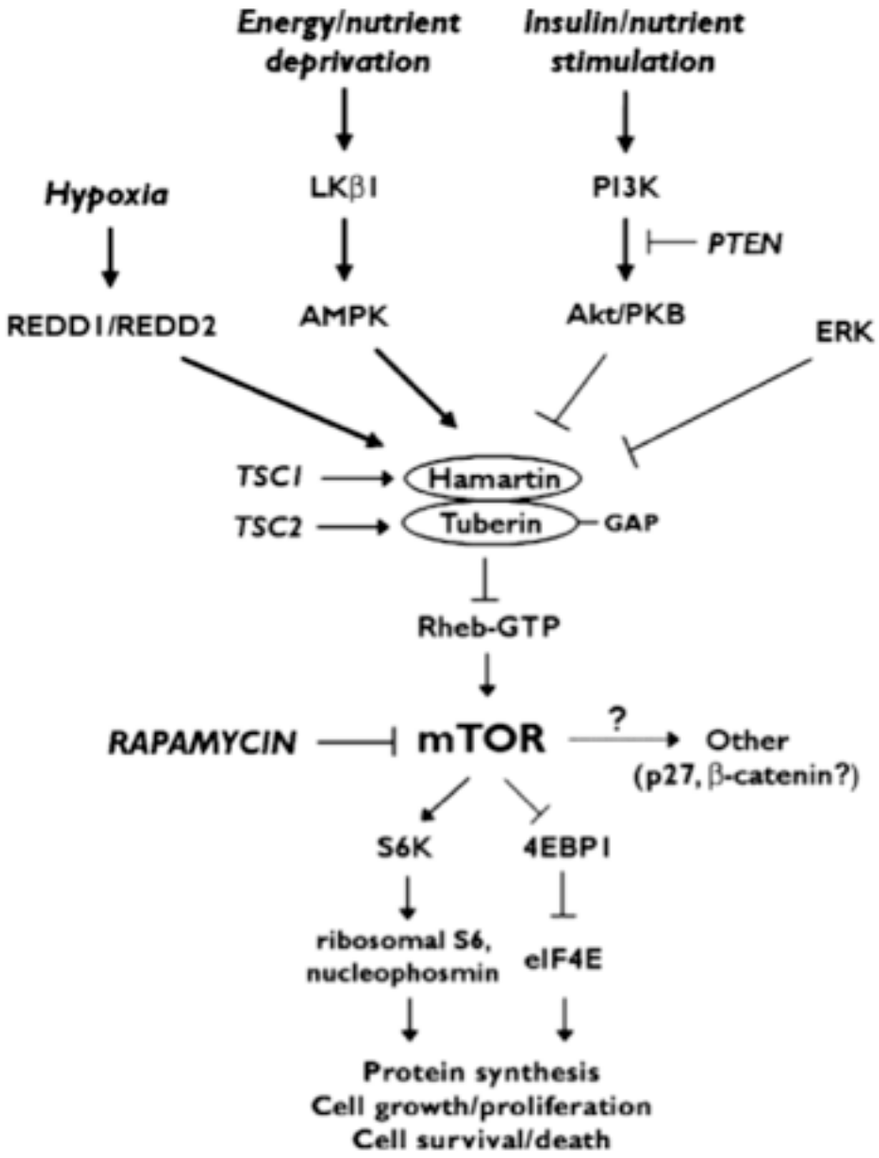
Epilepsia, 51(1):27–36, 2010
doi: 10.1111/j.1528-1167.2009.02341.x

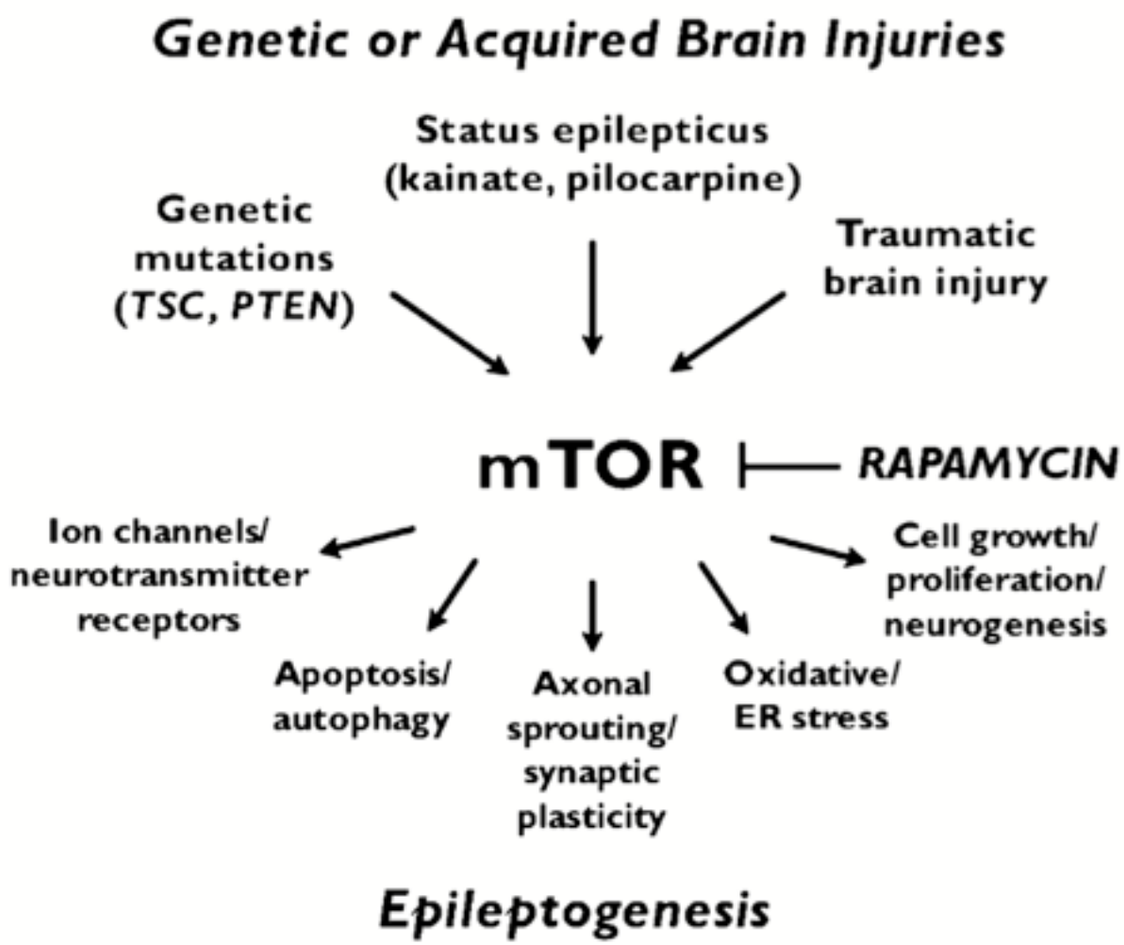
IF= 3.733

CRITICAL REVIEW AND INVITED COMMENTARY

Mammalian target of rapamycin (mTOR) inhibition as a potential antiepileptogenic therapy: From tuberous sclerosis to common acquired epilepsies

Michael Wong





Rapamycin Prevents Epilepsy in a Mouse Model of Tuberous Sclerosis Complex

Ling-Hui Zeng, MD, PhD,[1,2] Lin Xu, PhD,[1,2] David H. Gutmann, MD, PhD,[1] and Michael Wong, MD, PhD[1,2]

IF= 9.935

Objective: T
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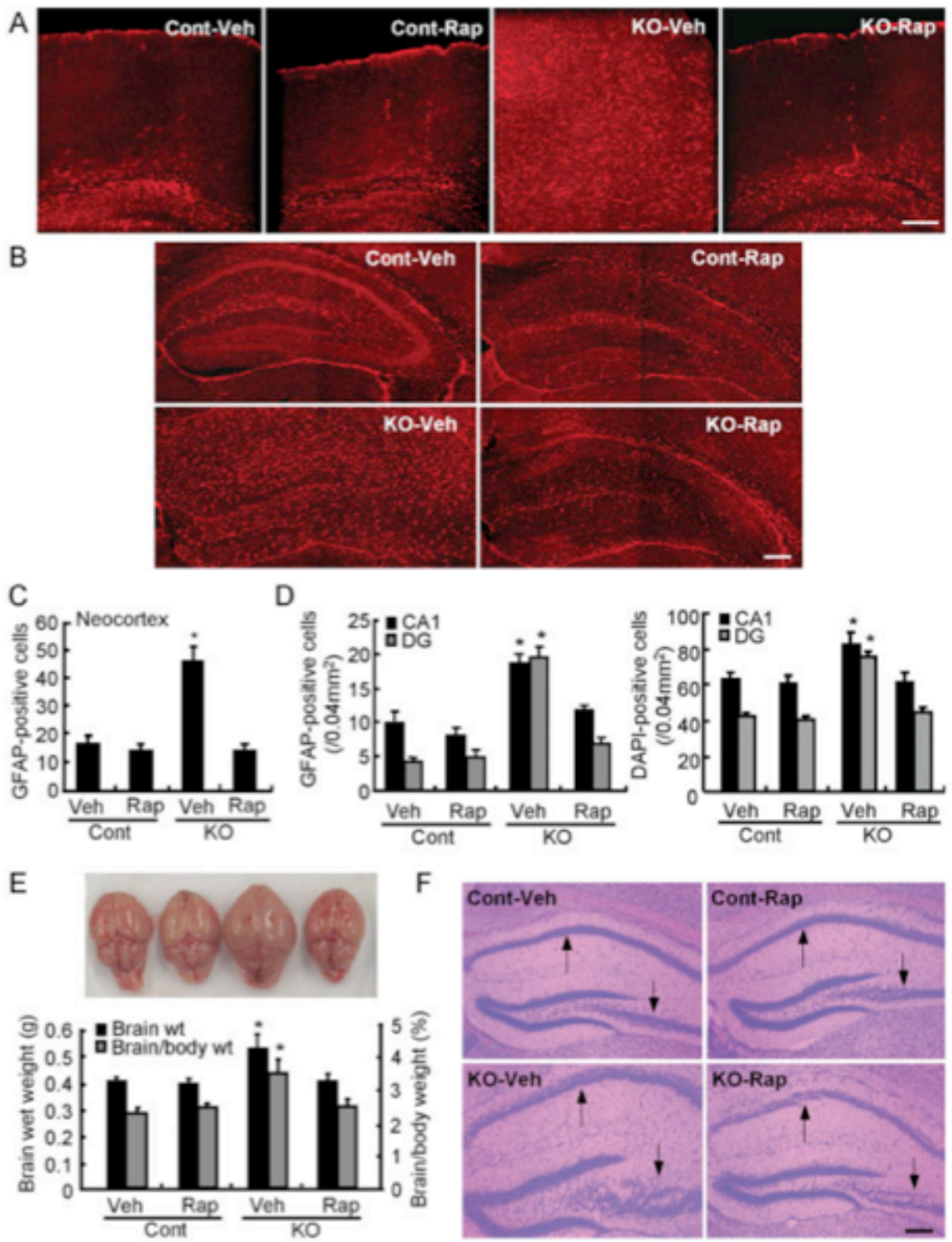
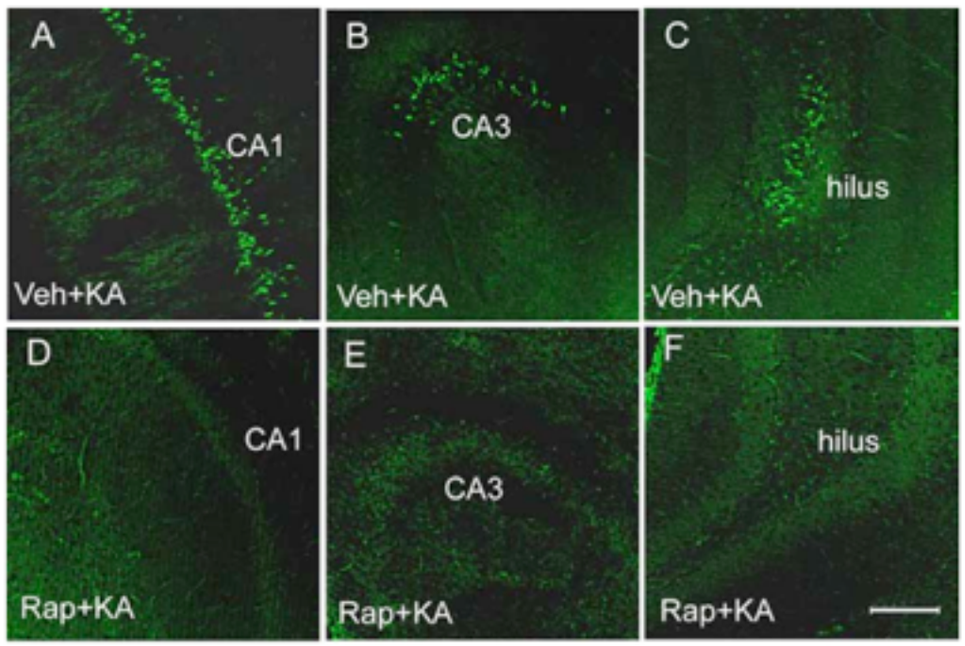
ırol 2008;63:444–453

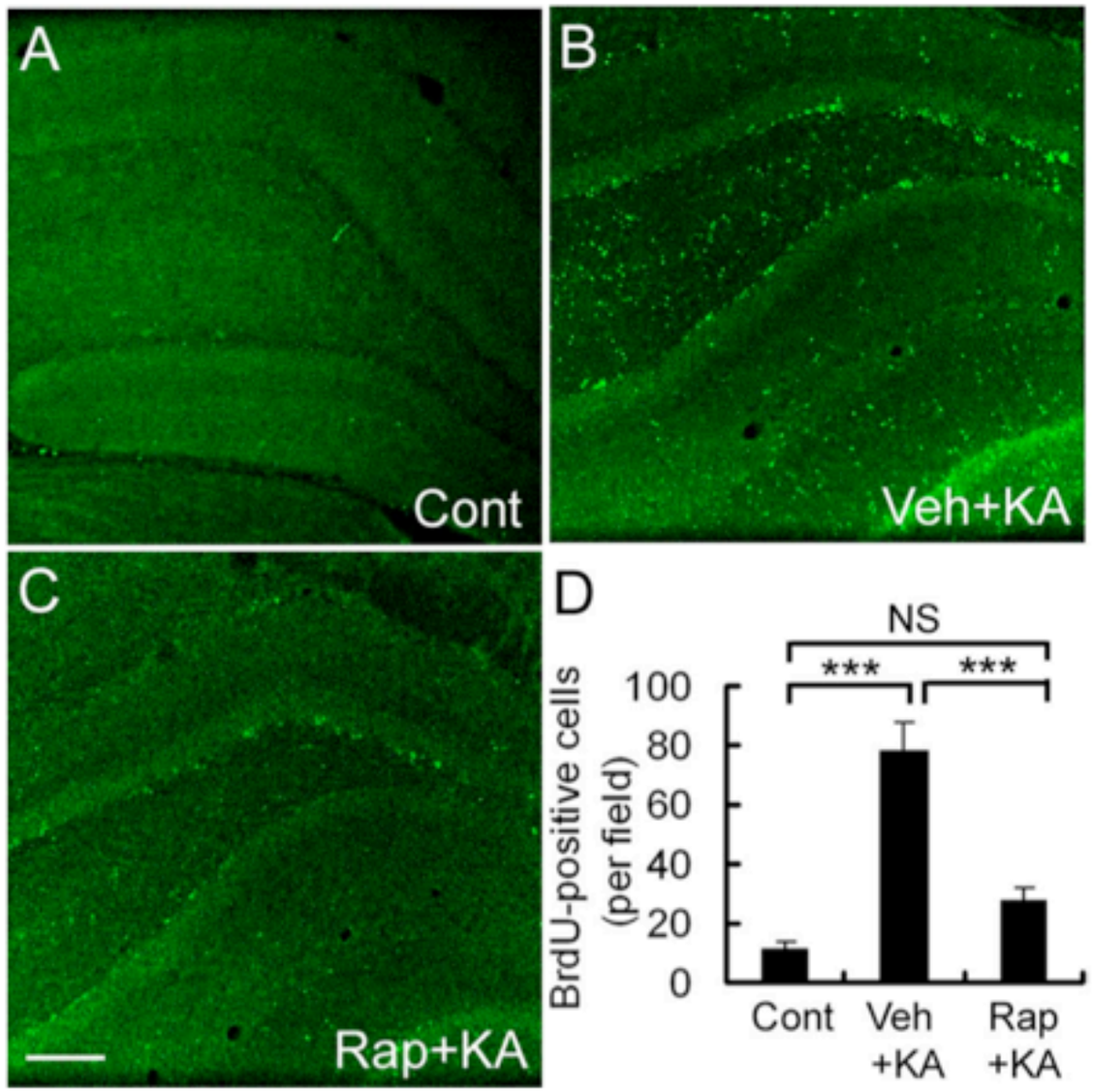


IF= 2.359

The Mammalian Target of Rapamycin Signaling Pathway Mediates Epileptogenesis in a Model of Temporal Lobe Epilepsy

Ling-Hui Zeng, Nicholas R. Rensing, and Michael Wong
Department of Neurology and the Hope Center for Neurological Disorders, Washington University School of Medicine, St. Louis, Missouri 63110





J Neurosci 2009; 21: 6964-72

Epilepsia, 51(6):1069–1077, 2010
doi: 10.1111/j.1528-1167.2009.02397.x

IF= 3.733

SPECIAL REPORT

Definition of drug resistant epilepsy: Consensus proposal by the ad hoc Task Force of the ILAE Commission on Therapeutic Strategies

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Department of Neu nstein College
of Medicine, ion, and
Department of osciences,
University of C y Center,

Level 1: Categorization of outcome to a therapeutic intervention

Level 2: Definition of drug resistant epilepsy

Primary target: medical practitioners at all health care level
Aid recognizing patients with drug resistant epilepsy for prompt referral to specialist centers for evaluation
Clinical research

Level 1: Categorization of outcome to a therapeutic intervention

Scheme for categorizing outcome of an intervention for epilepsy

Outcome dimension		
Seizure control	**Occurrence of adverse effects**	**Outcome category**
1. Seizure-free	A. No	1A
	B. Yes	1B
	C. Undetermined	1C
2. Treatment failure	A. No	2A
	B. Yes	2B
	C. Undetermined	2C
3. Undetermined	A. No	3A
	B. Yes	3B
	C. Undetermined	3C

Level 2: Definition of drug resistant epilepsy

Drug resistant epilepsy may be defined as failure of adequate trials of two tolerated and appropriately chosen and used AED schedules (whether as monotherapies or in combination) to achieve sustained seizure freedom.

CONCLUSION

- The primary target users of the definition are medical practitioners at all health care levels
- recognizing patients with drug resistant epilepsy for prompt referral to specialist centers for evaluation.
- limit in use the case of fist seizure
- other dimensions of outcome are not included in the current scheme,
- The definition aims to describe responsiveness to AED therapy but does not address the possible determining factors.
- inevitably assumptions were made that require testing and validation in future studies.

TREATMENT RELATED COMPLICATION

- Bone health in young adult form tropical country
- Atherosclerosis

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Prevalence and risk factors of low bone mineral density and 25-hydroxyvitamin D status in young healthy epileptic adult patients in a tropical Asian country taking antiepileptic drug

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ABSTRACT

Purpose: Antiepileptic drugs have been reported to reduce bone mineral density (BMD) in several countries with varying prevalence but in studies with small sample size and inadequate assessment of confounders, and rarely including young adults. We sought to determine the prevalence, vitamin D status and risk factors for low BMD in young adult epileptic patients in a tropical setting.
Methods: We prospectively examined left femoral neck and spine with dual-energy X-ray absorption. Demographic data, basic laboratory studies, history of clinical epilepsy, parathyroid hormone and vitamin D level were obtained.
Results: One hundred and twenty three patients were included. The mean (±SD) *T*-score was −0.31 ± 1.24 at the spine and −0.19 ± 1.11 at the left femoral neck. 36% had osteopenia and 4.1% had osteoporosis at either site. Four patients had vitamin D deficiency. Vitamin D levels were not correlated with BMD. Twenty-five patients had vitamin D insufficiency. Multivariate logistic regression analysis identified low body mass index (BMI) and male sex as risk factors for low BMD at the spine and low BMI and duration of treatment as risk factors for low BMD at the left femoral neck.
Conclusion: Chronic use of antiepileptic drug (AED) in young adult patients is associated with low BMD.

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20 – 50 years old with taking AED(s) ≥ 6 months
stable dosage of AED(s)
no other risk factors of low BMD

36% had osteopenia
4.1% had osteoporesis

Risk factors for low MBD (T score at spine) on multivariate analysis

Variable	Level	Odds ratio	95% CI	*p*-value
Sex	Female	1	-	0.001
	Male	3.07	1.27 - 7.42	
BMI	< 18.5	1	-	< 0.001
	18.5 - 22.9	0.44	0.12-1.58	
	> 23	0.06	0.01-0.28	

Risk factors for low MBD (T score at femur) on multivariate analysis

Variable	Level	Odds ratio	95% CI	*p*-value
Duration of treatment (Yr)	0.5-1	1	-	< 0.001
	1-5	1.65	0.14-20.00	
	5-25	2.17	0.22-21.00	
	> 25	8.60	0.75-98.71	
BMI	< 18.5	1	-	0.057
	18.5-22.9	1.1	0.27-4.14	
	> 23	0.15	0.03-0.78	

3.3% had 25-hydroxyvitamin D deficiency
20.3% had 25-hydroxyvitamin D insufficiency
25-hydroxyvitamin D did not correlate with BMD at either measured site
Parathyroid hormone level was not correlated with BMD at euther site or with 25-hydroxyvitamin D level

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FULL-LENGTH ORIGINAL RESEARCH

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Bone mineral density in children, adolescents, and young adults with epilepsy

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†Marco Salvatore

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96 patients (3-25 years) VS 63 healthy control
Taking AED(s) ≥ 2 years

48.9% had cerebral palsy (spastic tetraparesis, spastic diaplegia, congenital hemiplegia and dyskinesis palsy
68.7% had MR
11,4% walk with help; 28.1% could not walk
39% had history of fracture

60% had abnormal BMD
74%had osteopenia and 25% had osteoporesis include with or without cerebral palsy

Table 4. Comparison of vitamin D levels and other biochemical parameters of bone metabolism in patients with epilepsy and those in the control group

	Epileptic group	Healthy group
Vitamin, 1-25(OH)D (ng/ml)	21.6 (1.25–77.9)	26.6 (11.8–68.4)
Osteocalcin (ng/ml)	24.6 (2.39–153.7)	20.8 (3.0–70.2)
PTH (pg/ml)	37.3 (2.63–84.5)	30.3 (3.3–59.9)
Calcitonin (pg/ml)	4.9 (0.1–19.3)	4.5 (0.1–17.9)
Alkaline phosphatase (IU/l)	407.9 (50–2384)	390 (112–840)
Calcium (mg/dl)	8.13 (6.0–11.4)	10.0 (9.1–12.9)
Phosphorus (mg/dl)	4.5 (2.8–6.1)	4.9 (3.0–6.1)

One-way analysis of variance (ANOVA). NS, not significant; PTH, parathormone.

Table 6. Multivariate analysis of independent factors on BMD

	Odds ratio	Lower[a]	Upper[a]	p-value
%Const	0.36	0.04	3.24	0.363
Sex	0.27	0.10	0.74	0.011
Age	1.97	0.26	14.71	0.507
Mental retardation	3.90	1.07	14.26	0.040
AEDs	1.42	0.40	5.04	0.585
Pubertal age	1.72	0.61	4.89	0.308
BMI	0.82	0.16	4.14	0.806
Cerebral palsy	2.41	0.62	9.36	0.203
Epilepsy type	0.60	0.14	2.63	0.501

BMI, body mass index; antiepileptic drugs, AEDs—mono- versus polytherapy.
[a]95% confidence interval for odds ratio.

EFFECTS OF AEDS ON LIPIDS, HOMOCYSTEINE, AND C-REACTIVE PROTEIN

IF= 9.935

Effects of Antiepileptic Drugs on Lipids, Homocysteine, and C-Reactive Protein

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Objective: The widely prescribed anticonvulsants phenytoin and carbamazepine are potent inducers of cytochrome P450 enzymes, which are involved in cholesterol synthesis. We sought to determine whether these drugs have an effect on cholesterol and other serological markers of vascular risk.

Methods: We recruited 34 epilepsy patients taking carbamazepine or phenytoin in monotherapy whose physicians had elected to change treatment to one of the noninducing anticonvulsants lamotrigine or levetiracetam. Fasting blood samples were obtained both before and 6 weeks after the switch to measure serum lipid fractions, lipoprotein(a), C-reactive protein, and homocysteine. A comparator group of 16 healthy subjects underwent the same serial studies.

Results: In the epilepsy patients, switch from either phenytoin or carbamazepine produced significant declines in total cholesterol (−24.8mg/dl), atherogenic (non–high-density lipoprotein) cholesterol (−19.9mg/dl), triglycerides (−47.1mg/dl) (all $p < 0.0001$), and C-reactive protein (−31.4%; $p = 0.027$). Patients who stopped taking carbamazepine also had a 31.2% decline in lipoprotein(a) level ($p = 0.0004$), whereas those taken off phenytoin had a decrease in homocysteine level (−1.7μmol/L; $p = 0.005$). All of these changes were significant when compared with those seen in healthy subjects ($p < 0.05$). Results were similar whether patients were switched to lamotrigine or levetiracetam.

Interpretation: Switching epilepsy patients from the enzyme-inducers carbamazepine or phenytoin to the noninducing drugs levetiracetam or lamotrigine produces rapid and clinically significant amelioration in several serological markers of vascular risk. These findings suggest that phenytoin and carbamazepine may substantially increase the risk for cardiovascular and cerebrovascular disease.

Ann Neurol 2009;65:448–456

: Adult epileptic patient who taking
CBZ or PHT in monotherapy
: To cross them over to monotherapy with LTG or LVE

Table. Mean Change in Each Outcome Measure between Draws 1 and 2

Outcome (units)	Group	N	Baseline	Mean	95% CI	p (within	p (between

Switch from PHT and CBZ produced significant declines
: in total choresterol (-24.8 mg/dl)
: atherogenic (non-high-density lipoprotein) cholesterol (-19.9 mg/dl)
: triglyceride (-47.1 mg/dl) (all p< 0.0001)
: C-reactive protein (-31.4%, p=0.027)
: Pts taken off CBZ -31.2% decline in lipoprotein level (p=0.0004)
: pts taken off PHT a decrease in homocystein (-17 micromol/L, p= 0.005)
All of these changes were significant VS controls (p< 0.05)
Result were a similar whether plts were switched to LTG or LEV

*Geometric mean, standard deviation (SD) on log scale.
CI = confidence interval; CBZ/PHT = carbamazepine- and phenytoin-treated patients combined; NML = healthy subjects; NS = nonsignificant ($p > 0.1$); HDL-C = high-density lipoprotein cholesterol; PHT = phenytoin-treated patients; CBZ = carbamazepine-treated patients; LDL-C = low-density lipoprotein cholesterol; TRIG = triglycerides; HCY = homocysteine.

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IF= 3.733

Long-term antiepileptic drug therapy contributes to the acceleration of atherosclerosis

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: AEDs plays a pivotal role in the pathogenesis of atherosclerosis

: 195 patients with long term AEDs used and 195 healthy age- and sex- match

: age 15-65 years

: IMT at CCA by B-mode ultrasounography

Results: CCA IMT was significantly increased in patients with epilepsy, with male subjects exhibiting thicker IMT than their female counterparts. Whereas BMI, homocysteine, hs-CRP, and TBARS were significantly elevated, folic acid and thiols were significantly reduced in patients with epilepsy. Multiple linear regression analysis further revealed that duration of AED therapy, age, gender, and TBARS level (index for oxidative stress) were independently associated with CCA IMT. In addition, the log-transformed CCA IMT increased linearly with duration of AED therapy after adjustments for age, gender, and TBARS level.

Discussion: The duration of AED therapy is significantly associated with the acceleration of atherosclerosis in patients with epilepsy, alongside

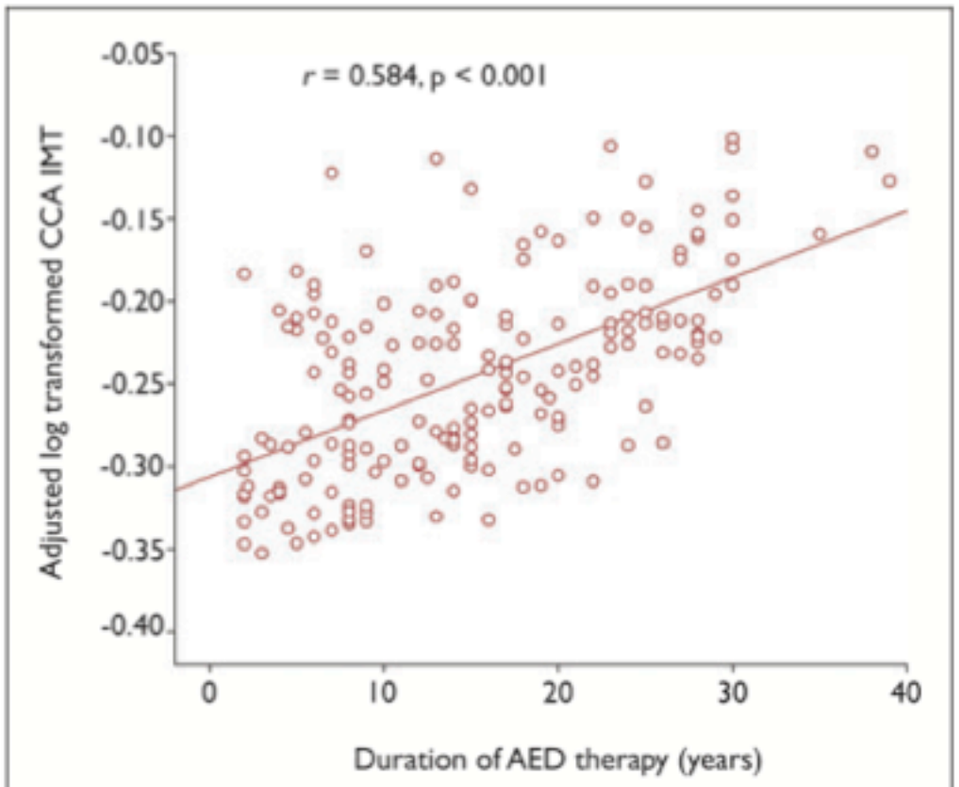

Figure 1.
Relationship between log-transformed common carotid artery (CCA) intima media thickness (IMT) and duration of antiepileptic drug (AED) therapy after adjustment for age, gender, and plasma thiobarbituric acid reactive substances level in 195 patients with epilepsy.
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