# 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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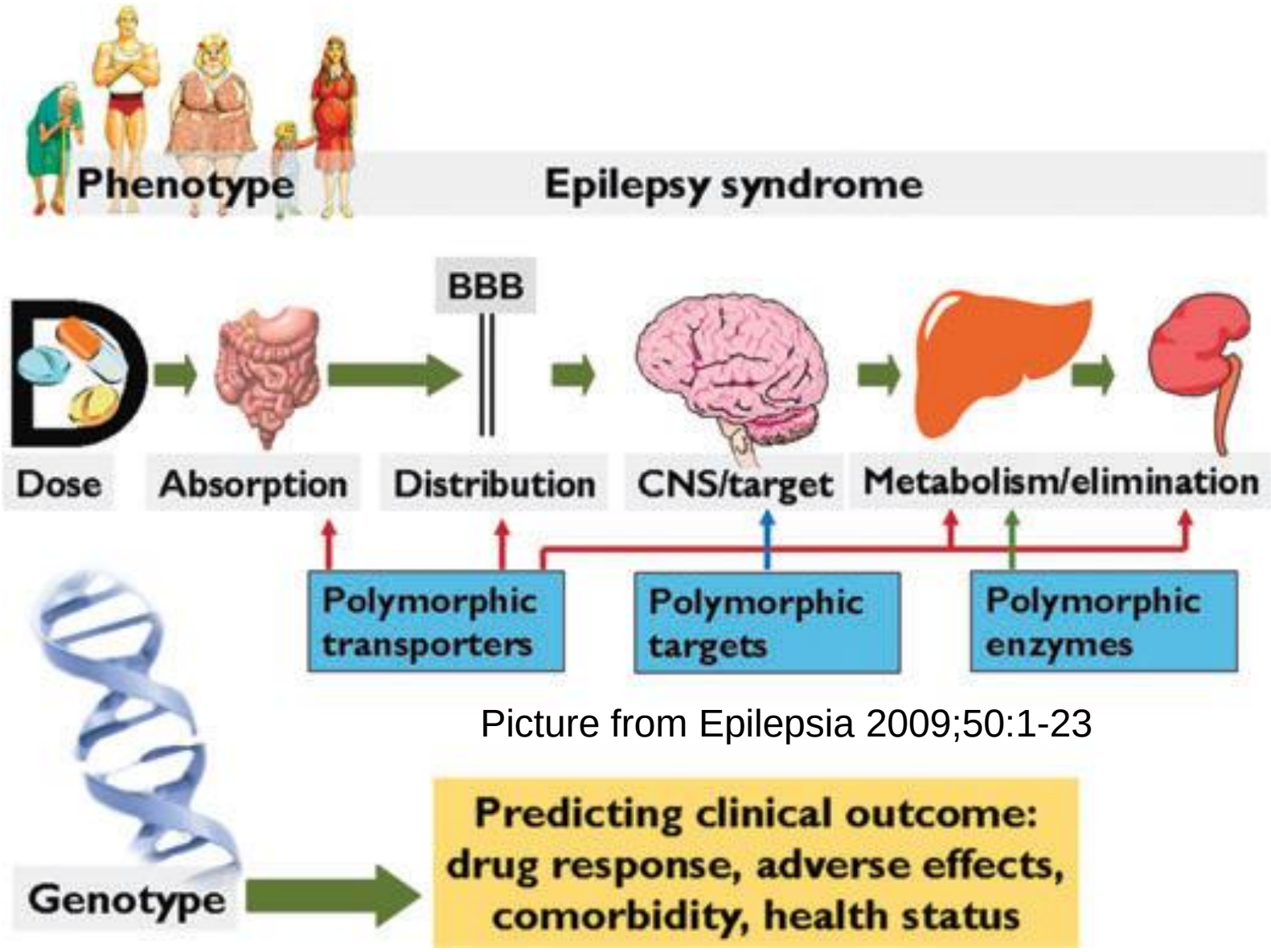


Picture from Epilepsia 2009;50:1-23

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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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FULL-LENGTH ORIGINAL RESEARCH

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

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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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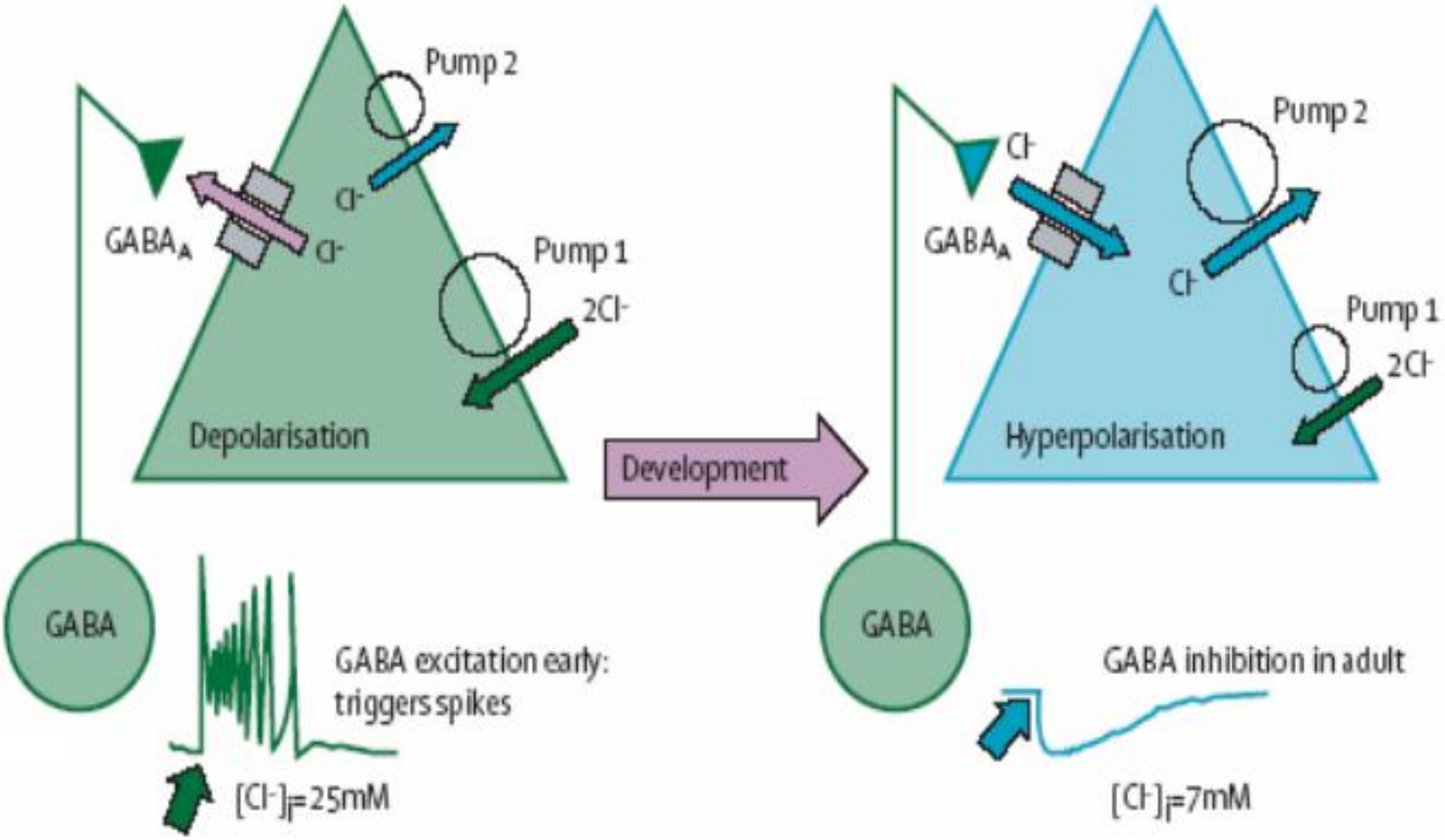
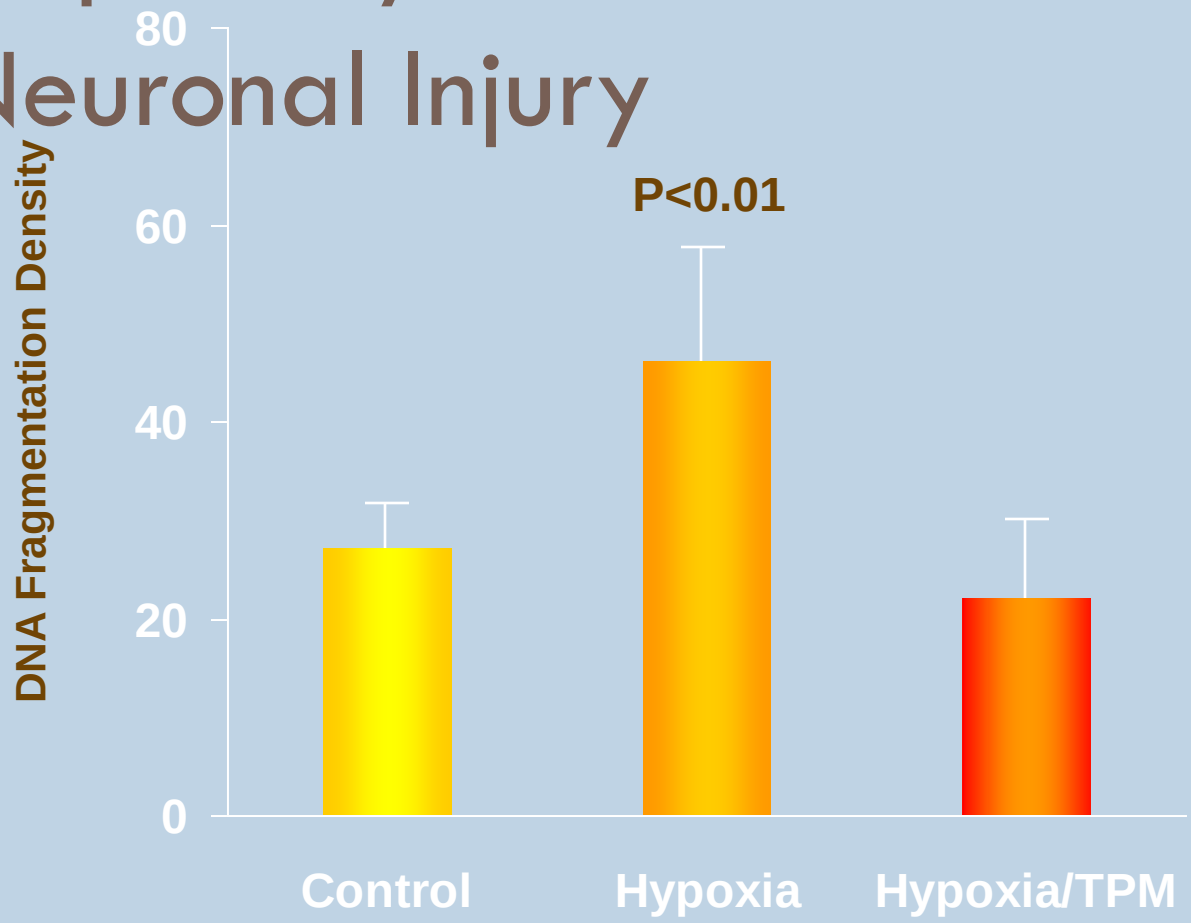



Picture from Epilepsia 2009;50:694

Pump 1 – $Na^+$-$K^+$-2$Cl^-$ (NKCCl)

Pump 2 –$K^+$-$Cl^-$ (KCC2)

# Hypoxia-Induced Long-Term Susceptibility to Neuronal Injury




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

# ThankYou