

AES News

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Recent Advances in Functional Neuroimaging

William Davis Gaillard, M.D.

Children's National Medical Center/Epilepsy Research Branch, NINDS

Introduction

Functional neuroimaging with PET and functional MRI (fMRI) provide a versatile means of the non-invasive assessment of cortical function in the evaluation and management of epilepsy patients considered for epilepsy surgery. These methods have been directed primarily toward identifying eloquent function to be spared during surgery for refractory partial epilepsy rather than for identifying or confirming the epileptogenic zone. They have certain advantages over invasive methods, such as the intracarotid amytal procedure and electrocortical stimulation, but they also have clear limitations.

Principles, Advantages, and Limitations

The most widely used means of functional neuroimaging are fMRI and ligand based studies using PET. They both rely upon identifying alterations in blood flow during cortical activation that are based upon the observation of Roy and Sherington that increased neuronal activity is associated with regional increases in blood flow. Alterations in blood flow may be monitored with the injection of a contrast agent, such as ^{15}O water, in the case of PET, spin tagging in the carotid with MR, or may rely upon hemoglobin as an endogenous contrast agent as used in most fMRI studies. Hemoglobin has a different MR signal in the oxygenated and deoxygenated state. Shortly after a neuronal population increases in activity — the delay is on the order of two seconds — there is an increase in blood flow accompanied by an increase

in oxyHgb/deoxyHgb reflecting an overabundant supply of oxygenated blood.¹ In effect blood oxygen level and blood flow dependent mechanisms identify a physiologic epiphenomenon rather than a direct marker of neuronal activity. Furthermore, blood flow dependent methods require ascertaining blood flow changes between two conditions, a task condition and a control condition. The choice of both control and task conditions is essential. Should the conditions be similar, and thus involving same brain regions, then no differences in blood flow will be detected. In addition, control conditions are in fact active states, and may involve brain areas in a manner completely different than assumed. When

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PRESIDENT'S MESSAGE



As we all continue to seek and comment on an improved national profile and situation for epilepsy patients, physicians and researchers, I want to mention some big accomplish-

ments and initiatives of which we should all be proud.

On March 30 and 31, a White House initiated conference, Curing Epilepsy: Focus on the Future, took place at the Natcher Center in Bethesda, MD. The conference was supported by NIH, AES, the Epilepsy Foundation, NAEC, CURE, and the pharmaceutical industry. Clinicians, researchers, industry representatives, epilepsy patients and families, and lay individuals spoke carefully considered words on our current and future understanding of and investigations into the etiology, development, prevention, and treatment of epilepsy. The expression and discussion of new ways of thinking directed toward the cure of epilepsy, defined as "no seizures, no side effects," should serve a new era of activism, attention, and inspiration for us all, but especially for young investigators to make this field their future career. We also hope that sources of funding will support these efforts. The ideas are already published in a booklet and will be carried further through a benchmark document from the conference, which is currently being prepared by the participants and organizers.

The excitement of this event was used by AES to begin efforts and a potential collaboration with the American Academy of Neurology and the Epilepsy Foundation to bring widespread understanding of the mechanisms, prevention and treatment of epilepsy to neurologists, epileptologists, patients, and researchers. This effort, and

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AES News

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Editor

Elaine Wyllie, M.D.

Executive Director

M. Suzanne C. Berry, CAE

Associate Director

Sandra L. Pizzoferrato

Director of Meeting Services

Steven J. Rugens

Program Director

Cheryl-Ann Tubby

Association Administrator

Karan A. Murray

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AES News

342 North Main Street
West Hartford, CT USA 06117-2507
Phone: (860) 586-7505
Fax: (860) 586-7550
E-mail: info@aesnet.org
Web site: www.aesnet.org

Membership consists of clinicians, scientists investigating basic and clinical aspects of epilepsy, and other professionals interested in seizure disorders. Members represent both pediatric and adult aspects of epilepsy. Active membership for one year is \$170 and includes a subscription to the journal *Epilepsia*. Junior Membership is \$130 annually; *Epilepsia* subscription is optional for Junior members. Active and Junior membership is limited to residents of the USA, Canada, and Mexico. Corresponding membership is limited to residents outside of North America. It does not include a subscription to *Epilepsia*, and fees are \$125. Senior membership is available to Active Members who have reached the age of 65.

Editorial Deadlines

Fall 2000 issue: August 25, 2000
Winter 2001 issue: January 19, 2001
Spring/Summer 2001 issue: April 27, 2001

President's Message

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an assessment of its outcome in influencing patient care, may provide a model for the future dissemination of the advances we hope will result from all of these efforts.

We expect to see AES soon launch its first publication, *Epilepsy Currents*. This monthly literature surveillance newsletter was approved by the AES Board of Directors and is in development. We hope it will allow rapid review of epilepsy-related scientific literature, providing abstracts and expert commentary. Drs. Michael Rogawski, Gregory Bergey, Robert Macdonald, Elaine Wyllie, and I are beginning the explorations, organization, and groundwork for what we hope will be introduced at our December meeting. The restructuring of our education committee and CME efforts is also well underway and will allow more diverse educational programs, both at the Annual Meeting and during the year.

One of our key concerns as a professional association is making the important work that is being accomplished by the Society and its members in the field of epilepsy known to a larger audience. The AES board believes that a carefully crafted communication strategy, well executed, can help AES influence research funding

decisions, attract high quality investigators and practitioners, raise public expectations and demand, and increase awareness of epileptology as a specialty. The Board of Directors accordingly has made external communications a priority concern for the AES, approved a budget, and engaged a marketing and communications consulting company. I appointed an external communications task force to work with this company to formulate the specific plan and begin implementation of specific directions. The working group consists of Joan Austin, Drs. Solomon Moshé, Steven Schachter, Tom Sutula (chair), and myself. We hope to make great strides towards promoting our efforts, accomplishments, ideas, and future plans through this initiative.

AES continues to actively work toward fulfillment of many of its missions in innovative programs because of the remarkable work of our members. We want to hear from and interact with an increasing number of our members; there is plenty for everyone to do. Let us know your talents, interests, and availability to participate. It seems to me no challenge is too much for this Society.

National Institutes of Health • Bethesda, MD • March 30-31, 2000

Curing Epilepsy

Focus on the Future

This conference was supported in part with grants from:

American Epilepsy Society
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AES thanks all the sponsors for their support.

AES CONVERSATION WITH . . .

Eric R. Hargis, *President and CEO, Epilepsy Foundation*



Eric Hargis became President and CEO of the Epilepsy Foundation in February 1999.

What attracted you to the Epilepsy Foundation?

I saw an opportunity to address a condition that does not get the attention it deserves in terms of public recognition, research funding, or services. Some health conditions have high prevalence but are not really life-changing events; others are life changing but have low prevalence. Seizure disorders are high impact both in terms of the numbers of people affected and of what having the condition means to the individual.

How would you describe the Foundation's key challenge?

Although I had worked in health care for over 20 years I really was not aware of epilepsy as a serious public health problem in America. And unfortunately I tended to represent what far too many people know, or don't know, about epilepsy. Many people have told me that when they have a seizure, the reaction of employers, colleagues and friends oftentimes is worse than the seizure itself. There is still a stigma surrounding epilepsy, mostly due to ignorance and fear. We have an opportunity to change that at the Epilepsy Foundation.

How will that change occur?

EF is a very small player dealing with a very big problem. We're a \$50 million organization, and we're taking on a \$12 billion health problem. We have several thousand volunteers, and we're dealing with 2.3 million Americans with epilepsy and their caregivers and families. So we have to focus on our core competencies and then collaborate with others, such as with AES, to address the range of needs.

What are EF's core competencies?

There are three things we as an organization are uniquely qualified to focus on. The first is to fund epilepsy research. The second is to serve as the unified voice for people with epilepsy, who are unheard in many of the discussions on Capitol Hill and throughout the country. The third is to serve as the authoritative source of accurate information about epilepsy for consumers. Our Web site is attracting nearly

100,000 visitors a month, and we want to make all the information resources we have available accessible to consumers in an online environment that allows them to select the level of detail that is helpful to them.

How can EF and AES best work together?

We recognize and have a real appreciation for the AES leadership in reaching out to work collaboratively with us. Immediately after I joined the Epilepsy Foundation, AES Executive Director Suzanne Berry and Bob Fisher, who then was AES President, came to talk with me about how our organizations could best work together. The real strength here is that the leadership of both organizations have a common commitment and are looking for ways to collaborate rather than being competitors. And what's good is that the winners are people with epilepsy.

What joint work is particularly effective?

Research funding is probably the strongest example of our partnership, because we can play a unique role together. Certainly, NIH and the pharmaceutical industry are the two major entities in research funding. But it's exciting what we can do, with AES, to fill gaps in the continuum of funding. We can provide dollars to take a new idea and move it forward, or bring a young investigator into the field, or make a small investment that will then be leveraged significantly in the future with NIH funding.

You attended your first AES Annual Meeting last December. What was your reaction?

The meeting was outstanding. It's a great conference—very well run, very focused, and very full from early morning to late evening. In fact, we may have to get the National Sleep Foundation involved, because there aren't too many opportunities to sleep!

What do you see in the future for people with epilepsy?

The way we look at epilepsy is changing. A good example is the recent NINDS conference on curing epilepsy, which EF and AES helped sponsor. I think in the future we'll look back and say that it was a landmark event. Because what we were talking about was a future with no seizures and no side effects for people with epilepsy.

Medical Education Program Materials Available on the Web

In 1991, the AES Board of Directors determined that the organization should undertake a formal approach to improving the education of medical professionals about epilepsy, beginning with medical students and neurology residents.

The original task force appointed by the board included Drs. Orrin Devinsky, chair, Edward Bromfield, Robert Clancy, Andrew Cole, Daniel Lowenstein, and Michael Privitera. Approximately 25 members have participated in what later became the Medical Student and Resident Education Committee, chaired since 1996 by Edward Bromfield. Other major contributors to the resident curriculum, completed in December 1999, include Drs. Jose Cavazos (who will become committee chair in December 2000), Frank Drislane, Frances Jensen, Anthony Ritaccio, and Steven Schachter.

The curriculum, which has been distributed along with a CD-ROM to all neurology residency directors in the U.S. and Canada, has been extremely favorably reviewed by recipients.

Interested AES members can view and download Medical Education Program materials from the AES Web site at www.aesnet.org.

The AES/VEC Is Open For Business

Be sure to check out the American Epilepsy Society Virtual Exhibition Center

at

www.aesnet.org

Hours: 24 hours a Days,
7 Days a Week



Functional Neuroimaging*(continued from page 1)*

assessing a patient it is important to assure that the subject can perform the tasks at hand, although it is the effort, rather than the performance itself, which may provide the bulk of activation.

When assessing a patient it is important to assure that the subject can perform the tasks at hand, although it is the effort, rather than the performance itself, which may provide the bulk of activation.

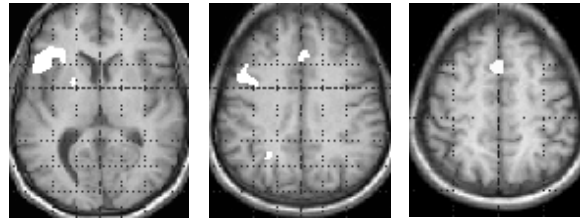
The two commonly used methods provide similar results, ¹⁵O water PET and fMRI. They both have advantages over the intracarotid amytal procedure [IAP] and electrocortical stimulation as they are less invasive and are associated with less morbidity and mortality. Invasive tests usually have a smaller margin of error and can not be readily repeated to re-evaluate uncertain or atypical results. In contrast, noninvasive functional imaging studies can be repeated, and a greater variety of functions can be assessed. PET confers radiation and, unlike fMRI, is not applicable to normal children. The number of experimental conditions is limited by radiation exposure. The half-life of the ligand requires a relatively long test session in the scanner. On the other hand, it is easier to monitor EEG during PET studies. It may be easier to perform studies in somewhat more inattentive patients, and those in whom MRI is contra-indicated (metal clips, pacemakers, etc.). Furthermore, PET identifies blood flow changes in the capillary bed rather than draining vein. The temporal resolution, however, is less than fMRI (one minute vs. two seconds).

The low signal to noise ratio in early PET studies necessitated group analysis of data warped into a standard space. For obvious reasons data placed into a standard space has little application for planning an operation on an individual patient. Furthermore epilepsy is a heterogeneous disease with great individual variability which is lost in group study analysis. However, recent advances in PET technology allow for individual studies. fMRI is more amenable to individual studies. As radiation is

not used studies can be performed repeatedly if necessary and different cognitive aspects may be examined. MRI is more sensitive to motion and requires a higher degree of cooperation. MRI has superior spatial and temporal resolution to PET, and, unlike PET, MR technology is almost universally available. Both techniques identify brain areas "activated" when there is a statistically significant difference signal between paradigm conditions for that brain region (voxel). The significant threshold may vary depending on experimental conditions, age of subject, number of tasks and control conditions used.²

When interpreting blood flow studies it is important to bear in mind that minor alteration in the paradigms may have significant results in activation patterns. For example, reading words silently is more likely to utilize semantic networks, while reading out loud may preferentially engage phonemic language networks.⁴ Most studies have been performed to identify location of language function. Yet, language has many facets and prudence would dictate that multiple paradigms be designed to assess various aspects of language. What is activated may not be essential to the cognitive task, or may reflect other cognitive aspects of the task. As an example, most tests of verbal fluency identify SMA and cingulate gyrus, areas involved in attention and motor planning but not language per se.⁵ Also, areas involved in the task may not be identified for a variety of reasons: the area may not exceed the statistical threshold, the task may be sufficiently automatic not to elicit a blood flow response, or the paradigms control and experimental conditions may be too similar.

There are few studies which have sought to validate blood flow mapping techniques.^{5,6} They show that there is good but not complete agreement between the two electrocortical stimulation and blood flow maps. Typically the areas "activated" during functional imaging studies and areas "disrupted" by stimulation with the same tasks occur in the same location, thus vali-

**Figure 1.**

fMRI map showing typical activation found in left inferior frontal and left middle frontal gyrus during a verbal fluency task. The task compares generating words beginning with the letters (C,L,F,P,R,W) and rest. Results are from a group of five normal adult volunteers. The left side of the image is left side of the brain. Verbal fluency tasks are reliable identifiers of anterior language cortex in patients with partial epilepsy.

dating functional imaging techniques. However there may be as much as a 5 mm difference between the two. These may reflect the resolution of imaging techniques (5-10 mm), the error in registration, and that some blood flow techniques identify blood flow changes millimeters distant from the active neuronal population.

Applications

Most functional imaging has been used to lateralize and localize language function in patients. Most studies involve adults, but children as young as seven years may be

Most functional imaging has been used to lateralize and localize language function in patients.

reliably studied. Motor and sensory mapping have also been used in both epilepsy and tumor surgery. Recently fMRI and PET methods have also been applied to identifying memory in individual subjects. In rare instances fMRI has been used for ictal localization, though the anatomic correlate of interictal spike origin appears more practicable.

Motor and Sensory

Primary sensory and motor cortex can readily be identified with either PET or fMRI. Finger, tongue or toe movement paradigms may be used for identifying the motor strip; sensory cortex stimulation may be identified with tactile stimulation with a brush on the anatomic area of interest.⁷ The

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Functional Neuroimaging

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sensory-motor response is robust; typically a 5-7% change in signal using a 1.5 T scanner is seen, in contrast to 1-2% signal change commonly observed for cognitive tasks. Identification of sensory-motor cortex has been demonstrated in patients mostly undergoing evaluation for tumor or vascular malformation surgery, but may also be useful in planning frontal or parietal epilepsy surgery especially in children younger than five years in whom cortical stimulation is less reliable.

Language

A number of investigators have used fMRI or PET to lateralize language function. They report excellent but not complete agreement with IAP when the methods are compared.^{2,8,9,10,11} Most groups have used tests of verbal fluency or semantic decision. These tasks are strong and reliable identifiers of frontal cortex, mostly IFG and MGF in patients and normal volunteers. The most commonly employed tasks use verbal fluency: generating a list of words to a letter (C,L,F; a phonemic task), generating a list of words belonging to a category (animals, food; a semantic task), or generating a verb to a noun (e.g. clue "ball", answer "hit"; a semantic task).^{2,3,6,10,12,13,14} The test items may be presented visually or aurally. Activation is almost entirely confined to frontal lobe language cortex, with only a minority of patients showing temporal lobe activation. The bulk of the activation is in the dominant hemisphere: when using an asymmetry index [$AI=(L-R)/(L+R)$] to quantify regional laterality, typically two to seven times more activation is seen in the dominant hemisphere than the non-dominant one. Visual reading may be as reliable as the use of regional asymmetry indices.¹⁵ Some investigators have used semantic decision tasks, such as deciding whether two words fall in the same category (e.g., abstract or concrete) or whether a word meets criteria for a particular category (e.g., whether an animal is indigenous to the North American continent and useful to man).^{8,16} Although there is excellent agreement between IAP and either fMRI or PET, discrepancies have been noted in about 3-5% of the 120 or so reported cases; there is some discrepancy; usually one method suggests bilateral language and the other unilateral.^{9,10,17} Outright disagree-

ment is unusual. Which method is better, PET and fMRI or IAP, is a matter of debate as some centers report functional imaging to be correctly lateralizing when compared to surgical and IAP results.^{12,15} Tasks using object naming and reading single simple words have not been particularly helpful for lateralizing language function.^{6,10} In part these stimuli do not sufficiently stress language cortex.

Most tasks employed identify anterior language areas and not temporal ones. Tasks which require subjects to read a text (semantic retrieval or reading a story), unlike single word paradigms, are able to lateralize and localize receptive language cortex in the temporal lobe.¹⁷ Paradigms which use listening to stories, sentences, or auditory response naming (listening to a description of an object which is then named) may also be useful when control conditions are used which mask primary (bilateral) temporal auditory cortex.^{4,15,18}

Memory

Unlike language, functional imaging of memory has had more variable results. This in part reflects the high level of hippocampal neuronal activity, for almost everything we do invokes monitoring of short term memory. Also, the hippocampal formation is small and is surrounded by sinuses and bony structures, which result in a significant partial volume averaging effect as well as MR signal distortion. Some recent studies have identified activation in parahippocampal structures for encoding of complex verbal and visual items.^{19,20} However, unlike language paradigms there is no substantial control data, and individual studies have only been reported in preliminary fashion. In this regard functional imaging has not yet met the capacity for IAP (though not ideal) in assessing the integrity of hippocampal memory function. These issues are likely to be resolved in the next few years.

Ictal and Interictal Studies

Most functional imaging has been used to identify cognitive areas to be spared during epilepsy surgery rather than helping to identify or confirm the ictal location. PET does not lend itself to ictal studies for a host of technical and logistical reasons (principally ligand availability and half-life). Some ictal fMRI studies have been obtained and

have been reported as rare case reports.^{21,22} They generally have been serendipitous, occurring in the scanner while other tasks were being performed. To be effective, seizures must be frequent, and be associated with minimal motion. When obtained, ictal blood flow maps have agreed both with ictal SPECT and intra-cranial recording. One advantage of fMRI is that the propagation of the ictus may be traced, which is not feasible with SPECT.

If ictal fMRI is uncommonly captured, then interictal fMRI may be more practicable. A number of exploratory studies have demonstrated that blood flow changes associated with interictal spikes may be identified using event related fMRI and single spike detection triggered by EEG.²³ These results are promising as they show replicable anatomically restricted blood flow changes, but like most interictal studies they require frequent spikes and have not been used in patients with multi-focal activity. Although potentially useful to identify the anatomic origin of interictal activity the clinical utility ultimately depends on the relative proximity of interictal activity and the generation of ictal event.

Functional neuroimaging of cognitive capacities with PET and fMRI allows for non-invasive assessment of cortical function in patients with partial seizure disorders.

Conclusion

Functional neuroimaging of cognitive capacities with PET and fMRI allows for non-invasive assessment of cortical function in patients with partial seizure disorders. Rarely they may be used to identify ictal events, but this is not sufficient to be of practical use. Interictal mapping may be more feasible but the clinical utility uncertain. The use of fMRI and PET for memory is promising, but not yet ready for widespread application. Currently, functional imaging techniques are most reliably applied to identify language cortex. Studies suggest that they are more reliable identifiers of lateralization, rather than localiza-

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tion, and are best used as a guide for intra-operative mapping. Some discrepancies are found which require further investigation. Prudence dictates that paradigms be designed for individuals and that a panel of paradigms be performed to assess the varied aspects of language. Atypical results should either be re-evaluated or confirmed by other means.

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We're Interested!

Please send news of appointments, honors, and awards to: AES People in the News, 342 North Main Street, West Hartford, CT 06117-2507

Alert:**Basic Researchers**

Philip A. Schwartzkroin, Ph.D., Chair, Commission on Neurobiology, ILAE

Kainic Acid (KA) Availability

As most of you know, kainic acid (KA) supplies have been extremely low for several months—due, I'm told, to the poor seaweed harvest (blame it on El Nino or La Nina). Although some companies (Tocris, Wako, Biomolecular) continue to provide limited supplies at relatively high prices, many laboratory investigators have been concerned that their research would be significantly impacted by this KA shortage. I have been alerted to the existence of a new source of kainate, and would like to pass on this information to those of you whose work involves the KA model.

Starting in June, 2000, Ocean Produce International will be able to supply kainate (derived from a novel source). According to their preliminary communications, their KA is ~99.7% pure, and will sell for approximately \$1.00 (US) per milligram. The company provides information about KA at the following the Web sites:

- background information
www.kainic-acid.com
- questions and answers
www.kainic-acid.com/qa.html
- order information
www.kainic-acid.com/orderinfo.html
- order form for quote
www.kainic-acid.com/orderform.html

The Ocean Produce International contact is:

A.A. "Ed" Cayer
Vice President, Life Sciences
Research & Development
Ocean Produce International
P.O. Box 995
2882 Sandy Point Road
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PRACTICE RX

The Cost of Medications for Treating Epilepsy

Conclusion: It Ain't Cheap!

John R. Gates, M.D., Chair, Practice Committee

The table below reflects a totally unscientific survey I performed with my own pharmacy here in St. Paul, Minnesota to obtain the average wholesale price per tablet for the most frequently prescribed doses of the most common antiepileptic drugs. I've used typical dosage ranges that I have found useful in my clinical experience and calculated an average wholesale cost per month. (The cost to the patient and/or his/her health plan would be higher due to the mark-up from the pharmacy, which is quite variable.) Despite these qualifiers, this chart certainly presents an idea of the monthly cost of medication treatment of epilepsy.

MEDICATION	*AWP/TAB	TYPICAL DOSE RANGE/DAY	COST/MONTH
Dilantin	.27/100 mg	300-400	\$24.30-\$32.40
Tegretol-XR	.48/200 mg	400-800	\$28.80-\$57.60
	.97/400 mg	400-800	\$29.10-\$58.80
Tegretol	.49/200 mg	400-800	\$29.40-\$58.80
Carbatrol	.43/200 mg	400-800	\$25.80-\$51.90
	.65/300 mg		
Depakote	.89/250 mg	750-3000	\$80.10-\$295.80
	\$1.64/500 mg		
Gabapril	\$1.18/4 mg	12-48	\$106.20-\$250.80
	\$1.57/12 mg		
	\$2.09/16 mg		
Neurontin	\$1.16/300 mg	1200-3600	\$139.20-\$356.40
	\$1.98/600 mg		
Lamictal	\$2.18/100 mg	300-800	\$196.20-\$289.20
	\$2.41/200 mg		
Topamax	\$2.95/100 mg	100-400	\$88.50-\$354.00
Zonegran	\$1.68/100 mg	200-400	\$100.80-\$201.60
Trileptal	\$1.63/300 mg	600-2400	\$97.80-\$358.80
	\$2.99/600 mg		
Keppra	\$1.70/500 mg	2000-3000	\$204.00-\$306.00

* AWP (Average Wholesale Price)

Currently, the AES Practice Committee is in the process of revising the Patient Assistance Program brochure. This brochure provides, in one convenient place, all the pertinent information for the various antiepileptic patient assistance programs currently available, including contact numbers and patient qualification information. We plan to have our new edition out by Fall 2000, now that all three new medications—Keppra, Trileptal and Zonegran—have been officially approved. Clearly, from the cost data presented in the above table, there is an obvious need for patient assistance programs. We are pleased the pharmaceutical industry does offer these resources, and the various companies have worked with us to make the information available for our patients.

Interestingly, there is a certain element about these prices that shows remarkable consistency, reminding me of the great line from "Car Talk" on Public Radio. The worried car owner asked the mechanic how much the repair to his car would cost, and the reply was, "Don't know what it is, but it'll be about \$200, if that's what it is." Clearly, the pharmaceutical industry has issues with limited exclusive patent rights, as well as the necessity of recouping significant R&D costs. Nonetheless, it does seem fair to comment: These drugs ain't cheap!

How are the current patient assistance programs for AEDs working for you and your patients? Let us know at ctubby@aesnet.org or (860) 586-7505.

Drs. Litt and Berkovic Receive Research Initiative Awards

Under its Research Initiative Awards program, which provides seed support to encourage innovative collaborative research in epilepsy, the American Epilepsy Society has awarded grants of \$50,000 each to AES members Brian Litt, M.D. and Samuel Berkovic, M.D.

Brian Litt's research on mechanisms underlying generation of seizure precursors in cortex and thalamus in mesial temporal lobe epilepsy is being conducted in collaboration with George Vactsevanos, Ph.D. of the Georgia Institute of Technology; and Diego Contreras and Douglas Coulter, Ph.D., both of the University of Pennsylvania. Dr. Litt is director of the Epilepsy Surgery Program and co-director of the EEG Laboratory, Department of Neurology at the Hospital of the University of Pennsylvania.

In collaboration with Professors Miriam Neufeld and Amos Korczyn of the Tel Aviv Sourasky Medical Center, Dr. Berkovic is working on research directed at determining whether new clinical epilepsy syndromes described in European-derived populations are present in Israel. The team also will consider whether special populations in Israel can be utilized to isolate epilepsy genes. Samuel Berkovic is director of the Epilepsy Research Institute of Australia's Austin & Repatriation Center.

"We are delighted to make these awards to support exactly the kind of novel, collaborative research that the program was designed to foster," commented AES Executive Director M. Suzanne C. Berry.

The Research Initiative Awards program was launched by the Society in 1999.

EF UPDATE

EF Lobbies Congress for More Research Dollars

Ann Scherer, Epilepsy Foundation

In early April, a total of 89 Epilepsy Foundation grassroots advocates, organized under its recently developed "Speak Up, Speak Out" program, converged on the nation's capital to make the case for greater federal investment in epilepsy research.

In approximately 150 visits to their respective U.S. Representatives and Senators, these grassroots advocates, many of whom either live with seizures themselves or have a family member with epilepsy, spoke out on the need for new treatments and the promise of research.

They urged increasing budgets for NIH and CDC; tripling the amount spent on epilepsy research; and passing the Children's Health Bill and a Patient's Bill of Rights to improve access to care (especially specialist care).

The outreach to Congress was preceded by two days of advocacy training at the Foundation's 2000 Public Policy Institute, held in Washington, DC and supported by grants from AES and Pfizer Inc. Institute attendees took part in intensive sessions on how to present a compelling case on Capitol Hill.

They also heard presentations from Susan Spencer, M.D. and Martha J. Morrell, M.D., who summarized the promise of research as described in the March 2000 White House initiated conference on "Curing Epilepsy: Focus on the Future."

This was the seventh year of Epilepsy

The "Speak Up, Speak Out" Network is an important part of those advocacy investments. It is a campaign to develop a nationwide voice for people with epilepsy, which will respond to special alerts on key legislative issues.

Foundation Public Policy Institutes and, according to the evaluations, one of the most effective. Since the Institutes and grassroots Congressional visits began in 1994, NINDS's estimated funding of epilepsy-related projects has doubled, from \$45 million to a projected \$90 million this year.

"While we cannot take full credit for the steady increase in funding," said Cindy Brownstein, the Foundation's Executive Vice President, "the investments we are making in advocacy are realizing gains."

The "Speak Up, Speak Out" Network is an important part of those advocacy investments. It is a campaign to develop a nationwide voice for people with epilepsy, which will respond to special alerts on key legislative issues. Interested people can join through the Foundation's Web site (www.epilepsyfoundation.org).

AES CIRCUIT

Members Suggest Site Enhancements



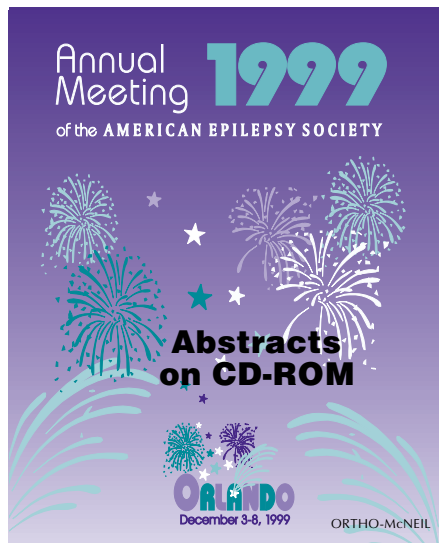
The results of the AES Technology Survey have confirmed member interest in further developing the AES Web site in order to provide more information resources for epilepsy practice and research.

The survey, which was developed and administered by the multimedia consulting firm Fusion Productions, was distributed to some 2100 members in January 2000. Members responding provided information on their current use of the AES site www.aesnet.org and offered suggestions for improving the utility and comprehensiveness of the site.

Nearly 80 percent of the respondents indicated they have visited aesnet.org. Obtaining information on the Annual Meeting and keeping current on Society activities were cited as primary reasons for accessing the site. Over 80 percent rated the current site as "very" or "somewhat" valuable overall.

Asked to assess the relative importance of various applications and services, respondents pointed to information resources as their primary area of interest. These included links to epilepsy journals, a searchable database of epilepsy journal articles, and abstracts online. The ability for online Annual Meeting registration and abstract submission also received a high importance rating from the respondents.

In a summary report on the survey results, Fusion Productions said the AES membership appears to be at a level of technical sophistication that is ready for increases in online activity, and pointed to the strong demand for specific programs and resources as highlighted by the survey respondents.



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NINDS REPORT

Conference on Curing Epilepsy Forsees “No Seizures, No Side Effects”

Margaret Jacobs, Program Director for Epilepsy, NINDS

NINDS recently coordinated a two-day international scientific conference focused on advances in epilepsy treatment. Initiated by the White House, the “Curing Epilepsy: Focus on the Future” conference was hailed by participants as an important occasion in epilepsy research, with many envisioning a future when epilepsy not only can be cured (defined as “no seizures, no treatment side effects”) but also prevented. More than 500 people attended the meeting at NIH in Bethesda, MD, and scores more participated in the proceedings via Internet-based technology.

The conference featured presentations and roundtable discussions by more than 30 clinicians and scientists, and several lay representatives who related their personal experiences with epilepsy. Scientific topics included prospects for interrupting and monitoring epileptogenesis, the processes by which epilepsy develops; genetic strategies for curing epilepsy; and strategies for developing new therapies. The conference was co-sponsored by the Epilepsy Foundation, the American Epilepsy Society, Citizens United for Research in Epilepsy (CURE), and the National Association of Epilepsy Research Centers.

“There is no question that epilepsy research is ready for a new infusion and for a dramatic expansion, both in the kinds of research going on and in the quality of that

research,” said Dr. Gerald Fischbach, director of NINDS, during his introductory address. He praised the co-sponsors for their support of the conference and of biomedical research in general, saying, “One of the really gratifying things about this job is to see private citizens and individuals who . . . get involved in biomedical research.”

Highlights of the conference included a videotaped presentation by Hillary Rodham Clinton and an address by U.S. Representative Neil Abercrombie (D, HI), who related how he developed epilepsy more than 30 years ago and urged participants to make themselves known to their representatives in Congress. Former NINDS Deputy Director Dr. Roger Porter also presented an award to Dr. Harvey Kupferberg, who has led the NINDS Antiepileptic Drug Development Program (now the NINDS Epilepsy Therapeutics Research Program) for 18 years and has announced he will retire in June.

Scientific presentations at the conference were interspersed with roundtable discussions on strategies emerging from new discoveries, bioethical issues of gene discovery, and the process of moving discoveries from the laboratory to the clinic. For the first time at an NINDS conference, people viewing the lecture via Webcast were given the opportunity to submit ques-

tions to the speakers by sending email to a special address set up for this purpose.

While the focus of the conference was on the scientific presentations, several unique opportunities surrounded the event. These included a special meeting for junior investigators, introducing a new RFA targeting translational epilepsy research by junior investigators. The conference also included sessions that allowed members of the general public to interact with the researchers attending the conference. Finally, a partnership between the Epilepsy Foundation and WebMD provided several online epilepsy discussion panels and an online epilepsy chatroom hosted on the WebMD during and just after the conference.

Dr. Fischbach described the conference as a wonderful experience that left him with “a great sense of hope and optimism” about prospects for advances in epilepsy research. He also announced the creation of a planning panel that will meet during the next six months to develop a five-year research plan to move toward curing epilepsy. He concluded by calling for industry and academia to find ways to work together to solve the enormous challenge of curing this devastating disorder.

This report is adapted from an article by Natalie Frazin, which appears in its entirety at www.ninds.nih.gov.



Attendees at General Session



First Lady Hillary Clinton speaks to the attendees.



Margaret Jacobs, AES



Dr. Susan Spencer, AES



Dr. Timothy Pedley, Keynote Speaker



Break for attendees



Ann Scherer, EF staff; Sue Berry, Cheryl-Ann Tubby, AES staff

In Memoriam

John Frederick Annegers died suddenly and unexpectedly on February 20, 2000 at the age of 55.

Dr. Annegers received his Ph.D. from Michigan State University in 1972, and conducted research on the epidemiology of epilepsy at the Mayo Clinic for seven years. He then moved to the University of Texas School of Public Health at the Health Science Center at Houston, where he was a professor of epidemiology until his death.

Dr. Annegers was an exceptional methodologist who developed strategies to study epilepsy in populations. He made seminal contributions to the understanding of remission of epilepsy, teratogenesis associated with antiseizure medication, family aggregation of epilepsy, risk factors for epilepsy, and mortality in people with epilepsy including several studies of sudden death. He also initiated studies on the cost of epilepsy.

Fred Annegers was an avid bicyclist and he will be equally remembered for his arrival at epilepsy centers worldwide equipped with his cycle and panniers along with his wry wit, sharp intellect, and critical assessment of a research strategy.

He is survived by his wife Carolyn and their two children. The many students and colleagues who have learned from him and benefited from his insights about study design, research, and life also remember him.

*An Internet-Based
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CALENDAR OF EVENTS

- JUNE 9-11 4TH ETNEAN EPILEPSY WORKSHOP**
St. Thomas Convent in Linguaglossa
at the slopes of Mt. Etna
Contact: Dr. Antonino Pavone, Neurology Department,
Ospedale Garibaldi, 95100 Catania, Italy
Fax: (39) 095-31-21-52, E-mail: hsepa@tin.it
- JUNE 18-22 10TH MEETING OF THE EUROPEAN NEUROLOGICAL SOCIETY**
Jerusalem, Israel
Contact: <http://www.akm.ch/ens2000>
- JUNE 25-29 FIFTH EILAT CONFERENCE ON NEW ANTI-EPILEPTIC DRUGS (EILAT V)**
Dan Hotel, Eilat, Israel
Contact: Conference Secretariat: Target Tours Ltd., Eilat V,
P.O. Box 29041, Tel Aviv 61290, Israel
Phone: +972 3 5175150, Fax: +972 3 5175155
E-mail: trgt@netvision.net.il
- JUNE 30- JULY 2 NATURE AND NURTURE IN EPILEPSY AND PSYCHIATRY**
Holmenkollen Park Hotel, Oslo, Norway
Contact: Ms. Kirsten Haga
Department of Anatomy, University of Oslo
E-mail (preferred) k.s.haga@basalmed.uio.no
Fax: +47 22 85 12 78
- SEPT. 13-17 AMERICAN ASSOCIATION OF ELECTRODIAGNOSTIC MEDICINE MEETING**
Philadelphia Marriott, Philadelphia, PA
Phone: (507) 288-0100 Fax: (507) 288-1225
- SEPT. 21-23 EPILEPSY, INFANTILE SPASMS AND DEVELOPMENTAL ENCEPHALOPATHY**
Sheraton Hotel and Towers, Seattle, WA
Contact: Pediatric Epilepsy Research Center,
University of Washington, Box 356470, Seattle, WA 98195-6470
Phone: (206) 221-5364, Fax: (206) 221-5721
E-Mail: perc@u.washington.edu
- OCT. 7-12 4TH EUROPEAN CONGRESS ON EPILEPTOLOGY**
Fortezza da Basso, Firenze, Italy
Phone: +39 06 85832576 - 85832569
Fax: +39 06 85356060
E-Mail: ptscongr@tin.it, E-Mail: eceflo@tin.it
- OCT. 25-28 29TH ANNUAL MEETING, CHILD NEUROLOGY SOCIETY**
Adams Mark Hotel, St. Louis, MO
Contact: Child Neurology Society
3900 Northwoods Drive, Suite 175
St. Paul, MN 55112
Phone: (651) 486-9447 Fax: (651) 486-9436
E-Mail: cns@tc.umn.edu
- NOV. 4-9 SOCIETY FOR NEUROSCIENCE, 30TH ANNUAL MEETING**
New Orleans, LA
Contact: [http://www.sfn.org/info@sfn.org/About the Society](http://www.sfn.org/info@sfn.org/About%20the%20Society)
Phone: (202) 462-6688
- DEC. 1-6 AES ANNUAL MEETING, LOS ANGELES, CA**
Century Plaza Hotel and Tower
Information: www.aesnet.org

Communicate Electronically With AES



AES Home Page

Address: aesnet.org

Log In: Logging in to aesnet.org is easy, and you only have to do it once. Visit the "Members Only" section at aesnet.org/CM.O.D., log in, and save the information to your computer.

Annual Meeting: Information on the 54th Annual Meeting in Los Angeles.

Research: Check out the Surgery and Genetics section of the home page.

Medical Education Book: Medical Education Program materials (Resident Version) are available at aesnet.org/educ/medbook for downloading as PDF files. Individual PowerPoint slides are at aesnet.org/educ/index.

Membership: AES On-Line Membership Roster—"Members On-Line" is updated monthly. Use your user ID and password and have access to the latest addresses for AES members. This is the "Members Only" section.

Practice Management: Patient Assistance Programs, Drug Updates and other articles.

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General: info@aesnet.org

Listservs

Pharmacology:

Pharmacy@aesnet.org
Several committees and SIGs

Fax Number

AES Office: (860) 586-7550

Fax-on-Demand

Information is available on the fax-on-demand service, (860) 586-7575; request the index to see all that's available. For a directory of all of AES's documents, call AES's fax-on-demand and order document 30000.

Genetics, Networks Among Year 2000 Annual Meeting Topics

The first AES Annual Meeting of the millennium, scheduled for December 1-6, 2000 at the Century Plaza Hotel and Tower in Los Angeles, will take up questions of genetics and neuronal networks as part of a rigorous and broad-based program.

The Annual Course on Sunday, December 3, will focus on epilepsy genetics. Sessions are scheduled on genetics of cortical dysplasia, partial epilepsy, and channelopathies; pharmacogenomics; and the AES Gene Discovery Project.

The Investigators' Workshop on Sunday also will offer a session on genetic technologies. The preliminary agenda for the Investigators' Workshop includes presentations on epilepsy classification; glia, neuronal excitability and epilepsy; and neuroimaging and cognitive function localization. Carl Stafstrom, M.D., Ph.D. chairs the Investigators' Workshop and Michael Sperling, M.D., the Clinical Investigators' Workshop.

Epilepsy as a Disorder of Large-Scale Neural Networks is the Presidential Symposium topic, with AES President Susan Spencer, M.D. discussing a "Neural Networks in Human Epilepsy: Evidence and Implications for Treatment." William Theodore M.D. is serving as chair of the Scientific Program, which runs from Monday, December 4 through Wednesday, December 6. Other topics are *Neurostimulation: Existing and Emerging Treatments for Epilepsy*, including transcranial magnetic stimulation and vagus nerve stimulation; and *Psychological Issues in Epilepsy*, such as non-epileptic seizures and behavioral disorders associated with epilepsy.

The AES Antiepileptic Therapy Symposium will present case studies to cover topics on AED use in specific populations such as women and the elderly, treatment of benign childhood seizures, and behavioral pros and cons of AEDs.

The 54th Annual Meeting also offers an extensive group of platform and poster presentations, satellite symposia, and industry-sponsored scientific exhibits focusing on such topics as results of clinical trials and drug development. Three days of exhibits from over 50 commercial, governmental and educational companies will provide attendees with the latest in pharmaceuticals, publications, technology and products in the field of epilepsy.

The historic Century Plaza Hotel will serve as this year's Annual Meeting Headquarters. Located in the fashionable West Side of Los Angeles between Beverly Hills and Santa Monica, the hotel is convenient to a variety of restaurants, shopping and nightlife, as well as the new and richly endowed Getty Center museum. More information on the Annual Meeting and Los Angeles is available through the AES Web site at www.aesnet.org.



Los Angeles offers an exciting venue for the 2000 Annual Meeting.

American Epilepsy Society

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December 1-6

The American Epilepsy Society Announces

Call For Nominations for Distinguished Achievement Awards

The following awards are given annually by the AES, and will be presented at the December 2000 AES Annual Meeting in Los Angeles.

Epilepsy Research Award

A public recognition program funded by the Milken Family Foundation to encourage and reward clinical and basic science investigators whose research contributes importantly to understanding and conquering epilepsy.

William G. Lennox Award

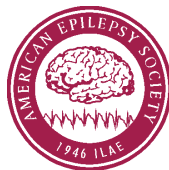
Funded by the William G. Lennox Trust Fund to advance and disseminate knowledge concerning epilepsy in all of its phases presented to an individual who has made a significant contribution to the field of epilepsy.

AES Service Award

Presented to an AES member in recognition of outstanding service in the field of epilepsy (including non-educational and non-scientific) and exemplary contributions to the welfare of AES and its members.

J. Kiffin Penry Award for Excellence in Epilepsy Care

Funded by Abbott Laboratories to recognize an individual whose work has had a major impact on patient care and improved the quality of life for persons with epilepsy.



The following awards are given biennially by the International League Against Epilepsy and the International Bureau for Epilepsy, and will be presented at the May 2001 International Epilepsy Congress in Buenos Aires.

Ambassador for Epilepsy Award

Recognizes outstanding contributions to activities advancing the cause of epilepsy, either at an international level or with an international impact.

Award for Social Accomplishment

Presented to recognize a longstanding record of activities promoting improvement in the social circumstances of people with epilepsy, or a single action resulting in a major breakthrough in improving social conditions for people with epilepsy.

Instructions and forms for submitting nominations for Distinguished Achievement Awards are available at www.aesnet.org or from the American Epilepsy Society, 342 North Main Street, West Hartford, CT 06117.

Please Note: The deadline for receipt by AES of all award nominations is September 1, 2000.