Epilepsy Highlight 2009

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Epilepsy Highlight2009

- Pharmacogenomics/ Pharmacogenetics
- Pregnancy & epilepsy
- Novel RX:Carisbamate, Lacosamide, Retigabine, Rafinamide, Brivaracetam, Talampanel, Neuropace
- New drug in Thailand: Fosphenytoin, Levetiracetam syrup
- Upcoming drug to Thailand:I.V. Levetiracetam, Zonisamide
- New syndrome: new epileptic syndrome

Epilepsy Highlight2009

- New therapy: DBS, Neuropace

Epilepsia, 49(12):2087–2091, 2008
doi: 10.1111/j.1528-1167.2008.01719.x

FULL-LENGTH ORIGINAL RESEARCH

Carbamazepine and phenytoin induced Stevens-Johnson syndrome is associated with HLA-B*1502 allele in Thai population

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CRITICAL REVIEW AND INVITED COMMENTARY

The clinical impact of pharmacogenetics on the treatment of epilepsy

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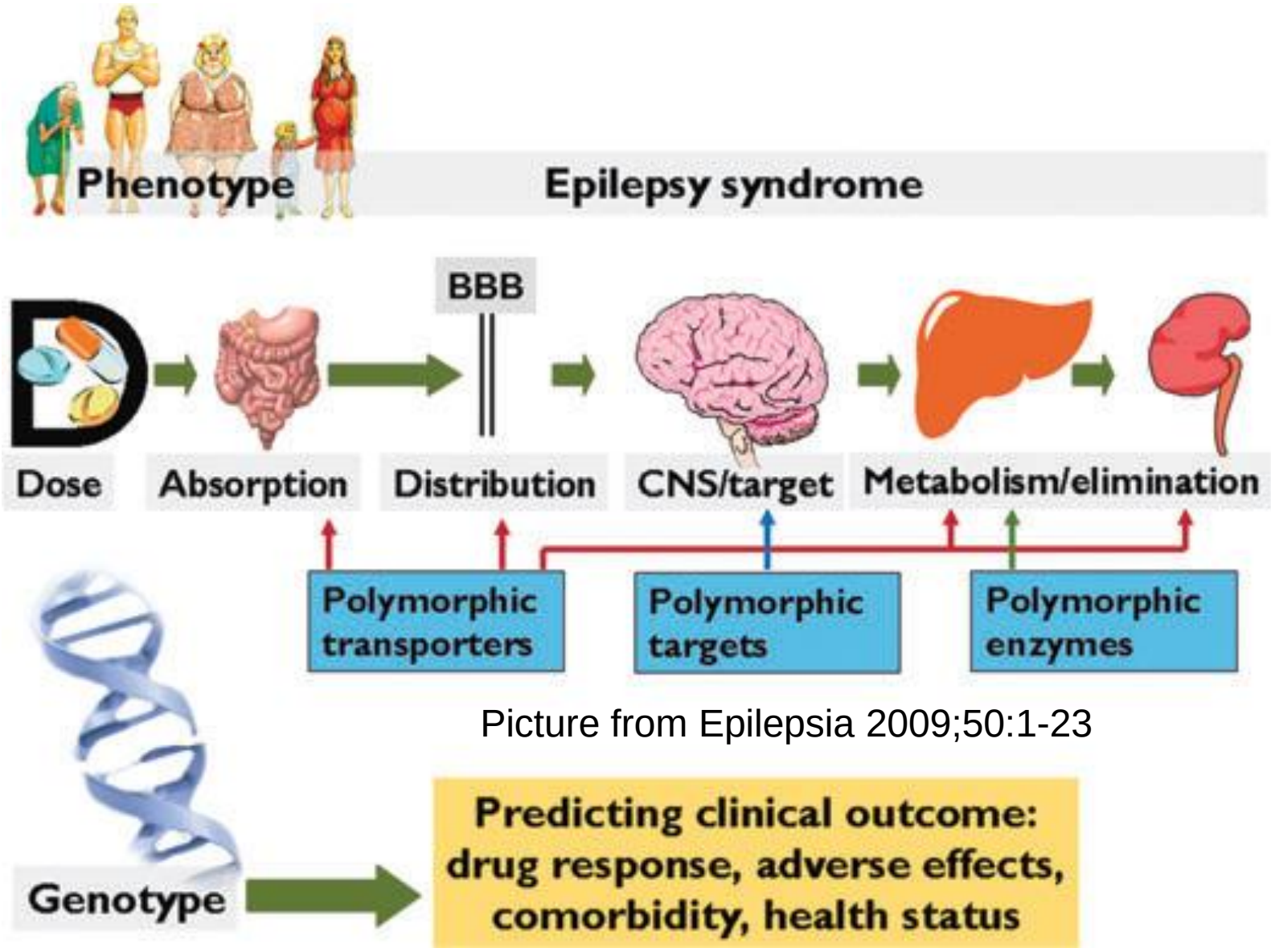

Picture from Epilepsia 2009;50:1-23

Epilepsia, 50(1):24–32, 2009
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CRITICAL REVIEW AND INVITED COMMENTARY

Gene therapy in epilepsy

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Table 1. Summary of studies for gene therapy of epilepsy

Gene	Vector	Model	Authors
Adenosine	Cells expressing adenosine	Kindling	Huber et al., 2001
	Myoblasts delivering adenosine	Kindling	Guttinger et al., 2005
CCK	Lipofectin	Audiogenic rats	Zhang et al., 1997
ICP10PK	HSV-2	Kainate ip	Laing et al., 2006
GAD	Cells expressing GAD65	Kindling	Gernert et al., 2002
	Fetal cells	Kainate icv	Shetty & Turner, 2000
	Immortalized astrocytes expressing GAD67	In vitro	Sacchettoni et al., 1998
	Immortalized GABAergic cells	Kainate ip	Castillo et al., 2006
	AAV-GAD67	In vitro	Robert et al., 1997
	Fibroblasts, GAD65, GAD67	In vitro	Ruppert et al., 1993
	Cells expressing GAD65	Kindling	Thompson et al., 2000
	AAV-antisense GABA-A alpha1	Stim. of IC	Xiao et al., 1997
Galanin	AAV-preprogalanin	Kainate ih	Lin et al., 2003
	AAV-FIB-galanin	Kainate ip/stim. of IC	McCown, 2006
	AAV-FIB-galanin/AAV-galanin	Stim. of IC	Haberman et al., 2003
GDNF	Ad-GDNF	Kainate ip	Yoo et al., 2006
	AAV-GDNF	Kindling, SSLSE	Kanter-Schlifke et al., 2007
Glut1	HSV1	Kainate ih	McLaughlin et al., 2000
HSP72	HSV	Kainate ip	Yenari et al., 1998
Homer1	AAV	SSLSE	Klugmann et al., 2005
NPY	AAV-preproNPY	Kainate ip, kindling	Richichi et al., 2004
NPY	AAV-preproNPY	SSLSE	Noé et al., 2008
NR1	AAV – NR1 oral vaccine	Kainate ip	During et al., 2000
	AAV-NR1A/AAV tet off	Stim. of IC	Haberman et al., 2002

Ad, adenovirus; CCK, cholecystokinin; icv, intracerebroventricular; ih, intrahippocampal; ip, intraperitonneal; SSLSE, self-sust
ing limbic status epilepticus; stim, stimulation.

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Epilepsia, 50(7):1689–1696, 2009
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FULL-LENGTH ORIGINAL RESEARCH

Multidrug-resistant genotype (*ABCB1*) and seizure recurrence in newly treated epilepsy: Data from international pharmacogenetic cohorts

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doi: 10.1111/j.1528-1167.2008.01926.x

SUPPLEMENT – 2007 ANNUAL COURSE

Antiepileptic drugs during pregnancy: What is known and which AEDs seem to be safest?

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EPILEPSY SYNDROMES IN DEVELOPMENT

Transient epileptic amnesia: An emerging late-onset epileptic syndrome

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Table 1. Differential diagnosis between transient global amnesia (TGA) and transient epileptic amnesia (TEA)

	TGA	TEA	Comments
Duration of attacks	1–24 h	<1 h	Up to 30% of TEA episodes last longer than 1 h
Interictal EEG	No epileptiform abnormalities	Epileptiform abnormalities on temporal or fronto-temporal regions	Up to 70% of cases of TEA have normal interictal EEG
Other ictal symptoms (accompanying the amnesic attack, or occurring independently)	No	Yes	Up to 30% of cases of TEA have only pure amnesic attacks; additional minor ictal phenomena may be unnoticed
Recurrence of attacks	Rare	Frequent	–
Response to antiepileptic treatment	Absent	Common	–

EEG, electroencephalography.

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FULL-LENGTH ORIGINAL RESEARCH

A case-control evaluation of the ketogenic diet versus ACTH for new-onset infantile spasms

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Table 2. Demographics and outcomes of children started on the KD (n = 13). Patients are ordered based on the sequence in which they were treated over the 11-year study period

Patient	Age at spasm onset (months)	Duration of spasms (days)	Gender	EEG[a]	Etiology (specified if symptomatic)	Spasm-free at 1 month?	Time to spasm freedom (days)	EEG at 1 month[a]	Spasm-free with ACTH after therapy switched	Developmental outcome at 6 months
1	5	24	Male	Modified	Cryptogenic	Yes	18	Modified	N/A	Mild delay
2	5	14	Female	Modified	Congenital CMV	Yes	7	None (normal at 4 months)	N/A	Moderate delay
3	2	21	Male	Classic	Hypoxic-ischemic encephalopathy	Yes	1	None (normal at 2 months)	N/A	Severe delay
4	5	5	Female	Classic	Idiopathic	Yes	6	Classic (normal at 3 months)	N/A	Normal
5	5	30	Male	Modified	Cryptogenic	No	N/A	Modified	Yes	Severe delay
6	5	3	Female	Classic	Congenital hydrocephalus	No	N/A	Modified	Yes	Moderate delay
7	10	4	Female	Classic	Group B streptococcal meningitis	Yes	9	Modified (normal at 5 months)	N/A	Mild delay
8	5	10	Male	Classic	Idiopathic	No	N/A	Classic	Yes	Normal
9	10	3	Male	Modified	Left hemispheric astrocytoma and infarction	No	N/A	Modified	Yes (topiramate used, not ACTH)	Mild delay
10	5	4	Female	Classic	Partial agenesis of the corpus callosum	Yes	3	Modified (normal at 2 months)	N/A	Mild delay
11	8	45	Male	Modified	Periventricular leukomalacia	Yes	10	Normal	N/A	Mild delay
12	5	7	Female	Classic	Idiopathic	Yes	3	Minor asymmetry (normal at 2 months)	N/A	Normal
13	3	14	Female	Modified	Aicardi syndrome	No	N/A	Modified	No	Moderate delay

[a]classic, classic hypsarrhythmia; modified, modified hypsarrhythmia.

Table 3. Demographics and outcomes of children started on ACTH (n = 20). Patient numbers are ordered based on the sequence in which they presented over the 11-year study period

Patient #	Age at onset (months)	Duration of spasms (days)	Gender	EEG[a]	Etiology (specified if symptomatic)	Spasm-free at 1 month?	Time to spasm freedom (days)	EEG at 1 month[a]	Developmental outcome at most recent follow-up
1	4	16	Male	Classic	Dysgenesis of the corpus callosum	Yes	1	Modified	Normal
2	7	22	Female	Modified	Idiopathic	Yes	3	Normal	Normal
3	5	3	Male	Classic	Trisomy 21	Yes	1	None (normal at 6 months)	Moderate delay
4	5	25	Female	Classic	Trisomy 21	Yes	3	Normal	Mild delay
5	9	14	Male	Modified	Idiopathic	Yes	4	Normal	Mild delay
6	6	42	Male	Classic	Hemispheric atrophy	Yes	5	Normal	Normal
7	6	12	Male	Classic	Pachygyria	Yes	14	None	Moderate delay
8	5	30	Female	Modified	Periventricular leukomalacia	Yes	21	None (modified at 3 months)	Mild delay
9	6	25	Male	Classic	Cryptogenic	Yes	5	Focal spikes	Mild delay
10	7	90	Female	Classic	Trisomy 21	Yes	1	Normal	Moderate delay
11	1	50	Male	Modified	Periventricular leukomalacia	Yes	5	Focal spikes	Severe delay
12	6	4	Female	Classic	Periventricular leukomalacia, hydrocephalus	Yes	6	Focal spikes	Severe delay
13	5	21	Male	Classic	Cryptogenic	Yes	2	Normal	Normal
14	8	35	Female	Modified	Idiopathic	Yes	6	Normal	Normal
15	8	18	Male	Modified	Schizencephaly	Yes	2	Modified	Mild delay
16	5	25	Female	Classic	Chromosome 5,9 translocation	Yes	1	Modified	Mild delay
17	12	90	Male	Classic	Trisomy 21	Yes	5	Normal	Mild delay
18	6	21	Male	Classic	Linear nevus sebaceous syndrome	Yes	4	Normal	Normal
19	1	100	Male	Classic	Cryptogenic	No	N/A	Modified	Moderate delay
20	6	21	Male	Modified	Hearing loss, optic nerve atrophy	No	N/A	Modified	Moderate delay

[a]classic, classic hypsarrhythmia; modified, modified hypsarrhythmia.

Epilepsia 2008:49;1504

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FULL-LENGTH ORIGINAL RESEARCH

Talampanel suppresses the acute and chronic effects of seizures in a rodent neonatal seizure model

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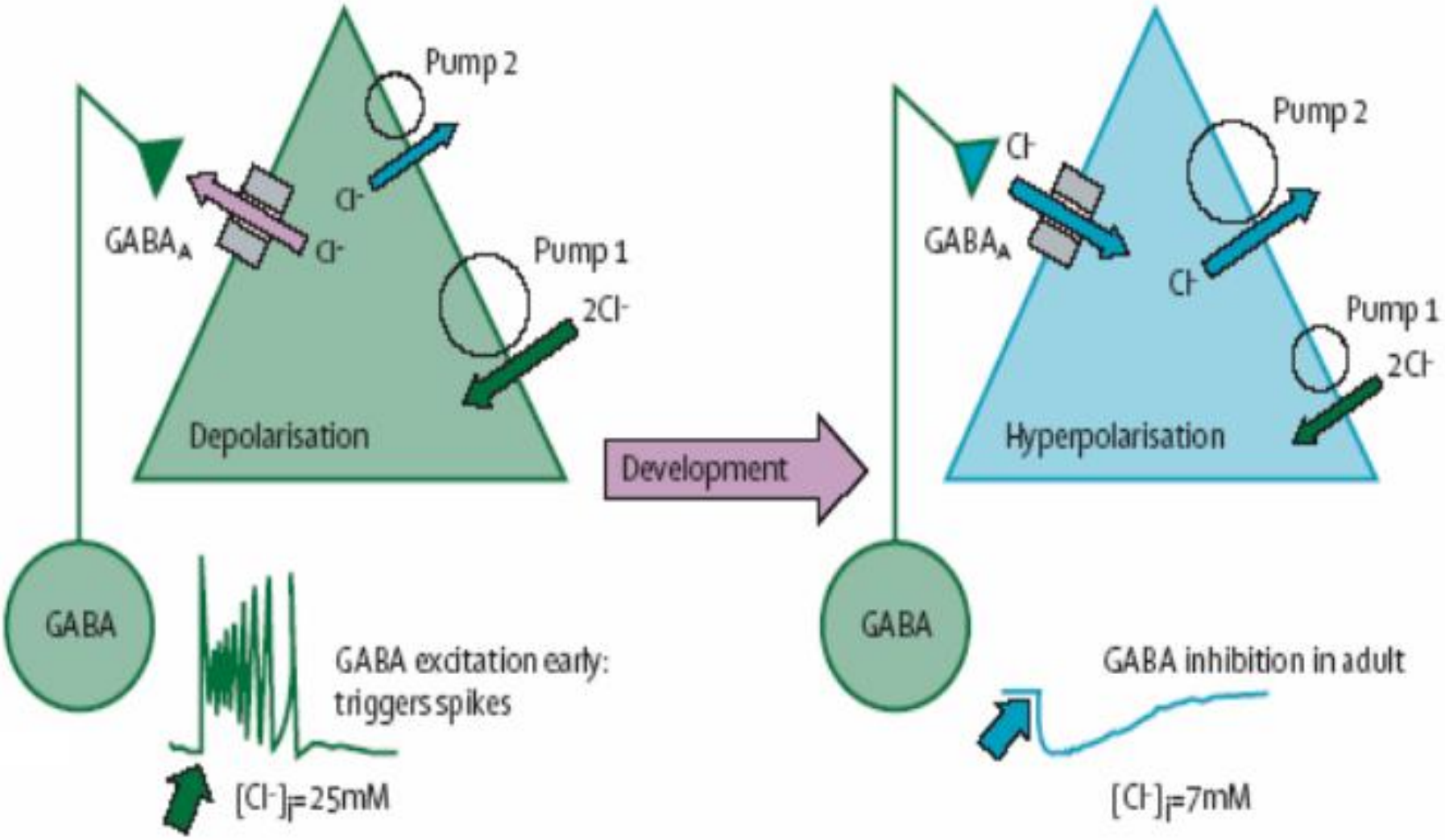
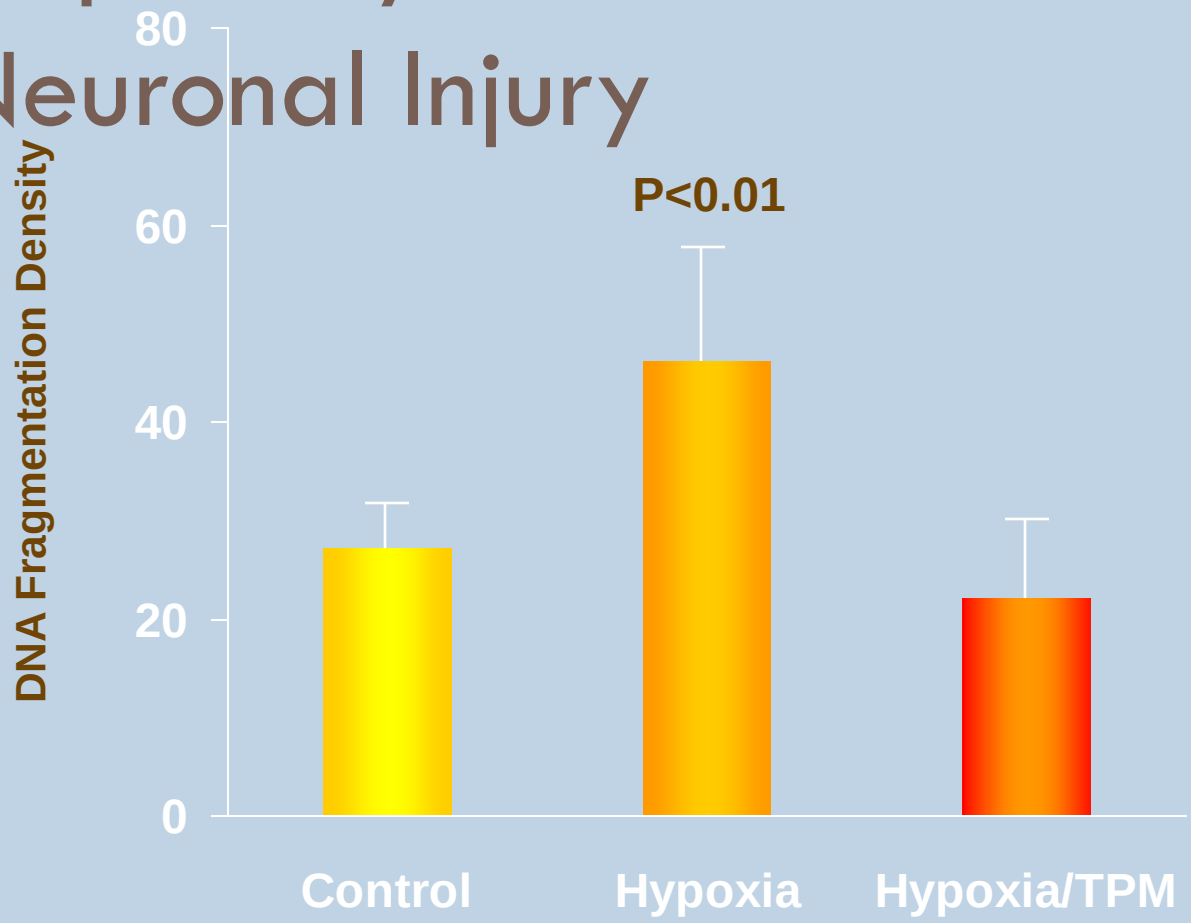


Picture from Epilepsia 2009;50:694

Pump 1 – Na^+-K^+-2Cl^- (NKCCl)

Pump 2 –K^+-Cl^- (KCC2)

Hypoxia-Induced Long-Term Susceptibility to Neuronal Injury



Koh S, Jensen FE. Ann Neurol 50:366, 2001

ThankYou