Is postresective intraoperative electrocorticography predictive of seizure outcomes in children?

Clinical article

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Object. Intraoperative electrocorticography (ECoG) is commonly used to guide the extent of resection, especially in lesion-associated intractable epilepsy. Interictal epileptiform discharges on postresective ECoG (post-ECoG) have been predictive of seizure recurrence in some studies, particularly in adults undergoing medial temporal lobectomy, frontal lesionectomy, or low-grade glioma resection. The predictive value of postresective discharges in pediatric epilepsy surgery has not been extensively studied.

Methods. The authors retrospectively examined the charts of all 52 pediatric patients who had undergone surgery with post-ECoG and had more than 1 year of follow-up between October 1, 2003, and October 1, 2009.

Results. Of the 52 pediatric patients, 37 patients showed residual discharges at the end of their resection and 73% of these patients were seizure free, whereas 15 patients had no residual discharges and 60% of them were seizure-free, which was not significantly different (p = 0.36, chi-square).

Conclusions. Electroencephalography-guided surgery was associated with excellent postsurgical outcome. Although this sample size was too small to detect a subtle difference, absence of epileptiform discharges on post-ECoG does not appear to predict seizure freedom in all pediatric patients referred for epilepsy surgery. Future studies with larger study samples would be necessary to confirm this finding and determine whether post-ECoG may be useful in some subsets of pediatric epilepsy surgery candidates.

Key Words • epilepsy surgery • intraoperative electrocorticography • postresective • neocortical • extratemporal

Epilepsy is a relatively common disorder in children, with an incidence of 82 per 100,000 people,25 and approximately 20% of these children will become refractory to medications.23 Of those with medically intractable epilepsy, many may be candidates for resection of the seizure onset zone, a procedure that is potentially curative and may allow them to discontinue medications. Prediction of long-term seizure outcome remains suboptimal in epilepsy surgery.

Intraoperative ECoG is the monitoring of brain activity with electrodes directly on the brain during the surgery. It can be used to evaluate resection margins for ongoing epileptiform discharges and to define the epileptic zone. It is typically performed prior to resection (pre-ECoG) and can be repeated intraoperatively after resection is complete (post-ECoG). There is disagreement on the superiority in determining resection margins and outcomes of surgery as guided by either intraoperative ECoG or extraoperative ECoG from chronic implantations.25 The subpopulations of patients best helped by ECoG likely have more focal pathology. The risks of a prolonged single operation need to be weighed against those of multiple surgeries and extraoperative monitoring. Patients with more diffuse diseases may not have an increase in benefits, but rather a larger deficit, if subjected

Abbreviations used in this paper: ECoG = electrocorticography; EEG = electroencephalography; pre-ECoG = prereseective ECoG; post-EEG = postresective ECoG.

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to a broader resection. Interpretation of intraoperative ECoG is complicated by the effect of the anesthetics and medications used during the procedure. The important ECoG measures are also changing as recording technology advances. Potential ECoG characteristics undergoing investigation include the presence or absence of interictal spikes, quantitation of spike frequency, and the presence of high-frequency “fast ripples” or gamma discharges in the epileptogenic zone.

Electrocorticography may be helpful for patients without lesions, but many institutions will only operate on such patients after extraoperative intracranial monitoring demonstrates a reproducibly localized seizure onset zone. A dogmatic approach raises the barriers to care for some patients who have medically intractable focal onset epilepsy. Electrocorticography is used exclusively as the operative electrophysiological modality at some institutions, while at others it is never used. Proponents of ECoG argue it can alleviate the need for invasive EEG monitoring in some of these patients, which merits validation by other centers.

Electrocorticography is not the sole predictor of surgical outcomes. The presence of a lesion on MRI, and its complete resection, often also predicts seizure freedom. Location of the resection may influence outcomes, with temporal resections having better outcomes than other locations. Despite using pre-ECoG, many institutions are not using it after resection, based on the view that it will lead to excessive resection.

Some studies have shown that interictal epileptiform discharges on post-ECoG are predictive of seizure recurrence in adults receiving temporal lobe resection or those with frontal lobe lesions. Other studies have shown improved outcomes with the removal of discharges on post-ECoG in patients with low-grade gliomas or in all pathologies and all locations. Other studies have not shown post-ECoG discharges to be predictive of seizure recurrence.

There is a need for more data from children, as few case series include more than 50 patients. Most children with medically intractable seizures also have extratemporal epilepsy. Intercitial preoperative pediatric extrapetotal ECoG spike frequency may give additive clinical impact to ictal ECoG and neuroimaging data. Electrocoercicography-augmented lesionectomies for pediatric ganglioglioma may have better seizure control for temporal lesions, although it is less helpful in other locations.

The approach of guiding a resection by discharges on post-ECoG implies that leaving behind significant abnormalities would be a predictor of bad outcomes. However, “chasing spikes” may lead to greater morbidity by expanding the resection beyond the seizure onset zone. We do not seek to address the debate between the use of ECoG and extraoperative monitoring, but rather the utility of pre-ECoG versus pre- and post-ECoG, particularly in children. We hypothesized that the presence of epileptiform discharges on post-ECoG is predictive of seizure recurrence in children with extratemporal, as well as temporal, onset seizures.

Methods

Study Sample

We retrospectively examined the charts of all patients who had undergone epilepsy surgery with ECoG at Seattle Children’s Hospital between October 1, 2003, and October 1, 2009. This time period started with the implementation of our current strategy and ended to allow more than 1 year of follow-up. We retrospectively reviewed our operative experience under an institutional review board–approved protocol. Patients who did not have adequate follow-up were excluded from the study.

We reviewed the charts for patient demographic data, age at surgery, lesion, presence on neuroimaging, location of surgery, type of surgery, pathology, and seizure status at most recent follow-up. Fluorodeoxyglucose-PET was used to assist focus localization in almost all nonlesional cases.

Electrocorticography Procedure

Electrocorticography was performed by placement of either electrode strips or free-floating platinum electrodes (both made by Ad-Tech Medical Instrument Co. and Integra LifeSciences Co.) at the margins of resection. Typically 12 electrodes were used to record around the resection cavity at the direction of the surgeon (J.G.O.). Recording averaged 9 minutes and 31 seconds (range 2 minutes 48 seconds to 29 minutes 27 seconds ± 7 minutes 27 seconds) after resection was complete. The EEG recording was obtained using 32- or 128-channel Telefactor (Grass Technologies) or Xltek (Natus Medical Incorporated) digital systems. Sampling frequencies ranged from 200 to 2000 Hz. Post-ECoG was not performed if the pre-ECoG was not actively spiking. Resection was based on the preoperative extraoperative and/or intraoperative ECoG, and postresection spiking tissue was not removed unless the spikes were isolated to the immediate resection boundary. The interpretation report of the ECoG by the clinical epileptologist was reviewed regarding the presence or absence of postresection spikes and/or sharp waves. When the digital traces could be retrieved, the ECoG recordings themselves were reviewed for spikes and/or sharp waves by 1 author (C.D.W.), who was blinded to the original ECoG results and the outcomes.

Outcome Assessment

Outcomes were measured as seizure freedom, measured by the Engel classification system as Class I, meaning seizure free with or without residual auras versus all other outcomes at most recent follow-up. For statistical analysis, the Fisher exact test for small cell counts was performed using Graphpad (http://www.graphpad.com/quickcalcs/contingency1.cfm). Interrater agreement was measured using the Online Kappa Calculator (http://justusrandolph.net/kappa). For 1-way ANOVA the Free Statistics Calculators website was used (http://danielsoper.com/statcalc3/default.aspx). A probability value < 0.05 was considered statistically significant.
Results

During the 6 years studied, 161 resective epilepsy surgeries were performed at our center, of which 91 involved ECoG on 87 patients. We used extraoperative monitoring with grids followed by ECoG in 27 patients. Only pre–ECoG was performed in 26 surgeries, while 75 had both pre- and post-ECoG. We collected more than 1 year of follow-up data on 52 patients who underwent post-ECoG, of whom 28 were females (54%). Mean age at surgery was 9.3 years (range 3 months to 17.4 years). There were lesions detected on neuroimaging in 46 (88%) of the patients. Resections were performed in 51 patients, and 1 patient underwent multiple subpial transections due to seizure onset over eloquent cortex. The locations of resection or multiple subpial transections are listed in Table 1. Our records could not reliably separate medial from lateral temporal lobe recordings. Our patients who underwent parietal resection had better outcomes, although there was not a significant difference in seizure freedom based on location (p = 0.123, 1-way ANOVA), nor was the location associated with presence of spikes on post-ECoG (p = 0.282, 1-way ANOVA). Average length of follow-up was 3 years.

The digital ECoG recordings were reviewed in 47 patients (90%). Second evaluations concurred with the initial clinician’s interpretation in 45 patients (κ = 0.893), and 2 patients were reclassified from no post-ECoG discharges to having post-ECoG discharges. For the other 5 patients, the initial interpretation was used to classify the presence of post-ECoG discharges.

The patients’ histopathological results, presence of postresection spikes on ECoG, and seizure outcomes are listed in Table 2. Residual discharges were present on post-ECoG in 37 patients and 73% of them were seizure free; there were 15 patients who had no residual discharges on post-ECoG and 60% of them were seizure free. The OR of seizure freedom among those who had residual epileptiform discharges on post-ECoG versus the odds of seizure freedom among those who did not was calculated as (27/10)/(9/6) = 1.80 (95% CI 0.509–6.361), in the opposite direction of the hypothesis, but was not statistically significant (p = 0.36, chi-square).

The presence of a ganglioglioma was associated with better outcomes than other pathologies (p = 0.01, Fisher exact test for small cell counts), despite 80% of them showing spikes on post–ECoG. There was a nonsignificant trend toward patients who had lesions on neuroimaging having a better seizure-free rate (74%), while only 33% of the nonlesional patients were seizure free (p = 0.06, Fisher exact test for small cell counts).

Discussion

While our sample size was insufficient to detect a small difference, absence of epileptiform discharges on post–ECoG does not appear to predict seizure freedom in all pediatric patients referred for epilepsy surgery. In fact, our patients with postresective discharges did slightly better than those without. The presence of discharges on pre–ECoG was predictive of better outcomes in patients with dysembryoplastic neuroepithelial tumors.70 Future studies with larger samples are necessary to confirm this finding and to determine whether post–ECoG may be useful in subsets of pediatric epilepsy surgery candidates. In particular, we did not specifically study post–ECoG investigation of the medial temporal lobe. Residual activity in the hippocampus during medial temporal lobectomy in adults is associated with outcome in some studies4,15,25 but not in others.5,12,14,18,25,37,39,43 Our data do not address that finding adequately. Our data suggest that post–ECoG is not predictive of outcome in extratemporal, neocortical resections, which comprise the majority in pediatric epilepsy surgery, as has been suggested elsewhere.22

Our data are consistent with the observation of Marsh et al.24 that interictal EEG spikes on extraoperative intracranial recordings identify the region of electrophysiographic seizure onset in some, but not all, pediatric epilepsy patients. Some papers have suggested amplitude, frequency,30 or morphology37 of discharges is predictive of seizure recurrence, although this has not been found in other studies.15 Post–ECoG was also not predictive of seizure outcome in the 94 pediatric patients who underwent temporal lobe resection at the Hospital for Sick Children in Toronto.5 Our data are also consistent with the suggestion that the “resection of the entire epileptogenic zone defined by EEG may not be absolutely necessary to achieve seizure freedom,”31 although there is not complete agreement as to how to use EEG to define the epileptogenic zone.

Our outcomes in patients with gangliogliomas were better than other pathologies, similar to 92% Engel Class I or II outcomes from other series.3 In our patients, the good outcomes were irrespective of the frequent presence of postresection spikes. Other authors advocate pre–ECoG to augment lesionectomies for pediatric ganglioglioma, although they have not found a significant difference in the rate of seizure freedom.28,29 Multiple studies in adults with gangliogliomas suggest that post–ECoG is helpful.27,32,38 Although these series may not be applicable to the pediatric patient population, our outcome data have reinforced our use of pre–ECoG, whether intraoperative or extraoperative, for lesion-associated epilepsy surgery.

Our patients with dysembryoplastic neuroepithelial tumors all also had good outcomes. We did not find dual
pathology in these patients as has been noted to be present in 52% of them in a larger series.10 Multiple pathologies are also frequently present, especially in children with temporal lobe pathology.26 Both of our patients with cavernous angiomas had good outcomes despite residual epileptiform discharges. Two groups indicated good outcomes in this patient population with ECoG, although one used it only preresection,41,42 and the other did not specify when recording occurred.11

One potential source of bias is that patients who were seizure free were more likely to be lost to follow-up, while patients with ongoing seizures were more likely to seek ongoing care. We operated on a large number of patients from neighboring states who underwent the majority of their follow-up evaluations with providers there. Another limitation is that individual epileptologists determined the relevant signature of epileptiform activity. Specifically, our data do not address the presence of high frequency (250–500 Hz) fast ripples on ECoG.

With all surgical series, there is a selection bias given the choice of patients we operated on, which was influenced heavily by their presentations. The procedures and approaches offered to patients have been tailored to their individual cases and have evolved with advances in our understanding of how to maximize outcomes while minimizing deficits. To minimize deficits, resection was incomplete due to proximity to eloquent brain in 2 cases. Only 1 surgeon operated on all cases, which provides both consistency but also potential bias. Four epileptologists interpreted the ECoG data originally and had excellent agreement with subsequent review.

Pre-ECoG is a potentially very powerful tool with many opinions about its use but is associated with good outcome in many series including ours.17,39,38 Post-ECoG may be useful in adult, mesial temporal resections.25 Our data indicate that post-ECoG in pediatric neocortical epilepsy resections is not necessarily predictive of seizure recurrence in all children, and, in many circumstances, good outcome can be achieved despite leaving unresected the tissue that is generating discharges. Postresective discharges may reflect irritability of the cortex due to the trauma of surgery. As a result of these findings, we are not concerned about diffuse changes in post-ECoG recordings on extratemporal cases. More data are needed to confirm these findings and help inform ongoing debates about the use of ECoG.

Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author contributions to the study and manuscript preparation include the following. Conception and design: Wray, Saneto, Novotny, Ojemann. Acquisition of data: Wray, Ojemann. Analysis and interpretation of data: Wray. Drafting the article: Wray. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Wray. Statistical analysis: Wray.

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