HIGHLIGHTS FROM INTERNATIONAL NEUROSCIENCE MEETINGS

American Epilepsy Society (AES) 64th Annual Meeting 3rd Biennial North American Regional Epilepsy Congress San Antonio (TX), December 3rd-7th 2010

Raidah Al-Baradie, *MD.*
Neuroscience Center, King Fahd Specialist Hospital & Pediatric Department, Dammam University, Dammam, Saudi Arabia.

This year's meeting was held in San Antonio, Texas, USA over 5 days from 3-7 December 2010. The program included sessions on basic science, clinical research, and clinical practice for adults or children, psychiatry, neurosurgery, nursing, and professionals in epilepsy care. The scientific material was presented as courses, plenary sessions, special interest group meetings, investigators workshops, satellite symposia, platforms, poster sessions, and poster walking tours. A brief overview of interesting abstracts from the meeting will be presented in the following pages.

Abstracts

The relation between interictal spikes and seizures in rat models of epilepsy
M. Dichter, H. Juul, J. Keating

Interictal spikes (ISs) are biomarkers for excessive brain excitability in epilepsy. However, the relationship between IS frequency and pattern and seizure development is not well understood. In some acute seizure models, ISs increase in frequency and complexity just before seizures and appear to be the triggering event. In other epilepsy models, there appears to be little relationship. In human patients, there is a suggestion that spikes increase after seizures and then decline thereafter. If there is a relationship between seizures and ISs, it is likely to be more clearly seen in animals that exhibit clustered seizures. They found that clusters of seizures are most likely to occur during periods of reduced IS firing. Also, repetitive seizures can induce normally glutamatergic granule cells to produce and secrete GABA and that this change in neuronal phenotype lasts for approximately one week. It is likely other homeostatic mechanisms are also involved in dampening excessive brain excitability. Identifying these mechanisms may provide new targets for innovative anti-seizure therapy.

mTOR inhibition has potential antiepileptogenic effects in a controlled cortical impact model of traumatic brain injury
D. Guo, L. Zeng, D. Brody, M. Wong

Traumatic brain injury (TBI) is a major cause of disability and death. The TBI is often accompanied by the subsequent development of posttraumatic epilepsy (PTE). Seizures of PTE are frequently intractable to available treatment options, and attempts at preventing PTE have been unsuccessful. Understanding basic mechanisms of posttraumatic epileptogenesis is important for developing antiepileptogenic therapeutic approaches to PTE. The mammalian target of rapamycin (mTOR) pathway has been implicated in mediating mechanisms of epileptogenesis in other models of epilepsy and has also been reported to be activated in models of TBI. It was concluded that the mTOR pathway is strongly activated following experimental TBI and may mediate mechanisms of epileptogenesis in the CCI model of TBI. The mTOR inhibitor rapamycin may have antiepileptogenic effects in this model.

HIGHLIGHTS FROM INTERNATIONAL NEUROSCIENCE MEETINGS

Correlation between interictal high-frequency oscillations and seizure outcome in pediatric resective epilepsy surgery

T. Akiyama, C. Go, A. Ochi, I. Elliott, E. Donner, S. Weiss, O. Snead III, J. Rutka, J. Drake, H. Otsubo

High-frequency oscillations (HFOs) >80 Hz (ripples at 80-200 Hz and fast ripples [FRs] at >250 Hz) have been recorded in the intracranial EEG from the epileptogenic brain. There has been no diagnostic modality to date to measure the epileptogenic zone directly. Interictal HFOs may be a valuable marker to localize the epileptogenic zone, removal of which is necessary and sufficient to achieve seizure freedom. In this study, a correlation between resection of the brain region with interictal HFOs and seizure outcome using automated detection of HFOs. was investigated. Interictal FRs are indicative of the epileptogenic zone if they are present in at least 3 channels. Interictal ripples are considered to reflect the irritative zone rather than the epileptogenic zone. The HFOs have no correlation with the seizure outcome.

Short-term outcome prediction by electroencephalographic features in children treated with therapeutic hypothermia after cardiac arrest.

N. Abend, S. Kessler, A. Topjian, A. Gutierrez-Colina, R. Ichord, M. Donnelly, V. Nadkarni, R. Berg, D. Dlugos, R. Clancy

Thirty-five children managed with a standard clinical TH algorithm after cardiac arrest were prospectively enrolled. The EEG recordings were scored in a standardized manner and categorized. The EEG category one consisted of continuous and reactive tracings. The EEG category 2 consisted of continuous but unreactive tracings. The EEG category 3 included those with any degree of discontinuity, burst suppression, or lack of cerebral activity. The primary outcome was unfavorable short-term outcome defined as Pediatric Cerebral Performance Category score of 4-6 (severe disability, vegetative, death) at hospital discharge. Patients with EEG scores of 2 or 3 were far more likely to have poor outcomes than those with a score of one.

Automatic seizure detection in SEEG using high frequency activities in wavelet domain

L. Ayoubian, J. Gotman

It is known that analysis of high frequency activities (HFs), ranging from 80-500 Hz, indicates that these activities are prominent in many seizures and occur at seizure onset (Jirsch et al 2006, Ochi et al 2007). This study explores the use of HFs for automatic seizure detection in SEEG. So the SEEG was recorded after 500 Hz filtering with 2000 Hz sampling rate. The method was designed using 2 h of SEEG from 8 patients and a total of 10 seizures. The SEEG signals were transformed into wavelet domain using the complex Morlet wavelet. The frequency ranges of interest are between 80-500 Hz. It was found that HFs are very prominent at seizure onset. It was demonstrated that in SEEG it is possible to detect many seizures automatically through HFs only. As some seizures show minimal amounts of this activity, HFs are not sufficient to detect all seizures. However, HF detection could be combined to existing seizure detection methods due to the fact that HFs are prominent early in the discharge and are relatively specific to seizures; this would thus improve seizure detection performance.

To laugh or not to laugh: dichotomy favoring right temporal lobe onset of seizure

P. Paul Pritchard, P. Lajeunesse, M. Wagner

As an epileptic manifestation, laughter most commonly occurs in children who have hypothalamic hamartoma. Among adults, gelastic seizures take origin from other limbic structures, including temporal lobes, cingulate gyrus, and frontal lobes. Previous citations of gelastic seizures have not suggested a predictable laterality of seizure onset. In this retrospective study, a chart review was carried out of 19 adult patients at the institution who reported a gelastic component to their seizure semiologies. Also case histories, brain imaging, interictal EEG, and results of VEEG

monitoring were studied. Three of this group had seizures, which arose independently in right and left temporal lobes. Half of the seizures with right temporal onset were gelastic, versus none of those of left temporal onset, and none of those of indeterminate laterality. Gelastic features of the seizure occurred exclusively with events of right temporal lobe onset. This finding appears to confirm the concept of the cerebral laterality of emotive function.

Rufinamide for refractory epilepsy in a pediatric and young adult population

J. Joseph, R. Schultz, A. Wilfong

This study indicates that rufinamide is a helpful adjunct in the therapy of a variety of refractory seizure types both in children and in young adults. This is consistent with data from previous studies. Forty-six percent of patients exhibited a reduction in seizure frequency, with 37% of the responders showing a more than 50% decline in seizure frequency. Rufinamide appeared to have had a relatively good safety profile, as only 2 patients stopped the medication due to adverse effects. However, 15 patients did not think that the medication helped them, and 5 actually had an increase in seizure frequency on rufinamide. These data shows that rufinamide therapy may be a relatively safe adjunct in the treatment of refractory epilepsy.

Intravenous lacosamide in refractory status epilepticus and seizure aggravation

J. Larch, J. Dobesberger, G. Kuchukhidze, G. Walser, I. Unterberger, E. Trinka

In this series of patients with seizure clusters and status epilepticus (SE) after failure of first line treatment benzodiazepines, intravenous (IV) lacosamide (LCM) was used. The initial dose was mean 257.9 mg (SD 90.2), median 200 mg (range 200-400). The rate of infusion in patients with SE ranged between 40-57mg/min, in patients with seizure clusters 20-57mg/min. An LCM IV was used as a third drug. Nonconvulsive SE was terminated with LCM IV in 3/3 patients, convulsive SE in 1/6 patients, and in 8/10 patients with seizure clusters LCM IV was effective. These data support consideration of LCM IV use as a safe alternative to standard AED therapies for acute treatment of seizure emergency situations. Further studies on optimal dose, rate of infusion efficacy and safety are needed.

A phase II study evaluating the safety, tolerability, and efficacy of Perampanel, a selective AMPA receptor antagonist, in patients with refractory partial seizures

D. Squillacote, G. Krauss, N. Vaiciene-Magistris, D. Kumar

Perampanel is an orally-active, selective, non-competitive AMPA receptor antagonist with a long half-life, which has shown broad-spectrum anti-seizure effects in various animal models. Following favorable tolerability in Phase I studies, this study evaluated the maximum tolerated dose and safety of perampanel in a randomized, double-blind, placebo-controlled, parallel-group phase II trial with a secondary endpoint of efficacy. The study demonstrated the tolerability of perampanel doses of 2 mg to 12 mg/day with no safety issues identified in this small study. There was also a preliminary suggestion of efficacy. Based on results from this and other studies, 3 phase III studies are ongoing to further evaluate the efficacy and safety of perampanel.

Vagal nerve stimulator: cognitive and mood aspects

A. Piazzini, K. Turner, V. Chiesa, E. Gardella, E. Zambrelli, F. La Briola, A. Vignoli, M. Canevini

In this study, a small number of patient were treated with VNS for refractory seizure. A complete neuropsychological battery has been administered to all 14 selected patients. This battery includes tests for the assessment of intelligence level, attention, short-term verbal memory, short-term visual memory, long-term verbal memory, long-term visual memory, language, a questionnaire on mood status and another one on Quality of Life. The first one-year follow-up

highlights an improvement of Quality of Life and mood conditions. The cognitive functions seem stable. This first data are encouraging; it is important to enlarge this sample, to have more reliable results.

Prolonged febrile seizures and memory development

M. Martinos, M. Yoong, R. Scott, M. de-Haan

In this study, differences were found between a group of healthy controls and children following prolonged febrile seizures (PFS) on a hippocampally dependent task. Namely, patients following a PFS spent less time looking at a novel face following a delay when compared to their normal counterparts. Also, the relationship between mean hippocampal volumes in the PFS group and their degree of novelty preference corroborates the important role of the hippocampus in these processes.

Scalp temporal positive sharp waves may originate from the mesial temporal cortex

R. Serafini, G. Barkley, K. Elisevich, K. Mason

In this study, EEG recordings presenting these positive waves were identified and reviewed for evidence indicating a source in any of these regions. The MRI showed temporal lobe abnormalities in 4 patients (with mesial temporal sclerosis, and cavernoma in one patient). In the remaining 2 patients, no temporal lobe lesions were seen. An MEG was performed in 3 patients and showed basal or mesial temporal epileptiform discharges. On a theoretical basis, interictal epileptic discharges (IEDS) originating from the mesial temporal cortex may be recorded by ipsilateral scalp electrodes as low voltage sharp transients of positive polarity. These positive discharges are more pronounced in patients with ipsilateral hippocampal atrophy. Some patients exhibit scalp temporal IEDS with an initial low voltage positive component, and this may correspond to an initial source over the mesial temporal cortex.

Use of intravenous levetiracetam in acute seizure management in neonates

O. Khan, E. Chang, C. Cipriani, C. Wright, P. Ritch, E. Crisp, B. Kirmani

Neonatal seizures affect approximately 1 to 4 of 1000 live births in North America and are a major predictor of future adverse neurologic outcomes. Levetiracetam (LEV) is an anti-epileptic drug (AED) with a novel mechanism of action; the intravenous (IV) form is currently approved as adjunctive treatment for a variety of seizures in patients 16 years of age and older. A retrospective chart review was conducted on all term and late preterm neonates who received intravenous LEV. Twenty-two neonates, 12 females, and 10 males with partial epilepsy who received intravenous LEV. A bolus administration of 50 mg/kg was administered in most patients followed by a maintenance dose of 25 mg/kg every 12 hours. Nineteen patients (86%) experienced immediate seizure control within one hour of the loading dose. These patients responded to intravenous LEV both electrographically and clinically with improvement seen one hour after commencing the loading dose. Twenty-two patients (100%) were switched to oral LEV and of those, 18 (81%) were discharged home on oral LEV monotherapy. No major immediate or long-term adverse effects were reported. Duration of follow up ranged between 2-6 months. It was concluded that IV LEV appears to be safe and efficacious in acute seizure management in neonates.

Recent advances in stereoelectroencephalography (SEEG)

J. Hall

In this poster, commercial electrodes developed with input from French neurosurgeons are fully MRI compatible. A novel technique of SEEG placement without a traditional frame or the need for intra-operative x-rays or angiogram has been perfected. It allows accurate placement in virtually any trajectory, and thus fewer electrodes may be necessary. Experience over the past several years has allowed the adaptation of this method of SEEG placement to commercially available electrodes. This new technique is demonstrated by intra-operative photographs and post-

implantation MRI. With the fusion of these technologies we may: accurately place fewer electrodes, acquire MRI with the electrodes in place, perform radiofrequency lesions, and avoid a second surgery for removal. This advance permits image-guided stereotaxic resection using MRI acquired with the electrodes in place, thus ensuring adequate removal of tissue around specific electrodes and/or specific electrode contact.

Drug withdrawal protocol after temporal lobe epilepsy surgery

R. Centeno, M. Guimarães, L. Caboclo, H. Carrete, E. Yacubian

In this series, patients with clinically intractable temporal lobe epilepsy (TLE) submitted for surgical treatment that became seizure free for a period of 2 years and had serial EEG exams without epileptic discharges were candidates to be submitted to the protocol of AED withdrawal. Patients and their families were informed about the risks, and they joined the protocol after informed consent. As a first step they were taken off benzodiazepines, followed by an AED, which was not considered a first choice for the clinical treatment of TLE, and finally an AED that was a first choice for TLE, such as carbamazepine, oxcarbazepine, and phenytoin. The withdrawal was performed gradually, and the drug was reduced by 25% of the total dose in a period of 5 half-lives of the drug. After each step the EEG was repeated. In patients whose EEG showed epileptic discharges the withdrawal was stopped and in those whose seizures recovered the AED were re-introduced integrally. Patients were followed and analyzed prospectively for a mean period of 2 years (range 0.5 to 4 years). The results are compatible with data available in the literature representing a safety protocol, as from the 40 patients included, 72.5% did not have seizure recurrence, and 50% were seizure free without medication. Finally, after seizure recurrence only 90% showed refractoriness.

Mutation screening of GRIN2A as a candidate gene for idiopathic focal epilepsies

S. von Spiczak, K. Finsterwalder, C. Reutlinger, H. Muhle, A. Caliebe, T. Obermeyer, M. Schilhabel, A. Franke, I. Helbig, U. Stephani

Mutation analysis of GRIN2A in patients with CTS and epilepsy syndromes of the Rolandic spectrum identified one missense mutation localized in the ligand-binding domain of the alpha-2 NMDA receptor subunit. This further supports earlier findings suggesting the involvement of altered glutamatergic transmission in the generation of centrotemporal spikes. Further studies including larger patient cohorts and functional analysis of the mutant protein are needed to validate these findings.

Cortical dysplasia in patients with temporal lobe epilepsy: Morphological study of 60 cases

J. Villeda Hernandez, M. Alonso, L. Rocha, S. Orozco

In the present study, neocortical malformations in cases of refractory temporal lobe epilepsy and cortical dysplasia (CD) we characterized. They studied 60 cases (40 males and 20 females), mean age 34.6 years, of refractory temporal lobe epilepsy and CD, only 8 with preoperative MR imaging were suggestive of CD. They found marked dislamination in all areas of the cortex, neuronal loss, amylaceous bodies, neuronal cytomegaly with cytoskeletal disorganization containing dense fibrillar cytoplasmic aggregates, dysplastic neurons, balloon cells with atypical nuclei, often with binucleation, and abundant glassy eosinophilic cytoplasm. The CD was classified as type IA in 8.3%, type IIA in 50%, and type IIB in 15% of cases. Combined type IA and IIA were found in 5%, type IIA and IIB in 16.6% and type IA and IIB in 1.6% of cases. GFAP, nestin, and vimentin were highly expressed in the majority of neurons in the cortical areas as well as the hippocampus. The majority of balloon cells were found in the white substance. Expression of nestin was increased only in balloon cells and dysplastic neurons. These findings suggest that malformations of cortical development, up regulation of the astrocytic response as an astroglial dysfunction, and possible alterations in the blood brain barrier contribute to high epileptogenic activity in these patients.

HIGHLIGHTS FROM INTERNATIONAL NEUROSCIENCE MEETINGS

Screening for GLUT1 deficiency is a diagnostic test in early-onset absence epilepsy: A replication study

S. Mullen, T. Arsov, K. Lawrence, J. Damiano, S. Berkovic, I. Scheffer

In this study, they sought to replicate this finding and thereby to confirm that mutational analysis of SLC2A1 for the treatable metabolic condition GLUT1-deficiency is a useful diagnostic test in early-onset absence epilepsy (EOAE). The EOAE was defined as epilepsy of unknown cause with predominantly absence seizures, generalized spike wave (>2.5Hz) and onset under 4 years. Those with tonic or atonic seizures were excluded. A total of 40 new cases underwent SLC2A1 mutational analysis by direct sequencing. The result of this study replicates their previous finding that over 10% of EOAE is due to GLUT1-deficiency in an independent cohort. A total of 8 EOAE cases with SLC2A1 mutations in a total of 72 EOAE patients screened to date have now been identified. Given the major treatment and genetic counselling implications, SLC2A1 mutational analysis should be part of the routine diagnostic work-up for EOAE.

Increased incidence of sudden unexpected death in epilepsy (SUDEP) with lamotrigine in Rogaland County, Norway

D. Aurlien, J. Larsen, E. Taubøll, L. Gjerstad

In this study, they present a retrospective population based study on the incidence of SUDEP in Rogaland County, Norway, (375,000 inhabitants) over 10 years from 1995 to 2005. The incidence of SUDEP associated with each antiepileptic drug (AED) was estimated. The SUDEP victims were identified by review of hospital records and post mortem reports of deceased individuals with a diagnosis of epilepsy and data from the National Causes of Death Registry. The incidence of definite and probable SUDEP for patients treated with LTG was 3.9 per 1000 patient-years and 0.46 per 1000 patient-years for patients that were not treated with LTG (p<0.001, odds ratio 8.8 with 95% confidence interval 3.6-21.6). Among the 26 cases, 7 were treated with carbamazepine (CBZ) (4 in monotherapy), and 8 with valproate (VPA) (4 in monotherapy). The SUDEP incidence for CBZ and VPA was not significantly different from the incidence among those not treated with these AEDs. The incidence of SUDEP in patients treated with LTG was significantly increased compared to other AEDs. The findings may suggest a gender difference with a higher incidence in women. The total incidence of SUDEP in Rogaland County was similar to that of previous population based studies.