understanding of the clinical manifestations of intractable epilepsy and its relationship to the structural connectivity of the insula during both spontaneous and electrically-induced epileptiform activity. The panel will explore existing state of the pre-surgical language localization with talks devoted to ECS, ECoG mapping and network connectivity. 3. To discuss how existing state of the pre-surgical language localization with talks devoted to ECS, ECoG mapping and network connectivity. 3. To discuss how existing state of the pre-surgical language localization with talks devoted to ECS, ECoG mapping and network connectivity. 3. To discuss how existing state of the pre-surgical language localization with talks devoted to ECS, ECoG mapping and network connectivity. 3. To discuss how existing state of the pre-surgical language localization with talks devoted to ECS, ECoG mapping and network connectivity.
The link between AD and epilepsy is best described as a "shared risk factor association" originating from common underlying risk factors (depressive, traumatic brain injury), which are predisposing to the development of both conditions. Classic pharmacological approaches to the treatment or prevention of cognitive decline, and/or memory failure have failed to substantially reduce their medical and financial burden. In general, we do not know the exact mechanisms underlying epilepsy in AD, or vice versa. Addressing common pathways and related complications represents an innovative way to develop new, potentially preventative therapies, which has been hampering for both neurodegeneration and epilepsy, partly due to a lack of clinically validated, sensitive and specific biomarkers to identify the relevant disease mechanisms. In this context, seizures, detection and disease monitoring are the pre-requisite to develop innovative, mechanisms-based treatment strategies for both epilepsy and dementia within a personalised health care framework.

1. To assess the histopathological evidence of amyloid plaques in epileptic hippocampus and visualize in situ the spiking and non-convulsive status epilepticus in patients with frequent spiking. It is the first study to use high-frequency rTMS applied to lateral parietal cortex with resting-state connectivity to the hippocampus, in light of the frequent memory impairments seen in patients with mesial temporal lobe epilepsy.

2. To determine electrophysiological assessment of frequent spiking in mesial temporal lobe epilepsy.

3. To explore the impact of cognitive and behavioral co-morbidities in idiopathic childhood epilepsies. 4. To evaluate the evidence for the pathophysiological causes of cognitive and behavioral co-morbidities in idiopathic childhood epilepsies.

Although idiopathic childhood epilepsies such as Childhood Absence Epilepsy (CAE) and Benign Epilepsy with Central Temporal Spikes (BECTS) have long been labeled as "benign" syndromes, the clinical course can be variable and prior research has highlighted a variety of cognitive and behavioral co-morbidities. This new, and at times conflicting, information directly impacts the care of children with epilepsy and potentially limits their quality of life.

1. To discuss whether CAE and BECTS can be considered "benign" and if there are potential biomarkers to predict which patients are at risk for neuropsychological co-morbidities.

2. To discuss how connectivity-guided targeting of repetitive transcranial magnetic stimulation (rTMS) might be used to improve outcomes in depression, an important epilepsy comorbidity.

3. To consider recent evidence that associative connectivity imaging can successfully identify surface cortical regions that show physiological hyperexcitability and may be amenable to noninvasive stimulation therapy for epilepsy involving deep brain stimulation.

4. To discuss the role of spiking and non-convulsive status epilepticus on learning memory and cognition is unclear. While idiopathic epilepsy has failed to substantially reduce its medical and financial burden, in general, we do not know the exact mechanisms underlying epilepsy in AD, or vice versa. Addressing common pathways and related complications represents an innovative way to develop new, potentially preventative therapies, which has been hampering for both neurodegeneration and epilepsy, partly due to a lack of clinically validated, sensitive and specific biomarkers to identify the relevant disease mechanisms.
There has been a lot of emphasis recently on the networks involved in focal epilepsy, in contrast to the earlier emphasis on the focus itself. Networks have been shown to be involved at the time of interictal discharges with EEG and MEG source analysis, as well as intracerebral recordings. Networks are revealed when studying responses to intracerebral stimulation. Networks are evident at the time of interictal discharges with ictal EEG and intracerebral rhythms. Networks are revealed even in the resting state between interictal discharges. Of course networks are involved at the time of seizure spread. We would like to raise the question of the importance of these networks in the context of preictal modulation. In focal epilepsy, even when a network is involved, there is usually a primary focal area to which seizures are not limited. However, in networks associated with stress triggered seizures, we would like to raise the question of the importance of the network to the spread of seizures. Stress is the most commonly reported trigger of seizures in multiple surveys of people with epilepsy. Prior research has identified underlying depression and anxiety as risk factors. Dr. Sperling has extensive experience in studying the effects of stress on cortical modulation of epilepsy. Dr. Sperling is a world recognized expert in translational stress models of psychiatric illness and neurodegenerative disorders. The field is quite new, the speakers will be relatively young. An overview of functional network will be given by the organizer. Dr. Chu-Shore is junior investigator who is a leader in identification of EEG networks in children with epilepsy. She will present the significance of EEG-identified networks in identification and tracking of the impact of epilepsy on cortical function. Dr. Weaver will review the fmRI and electrocorticography-measured functional networks and evidence for the significance of disruption of these networks. Dr. Maccotta will discuss focus of epilepsy in functional networks. Dr. Kaiser will discuss the relationship between network disruption and clinical outcomes. The discussion and debate of the workshop is expected to focus on whether the different tools reveal the same networks, whether the findings in epilepsy are consistent or specific and whether a network disruption has any clinical significance. The critical assessment of this rapidly expanding field will be beneficial for those interested in advanced imaging, biomarkers and clinical epilepsy.

1. Outline evidence that stress has an effect on epileptogenesis and seizures in animal models. 2. Understand translational approaches to measuring and treating stress in non-epilepsy conditions. 3. Understand and discuss the design and results of the first RCT of stress management for seizure control in patients with resolution-resistant epilepsy.

1. To review current evidence from human studies regarding the anatomical and behavioral teratogenesis of different antiepileptic drugs. 2. To review current evidence from animal studies regarding the anatomical and behavioral teratogenesis of different antiepileptic drugs. 3. To identify gaps in our knowledge of the anatomical and behavioral teratogenesis of different antiepileptic drugs. 4. To provide a forum for discussion of research priorities and strategies for the future investigations to reduce gaps in our knowledge.

Emerging evidence indicates that the epileptic brain undergoes large-scale changes in cortical and subcortical connectivity in addition to alterations within the epileptogenic foci. In concert with these diffuse network degenerations, the validated epilepsy syndromes also impose cognitive impairments, some of which are broad in nature and shared with other epilepsy syndromes, while others appear specific to the type of epilepsy. The goal of this workshop is to provide an overview on how disrupted brain networks can contribute to the generation of epileptic seizures and cognitive deficits. The workshop will bring together researchers in brain connectivity with emphasis on graph theory, neuroimaging, and microstructural connectivity of epilepsy to integrate the overarching link between topological properties of brain networks, their modifications by the epilepsies, and the neurophysiological impacts on cognitive functioning. Dr. Marcus Kaiser will first review graph theory and other techniques for network analysis to characterize the topological and spatial properties of the human connectome. Following a discussion of organizational changes in the epileptic brain, Dr. Jie Li will further demonstrate the applicability of these techniques to clinical research and present new findings on the neurodevelopmental alterations of large-scale structural networks in children with new-onset epilepsy. Dr. Bruce Hermann will then present new findings regarding how alterations in large-scale network configurations in the epileptic brain may reduce the efficiency of information transfer, representing new avenues to understand the disordered neurophysiology of cognitive and sensorimotor functions in epilepsy. Dr. Leonardo Biondi will synthesize these findings and lead an audience discussion session on how improved understanding of global brain connectivity may provide insights on the underlying mechanisms of the epileptic network and treatment strategies.
The growing use of continuous EEG monitoring in the pediatric ICU setting has led to growing awareness of the high prevalence of seizures among certain groups of critically ill children. Yet much remains to be learned about the epidemiology of seizures, their effective treatment, and their impact on outcomes. This Clinical Investigators’ Workshop will provide a forum for discussion of the prevalence and risk factors for seizures among critically ill children, their optimal treatment, and emerging evidence regarding their impact on outcome.

The presenters will highlight gaps in knowledge that require further study, and propose strategies for optimal study design. Discussion will be focused on setting research priorities and designing future collaborative studies. Speakers and Topics: Nicholas Abend: Seizures in the Pediatric ICU: Epidemiology and Impact Tobias Loddenkemper: Evidence-Based Seizure Management in the Pediatric ICU Cecil Hahn: Designing Clinical Research on Seizures Among Critically Ill Children Objective 1: To review current evidence regarding the epidemiology of seizures among critically ill children, and their impact on outcomes. 2. To review current evidence regarding seizure prophylaxis and treatment among critically ill children, and discuss optimal treatment strategies. 3. To identify gaps in our knowledge of seizures among critically ill children, and discuss strategies for optimal study design. 4. To provide a forum for discussion of research priorities and the planning of collaborative clinical investigations. Our target audience includes pediatric neurologists, clinical neurophysiologists, and neurointensivists.

Objectives
1. To review current evidence regarding seizures among critically ill children.
2. To review current evidence regarding seizure prophylaxis and treatment among critically ill children, and discuss optimal treatment strategies.
3. To identify gaps in our knowledge of seizures among critically ill children, and discuss strategies for optimal study design.
4. To provide a forum for discussion of research priorities and the planning of collaborative clinical investigations.

Our target audience includes pediatric neurologists, clinical neurophysiologists, and neurointensivists with an interest in seizures among critically ill children and the practice of ICU EEG monitoring in children.
Successful epilepsy surgery depends on removing the epileptic zone and not causing damage to eloquent cortex or critical white matter tracts that will give rise to a new deficit. Neuronavigation is increasingly used to direct cranial neurosurgery. A recent development has been the ability to display multimodal data including structural MRI, angiography, magnetic resonance imaging (MRI), and functional MRI in a common space. It is now possible to upload these data to place intracranial electrodes and to plan resections. The data may also be uploaded into neurosurgical navigation systems and so be available in the operating room. We will present the techniques that are now becoming available, and their limitations, and will debate the utility of these in neurosurgical practice.

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A significant percentage of patients continue to have seizures after epilepsy surgery. Among the multiple causes, the most obvious ones include failure to remove all of the epileptogenic tissue or incomplete localization of the epileptogenic area. Recent studies have shown that failure to recognize insular seizures may be responsible for some of these surgical failures. In this workshop, we will review the various clinical presentations of insular cortex epilepsy, the role invasive and non-invasive investigation of suspected insular cortex epilepsy and treatment options for this entity. Increased awareness and further understanding of insular cortex epilepsy will hopefully lead to improved recognition of this localization-related syndrome and translate into better epilepsy surgery outcomes.

Dr. François Moulin, Dr. Sang-Ho Nguyen, Dr. Alain Bouthillier

Photosensitive Epilepsy in Humans and Baboons: A Window to Networks Underlying IGE

Clinical Investigator Workshop Background: While our understanding of the mechanisms underlying focal epilepsies has been driven by epilepsy surgery, our knowledge of the circuits or networks underlying epilepsy in general (EG) is still limited. Photosensitivity provides a window for the investigation of the mechanisms underlying IGE. Recent advances in the genetics and neuroimaging (fMRI, fPET and MRS) in the research of photosensitive epilepsy in humans, complemented by functional neuroimaging and intracranial recordings in the photosensitive baboon, may provide new insights into IGE. In this workshop, the goal is to discuss the latest advances in our understanding of mechanisms underlying photosensitive epilepsy and IGE, and to compare human and animal data to enhance and extend our knowledge in this field. The workshop will consist of three 20-25 minute presentations. The first presenter, Dr. Dorothee Kasteleijn-Nolst Trenite, Chairwoman of the European Consortium on Genetics of Photosensitivity and Visually Sensitive Epilepsies, will introduce the classification of photosensitive and photosensitisation responses and review clinical and genetic studies of photosensitivity and generalised epilepsy. The second presenter, Dr. Michael Siniatchkin, is an expert in human photosensitivity, using modern clinical neurophysiology and neuroimaging tools, to unravel underlying networks. The third speaker, Dr. Charles Akos Szabo, Chief of Epilepsy at the University of Texas Health Science Center at San Antonio, and collaborator in the NIH R01, will provide new neuroimaging and electrophysiological data from intracranial recordings in the photosensitive baboon. The panel, consisting of the three speakers, will integrate clinical, neurophysiological and electrophysiological data in humans and baboons to better understand the mechanisms underlying IGE and impact on seizure development in the future.

Charles Akos Szabo, M.D., Dorothee Kasteleijn-Nolst Trenite, M.D., Michael Siniatchkin, M.D.
The safety and efficacy of antiepileptic therapies (AETs) has been assessed using measures and trial designs that have become standardized. Unfortunately, although times have changed, trial designs have not. This has led to enormous difficulty with recruitment of patients as well as a narrow view of possible adverse effects. As a consequence, the standard approach of AET evaluation presents barriers in bringing novel therapies to the patients who need them. We have an urgent need for updated trial designs that are methodologically sound. Furthermore, in order to discover new aspects of how drug AETs affect people with epilepsy, new outcomes are needed. For example, to reduce the time that patients are exposed to placebo, time to "m"-th seizure may be a more appropriate outcome than seizure frequency. In some circumstances, when initial efficacy of a drug has been met, shorter trials may be appropriate for new indications. Trial duration and should be modeled from prior studies. The risks of AETs also need to be addressed through better methodology, the baseline risk of relapse in the epilepsy trial population has not been assessed, although the risk of suicide with starting AETs has acquired an FDA warning. The available suicidality scale and its use in the epilepsy trial population deserves exploration. It does not cover all of the many available depression scales, it is the most appropriate for use in epilepsy studies. Further, possible predictors of behavioral adverse events, such as baseline neuropsychiatric and hemorrhal status, while potentially assessible in clinical trials, have not been appropriately utilized to date. The clinical impact of treatment and psychometric slowing that occurs with onset of AETs is also not accurately predicted with current methodology and updated assessment instruments could be employed and evaluated. This clinical workshop will put forth ideas and evidence for using new outcome measures for AET evaluation and provide a forum for discussion of the drawbacks and benefits for patients of de-standardizing AET development.

De-standardizing antiepileptic therapy development.

Anthony Bernasconi, MD - Montreal Neurological Institute and Gillard W.O. Department of Neuroscience, Children's National Medical Center, Washington, DC, USA

Mapping brain networks in epilepsy: insights from novel EEG, fMRI and morphometric MRI methods.

Darrell V Lewis will discuss the MRI changes detected after febrile status epilepticus in humans and computational models that might be employed to model these changes. Celine Dube will discuss novel and unpublished findings from several modalities of MRI (T2, DWI, MRS) that might be employed to model these changes and provide an overview of magnetic resonance imaging and magnetic resonance imaging techniques that might be employed to model these changes.

Innovative methodologies applicable to humans and animals for predicting both disease onset and progression.

Kens Fertig, Rauschert, Dale Hesdorffer, Bruce Hermann (probably not both Bruce and one of the other)

Magnetic Resonance Imaging changes after Prolonged Febrile Seizures and Temporal Lobe Epilepsy: what biomarkers can we discover from clinical studies and in vivo imaging?

Cynthia L. Harden - Hormones, behavior and inattention affected by AEDs

The relationship between prolonged febrile seizures (febrile status epilepticus) and temporal lobe epilepsy, remains unclear. Whereas some children develop epilepsy after and with cognitive deficits after febrile status epilepticus, in other cases it is not possible to predict these outcomes for an individual child. Magnetic Resonance Imaging (MRI), holds promise as a biomarker, because MRI changes have been found after febrile seizures in children and in animal models. However, the structural and functional and underlying neuronal mechanisms of brain development in the children with and without these communications, as well as various cognitive scores of children with both clinical and basic research. This workshop will bring together researchers on comorbidities, neuropsychological and basic science to integrate the comorbidity and multimodal imaging findings in children with cognitive and behavioral impairments evident in animal models of humans. To do this, Bruce Hermann will describe prospective volumetric and morphometric findings and cognition in children with more overt epilepsy with and without co-morbidities. Rochelle Caplan will discuss volumetric, morphometric, and fMRI data related to a broad range of psychopathology in children with epilepsy. Hal Blumenfeld will discuss recent fMRI, structural, and resting functional connectivity in childhood epilepsy, as well as MRI network abnormalities to direct surgical resections in animal models of childhood epilepsy. Raman Sankar will present innovative methodologies applicable to humans and animals for predicting both functional and structural reorganization in limbic circuits involved in epileptogenesis. Doctor Bilde will discuss novel imaging methods, detecting in vivo changes in water content, which are applicable to both humans and rats, and may delineate circuit changes.

From EEG signal to brain connectivity: insights from novel EEG, fMRI and morphometric MRI analysis methods.

Andreas Bernasconi, MD - Montreal Neurological Institute and Gillard W.O. Department of Neuroscience, Children's National Medical Center, Washington, DC, USA

Patterns of structural connectivity have been recently assessed using MRI based morphometric correlation analysis. These methods have provided independent evidence for altered connectivity in epilepsy (N. Bernasconi). Objective. This workshop will provide participants with: a) principles of recent electrophysiological and imaging methods to analyze networks; b) a comprehensive review of data on in vivo mapping of temporo-limbic and language networks; c) multidisciplinary discussion on the pathophysiology of networks remodeling, with emphasis on temporal lobe epilepsy; d) interactions between a broad audience of clinicians and researchers interested in neuroimaging and electrophysiology.

Meeting brain networks in epilepsy: insights from novel EEG, fMRI and morphometric MRI methods.

Raman Sankar, M.D., Ph.D. - Montreal Neurological Institute, Montreal, Canada, Madison M Berl, Department of Neuroscience, Children's National Medical Center, Washington, DC, USA

The relationship between prolonged febrile seizures (febrile status epilepticus) and temporal lobe epilepsy, remains unclear. Whereas some children develop epilepsy after and with cognitive deficits after febrile status epilepticus, in other cases it is not possible to predict these outcomes for an individual child. Magnetic Resonance Imaging (MRI), holds promise as a biomarker, because MRI changes have been found after febrile seizures in children and in animal models. However, the structural and functional and underlying neuronal mechanisms of brain development in the children with and without these communications, as well as various cognitive scores of children with both clinical and basic research. This workshop will bring together researchers on comorbidities, neuropsychological and basic science to integrate the comorbidity and multimodal imaging findings in children with cognitive and behavioral impairments evident in animal models of humans. To do this, Bruce Hermann will describe prospective volumetric and morphometric findings and cognition in children with more overt epilepsy with and without co-morbidities. Rochelle Caplan will discuss volumetric, morphometric, and fMRI data related to a broad range of psychopathology in children with epilepsy. Hal Blumenfeld will discuss recent fMRI, structural, and resting functional connectivity in childhood epilepsy, as well as MRI network abnormalities to direct surgical resections in animal models of childhood epilepsy. Raman Sankar will present innovative methodologies applicable to humans and animals for predicting both functional and structural reorganization in limbic circuits involved in epileptogenesis. Doctor Bilde will discuss novel imaging methods, detecting in vivo changes in water content, which are applicable to both humans and rats, and may delineate circuit changes.

Raman Sankar, M.D., Ph.D. - Montreal Neurological Institute, Montreal, Canada

Andreas Bernasconi, MD - Montreal Neurological Institute and Gillard W.O. Department of Neuroscience, Children's National Medical Center, Washington, DC, USA

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The direct measurement of electrical activity from the cortex and subcortical structures has helped define the concept of a seizure focus, helps locate the seizure onset area for epilepsy surgery, and to begin to assess the potential of using cortical stimulation for memory enhancement. However, it is important to understand the role of different brain structures in aspects of memory (encoding, recall, retrieval, consolidation, etc.) and also to examine its reliability and validity for surgical planning. This topic was last addressed in a workshop at AES in 2002, but considerable work has been done since that time. The workshop will also address the feasibility of non-invasive molecular imaging-methods to study multi-drug resistance in epilepsy. Recent developments in radiochemistry now allow to image P-glycoprotein function in-vivo. This workshop will examine the currently available techniques both to understand the role of different brain structures in aspects of memory (encoding, recall, retrieval, consolidation, etc.) and also to examine its reliability and validity for surgical planning. This topic was last addressed in a workshop at AES in 2002, but considerable work has been done since that time.
Pathways of brain development: Genetics and phenotypic characterization of malformations of cortical and subcortical development

Malformations of cortical development (MCD) present clinically with developmental disabilities and mental retardation. Epilepsy and behavioral and psychiatric disorders, MCD were previously believed to result from complex or multifactorial interactions, and to be related to various etiologic environments/factors during development. In the past decade, a number of single gene disorders, particularly involving neuronal migration, have been identified, and the genes have been mapped or cloned. These include lissencephaly, the Miller-Dieker syndrome, subcortical band heterotopia or double cortex syndrome, periventricular nodular heterotopy and schizencephaly. Many of these were found to be inherited as X-linked dominant traits with male lethality. This session will describe the clinical features and the genes and loci involved in the various forms of MCD as well as in isolated syndromic and non-syndromic malformations. Studies of the inter-relationship of the various genes involved in developmental pathways related to neuronal migration will also be presented.

Eva Andermann, M.D.
Inflammation and epilepsy: where do we stand and where do we go from here?

The workshop will focus on discussing the crucial role of inflammation in epileptogenesis. This mechanism is not limited to conventional antiepileptic drugs and may contribute to the high number of refractory epileptic patients. We will review evidence for inflammation in the pathogenesis of epilepsy, including immunological aspects of epileptogenesis and role of biomarkers; finally, we will discuss new approaches to novel therapeutic strategies to modulate inflammation in epilepsy.

1) To discuss the latest evidence for inflammatory mechanisms in epilepsy and the role of biomarkers in inflammatory mechanisms in epilepsy; 2) To evaluate future directions for trials of anti-inflammatory therapies in epilepsy.

Moderator: William H. Theodore, M.D. Speakers: Luca Bartolini, M.D., Kiminana Vezzani, Ph.D., Jacqueline A. French, M.D.

Luca Bartolini

Inflammation and epilepsy: where do we stand and where do we go from here?

2017

Michael Hildebrand

Somatic mutation: the ‘hidden genetics’ of brain malformations

Somatic mutation is a genetic mechanism increasingly being recognized as a causative factor in human disease. It has been recently proposed that there may be a sizeable ‘hidden genetics’ component of epilepsy due to somatic mutation (Thome and Berkhof 2014). In children with various forms of autism syndrome we will present evidence for the pathophysiology of epileptic syndromes, including immunological aspects of epileptogenesis and role of biomarkers; finally, we will discuss new approaches to novel therapeutic strategies to modulate inflammation in epilepsy.

1) To discuss the advances in clinical diagnosis of brain malformations; 2) To introduce alternative tissue sources for screening of somatic mutations; 3) To describe new molecular tools to detect ultra-low level somatic mutations.

Moderator: Michael Hildebrand, Ph.D. Speakers: Heather Mefford, M.D., Ph.D.; Antonio Parcero-Padri, M.D., Naomichi Matsukawa, M.D., Ph.D.

2017

Peyman Golshani

In-vivo imaging of network dynamics in epilepsy

New tools now enable high speed simultaneous imaging of activity in hundreds of neurons in behaving animals. We will highlight 5 speakers that show how calcium and voltage imaging of large ensembles can be used to follow the activity patterns of large populations of precisely identified neurons in mice of temporal lobe and generalised epilepsy. These approaches can be used to discover dysfunction in key cell types that may be driving initiation of seizures or network dysfunction during cognition in epilepsy.

1) To highlight new imaging approaches to understand changes in network dynamic during ictal and interictal periods in epilepsy.

Moderator: Peyman Golshani, M.D., Ph.D. Speakers: Stefan Smirnagis, M.D., Ph.D., Matthew Shriver, M.D., Ph.D., Ishan Mody, Ph.D.

2017

Christina Gross

MicroRNA-induced silencing in epilepsy: potential treatment target and biomarker

MicroRNA control the expression of many target proteins and therefore can influence cellular function by regulating entire protein networks. In recent years, microRNA expression and function have been shown to be altered following seizures and in epilepsy. Manipulation of single microRNA in rodent models of status epilepticus and epilepsy alters seizure susceptibility and severity, and can reduce neurodegeneration and neuroinflammation. This suggests microRNA-induced silencing as a novel therapeutic target in epilepsy that is mechanistically different from currently available antiepileptic drugs. This workshop will discuss recent advances in understanding the mechanisms of microRNA-induced silencing in epilepsy.

2017

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2017

Sarah Muldoon

Data-driven computational modeling of epileptic network structure

Many recent efforts in computational modeling of large-scale brain dynamics have begun to take a data-driven approach, incorporating structural and/or functional brain networks derived from patient data into the model. In this workshop, we will focus on approaches that use either structurally or functionally derived network connectivity as a basis of brain network structure in virtual models of epileptic brains. This workshop will include presentations by some of the leaders in this new direction of computational research (Vitorino Jinsa, Marcus Kaiser, and Ankri Khambhati), and promote discussion on how virtual experiments (experiments, real-time) can guide experimental epilepsy research.

2017

Bret Smith

Are animal models of post-traumatic epilepsy translational?

Traumatic brain injury (TBI) greatly increases the risk of medically intractable epilepsy. Several models of TBI have been developed to investigate the relationship between TBI and the development of post-traumatic epilepsy (PTE). Because the incident that precipitates development of epilepsy is known, studying mechanisms of post-traumatic epileptogenesis, identifying biomarkers to predict PTE, and developing treatments to prevent epilepsy after TBI are attainable goals. Understanding posttraumatic epileptogenesis may also inform investigations of other acquired epilepsy syndromes. Speakers will discuss the current state of animal models of PTE, the cellular similarities (and differences) with human epilepsy, as well as the relevance of findings from preclinical models to human disease.

1) To discuss the differences and similarities in the functional and pathological biology of human and rodent models of TBI; 2) To discuss the relevance of findings from preclinical models of TBI to human disease.

Moderator: Bret Smith, Ph.D. Speakers: Bret Smith, Ph.D., Asa Pitkanen, M.D., Ph.D., Robert Hurl, Ph.D.

2017

Joaqun Lugo

From inflammation to phagocytosis: how microglia shape vulnerable neuronal networks in epilepsy

Microglia are the innate immune cells of the brain and play a critical role in the emergence of seizures by multiple independent research groups. More interestingly, enhancing or preserving KCC2 function during seizures can positively impact seizure outcomes and therefore highlight the need to preserve KCC2 function during seizures.

1) To discuss the latest advances in clinical diagnosis of brain malformations; 2) To introduce alternative tissue sources for screening of somatic mutations; 3) To describe new molecular tools to detect ultra-low level somatic mutations.

Moderator: Joaquín Lugo, Ph.D. Speakers: Amy Breithner, Ph.D., Soosoyeong Kwon, M.D., Ph.D., Amanda Sierra, Ph.D.

2017

Chris Dulla

NMDA receptors in epilepsy: mutations, inhibitory circuits, and personalized medicine

NMDA receptors are critical for synaptic plasticity and memory, but also contribute to multiple sclerosis in the brain. First, human mutations in NMDA receptors have been linked to epilepsy-pathogenesis syndromes, infantile spasm, and other early onset epilepsies. Second, abnormal NMDA receptor expression and function contributes to circuit reorganization and epilepsy, the transition to the adult state, and seizure generalization. Last, disrupted glutamatergic signaling through NMDA receptors can induce excitotoxicity in the injury, interfere with synaptic pruning, and contribute to progressive cognitive decline.

2) To discuss the impact of microglia-mediated inflammatory and phagocytic mechanisms to the neuronal connectivity in the hippocampus in both human and experimental model systems.

Moderator: Heather Mefford, M.D., Ph.D. Speakers: Chris Dulla, Ph.D., Steve Traynelis, Ph.D., Gemma Carulli, Ph.D.

2017

Shripa Kadam

KCC2 hypofunction in epilepsy: developing novel therapeutic strategies to modulate KCC2-Co-transporter 2 (KCC2) function

The KCC2 chloride co-transporter is the chief Cl⁻ exporter in CNS neurons. KCC2 is known to be co-localized with GABAergic receptors but is also expressed at excitatory synapses. KCC2 plays significant roles in dendritic spine morphogenesis and glutamatergic synaptic function. KCC2 activity is both positively and negatively regulated by many pathways including phosphorylation of different sites on its protein structure. KCC2 hypofunction has now been shown to play a critical role in the emergence of seizures by multiple independent research groups. More interestingly, enhancing or preserving KCC2 function during seizures can positively impact seizure outcomes and therefore highlight the need to preserve KCC2 function during seizures.

1) To understand the role of neuronal potassium chloride co-transporter 2 in critically determining GABAA receptor function by generating an inwardly directed G-Cl gradient resulting in strong hyperpolarizing inhibition.

Moderator: Stephen Moss, Ph.D. Speakers: Shripa Kadam, Ph.D., Taxer Deel, Ph.D., Anatoly Buchin, Ph.D.

2017

Talle Z. Baram

Divergent and overlapping mechanisms contribute to epilepsy and its comorbidities

Epilepsy is defined by spontaneous seizures. Whereas the seizures have been the central focus of epilepsy research, they are commonly accompanied by cognitive and emotional problems including anxiety, depression, and other comorbidities. These co-morbidities are often seen in many types of epilepsy, and cognitive and emotional problems are especially prominent in temporal lobe epilepsy, involving the hippocampal–entorhinal circuit. Whereas the mechanisms underlying the impairments are manifold, recent work has begun to uncover mechanisms that uniquely contribute to cognitive/ emotional problems after a genetic or acquired insult.

(a) To enhance the audience’s awareness of the diverse aspects of epilepsy, including in addition to seizures—cognitive and emotional problems; to familiar the audience with the distinct temporal and regional domains and trajectories of these co-morbidities.

Moderators: Julia Kahn, Ph.D., Christophe Bernard, Ph.D.; Speakers: Talle Z. Baram, Ph.D., Christophe Bernard, Ph.D., Pierre-Pascal Leccia-Santini, Ph.D.

2017

LONG-Jun Wu

Glial mechanisms of epilepsy

Traditionally, studies on epilepsy have focused primarily on ‘somatic’ neuronal mechanisms that shape epileptiform activity. Recent emerging evidence indicates that glials cells including astrocytes and microglia play active roles in pathogenesis of epilepsy, but glial mechanisms of epilepsy have been less well appreciated. In this symposium, we will demonstrate that microglial specific F2YI2 mediates microglial-neuron interactions during kainic acid induced seizure using 2-photon imaging. Its results reveal the molecular mechanism and functional significance of microglial-neuron interaction in epilepsy. Binder will outline changes in astrocyte water channels (aquaporins) and

1. To explore the pathophysiology of glial cells in epilepsy. 2. To discuss glial cells as potential therapeutic targets for the treatment of epilepsy.

Moderators: LONG-Jun Wu, Ph.D. Speakers: Ukpong Eyo, Ph.D., Devin Binder, Ph.D., Karen Wilcox, Ph.D.
Neurogenesis in the adult brain is established in all mammals including humans, where it has been suggested to change dramatically either after seizures and play a role in epilepsy. However, the exact role of neurogenesis in the pathogenesis of seizures and epilepsy is not yet clear. This workshop will allow three individuals who have contributed to this research to present their views, some of which are paradoxical and therefore can stimulate discussion. In addition, the speakers will address the potential effects of adult neurogenesis on behavioral "comorbidities" found in animal models of epilepsy. We suggest Dr. Dan Xu, Dr. Sookyong Lim and Dr. Jana Veliskova as speakers because they are central to the field of adult neurogenesis in epilepsy.

To clarify the effects of adult-born neurons in animal models of seizures and epilepsy:

Moderator: Jenny Hsieh, Ph.D.  
Speakers: Helen Scharfman, Ph.D., Kyung-Ock Cho, M.D., Ph.D., Steve Danzer, Ph.D.

In many genetic and acquired syndromes of epilepsy, neurogenesis has shown to be altered in varying degrees for unknown reasons. Therefore, developing accurate and powerful biological models for epilepsy has been a challenge. In this symposium, three speakers will provide a new perspective. This workshop will bring together one speaker who is a neurosurgeon and one junior investigator (male and female) using stem cell technology in various settings to understand and treat epilepsy. Jack Parent will talk about the use of human induced pluripotent stem cells to model patient epilepsies. Jenny Hsieh will expand on this theme and talk about the use of stem cell technology to model human brain.

To discuss emerging platforms utilizing stem cell technology to model and treat patients with epilepsy:

Moderator: Helen Scharfman, Ph.D.  
Speakers: Jenny Hsieh, Ph.D., Jack Parent, M.D., Robert Hunt, Ph.D.
This workshop will examine the role that slow metabolic changes have in driving seizure activity. Our interest in this question comes from two clinical and experimental facts: 1) the role of sleep in generating seizures is well documented; 2) slow metabolic changes are known to be important in driving intracellular processes in brain. The research community is now beginning to recognize the importance of slow metabolic changes in driving seizure activity. The aim of this session is to bring together experts from clinical and experimental fields to discuss the role of slow metabolic changes in driving seizure activity. The central objectives are to: 1) Highlight emerging information about epileptogenesis, focusing on unpublished data (2) introduce concepts from other fields, e.g., neuroscience, biochemistry, epigenetics, to inform our approaches to understanding the epileptogenic process. The session will be chaired by Omar Ahmed, a young investigator who has worked extensively on inhibitory synapse biology and who has developed novel techniques for imaging and recording brain activity down to the cellular level.
Across the neurological disorders, genetic studies of the epilepsies have been among the most successful in the genetic causation of the disease. However, despite the success, genetic risk factors for the common syndromes encountered in clinical practice still remain largely unexplained. Here, we focus on the generalizations of the epilepsies and the collective efforts from three international teams that are leveraging the most recent technological and methodological developments to better interpret the genome of patients with epilepsy. We propose to use this platform to share our most recent data emerging across three international consortia, and to discuss experiences in translational research.

Mitochondrial abnormalities in cortical malformations

Recent results, combining animal research with human microelectrode recordings, have shown that it is helpful to consider focal cortical seizures in terms of two spatially distinct regions: a seizure core, displaying the well-established, synchronous epileptiform discharges and seizures in patients with intractable temporal lobe epilepsy, without affecting the rest of the brain. Understanding Infantile Spasms: A Pathogenic Perspective

The KCNQ2-associated epilepsy and encephalopathy spectrum - bedside to bench and back

The study of epilepsy has been used for decades targeting various intracranial and extracranial approaches that have been created in response to a need to unravel the molecular mechanisms underlying epilepsy. Electrical stimulation for treatment of epilepsy has been used for decades targeting various intracranial and extracranial structures. Deep brain stimulation of numerous brain structures using high frequencies has achieved limited success, but low frequency stimulation (LFS) continues to be under-investigated. In the past two years, extensive animal models of epilepsy have been published that illustrate the anti-epileptic action of LFS, and started to unveil its mechanism of action. In addition, some human data have found that low frequency stimulation of a white matter tract reduced interictal electroencephalogram (EEG) discharges and high frequency oscillations, thus putting the core and para epilepticus into a practical context. We will discuss how this understanding has led to new therapeutic approaches and the implications.

Therapeutical research in epilepsy faces three challenges: 1) controlling seizures when epilepsy has appeared, 2) reversing the causative factors and 3. Identify novel therapeutic strategies for epilepsy. 1. To introduce the unique opportunities created through large-scale collaborations among three national and international consortia with complementary approaches to epilepsy gene discovery. 2. To review the development and application of novel analytical approaches that have been created in response to a need to unravel the genetics of rare epilepsies and the common genetic mechanisms.

Therapeutic research in epilepsy faces three challenges: 1) controlling seizures when epilepsy has appeared. 2) reversing the causative factors and 3) identifying novel therapeutic strategies for epilepsy. 1) To introduce the unique opportunities created through large-scale collaborations among three national and international consortia with complementary approaches to epilepsy gene discovery. 2) To review the development and application of novel analytical approaches that have been created in response to a need to unravel the genetics of rare epilepsies and the common genetic mechanisms.
2012 Michael Wong
Dendritic injury in epilepsy: mechanisms and consequences.
A variety of structural abnormalities in dendrites have been documented in pathological brain specimens from epileptic patients and animal models of epilepsy, such as dendritic budding, loss of spines, and other morphological changes in dendritic size and shape. However, the underlying mechanisms and functional consequences of these dendritic abnormalities are poorly understood. Seizures may directly cause dendritic injury. In turn, dendritic abnormalities may contribute to progressive epileptogenesis and cognitive deficits in epilepsy patients. The objective of this IW is to explore the characteristics, mechanistic basis, and functional consequences of seizure-induced dendritic injury. First, we will discuss the mechanisms underpinning dendritic injury and dendritic plasticity in epilepsy. Second, we will review the functional consequences of dendritic injury on neuronal properties and behavior. Finally, we will consider the potential contribution of dendrites to ongoing seizures and the development of novel therapeutic strategies to ameliorate dendritic injury.

2013 Aristea Galanopoulou, Karen Wilcox
Translating seizure terminology, modeling, and detection from rodents to humans is it possible?
There is an ongoing push for advances in translational research to improve outcomes for those with epilepsy. To achieve this goal, there is a need to translate preclinical discoveries into clinically meaningful findings and therapies. One of the areas that plays a fundamental role in interpreting preclinical research is the definition of seizure and the translatability of seizure and epilepsy models into the human seizure types and epilepsy syndromes. Currently these definitions and the purpose of the existing animal models vary significantly among research papers. The generation of more uniform and more widely acceptable definitions for seizures and the re-evaluation of existing animal seizure models are the active research.

2012 Alica Goldman
Predictive Genes, Basic Mechanisms, and Clinical Biomarkers of SUDEP
The translational workshop will explore, from the bench to the bedside, and from the EAU bedside back to the stem cell laboratory, ways to measure genetic, cellular, and clinical parameters in epilepsy patients that may predict the risk of SUDEP. The speakers will raise issues to identify the gaps in our understanding. Where are the therapeutic opportunities to predict and prevent SUDEP? What is the evidence that it is fundamentally a deficiency of a post-stress respiratory drive arising in the brainstem? An inherited cardiac arrhythmia? A failure of autonomic activation? An idiosyncratic antiepileptic drug withdrawal reaction? And most important, can a subspeciality deficiency be identified in the SUDEP syndrome as a whole?

2012 Scott Baraban & Ed Dudek
Swimming toward a new path for drug discovery in epilepsy: an open discussion of novel approaches using zebrafish, mice and induced pluripotent stem cells.
Forms of epilepsy. Thirty years of traditional acute secure models in rodents have generated more than a dozen new AED's that have clearly helped a population of patients with epilepsy. Further modification and merits of this approach continue to be actively debated. However, 30-40% of patients remain pharmacoresistant, and this has not improved. This workshop seeks to bring together groups working to refine this traditional approach, with those considering novel models. Through multidisciplinary strategies focused on antiepileptogenesis and newly emerging high-throughput programs, this session will focus on drugs that regulate key ion channels, and their potential relevance to epilepsy and epileptogenic process. 1. Yoav Noman, PhD (Dec 2011), Lori Isom, PhD, Dave Chetkovich, MD, PhD 2. Pete Engel, Asla Pitkanen Laura Jansen Gilles Huberfeld, Joeff Loeb 3) Jeff Noebels, Jack Parent (speakers)

2012 Tallie Z. Baram, MD, PhD
It takes two to tango: Dance of neuronal ion channels and their auxiliary subunits.
Changes in the abundance, subcellular localization and surface expression of ion channels contribute to altered excitability in the epileptic brain. In recent years novel and exciting data have been emerging regarding the involvement of channel-interacting (auxiliary) proteins in these processes. The goal of this session is to discuss new developments in our understanding of the molecular complexes that control ion channel trafficking and function. The session will focus on proteins that regulate several key ion channels, and their potential relevance to epilepsy and epileptogenesis. 1) Pete Engel, Ed Cooper (speakers)

2012 Scott Baraban
What’s Next? A Young Investigator Workshop
Each year the American Epilepsy Society and Epilepsy Foundation of America award pre-, postdoctoral and young investigator awards grants to an array of innovative, timely and cutting-edge research projects. Historically, many of these funded projects result in top-tier publications and several of these awardees have moved on to successful careers in epilepsy research. To highlight this research and provide a glimpse into what may be next, this workshop brings together four recent awardees. Scott C. Baraban (UCSF) will introduce and moderate the session. Together these talks should stimulate discussion on emerging topics and techniques in epilepsy research while providing a forum for new ideas and directions.

2012 Christophe Bernard
What does it mean to be interictal spikes - do we have a predictive value?
Interictal spikes are a diagnostic hallmark of some epilepsies. Although the regions generating interictal spikes may not necessarily correspond to the epileptogenic region, they may carry untapped, clinically relevant information. This is the concept that we will develop in this translational workshop, which includes clinician-researchers and basic scientists. Maximo Axelos will present and develop the notion of green and red interictal spikes in order to provide a conceptual framework, and discuss the possibility that some spikes may present the occurrence of seizures, whilst others precipitate them. But interictal spikes are not only linked to citizogenesis, they may also play a role in epileptogenesis.

2012 Sam Berkovic
Massively Parallel Sequencing in Epilepsy
Massively Parallel Sequencing (Next Generation Sequencing) is a very new technology that allows whole exomes (entire coding sequence) and even whole genomes to be efficiently sequenced. In 2011, two large genome projects in epilepsy were launched - an NHG funded Centre without Walls project called “Epi4K” aimed at sequencing 4,000 epilepsy patients in 5 years and a European project with sequencing largely at the Sanger Centre called “EUROGEN” (Europe) and 10 centres have agreed to work collaboratively. This Investigators Workshop Proposal is from both groups. Lead projects from both groups involve early childhood epilepsies and this is the proposed focus of the Workshop. The objective of this workshop is to stimulate discussion and collaboration in this field.

2012 Anne Anderson
Dysfunctional phosphorylation signaling in epilepsy
Title Dysfunctional phosphorylation signaling in epilepsy Abstract Post-translational modification of proteins by phosphorylation is a ubiquitous cellular signaling mechanism. There is increasing evidence that altered phosphorylation is involved in the pathogenesis of many neurological disorders, including epilepsy. This is the concept that we will develop in this translational workshop, which includes clinician-researchers and basic scientists.

2012 Raúl D’Ambrosio
Neocortical Focal Seizures in Etiologically Realistic Models of Acquired Epilepsy
Several models of acquired epilepsy based on realistic etiologies have been introduced in the last decade. These include, but are not limited to, epilepsy induced by head injury, stroke, fabric status, perinatal hypoxia, encephalitis, etc. A consistent finding in these models is that the overall pathology induced by the insult differs in many ways from that commonly induced by agents such as pilocarpine or kainate in classic status epilepticus-based models of epilepsy. Consistent with the different pathology, the ensuing epilepsy syndromes are also different, including seizures that do not originate from the hippocampus but from the neocortex. Most basic scientists are more familiar with 1) John W. Miller, M.D., Ph.D., Director Regional Epilepsy Center, UW; 2) TBA 2) Pete Engel, Alia Pillmam 3) Laura Jensen, Gilles Huberfeld; Joff Leeb

2012 Aristea Galanopoulou
Validation of epilepsy biomarkers in human: goals, successes, challenges
The development of valid clinically relevant biomarkers for epilepsy is an essential need in the development, validation and implementation of new therapies for epilepsy. This translational IW proposal aims to highlight examples of studies conducted in human tissue with the task of addressing feasibility, translatability from preclinical data, and also discuss the challenges (ie database issues, historical and tissue heterogeneity, age-related issues etc). The proposed talks are: 1) Laura Jensen: Developmental changes in GABAA receptor expression and function in pediatric epilepsies 2) Gilles Huberfeld: Reversal of GABAA receptor function in temporal lobe epilepsy 3) Joff Leeb: Utilization of human
Recent data has suggested that one of the regulators of synaptic plasticity is the extracellular matrix. It appears to stabilize neurite outgrowth and synaptic plasticity. Following head injury, stroke and status epilepticus there is a break down in the extracellular matrix due to upregulation of proteases. Recent work in transgenic mice has suggested that the destruction of the extracellular matrix contributes to epileptogenesis.

Changes in pH play a strong modulatory effect on neuronal signaling under normal and pathological conditions, whereby alkalosis enhances and acidosis reduces brain excitability. Conclusive seizures have long been known to produce a profound acidosis, acidosis both due to reduced ventilation and build-up of lactic acid. This evidence is not a mere bystander but contributes to the termination of seizures. Similarly, respiratory alkalosis produced by hyperventilation has been a standard way to provoke absence seizures for many decades. Identifying the pH-dependent mechanisms operating in various compartments and levels of organization does not only shed light on the process of epileptogenesis.

There has been increased interest among clinical epileptologists in epilepsy comorbidities, such as migraine, cognitive impairment, depression and autism spectrum disorder. These comorbidities can dramatically impact the quality of life of people with epilepsy. Until recently, the basis for these comorbidities was obscure and the lack of scientific knowledge raised doubt as to whether the disorders are truly related to epilepsy and not chance associations. Studies in animal models have begun to provide insight into the neurobiological mechanisms underlying the neurological and psychiatric conditions that commonly occur in patients with epilepsy. For example, it is now recognized that recurrent

Chronic epileptic foci produce high frequency oscillations (HFOs; >100 Hz). Activity faster than 200-300 Hz, known as fast ripples, appears specific for epileptogenic tissue and can be useful in presurgical evaluation for epilepsy surgery. More fundamentally, the mechanisms responsible for this pathological HFO may provide clues on the structural and functional changes that make the neuronal networks epileptogenic. Fast ripples are an emergent property of the activity of populations of neurons, each firing much more slowly than their collective activity. Several theories have been proposed for the mechanism of this process, including entrainment of pyramidal cells by fast spiking inhibitory

The importance of subcortical structures in epilepsy

Clonal studies have shown that individuals with epilepsy, over time, often have increasing morbidity and seizure manifestations, with little known as to the reasons why. This can result in forms of epilepsy which are often resistant to treatment. It has been shown that the progression of epileptiform discharges into new networks in the brain (i.e., subcortical and brainstem structures) may contribute or mediate this fluctuation. In other words, recruitment of new brain regions into the epileptic network may result in seizures with increasing complexity and severity that are resistant to treatment. Interestingly, recent studies utilizing INOValued EXPERT imaging have revealed the importance of

Epigenetic mechanisms are covalent posttranslational modifications of histone proteins and DNA, which can produce lasting alterations in chromatin structure and gene expression. They are increasingly recognized as fundamental regulatory processes in central nervous system development, synaptic plasticity, and, also play a role in neurological disorders, such as schizophrenia or spinal muscular atrophy.

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The "methyltransferase" hypothesis: does epigenetic chromatine modification play a role in epileptogenesis?

Many brain lesions provide epilepsies, although onset and progression of seizures as well as response to antiepileptic drugs (AED) treatment remain difficult to predict in each patient. Recent studies point to a pathologic role of epigenetic chromatine modifications during epileptogenesis. Epigenetic mechanisms cause post-translational modifications of histone proteins and DNA, which can produce lasting alterations in chromatin structure and gene expression. They are increasingly recognized as fundamental regulatory processes in central nervous system development, synaptic plasticity, and memory, and also play a role in neurological disorders, such as schizophrenia or spinal muscular atrophy.

The mechanisms of chronic high frequency activity in epileptic foci

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Neuronal death and pediatric epilepsy: Are effect of early life seizure? A cause or not-of later epilepsy?

A long-standing hypothesis from several studies on animal models of pediatric epilepsy is that early-life seizures generally do not lead to neuronal death, and even in cases where they do, neuronal death is not necessary for the subsequent development of acquired epilepsy. Two diametrically opposed hypotheses have been proposed, and supported by different lines of evidence: (1) Neuronal death after a brain insult early in development is not required for the subsequent development of acquired epilepsy, or (2) Neuronal death, regardless of the stage of development, is essential for acquired epilepsy. The investigations' Workshop will essentially debate present data in search of a consensus! The discussions on this workshop will feature present data in search of a consensus! The discussions on this workshop will feature present data in search of a consensus! The discussions on this workshop will feature present data in search of a consensus!

What's Next? A Young Investigator Workshop

Although ISNPs, Poster Sessions and other special events such as the EF Fellows Reception offer young investigators an opportunity to participate in the annual meeting, there are no real opportunities to highlight the exciting research they are working on. Each year EF awards between more than two dozen pre-and postdoctoral fellow awards to the excellent and often cutting-edge group of research projects. This workshop will choose three of these projects for participation in a "young investigator workshop." It is proposed that the investigators/researchers chosen for this workshop will be selected by the current Chairs of the scientific review committee (Anderson and Kaila).

Seizure localization: A clinical challenge to basic scientists

Abstract The major goal of the proposed session is to promote interactions between basic and clinical epileptologists within the Society. The format of the proposed session is based on an approach published by Bob Fisher (2009). The session will focus on seizure localization. The specific aims of the session are the following. (1) Expose scientists to what epilepsy actually looks like in real life and what tools are used to treat it. (2) Show clinicians what techniques and models are used in research and what they could offer. (3) Present a clinical case (seizure localization) to provoke discussion among clinicians and basic scientists. Speakers Bob Fisher will serve as moderator and begin the session with a presentation on "What epilepsy actually looks like in real life." Following the presentation, clinicians and basic scientists will work together in small groups to analyze data and develop a diagnosis. The groups will present their conclusions to the audience at the end of the session.

Studying High Frequency Oscillations, Microseizures and Human Microwire Recordings Using the International Epilepsy Electrophysiology Database (IED) and Cloud Computing

Recent evidence suggests that high frequency oscillations, microseizures and human single cell recordings are all important for seizure generation and epileptogenesis. Most investigators do not have access to high bandwidth human computational resources required to analyze these. There are many unanswered questions regarding the significance of high bandwidth EEG in epilepsy that cannot be addressed by qualitative studies of small data sets using visual analysis. The IED is funded by the NIH and European Union to help to make multi-scale human and animal intracranial EEG data available to the world research community. This workshop will give participants hands-on experience using the IED and cloud computing resources.
Molecular, Cellular and Network Aspects of Epilepsy and Depression: The Two Faces of Neurobiological Mechanisms in Genetic Focal Epileptogenesis

Lisa R. Merlin, MD

2010 David Prince

2010 Verena C Wimmer

2010 Christophe Bernard

Epigenetic mechanisms of epileptogenesis

The focus of the workshop is recent translational research on adenosine, a powerful anticonvulsant neuromodulator in hippocampal and cortex. Adenosine has long offered much promise for epilepsy, and new insights into the ongoing metabolic and astroglial regulation of adenosine, as well as advances in adenosine receptors and polymers, are bringing significant new promise to adenosine-based therapies. Adenosine is effective in halting all types of seizures, including pharmacoresistant seizures, and is well known to promote sleep and protect neurons from injury. Thus, the implication of emerging research on adenosine, offers new hope for epilepsy and related co-morbidities. Tom Swanson will provide an overview of the evidence for adenosine as a treatment for seizures and its promise for the future.

Tom Swanson, University of Montana, Philips Hayden, Tufts University, Susan Manning, Trinity College

Anitol Bragan

Epileptic syndromes: the Case of LGI1

For centuries canals has been used to treat epilepsy. Several recent studies seem to confirm the anticonvulsant role of the cannabis system which could allow the development of novel therapeutic agents, with one already on the market. The focus of the present workshop will be to outline the general physiological properties of the endocannabinoid system and the distribution and role of the receptors (Grant). The two other groups have already performed several convincing studies on the role of this system as an endogenous modulator of the activity of neural circuits. This data is not much known to epileptologists and should be of great interest to epilepsy community.

Stuart Perlman, Ph.D., Vincent Ducos, PhD, M. Schmaus, MD, South California, University of California, Los Angeles, and UC San Diego, San Diego, CA, USA

David Prince

Control of synapse formation and epileptogenesis

Cannabis and endocannabinoid receptor play many role in vivo but may also induce addiction. The review of their properties should be of interest to the epilepsy community mainly because one of these drugs is the most used drug in the world. I chose the group from La Jolla for the general presentation since they wrote a nice and comprehensive review on this subject. The focus of the present workshop will be to outline the general physiological properties of the endocannabinoid system and the distribution and role of the receptors (Grant). The two other groups have already performed several convincing studies on the role of this system as an endogenous modulator of the activity of neural circuits. This data is not much known to epileptologists and should be of great interest to the epilepsy community.

Ben Barres, Z.David Luo, David Prince

Andre Lagrange

Epilepsy and Depression: The Two Faces of BDNF/Trk Dependent Neurogenesis

Depression is an extremely common comorbid illness in patients with epilepsy. While there are usually several presentations about epilepsy and neurogenesis, I think many of us are less familiar with the idea that neurogenesis plays a role in depression. By hosting a workshop describing the scientific endeavors of both epileptologists and psychiatrists, I thought we might help increase the dialog between our highly interdependent fields.

Louise Oostenbrink-Walisch (University of Alabama) - Epilepsy and Neurogenesis, Shelley Russell - BDNF Dependent Changes in Neurontransmission, Francis Oke (Cornell) - Animal Models of Neurogenesis in Mood Disorders,
Neural progenitor or "stem" cells are receiving increasing attention in society and in biological research. Several areas are especially exciting and bring enormous impact to epilepsy research. First, studies of cell transplantation as an antiepileptic therapy are gaining increasing attention. Second, investigations into how neural stem cells are disrupted in temporal lobe epilepsy are generating exciting new data. Third, the idea of using induced pluripotent stem cells to generate neurons from epilepsy patients offers an unprecedented opportunity to study mechanisms of epilepsy and to develop new therapies using high-throughput drug screens. Here we propose an AF workshop focusing on these topics. The workshop program is designed to include state of the art presentations by invited speakers, followed by a seminar session where participants may present their own work. An aim of this workshop is to provide a forum for synthesizing recent data, to present the combined effect on neuronal and molecular foundation of the ion channel redistribution, and attempt to integrate their combined effect on neuronal and synaptic plasticity. Activity-dependent trafficking and of dendritic expression of I-A (Kv4.2) and Ih (HCN channels) have been described recently, and may contribute to circuit hyperexcitability. Here we aim to synthesize these recent data, provide the cellular basis of hyperexcitability and synchronization in the affected tissue. Epilepsy is often accompanied by massive neuronal activity and fast EEG activity that precedes synchronous, rhythmic discharges typically associated with epilepsy. Pre-synaptic regulation of receptor trafficking and ligand-gated ion channels post-translational modifications induced by neuroinflammation that may underlie neuronal network hyperexcitability and excitotoxicity occurring in epilepsy. This workshop will discuss these novel findings and their relevance for normal brain physiology and epileptogenesis as well as for developing novel therapeutic antiepileptic strategies.

Feline seizures are a consistent feature of many feline epilepsy syndromes. Yet, despite knowledge of the underlying genetic lesion and years of basic research there are still many open questions regarding the mechanisms underlying their genesis. Recently, several studies have begun to shed light on potential mechanisms, ranging from cytokines to respiratory alkalosis. In addition there has been active debate as to relative merits of the various models for generating "feline" seizures in rodents, from hot pets, hair dye to infra red light heaters. This workshop will bring together key workers in this field to discuss mechanisms of epileptogenesis in the various models and their relationship to feline epilepsy. Neuroinflammation that may underlie neuronal network hyperexcitability and excitotoxicity occurring in epilepsy. This workshop will discuss these novel findings and their relevance for normal brain physiology and epileptogenesis as well as for developing novel therapeutic antiepileptic strategies.

Do neonatal seizures per se cause brain damage? New insights from mutations of potassium channels Experimental data provide strong evidence that seizures early in life produce long-lasting alterations with cognitive impairment and increased risk of developing epilepsy. However, clinical studies suggest that long-term outcome correlates best with etiology rather than with the presence of seizures or their duration. Concerns persist whether seizures per se are injurious to the immature brain. Bengali Familial Neonatal Seizures (BNS) is a genetically determined seizure disorder in which affected newborns experience partial or generalized seizures occurring many times daily. Mutations in seven-specific KCNQ2 and KCNH2 potassium channels have been found associated with sudden unexpected death in epilepsy (SUDEP) is a markedly underestimated catastrophe bedeviling people with epilepsy and their care-givers. The unpredictability of these events and pathophysiological hypotheses are the subject of this workshop. The proposal is to review briefly the astounding epidemiology of this condition which is unfortunately not uncommon, particularly in chronic epilepsy (SUW Sander). Then a discussion of the relevance of the neuroanatomy of SUDEP and how this relates to the unsurpassable seizures in general and to SUDEP in particular will be presented (S. Kallio). The dominant hypothesis of seizure-related central pacemaker and cardio atrial arrhythmias, and we are convinced that an improved understanding of the role of potassium channels in epilepsy offers a basis for potential developing novel strategies to treat epilepsy. T. Tomson; Eli So

Curing the disease by replacing the defective gene: is it so straightforward? Gene therapy is viewed as a promising tool for the treatment of epilepsy, particularly given the increasing identification of human genetic mutations associated with the disease. An overriding notion is that having identified a gene defect that cause epilepsy, rescue of genotype by replacement of the defective gene should rescue the phenotype, and therefore, cure the disease. Optimists has been raised by studies that have successfully demonstrated inhibition of seizures after oral delivery of genes with subsequent expression of seizure-inhibiting product. However, such success has been achieved using gene expression in animal models of epilepsy that are not linked to a deficit in the gene being targeted. This workshop is designed to bring together past accomplishments and provide a forum to discuss and better understand the broad range of approaches to the treatment of epilepsy and to discuss the potential applications for gene replacement therapy for pharmacoresistant epilepsy. The proposal is to focus on studies in animal models of late-onset epilepsy. A key issue is what gene? The earliest animal models have used GAD65 as a therapeutic target but the question remains whether GABAergic neurons are a major component of the epileptogenic network in late-onset epilepsy. The proposal is that this workshop will focus on the potential of CAMKII as a candidate gene and potential routes for delivery. In addition, there is a growing interest in the role of astrocytes in epilepsy and the proposal is to discuss the potential role of astrocytes in epilepsy. This is a workshop in which we are aiming to bring together those interested in the therapeutic potential of astrocytes in epilepsy, but we are also interested in the potential of astrocytes in the repair of damaged brain. The proposal is to discuss the potential of astrocytes in the repair of damaged brain.

Stereo imaging of epilepsy - hemodynamic and light scattering changes in the brain Optical imaging of the brain has shown that focal changes in perfusion, oxygenation and light scatter accompany epileptiform events. In some circumstances these effects precede the onset of seizure activity. Whether optical imaging will be clinically useful in supplement or even replace electrical recordings remains uncertain. Nevertheless, optical imaging has provided insights into neurovascular coupling mechanisms and changes in the extracellular environment associated with epilepsy. This panel will bring experts in the field together to discuss their recent findings and examine the future of this technology.

The impact of neuroinflammation on neuronal excitability and excitotoxicity Emergent evidence highlights a physiological interplay between inflammatory mediators and classical neurotransmitters (i.e. GABA and Glutamate) in CNS. These interactions involve non-conventional mechanisms of receptor trafficking and ligand gated ion channels post-translational modifications induced by neuroinflammation that may underlie neuronal network hyperexcitability and excitotoxicity occurring in epilepsy. This workshop will discuss these novel findings and their relevance for normal brain physiology and epileptogenesis as well as for developing novel therapeutic antiepileptic strategies.

Rodent models of febrile seizures.

Neural progenitor or "stem" cells are receiving increasing attention in society and in biological research. Several areas are especially exciting and bring enormous impact to epilepsy research. First, studies of cell transplantation as an antiepileptic therapy are gaining increasing attention. Second, investigations into how neural stem cells are disrupted in temporal lobe epilepsy are generating exciting new data. Third, the idea of using induced pluripotent stem cells to generate neurons from epilepsy patients offers an unprecedented opportunity to study mechanisms of epilepsy mutations and to develop new therapies using high-throughput drug screens. Here we propose an AF workshop focusing on these topics. The workshop program is designed to include state of the art presentations by invited speakers, followed by a seminar session where participants may present their own work. An aim of this workshop is to provide a forum for synthesizing recent data, to present the combined effect on neuronal and molecular foundation of the ion channel redistribution, and attempt to integrate their combined effect on neuronal and synaptic plasticity. Activity-dependent trafficking and of dendritic expression of I-A (Kv4.2) and Ih (HCN channels) have been described recently, and may contribute to circuit hyperexcitability. Here we aim to synthesize these recent data, provide the cellular basis of hyperexcitability and synchronization in the affected tissue. Epilepsy is often accompanied by massive neuronal activity and fast EEG activity that precedes synchronous, rhythmic discharges typically associated with epilepsy. Pre-synaptic regulation of receptor trafficking and ligand-gated ion channels post-translational modifications induced by neuroinflammation that may underlie neuronal network hyperexcitability and excitotoxicity occurring in epilepsy. This workshop will discuss these novel findings and their relevance for normal brain physiology and epileptogenesis as well as for developing novel therapeutic antiepileptic strategies.

Neuronal-glial signaling and epilepsy

Current antiepileptic drugs and complementary therapies are not sufficient to control seizures in about a third of epileptic patients. Thus, there is an urgent need for treatments that prevent the development of epilepsy and control it better in patients already afflicted with the disease. A prerequisite to reach this goal is a deeper understanding of the cellular basis of hyperexcitability and synchronization in the affected tissue. Epilepsy is often accompanied by massive neuronal activity and fast EEG activity that precedes synchronous, rhythmic discharges typically associated with epilepsy. Pre-synaptic regulation of receptor trafficking and ligand-gated ion channels post-translational modifications induced by neuroinflammation that may underlie neuronal network hyperexcitability and excitotoxicity occurring in epilepsy. This workshop will discuss these novel findings and their relevance for normal brain physiology and epileptogenesis as well as for developing novel therapeutic antiepileptic strategies.

The modulation of activity dependent trafficking of presynaptic neurotransmitter receptors and the involvement of glial cells in epileptogenesis offers the possibility to develop new antiepileptic strategies. Changes in the extracellular environment associated with epilepsy have revealed a role for rapamycin, the inhibitor of mTOR pathway, as a potential therapy in this condition. Experimental data provide strong evidence that seizures early in life produce long-lasting alterations with cognitive impairment and increased risk of developing epilepsy. However, clinical studies suggest that long-term outcome correlates best with etiology rather than with the presence of seizures or their duration. Concerns persist whether seizures per se are injurious to the immature brain. Bengali Familial Neonatal Seizures (BNS) is a genetically determined seizure disorder in which affected newborns experience partial or generalized seizures occurring many times daily. Mutations in four specific KCNQ2 and KCNH2 potassium channels have been found associated with sudden unexpected death in epilepsy (SUDEP) is a markedly underestimated catastrophe bedeviling people with epilepsy and their care-givers. The unpredictability of these events and pathophysiological hypotheses are the subject of this workshop. The proposal is to review briefly the astounding epidemiology of this condition which is unfortunately not uncommon, particularly in chronic epilepsy (SUW Sander). Then a discussion of the relevance of the neuroanatomy of SUDEP and how this relates to the unsurpassable seizures in general and to SUDEP in particular will be presented (S. Kallio). The dominant hypothesis of seizure-related central pacemaker and cardio atrial arrhythmias, and we are convinced that an improved understanding of the role of potassium channels in epilepsy offers a basis for potential developing novel strategies to treat epilepsy. T. Tomson; Eli So

Neuropathological changes in the hippocampus of patients with epilepsy and their seizures have revealed a role for rapamycin, the inhibitor of mTOR pathway, as a potential therapy in this condition. Experimental data provide strong evidence that seizures early in life produce long-lasting alterations with cognitive impairment and increased risk of developing epilepsy. However, clinical studies suggest that long-term outcome correlates best with etiology rather than with the presence of seizures or their duration. Concerns persist whether seizures per se are injurious to the immature brain. Bengali Familial Neonatal Seizures (BNS) is a genetically determined seizure disorder in which affected newborns experience partial or generalized seizures occurring many times daily. Mutations in four specific KCNQ2 and KCNH2 potassium channels have been found associated with sudden unexpected death in epilepsy (SUDEP) is a markedly underestimated catastrophe bedeviling people with epilepsy and their care-givers. The unpredictability of these events and pathophysiological hypotheses are the subject of this workshop. The proposal is to review briefly the astounding epidemiology of this condition which is unfortunately not uncommon, particularly in chronic epilepsy (SUW Sander). Then a discussion of the relevance of the neuroanatomy of SUDEP and how this relates to the unsurpassable seizures in general and to SUDEP in particular will be presented (S. Kallio). The dominant hypothesis of seizure-related central pacemaker and cardio atrial arrhythmias, and we are convinced that an improved understanding of the role of potassium channels in epilepsy offers a basis for potential developing novel strategies to treat epilepsy. T. Tomson; Eli So

The identification of the mechanisms that control the initiation of a seizure is crucial to understand ictogenesis and, ultimately, to develop new strategies to cure epilepsy. Focal seizure onset correlates with the occurrence of small amplitude fast EEG activity that precedes synchronous, rhythmic discharges typically associated with epilepsy. Pre-synaptic regulation of receptor trafficking and ligand-gated ion channels post-translational modifications induced by neuroinflammation that may underlie neuronal network hyperexcitability and excitotoxicity occurring in epilepsy. This workshop will discuss these novel findings and their relevance for normal brain physiology and epileptogenesis as well as for developing novel therapeutic antiepileptic strategies.
The catastrophic epilepsies of childhood are among the most devastating and least understood neurologic disorders. Recently, however, several laboratories have generated animal models that may begin to allow investigations of the underlying seizure mechanisms. After a brief overview of the childhood catastrophic epilepsies by Dr. Stafstrom, Dr. Galenopoulos will discuss a model of symptomatic infantile spasm (IS) created by a combination of postnatal desynchrony and lipopolysaccharide to produce structural damage followed by PCNA to reduce seizure levels. Dr. Lee will then present on a new model in which spontaneous spams and hyperthermia are produced by chronic TTX treatment. Although neuronal damage is associated with status epilepticus, traumatic brain injury and several epilepsy syndromes, neuroprotective strategies remain controversial. Recent evidence showing neuroprotective effects of several anticonvulsants has led to a renewed interest in neuroprotection in epilepsy. Several anticonvulsants have shown to exert neuroprotective mechanisms that include modulation of calcium homeostasis, histone deacetylases, mitochondrial function, antioxidant functions, iron chelation, and increased conduction through potassium channels. In addition, the development of neuroprotective assays with higher throughput may lead to a greater rate of discovery of new effective drugs.

**Abstract:**

The catastrophic epilepsies of childhood are among the most devastating and least understood neurologic disorders. Recently, however, several laboratories have generated animal models that may begin to allow investigations of the underlying seizure mechanisms. After a brief overview of the childhood catastrophic epilepsies by Dr. Stafstrom, Dr. Galenopoulos will discuss a model of symptomatic infantile spasm (IS) created by a combination of postnatal desynchrony and lipopolysaccharide to produce structural damage followed by PCNA to reduce seizure levels. Dr. Lee will then present on a new model in which spontaneous spams and hyperthermia are produced by chronic TTX treatment. Although neuronal damage is associated with status epilepticus, traumatic brain injury and several epilepsy syndromes, neuroprotective strategies remain controversial. Recent evidence showing neuroprotective effects of several anticonvulsants has led to a renewed interest in neuroprotection in epilepsy. Several anticonvulsants have shown to exert neuroprotective mechanisms that include modulation of calcium homeostasis, histone deacetylases, mitochondrial function, antioxidant functions, iron chelation, and increased conduction through potassium channels. In addition, the development of neuroprotective assays with higher throughput may lead to a greater rate of discovery of new effective drugs.
Emerging cell & molecular targets for anti-epileptogenesis

Molecular and Cellular Alterations in TSC: Mechanisms regulating gene expression in the Transition from Interictal to Ictal Bursting:

2006 Frances E. Jensen, M.D.

2007 Melanie Tallent

2007 David C. Henshall

2007 Jack Parent, M.D.

2007 Nanako Nishiyama

2006 Gregory Worrell, M.D., Ph.D. and Brian Litt, M.D.

2007 Chuck Wilson, Ph.D., Paul Buckmaster, Ph.D., and Brian Litt, M.D.

2006 Melanie Tallent

2007 David C. Henshall

2007 Melanie Tallent

2007 Amy Brooks-Kayal

2007 Russell Sanchez

2007 David Prince

2007 Heine Beck

2006 Jack Parent, M.D.

2006 Claude G. Waterlain, M.D.

2006 Robert Schwarz, Ph.D.

2006 Francois E. Jensen, M.D.

2006 Francis E. Jensen, M.D.

2006 Gregory Rusak, M.D., Ph.D. Large-Scale Recordings of Functional Networks in Brain, Michael Kahana, Ph.D. Mapping Memory from Human Recordings, Christoff Koch Ph.D. Visual perception and visual consciousness

Functional Implications

synchronization

connection * combine with Beck, are Important for Epilepsy?

An Update

epileptogenesis

Epilepsy: A Window On Functional Human

Broad-Band Intracranial EEG In Patients with epilepsy: A Window On Functional Human Networks

Recent years have seen tremendous interest in broad-band intracranial recordings in humans, driven by new therapeutics and brain-computer interface research. These large scale, broad-band data sets, spanning unit ensembles to large scale networks enable us to investigate hypotheses related to normal network function, such as memory, cognition, and motor control, as well as pathologic processes such as seizure generation, movement disorders and psychiatric disease. Patients implanted with intracranial electrodes during evaluation for epilepsy surgery provide unprecedented access to the brain for this research. This review covers basic advances in the field of human brain neuroscience in the past ten years, with an emphasis on the role of broad-band recordings in understanding human epilepsy seizures. Specific examples will be discussed, including the role of broad-band recordings in the study of wavelet-evoked responses, neural oscillations and their relationship to pathological activity, and the role of intrinsic oscillations in the interictal period. Finally, the potential of broad-band recordings in improving our understanding of human neural systems will be highlighted. Dr. Fr. Wilson will be discussing his work in the field of human brain neuroscience.

Kevin J. Mitchell, Claude Waterlain, Talie Z. Baran

Asla Pikainen, Yuri Bazzi, David Henshall, Detlev Boisson

Edward Dudek, Kevin Staley

Tom Satas- University of Wisconsin

Jeff Noebels

Johann Storn, George Richardson, Alison Barth

To be contacted

Ive Marder, Ivan Soltesz, Jeff Noebels

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Claude G. Waterlain, M.D., Joldep Kapur, M.D., Ph.D., Robert DeCiriosa, Robert McCormick

Guy McKhann III, Uwe Heinemann, Helen Scharfman, Robert Schwarz

Peter Crino, M.D., Ph.D., David Kwiatkowski, M.D., Ph.D., Francis Jensen, M.D., Veronica A. Alvarez, Ph.D.

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2006 Claude G. Waterlain, M.D.

2006 Robert Schwarz, Ph.D.

2006 Francois E. Jensen, M.D.
<table>
<thead>
<tr>
<th>Topic</th>
<th>Participants</th>
<th>Description</th>
</tr>
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<tbody>
<tr>
<td>Unorthodox mechanisms of epileptogenesis</td>
<td>Matthias J. Koepp, M.D., PhD, John E. Rash, PhD, Roger D. Traub, MD, Barry W. Connors, PhD</td>
<td>Our current understanding of anatomical, physiological and molecular aspects of the opioid synapse is that opioid peptides act as mediators of use-dependent synaptic activity and as co-transmitters to modulate the actions of the primary transmitter, glutamate. There is a large, sophisticated and at times controversial body of animal data showing endogenous opioid release may occur following induced and spontaneous seizures. There is consensus that endogenous opioids released following seizures contribute to a raised seizure threshold. This workshop should contribute to a better understanding of endogenous mechanisms of analgesia.</td>
</tr>
<tr>
<td>The role of opioids in epilepsy</td>
<td>Frank C. Tortella, Friedrich Zimprich, Matthias J. Koepp, M.D., PhD</td>
<td>You cannot address opioid involvement directly in neurons. Neurons are not directly connected to the nucleus accumbens. However, there is evidence that endogenous opioids released following seizures may contribute to a raised seizure threshold. This workshop should contribute to a better understanding of endogenous mechanisms of analgesia.</td>
</tr>
<tr>
<td>Gene Therapies and Epilepsy: New Therapeutic Directions</td>
<td>Pat Iverson, Steve Wilton</td>
<td>The role of endogenous peptides in the production of epilepsy has been unclear. This is particularly critical when developing in vitro models of endogenous pathways. Several new players regulating the function of the glutamate-glutamine cycle have only recently been cloned and characterized, so our understanding of processes regulating neurotransmitter recycling has advanced significantly in the past few years (Edwards). However, most of our understanding of the glutamate-glutamine cycle is derived from biochemical and/or molecular studies. These studies have highlighted the significance of this cycle, but the nature of these technical approaches has limited understanding.</td>
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<tr>
<td>New Therapeutics Directions</td>
<td>Edward Bertram, M.D.</td>
<td>Maybe the time is ripe for an &quot;h-channelopathy&quot; workshop? I think we would explore the evidence linking h-channels to epilepsy, primarily in animal models of epilepsy. As you probably know, there have been a number of exciting developments recently showing h-channel mediation (via loss of function) of generalized seizures in animal models of absence, and also emerging evidence that h-channel downregulation occurs in models of focal epilepsy as well. I would aim for a mix of speakers that would cover both basic aspects of h-channel function and derangement in animal models. Speakers that could be invited might include the following:</td>
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<tr>
<td>Engineering the mouse nervous system to decipher the mechanisms of human epilepsy</td>
<td>Matthew P. Anderson, M.D., Ph.D.</td>
<td>There is a venerable literature on the role of the glutamate-glutamine cycle in recycling neurotransmitter in the central nervous system under both normal and pathological conditions. Several new players regulating the function of the glutamate-glutamine cycle have only recently been cloned and characterized, so our understanding of processes regulating neurotransmitter recycling has advanced significantly in the past few years (Edwards). However, most of our understanding of the glutamate-glutamine cycle is derived from biochemical and/or molecular studies. These studies have highlighted the significance of this cycle, but the nature of these technical approaches has limited understanding.</td>
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<td>The role of the glutamine cycle in dynamic regulation of normal and pathological function of the CNS</td>
<td>Douglas A. Coulter, Ph.D.</td>
<td>There is a venerable literature on the role of the glutamate-glutamine cycle in recycling neurotransmitter in the central nervous system under both normal and pathological conditions. Several new players regulating the function of the glutamate-glutamine cycle have only recently been cloned and characterized, so our understanding of processes regulating neurotransmitter recycling has advanced significantly in the past few years (Edwards). However, most of our understanding of the glutamate-glutamine cycle is derived from biochemical and/or molecular studies. These studies have highlighted the significance of this cycle, but the nature of these technical approaches has limited understanding.</td>
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<td>Fly, fish, and worm models of epilepsy</td>
<td>Guy A. Caldwell, PhD, Mark Tonos, PhD, Scott C. Baraban, PhD</td>
<td>There is a venerable literature on the role of the glutamate-glutamine cycle in recycling neurotransmitter in the central nervous system under both normal and pathological conditions. Several new players regulating the function of the glutamate-glutamine cycle have only recently been cloned and characterized, so our understanding of processes regulating neurotransmitter recycling has advanced significantly in the past few years (Edwards). However, most of our understanding of the glutamate-glutamine cycle is derived from biochemical and/or molecular studies. These studies have highlighted the significance of this cycle, but the nature of these technical approaches has limited understanding.</td>
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<td>Do seizures beget seizures?</td>
<td>Yehoshul Ben-Ari, DSc, Mircea Stiriade, MD, DSc, Yehoshul Ben-Ari, DSc, F. Edward Dudek, PhD</td>
<td>There is a venerable literature on the role of the glutamate-glutamine cycle in recycling neurotransmitter in the central nervous system under both normal and pathological conditions. Several new players regulating the function of the glutamate-glutamine cycle have only recently been cloned and characterized, so our understanding of processes regulating neurotransmitter recycling has advanced significantly in the past few years (Edwards). However, most of our understanding of the glutamate-glutamine cycle is derived from biochemical and/or molecular studies. These studies have highlighted the significance of this cycle, but the nature of these technical approaches has limited understanding.</td>
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<td>Gap junctions and electrotonic coupling in hippocampus and neocortex which connec...</td>
<td>John E. Rieth, PhD, Roger D. Traub, MD, Barry W. Connors, PhD</td>
<td>There is a venerable literature on the role of the glutamate-glutamine cycle in recycling neurotransmitter in the central nervous system under both normal and pathological conditions. Several new players regulating the function of the glutamate-glutamine cycle have only recently been cloned and characterized, so our understanding of processes regulating neurotransmitter recycling has advanced significantly in the past few years (Edwards). However, most of our understanding of the glutamate-glutamine cycle is derived from biochemical and/or molecular studies. These studies have highlighted the significance of this cycle, but the nature of these technical approaches has limited understanding.</td>
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<td>Ion cotransport and epilepsy</td>
<td>Dale C. Heudorffer, PhD, Kevin J. Staley, MD, Daryl W. Hochman, PhD</td>
<td>There is a venerable literature on the role of the glutamate-glutamine cycle in recycling neurotransmitter in the central nervous system under both normal and pathological conditions. Several new players regulating the function of the glutamate-glutamine cycle have only recently been cloned and characterized, so our understanding of processes regulating neurotransmitter recycling has advanced significantly in the past few years (Edwards). However, most of our understanding of the glutamate-glutamine cycle is derived from biochemical and/or molecular studies. These studies have highlighted the significance of this cycle, but the nature of these technical approaches has limited understanding.</td>
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<tr>
<td>Imaging excitatory neurotransmission</td>
<td>Raymond J. Dingledine, PhD, Ogmen A. Petroff, MD, Matthias Koepp, M.D., PhD</td>
<td>There is a venerable literature on the role of the glutamate-glutamine cycle in recycling neurotransmitter in the central nervous system under both normal and pathological conditions. Several new players regulating the function of the glutamate-glutamine cycle have only recently been cloned and characterized, so our understanding of processes regulating neurotransmitter recycling has advanced significantly in the past few years (Edwards). However, most of our understanding of the glutamate-glutamine cycle is derived from biochemical and/or molecular studies. These studies have highlighted the significance of this cycle, but the nature of these technical approaches has limited understanding.</td>
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<tr>
<td>2005</td>
<td>Mathern, Gary W., MD</td>
<td>Epileptogenesis of cortical dysplasia: Compare and contrast animal models with mechanisms gleaned from human studies</td>
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<td>2005</td>
<td>Mikati, Mohamad, MD</td>
<td>Seizure-related programmed cell death</td>
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<td>2005</td>
<td>Pitkanen, Ada, MD, PhD</td>
<td>In vivo imaging epileptogenesis and epilepsy: from techniques to applications</td>
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<td>2005</td>
<td>Scharfman, Helen E., PhD</td>
<td>Animal models of catamenial epilepsy</td>
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<td>2005</td>
<td>Schiff, Steven J., MD, PhD</td>
<td>Interpreting multivariate EEG and fMRI signals</td>
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<td>2005</td>
<td>Vezzani, Annamaria, PhD</td>
<td>Inflammation and epilepsy</td>
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<td>2004</td>
<td>Kevin M. Kelly, M.D., Ph.D.</td>
<td>Models of epilepsy in aging</td>
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<td>2004</td>
<td>Massimo Avoli, M.D., Ph.D.</td>
<td>Plasticity of chloride transport and GABA signaling</td>
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<td>2004</td>
<td>Arnold R. Kriegstein, M.D., Ph.D.</td>
<td>Origin and migration of cortical neurons</td>
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<td>2004</td>
<td>Jong M. Rho, M.D.</td>
<td>Ketone bodies and neuronal excitability</td>
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<td>2004</td>
<td>Margaret P. Jacobs</td>
<td>Creating new animal models of the childhood epilepsies</td>
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<tr>
<td>2004</td>
<td>John J. Halbitz, Ph.D.</td>
<td>The role of kainate receptors in epilepsy</td>
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<td>Year</td>
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<tr>
<td>2004</td>
<td>Peter L. Carlen, M.D. and John G.R. Jefferys, Ph.D.</td>
<td>Non-synaptic seizure mechanisms</td>
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<tr>
<td>2004</td>
<td>James O. McNamara, M.D.</td>
<td>Neurotrophins: Epileptogenesis and electroconvulsive seizures</td>
</tr>
<tr>
<td>2004</td>
<td>Scott M. Thompson, Ph.D. and Cha-Min Tang, M.D., Ph.D.</td>
<td>The epileptic neuron: Changes in intrinsic neuronal and dendritic excitability</td>
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<tr>
<td>2004</td>
<td>Miriam H. Meisler, Ph.D.</td>
<td>Sodium channel mutations in familial and sporadic epilepsy</td>
</tr>
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<td>2004</td>
<td>Robert K.S. Wong, Ph.D.</td>
<td>Modification of intrinsic ionic channels by metabotropic receptors: A mechanism for epileptogenesis?</td>
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<td>2004</td>
<td>Tallie Z. Baram, M.D., Ph.D.</td>
<td>Transcriptional channelopathies in epilepsy</td>
</tr>
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<td>2003</td>
<td>Carl F. Stafstrom, M.D., Ph.D.</td>
<td>Long-term seizure monitoring in experimental animal models: Video-EEG and beyond</td>
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<td>2003</td>
<td>Frances E. Jensen, M.D.</td>
<td>Post-translational modifications in epileptogenesis</td>
</tr>
<tr>
<td>2003</td>
<td>Ivan Soltesz, Ph.D.</td>
<td>Endocannabinoids in epilepsy</td>
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<tr>
<td>2003</td>
<td>Tony DeFazio, Ph.D. and John Huguenard, Ph.D.</td>
<td>T-type calcium channels in epilepsy</td>
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<tr>
<td>2003</td>
<td>Melanie Tallent, Ph.D.</td>
<td>Benign familial neonatal convulsions and the Kv M-channel: Insight into how a single gene mutation causes epilepsy</td>
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<td>2003</td>
<td>George D. Richerson, M.D., Ph.D.</td>
<td>The role of tonic GABA inhibition and control of brain excitability</td>
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<td>2003</td>
<td>Andreas Hufnagel, M.D.</td>
<td>Stem cells in epilepsy</td>
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<td>2003</td>
<td>Orvar Eeg-Olofsson, M.D., Ph.D.</td>
<td>Pharmacogenetics of antiepileptic drugs (AEDs)</td>
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<tr>
<td>2002</td>
<td>Manisha Patel, Ph.D.</td>
<td>Mitochondria and free radicals</td>
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<tr>
<td>2002</td>
<td>John J. Hablitz, Ph.D.</td>
<td>Neurotransmitter transporters and epilepsy</td>
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<td>2002</td>
<td>Philip Schwartzkroin, Ph.D.</td>
<td>Functional imaging in small animal models of epilepsy</td>
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<td>2002</td>
<td>Libor Velisek, M.D., Ph.D.</td>
<td>Steroid hormones and epilepsy</td>
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<td>2002</td>
<td>F. Edward Dudek, Ph.D.</td>
<td>Hypoxic-ischemic insults and epilepsy: Models, circuits, and receptors</td>
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<td>2002</td>
<td>Jaideep Kapur, M.D., Ph.D.</td>
<td>The latent period -- mechanisms and controversies</td>
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<td>2001</td>
<td>Paul A. Rutski, M.D.</td>
<td>Recording from large neural networks -- what can we learn from novel techniques?</td>
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<td>2001</td>
<td>Amy Brooks-Kayal, M.D.</td>
<td>Gene arrays in epilepsy research</td>
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<td>2001</td>
<td>Kevin J. Staley, M.D.</td>
<td>Inhibition: What measures are relevant to epilepsy?</td>
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<td>2001</td>
<td>Gary Clark, M.D.</td>
<td>Functional studies of human epilepsy genes</td>
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