Noninvasive testing, early surgery, and seizure freedom in tuberous sclerosis complex

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ABSTRACT

Background: The unambiguous identification of the epileptogenic tubers in individuals with tuberous sclerosis complex (TSC) can be challenging. We assessed whether magnetic source imaging (MSI) and coregistration of ^{18}F fluorodeoxyglucose PET (FDG-PET) with MRI could improve the identification of the epileptogenic regions noninvasively in children with TSC.

Methods: In addition to standard presurgical evaluation, 28 children with intractable epilepsy from TSC referred from 2000 to 2007 had MSI and FDG-PET/MRI coregistration without extraoperative intracranial EEG.

Results: Based on the concordance of test results, 18 patients with TSC (64%) underwent surgical resection, with the final resection zone confirmed by intraoperative electrocorticography. Twelve patients are seizure free postoperatively (67%), with an average follow-up of 4.1 years. Younger age at surgery and shorter seizure duration were associated with postoperative seizure freedom. Conversely, older age and longer seizure duration were linked with continued seizures postoperatively or prevented surgery because of nonlateralizing or bilateral independent epileptogenic zones. Complete removal of presurgery MSI dipole clusters correlated with postoperative seizure freedom.

Conclusions: Magnetic source imaging and ^{18}F fluorodeoxyglucose PET/MRI coregistration noninvasively localized the epileptogenic zones in many children with intractable epilepsy from tuberous sclerosis complex (TSC), with 67% seizure free postoperatively. Seizure freedom after surgery correlated with younger age and shorter seizure duration. These findings support the concept that early epilepsy surgery is associated with seizure freedom in children with TSC and intractable epilepsy. *Neurology*® 2010;74:392-398

GLOSSARY

AED = antiepileptic drug; **ANOVA** = analysis of variance; **FDG-PET** = ^{18}F fluorodeoxyglucose PET; **MEG** = magnetoencephalography; **MSI** = magnetic source imaging; **TSC** = tuberous sclerosis complex; **UCLA** = University of California, Los Angeles.

Up to 90% of patients with tuberous sclerosis complex (TSC) have epilepsy,¹ with a significant proportion having medication-resistant epilepsy. For children whose epilepsy is medically refractory, surgical resection of the epileptogenic tubers and surrounding cerebral cortex may offer seizure freedom.²⁻⁷ However, the unambiguous identification of the epileptogenic regions can be challenging in children with TSC. Consequently, many patients with TSC require invasive EEG monitoring^{8,9} or are denied surgery.

Our center has focused on exploring newer noninvasive methods to detect the epileptogenic zones among the many cortical tubers in patients with TSC. This includes the use of magnetic source imaging (MSI)¹⁰ and ^{18}F fluorodeoxyglucose PET (FDG-PET)/MRI coregistration¹¹ as separate diagnostic tests. In this study, we compare the use of these 2 techniques separately and in combination in the presurgical evaluation of children with TSC and intractable epilepsy.

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Study funding: Supported by NIH grants K23 NS051637 to J.Y.W., R01 NS046516 to R.S., and R01 NS038992 and P01 NS002808 to G.W.M.

Disclosure: Author disclosures are provided at the end of the article.

METHODS All children with TSC and medically refractory epilepsy referred to the University of California, Los Angeles (UCLA) Pediatric Epilepsy Surgery Program from July 2000 to June 2007 were consecutively and prospectively recruited. All children had intractable epilepsy, defined as monthly or greater seizure frequency, and had failed a minimum of 3 first-line antiepileptic drugs.

Patient evaluation. The institutional review board at UCLA approved the use of human subjects and waived the need for written informed consent, because all testing was deemed clinically relevant for patient care. There were no clear indications at the time of referral that any child would be a surgical candidate, and all children with TSC referred during the study period underwent a presurgical evaluation.

Patients with TSC underwent a standardized presurgical evaluation, which consisted of inpatient video-EEG telemetry, high-resolution cranial MRI (1.5 T), and FDG-PET. All children with TSC demonstrated multiple, often bihemispheric tubers on neuroimaging, and neuroimaging could not detect which tubers were epileptogenic. On video-EEG, the location of interictal abnormalities was multifocal and nonlateralizing in all children with TSC except 2 (table 1). The ictal video-EEG was the most important test because ictal onsets were localized to a quadrant in 39% ($n = 11$), lateralized to a cerebral hemisphere in 36% ($n = 10$), and nonlocalized in 25% ($n = 7$). At our institution, ictal EEG localization was considered insufficient to proceed with surgical resection without confirmatory data. Therefore, for this cohort of patients with TSC, the standard presurgical evaluation with video-EEG, FDG-PET, and MRI as individual tests was considered insufficient in identifying the epileptogenic tubers or zone by the consensus opinion of members of the UCLA Pediatric Epilepsy Surgery Program.

As part of our expanded protocol, every attempt was made to obtain MSI and FDG-PET/MRI coregistration for every patient with TSC. When appropriate, neuropsychological assessment, intracarotid amobarbital test (Wada), and functional MRI were also obtained. α -Methyl tryptophan PET was not used in this study.

Decisions for surgical candidacy and the resection zones were made by group consensus consisting of a case conference attended by adult and pediatric epileptologists, adult and pediatric epilepsy neurosurgeons, neuroradiologist, and neuropsychologist. Surgical decisions were based on all test results for each patient with TSC. Two or more tests localizing to a single tuber or group of tubers in close proximity were typically necessary to propose that a patient was a surgical candidate, balanced by the potential loss of motor, sensory, visual, and language functions.

Outcome. Postoperative follow-up occurred at 6 months, 12 months, 24 months, and 5 years after surgery, and in the majority of children, clinic visits occurred more frequently. Seizure outcome was noted at each of these visits, and medications were adjusted when appropriate.

Data analysis. Statistical results were obtained with Statview software, version 5.0.1 for Windows (SAS Institute Inc., Cary, NC). A priori, significant results were considered at $p < 0.05$.

RESULTS Cohort characteristics. A total of 28 children (aged 18 years and younger) with TSC and intractable epilepsy underwent presurgical evaluation from July 2000 to June 2007 (table 1). There were 14 boys, with an average age of 5.5 years (range 0.75–17 years) at the time of evaluation. Two children had prior resection at another institution, 1 had his entire evaluation at

UCLA but had surgery at another institution closer to home without invasive studies, and 1 patient had 3 prior nonresective surgeries at UCLA (vagal nerve stimulator implantation, 2-staged corpus callosotomy) before his resective surgery.

The MRI studies were assessed for tuber counts. MRI studies demonstrated 20 or more tubers for all children with TSC, except for patient 10, whose tuber count was 10 to 20, and patient 13, whose tuber count was slightly less than 10. Tubers were bihemispheric in all 28 patients with TSC. All 28 patients with TSC had FDG-PET/MRI coregistration, and 18 had both MSI and FDG-PET/MRI coregistration. Thirteen of the 18 children with TSC who had both tests went on to have resective surgery (table 1).

Of the 28 children with TSC who had presurgical evaluations, 10 did not proceed to resective surgery (table 1). Three (patients 19–21) had temporary cessation of seizures during their surgical evaluation, and surgery was not further pursued even when seizures recurred or changed (conversion of infantile spasms to complex partial seizures in 1 case). Another 6 children were not offered surgery after additional MSI and FDG-PET/MRI coregistration tests because of nonlateralizing results or multiple bilateral independent sites of interictal discharges. One child (patient 28) was offered surgery after additional MSI and FDG-PET/MRI coregistration detected a surgical target, but the family declined the offer because of the size of the proposed resection. All 10 of these children continued to have seizures at their last follow-up visit.

The remaining 18 children were offered and underwent resective surgery using the MSI and FDG-PET MRI coregistration in planning the surgery (figure), and 12 became seizure free (67%). Their average ($\pm$ SD) postoperative follow-up was 4.1 ± 1.4 years, with a range of 1.75 to 8.50 years.

Of the 12 seizure-free children, their antiepileptic drugs (AEDs) were reduced gradually after surgery. Preoperatively, the average number of AEDs was 2.2 ± 0.7 , which was reduced to an average of 0.7 ± 0.6 AEDs postoperatively (paired t test, $p < 0.0001$) at the last follow-up visit. Five postsurgical TSC children were using no AEDs and were seizure free.

Of the 6 children who did not gain seizure freedom after their first surgery, their seizures all returned within weeks after surgery. All except 1 underwent a second presurgical evaluation. Two of 5 children had seizures that were insufficiently localized for a second resective surgery, and they subsequently had a vagal nerve stimulator implanted. The remaining 3 children had localizable seizures, all originating from different tubers removed in the first

Table 1 Clinical characteristics and presurgical evaluation

Patient	Age at presurgical evaluation, y	Seizure duration, y	VEEGii/VEEGi	MEGi	FDG-PET/MRI coregistration	Resection
Postoperative, sz free						
1	0.8	0.8	Nonlat/Lat		Nonlocalizing	L H
2	1.0	0.9	Nonlat/Loc	L O	L TO	L TPO
3	1.3	1.1	Lat/Lat	R P	Nonlocalizing	R P
4 ^a	1.6	1.3	Nonlat/Lat	R TP	R P	R TP
5	1.8	1.8	Nonlat/Loc	L FC (i)	Nonlocalizing	L FC
6	2.6	2.2	Nonlat/Loc		R TP	R T
7	3.3	3.2	Nonlat/Lat	L P	L P	L TP
8	3.7	3.4	Nonlat/Loc	L FTP	L T	L TPO
9	4.8	4.5	Nonlat/Nonlat		R T	R T
10	5.4	3.9	Lat/Lat	L P	Nonlocalizing	L P
11 ^b	8.1	6.6	Nonlat/Nonlat	R FT	L T	R T
12	8.8	8.8	Nonlat/Lat	L P	L P	L P
Postoperative, cont sz						
13	2.2	1.8	Nonlat/Loc	R FC	L F, R F	L F
14 ^c	3.4	3.2	Nonlat/Loc		R T	R TP
15 ^c	4.6	4.3	Loc/Loc	L FCP	Nonlocalizing	L FC
16	9.6	9.3	Nonlat/Lat	L T (i)	L T	L T
17 ^c	10.4	10.0	Nonlat/Loc	R FT	L T	R TP
18	10.6	10.4	Nonlat/Lat		Nonlocalizing	L T
No surgery, cont sz						
19	1.3	0.8	Nonlat/Lat	R FP, L P	Nonlocalizing	
20	1.8	1.2	Nonlat/Loc	No dipole	Nonlocalizing	
21	2.2	1.8	Nonlat/Loc	No dipole	Nonlocalizing	
22 ^a	3.8	3.8	Nonlat/Nonlat	B indep dipoles	Nonlocalizing	
23	5.8	5.3	Nonlat/Nonlat		Nonlocalizing	
24	7.8	7.4	Nonlat/Lat		Nonlocalizing	
25	7.9	7.7	Nonlat/Nonlat		Nonlocalizing	
26	8.7	6.2	Nonlat/Nonlat		Nonlocalizing	
27	13.8	13.5	Nonlat/Loc		Nonlocalizing	
28	17.3	15.8	Loc/Nonlat	L F	Nonlocalizing	

Abbreviations: B = bilateral; C = central; cont = continued; F = frontal; FDG-PET = ¹⁸fluorodeoxyglucose PET; H = hemisphere; i = ictal; ii = interictal; indep = independent; L = left; lat = lateralizing (findings limited to 1 hemisphere); loc = localizing (findings limited to 1 quadrant); MEG = magnetoencephalography; nonlat = nonlateralizing (bilateral independent or generalized findings); O = occipital; P = parietal; R = right; sz = seizure; T = temporal; UCLA = University of California, Los Angeles; VEEG = video-EEG.

^aPrior resection at another institution.

^bAll evaluation at UCLA but resection at another institution.

^cFirst and second resection at UCLA.

surgery and not apparent in the first presurgical evaluation including MSI and FDG-PET/MRI coregistration. All 3 children underwent a second resective surgery (table 1), which removed tubers distant from the first surgical resection in patient 14 (who continued to have seizures after the second resection) and

extended and enlarged the previous resection zones in 2 patients (patient 15 continued to have seizures after the second resection, whereas patient 17 is seizure free 11 months after the second resection).

All surgical pathologic specimens from all resections, including first and second operations, found cortical tubers. One child had the additional finding of hemimegalencephaly (patient 1, table 1), and a second child had additional cortical dysplasia that was normal on MRI and not apparent as tubers or cortical dysplasia (patient 8, table 1). Both children with the additional pathologic findings achieved seizure freedom postoperatively.

Correlating clinical findings to seizure outcome. Clinical characteristics were compared between children who were seizure free and not seizure free after surgery (table 2). Age at the time of surgery differed, with a younger age for those who were seizure free (4.1 ± 2.9 years) compared with those whose seizures continued postoperatively (7.9 ± 4.0 years; *t* test, *p* = 0.036). Seizure duration, defined as the time from age at seizure onset to age at surgery, also differed, with a shorter seizure duration for those who attained seizure freedom (3.7 ± 2.7 years) compared with those not seizure free after surgery (7.6 ± 4.0 years; *t* test, *p* = 0.028).

When these comparisons included children who were not offered surgery (table 2), using age at presurgical evaluation rather than age at surgery, those who attained seizure freedom were the youngest (3.6 ± 2.7 years), those who continued to have seizures postoperatively were intermediate in age (6.8 ± 3.8 years), and those who were not offered surgery were the oldest (8.0 ± 3.3 years; analysis of variance [ANOVA], *p* = 0.023).

Similarly for seizure duration, modified to reflect the time span between age at seizure onset and age at presurgical evaluation, those who were seizure free had the shortest seizure duration (3.2 ± 2.5 years), those who continued with seizures had intermediate seizure duration (6.5 ± 3.8 years), and those who were not offered surgery had the longest seizure duration (7.3 ± 3.4 years; ANOVA, *p* = 0.024).

Age at seizure onset did not differ among these groups, and neither did seizure frequency on the video-EEG, seizure type, active infantile spasms, history of infantile spasms, use of vigabatrin, gender, type of surgical resection, side of resection, or tuber count (table 2). There also was no difference in the postoperative follow-up period between the 2 postoperative groups (ANOVA, *p* = 0.75). Similarly, there did not seem to be referral or patient selection bias, e.g., no difference in age at the time of presurgi-

A 3-year-old girl with tuberous sclerosis complex began having seizures at age 7 weeks. She did not have infantile spasms. Her seizures consisted of 8 to 10 complex partial seizures daily, lateralized to the left hemisphere without further clear localization within that hemisphere. Many abnormal interictal findings included diffuse slowing during wakefulness, intermittent slowing over the left anterior quadrant, and spike discharges seen independently over the left central and frontal regions as well as right central, frontal, and temporal regions. Her brain MRI (A) showed greater than 20 tubers over both hemispheres, and her 18 fluorodeoxyglucose PET (FDG-PET) (not shown) showed multiple focal areas of moderate to severe hypometabolism over the left occipital lobe and bilateral frontal, parietal, and temporal lobes corresponding to these tubers. Her FDG-PET/MRI coregistration (B) showed that the largest volume of hypometabolism, relative to actual MRI tuber size, was located in the left parietal lobe, not the right central tuber as may have been expected from the MRI alone. Her interictal magnetic source imaging (C) showed a large cluster of dipoles over the left parietal tuber with no dipoles elsewhere. She underwent a left craniotomy, with a group of tubers visualized over the left parietal lobe and adjacent posterior temporal lobe. Her intraoperative electrocorticography showed intermittent slowing diffusely over the temporal lobe, and continuous epileptiform discharges over the anterior parietal tuber and adjacent posterior temporal tuber, along with spikes and paroxysmal fast activity over the parietal tubers. The parietal tubers along with the posterior temporal tuber were removed, and the patient has been seizure free for more than 3 years after surgery.

cal evaluation between the 2 halves of the 7-year inclusion period (ANOVA, $p = 0.77$).

Magnetic source imaging. Eighteen children with TSC had MSI. All AEDs were maintained at their usual doses for the MSI study. Eight of the MSI studies were performed at Scripps, and 10 were performed at UCSF. MSI findings did not differ between the 2 facilities when dipole yield, correlation with video-EEG localization, correlation with FDG-PET hypometabolic locations, and correlation with seizure freedom were individually compared.

Four MSI studies were not localizing for presurgical evaluation, either because no dipoles were detected (2 studies) or because dipoles were multifocal (2 studies). In the remaining 14 MSI studies, interictal dipoles clustered over a single tuber or a single group of closely located tubers (6 at Scripps and 8 at UCSF). For this study, dipole clusters were defined as 5 or more epileptiform dipoles in 1 or contiguous subbar regions of the brain.¹² By chance, patients 5 and 16 had seizures during their magnetoencephalography (MEG) studies (table 1), and the ictal onset zone closely matched the region localized by the interictal dipoles in the same study.

Whereas 1 patient who had MSI elected not to undergo surgery, the other 13 children underwent surgery, with the final resection based on all noninvasive tests, and the intraoperative electrocorticography. Seven patients had complete removal of the dipole clusters and all became seizure free postoperatively, 5 children had partial removal of the dipole clusters (limited resection for 1 because of eloquent cortex [patient 16 with the ictal MEG study]) and 2 achieved postoperative seizure freedom, and 1 child had no removal of the dipole cluster and continued with seizures postoperatively (table 1). Thus, complete removal of MSI dipole clusters correlated with postoperative seizure freedom (χ^2 , $p = 0.025$).

For the 8 children whose video-EEG ictal onset was localized to a quadrant and had MSI, MSI confirmed that localization in 6 (75%) and was nonlocalizing in 2 (table 1). For the 7 children with MSI whose video-EEG ictal onset was lateralized to 1 hemisphere but not further localized within that hemisphere, MSI provided localization in 6 and was nonlocalizing in 1. For the 3 children whose video-EEG ictal onset was nonlateralized, MSI provided localization in 2 and was nonlocalizing in 1. Thus, for these 2 groups of children with

Table 2 Clinical characteristics comparison^a

Clinical characteristic	Postoperative, sz free (n = 12)	Postoperative, cont sz (n = 6)	No surgery, cont sz (n = 10)	p Value
Age at surgery, y	4.1 ± 2.9	7.9 ± 4.0	NA	0.036 ^b
Sz duration at time of surgery, y	3.7 ± 2.7	7.6 ± 4.0	NA	0.028 ^b
Age at presurgical evaluation, y	3.6 ± 2.7	6.8 ± 3.8	8.0 ± 3.3	0.023 ^b
Sz duration at time of evaluation, y	3.2 ± 2.5	6.5 ± 3.8	7.3 ± 3.4	0.024 ^b
Age at sz onset, y	0.4 ± 0.5	0.3 ± 0.1	0.7 ± 0.7	0.33
VEEG sz frequency, no./d	3.6 ± 4.4	3.8 ± 2.0	3.8 ± 4.8	0.99
No. of failed AEDs	5.7 ± 1.5	7.7 ± 3.0	5.8 ± 2.2	0.16
Tuber count category-20+ tubers	11	5	10	0.28
Sz type-complex partial seizures	8	4	8	0.76
Active infantile spasms	2	1	1	0.73
History of infantile spasms	5	2	3	0.84
Use of vigabatrin	7	6	5	0.11
Gender-female	5	3	6	0.69
Type of surgical resection-lobar	6	3	NA	0.99
Hemisphere of resection-left	7	4	NA	0.73

Abbreviations: AED = antiepileptic drug; cont = continued; NA = not applicable; sz = seizure; VEEG = video-EEG.

^aData are presented as mean ± SD.

^b $p < 0.05$.

hemispheric or generalized ictal onset, MSI was able to provide further localization over ictal EEG in 8 of 10 children (80%).

FDG-PET/MRI coregistration. All 28 children with TSC had coregistration of their FDG-PET and their structural MRI. Sixteen of these coregistrations were nonlocalizing because no single tuber or group of tubers had the larger volume of hypometabolism relative to the actual tuber volume on MRI. The remaining 12 studies found the largest volume of hypometabolism, relative to the actual tuber volume on MRI, over a single tuber or group of tubers. Of these 12 patients, 8 had complete removal of the hypometabolic volume and 6 became seizure free postoperatively. Two children had partial removal of the hypometabolism and 1 achieved postoperative seizure freedom, and 2 children had no removal of the hypometabolic volume and 1 was seizure free postoperatively (table 1). Complete removal of hypometabolism on the FDG-PET/MRI coregistration did not correlate with postoperative seizure freedom (χ^2 , $p = 0.69$).

For the 11 children whose video-EEG ictal onset was localized to a quadrant, FDG-PET/MRI coregistration confirmed that localization in 5 and was nonlocalizing in 6 (45%). For the 10 children whose video-EEG ictal onset was lateralized to 1 hemisphere but not further localized within that hemisphere, FDG-PET/MRI coregistration provided further localization in 4 and was nonlocalizing in 6. For the 7 children whose video-EEG ictal onset was

nonlateralized, FDG-PET/MRI coregistration provided localization in 2 and was nonlocalizing in 5. Thus, for these 2 groups of children with hemispheric or generalized ictal onset, FDG-PET/MRI coregistration was able to provide further localization over ictal EEG in 6 of the 17 children (35%).

Seven patients had combined MSI and FDG-PET/MRI coregistration findings that colocalized over a single area of the cerebral cortex. Six (86%) were seizure free after resection (table 1).

Complications. There were no surgical mortalities, and there were no known surgical complications, including no CSF shunts, no transient or permanent motor or sensory deficit, no language deficits, and no infections.

DISCUSSION This study supports the notion from prior studies²⁻⁹ that despite multiple cortical tubers and therefore multiple potential seizure foci, children with TSC and intractable epilepsy can be successfully operated on and achieve seizure freedom. Our findings further indicated that, for a proportion of children with TSC and intractable epilepsy, seizures that were not localized with standard presurgical evaluations were able to be localized with the addition of noninvasive MSI and FDG-PET/MRI coregistration. Of the children who underwent surgery, 67% became seizure free postoperatively. What is unknown is whether these patients with TSC who we treated with noninvasive tests would also have their seizures localized with intracranial recording. Thus,

these are 2 operative approaches that may or may not complement one another.

Our results may be somewhat limited because of the relatively small cohort of TSC children with intractable epilepsy and the short follow-up period after surgery. Studies with larger groups and longer postoperative follow-up periods may be needed to further confirm our findings. Despite these limitations, this study demonstrates that postoperative seizure freedom in TSC can be achieved without invasive recording by using MSI and FDG-PET/MRI coregistration. Indeed, compared with the 68% postoperative seizure freedom achieved with the typically 3-staged and often bilateral invasive intracranial recording approach,⁹ our noninvasive approach had no known surgical complications and had a similar seizure freedom rate of 67% with a longer postoperative follow-up period. Furthermore, it is interesting to note that complete removal of MSI dipole cluster correlated with postoperative seizure freedom in our study. This finding supports the notion that MSI yields highly localizing information in a subgroup of epilepsy surgery candidates with TSC who typically require intracranial recording. Thus, our presurgical approach may potentially replace invasive monitoring for seizure localization in many patients with TSC.¹²

This study also shows that younger age at surgery and shorter seizure duration was associated with higher rate of seizure freedom after surgery. Conversely, longer seizure duration was associated with lower rate of seizure freedom after surgery. Furthermore, the group of children with TSC not offered surgery was the oldest group and had the longest seizure duration. This age-dependent phenomenon of surgery candidacy and subsequent postoperative seizure freedom has not been previously reported to our knowledge. Although previous studies did not show a significant age-dependent correlation, 1 did show a trend of seizure freedom with younger age at surgery ($p = 0.09$), consistent with our findings.⁹ Seizure duration seems to have an important clinical role in the evolution of seizures in TSC. Why there is an age-dependent phenomenon in children with TSC and intractable epilepsy is not clear. A plausible explanation may be the secondary epileptogenesis theory set forth by Morrell^{13,14} or the concept of an epileptic network as a result of interconnectivity and entrainment between different epileptogenic foci,¹⁵ but further validation is needed to better determine the mechanism of this age-dependent phenomenon.

For the practicing neurologist, our study indicates that a noninvasive approach with MSI and FDG-PET/MRI coregistration enabled a proportion of children with TSC, initially not considered surgery candidates with our standard presurgical evaluation, to undergo

surgery with a 67% seizure freedom outcome comparable to that from invasive EEG recording of ictal onsets. The finding that younger age and shorter seizure duration at the time of presurgical evaluation further supports the notion that early consideration for surgery in children with TSC and medically refractory epilepsy may be warranted for the best seizure outcome, but further studies and validations are needed.

AUTHOR CONTRIBUTIONS

Statistical analysis was performed by Joyce Y. Wu and Gary W. Mathern.

DISCLOSURE

Dr. Wu receives research support from the NIH (NINDS K23 NS051637 [PI] and NIMH R34 MH089299 [Coinvestigator]) and a Novartis-sponsored clinical trial (Site PI). Dr. Salamon reports no disclosures. Dr. Kirsch received royalties from the publication of *The Johns Hopkins Atlas of Digital EEG: An Interactive Training Guide* (The Johns Hopkins University Press, 2007); has served as a consultant to GLG Pharma, LLC; and receives research support from the NIH (NINDS K23 NS047100 [PI] and NINDS 5U01NS053998 [Site PI]) and from the University of California at San Francisco. Ms. Mantle reports no disclosures. Dr. Nagarajan serves as an Associate Editor of *Frontiers in Human Neuroscience*; and receives research support from the NIH (R01DC006435 [PI] and R01DC004855 [PI]) and from the NSF. Ms. Kurelowech and Dr. Aung report no disclosures. Dr. Sankar serves on scientific advisory boards for and has received funding for travel from Ortho-McNeil-Janssen Pharmaceuticals, Inc., NeuroTherapeutics Pharma, Inc., and Valeant Pharmaceuticals International; has served as a Contributing Editor of *Epilepsy Currents* and on the editorial board of *Epilepsia*; receives royalties from publication of *Pediatric Neurology*, 3rd ed. (Demos Publishing, 2008); serves on speakers' bureaus for and has received speaker honoraria from Ortho-McNeil-Janssen Pharmaceuticals, Inc., Valeant Pharmaceuticals International, UCB, and Eisai Inc.; and receives research support from Valeant Pharmaceuticals International, Marinus Pharmaceuticals, Inc., the NIH/NINDS (NS046516 [PI], NS045911 [Co-PI], NS059505 [Coinvestigator], and MH079933 [Coinvestigator]), and from the Epilepsy Foundation. Dr. Shields has received research grants from and served on advisory boards for Lundbeck pharmaceuticals and Questcor pharmaceuticals. Dr. Mathern serves on the editorial board of *Neurology*; and receives research support from the NIH (R01 NS 38992 [PI] and P01 NS002808 [Coinvestigator]).

Received February 22, 2009. Accepted in final form November 5, 2009.

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CDC, AAN to Health Care Professionals: Monitor Patients for GBS

The Centers for Disease Control and Prevention (CDC) and the American Academy of Neurology (AAN) collaborated to reach out to neurologists across the US to monitor and report any possible new cases of Guillain-Barré syndrome (GBS) following 2009 H1N1 flu vaccination.

Neurologists and health care professionals nationwide who diagnose patients with vaccine-associated GBS should use the CDC and FDA Vaccine Adverse Event Reporting System (VAERS) to report their observations.

In addition, neurologists and all health practitioners in the 10 Emerging Infections Program (EIP) states—California, Connecticut, Maryland, Minnesota, New Mexico, New York, Colorado, Oregon, Georgia, and Tennessee—are asked to report all new cases of GBS, regardless of vaccination status, to their state’s surveillance officer.

The AAN hosted a series of webinars providing an in-depth look at H1N1 vaccination and how it may pose a risk for GBS and information about the vaccination monitoring campaign.

For additional information about the monitoring campaign, or to watch the webinars or download VAERS form and information on reporting to surveillance officers in your state, visit the AAN’s GBS toolkit page, www.aan.com/view/gbstoolkit.