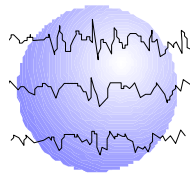


CONTRALATERAL ABNORMALITIES PREDICT OUTCOME OF PEDIATRIC EPILEPSY SURGERY

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ABSTRACT

RATIONALE: Selection of epilepsy surgical candidates requires the analysis of many variables with an objective to identify those patients likely to significantly benefit with minimal complication. This retrospective review strengthens identified predictive trends between diagnostic variables and outcome.

METHODS: We analyzed all pediatric patients who underwent initial resective surgery at Minnesota Epilepsy Group, PA from Jan 2000-Dec 2002. Seizure semiology, ictal/interictal scalp EEGs, and MRIs were analyzed. Sub-dural ictal/inter-ictal EEG, neuropsychological testing, MRS, SPECT, and PET with glucose, alpha-methylol-L-tryptophan, and flumazenil isotopes were reviewed if obtained in the evaluation. Diagnostic abnormalities were characterized by their lateralization/location in the frontal, temporal, parietal or occipital lobe. Findings were categorized by support, neutrality or conflict with the region of resection. Neutral findings were ipsilateral, but not within the region of resection. Any diffuse or contralateral abnormality to the region of resection was defined as a conflicting variable. Diffuse cognitive dysfunction was excluded. Patients were scored at follow-up at 6-, 12-, 24-months by Engel classification, percent seizure reduction, change in neuropsychological status, and complication.

RESULTS: Forty-six consecutive subjects were identified and reviewed; 23 (50%) underwent temporal lobe only resection; extra-temporal resections included 10 (22%) frontal, 1 (2%) parietal, and 12 (26%) multi-lobe. In subjects with available follow-up data, 23/41(56%) were seizure free at 12-months and 19/33 (58%) were seizure free at 24-months. Of subjects with <2 conflicting variables, 22/30 (73%) at 12 months and 19/27 (70%) achieved seizure freedom. Subjects with <2 conflicting diagnostic variables were significantly more likely have beneficial outcome of Engel I or II at 12 months (27/30: 90%, $p < 0.001$) and 24-months (24/27: 89%, $p < 0.001$) by Fischer's Exact Test. None of the six individuals with two or more conflicting variables attained Engel I or II outcome at 24 months. Supporting and neutral variables did not differ between the outcome groups.

CONCLUSION: A presurgical evaluation with less than two contralateral or diffuse diagnostic abnormalities improves prediction of Engel I-II outcome from 68-90% at 12 months. Only 9% of subjects with two or more conflicting abnormalities achieved Engel I-II at 12 months; none of the subjects maintained that success at 24 months.

Introduction:

Selection of pediatric epilepsy surgical candidates requires analysis of many variables to identify patients likely to significantly benefit with minimal complication. This retrospective review strengthens predictive trends between diagnostic variables and outcomes.

Methods:

We analyzed patients who underwent initial resective epilepsy surgery at Minnesota Epilepsy Group from January 2000 through December 2002. Seizure semiology, ictal/interictal scalp EEG, and MRI were analyzed on all patients. Neuropsychological testing, MRS, PET, and SPECT studies were reviewed if obtained in the presurgical investigation. PET studies utilized glucose, alpha-methyl-L-tryptophan, and/or flumazenil isotopes. Diagnostic abnormalities were characterized by their lobar location and lateralization to the surgical resection. Lobar determinations included frontal, temporal, parietal, or occipital. Findings were categorized by support, neutrality or conflict with the region of resection. Neutral findings were ipsilateral but not in the region of resection. Any diffuse or contralateral abnormality to the region was defined as a conflicting variable. Diffuse cognitive dysfunction or mental retardation was the only variable excluded. Patients were scored at follow-up intervals of 6, 12, and 24 months following surgery using a Modified Engel classification, percent seizure reduction, change in neuropsychological status, and complication.

Results

Forty-six consecutive pediatric subjects were identified and reviewed. Demographic variables are presented in Table 1. Average age of epilepsy onset was 3.6 years and the average duration of epilepsy was 7 years prior to surgery. Monthly seizure frequency averaged 124. The number of presurgical AED averaged 5.1 and the average number of AED prescribed at the time of surgery was 2.2. These variables are listed in Table 2 based on Engel Classification at 24 months post-operatively.

The distribution of surgical procedures is presented in Figure 2. Surgery was performed on the dominant hemisphere in 39% and non-dominant hemisphere in 37% (Figure 1). Twenty-three (50%) underwent temporal lobe only resections. Extra-temporal resections included 10 (22%) frontal, 1 (3.4%) parietal, and 12 (31%) multi-lobar areas. Thirty-two of 46 patients had complete resection of determined epileptogenic region. Ten of 46 had functional overlap with region of resection and received partial resection. Four had partial resections due to other reasons.

In subjects with available follow-up data, 23/42 (55%) were seizure free at 12 months. At 24 months, 19/34 (56%) were seizure free. Temporal lobe only resections demonstrated seizure freedom in 13/21 (62%) at 12 months and in 12/17 (71%) at 24 months. Extra-temporal resections were associated with seizure freedom in 10/21 (48%) at 12 months and in 7/17 (41%) at 24 months. Age of epilepsy onset, duration, and etiology did not vary between outcome groups of Engel I-II versus Engel III-IV.

The average number of supporting diagnostic variables was 5.3, and the average number of conflicting variables was 1.3. The average number of neutral variables was 2.5. The average net (supporting – conflicting) was 3.8 variables.

Subjects with <2 diagnostic variables in conflict were significantly more likely to be in Engel I or II at 12 months ($p < 0.001$) and 24 months ($p < 0.001$) by Fischer's Exact Test. Twenty-two of thirty (73%) subjects with <2 conflicting variables were seizure free at 12 months, and 5/30 (17%) were classified as Engel class II. At 24 months following surgery, 19/27 (70%) were seizure free and 5/27 (19%) were classified as Engel II. In subjects with 2 or more conflicting variables despite the number of supporting variables, only 1/12 (8%) was found to be seizure free at 12 months. None of the seven subjects with 2 or more conflicting variables were seizure free at 24 months. Supporting and neutral variables did not differ between the outcome groups.

The majority of conflicting variables were noted through scalp EEG recording, however conflicting MRI and neuropsychological variables also contributed to poor outcome.

Conclusion:

Subjects with <2 diagnostic abnormalities contralateral to the targeted epileptogenic zone achieved Engel class I or II surgical outcome in 90% and 89% of cases at 12 and 24 months respectively. None of the individuals with 2 or more conflicting variables attained Engel I or II outcome at 24 months.

24-Month Outcome: Beneficial Outcome v. Degree Surgical Resection

			BENF24		Total
			Engel I or II	Engel III or IV	
SURGCOM	Complete resection	Count	20	4	24
		% within SURGCOM	83.3%	16.7%	100.0%
		% within BENF24	83.3%	40.0%	70.6%
		% of Total	58.8%	11.8%	70.6%
	Partial resection	Count	4	6	10
		% within SURGCOM	40.0%	60.0%	100.0%
		% of Total	11.8%	17.6%	29.4%
Total	Count	24	10	34	
	% within SURGCOM	70.6%	29.4%	100.0%	
	% within BENF24	100.0%	100.0%	100.0%	
	% of Total	70.6%	29.4%	100.0%	

Table 1

Demographics	% of Patients
Gender: N=46	
Male	54
Female	46
Hand Dominance	
Right	74
Left	20
Undetermined	6
Developmental Assessment	
Normal	33
Global Delay	52
Behavioral	2
Speech Delay	9
Motor Delay	4
Pre-surgical Etiology	
Mesial Temporal Sclerosis	28
Encephalomalacia	7
Trauma	2
Tumor	22
Genetic/Degenerative	2
Congenital	17
Undetermined	20

Figure 1

Resection Lateralization: Language Dominance

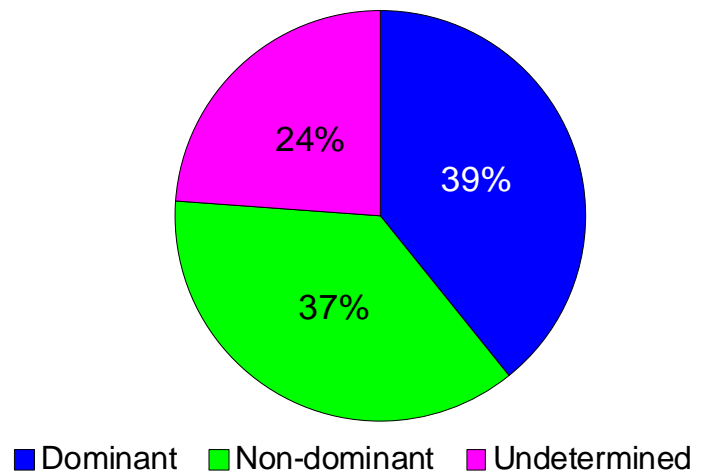


Figure 2

Area of Resection

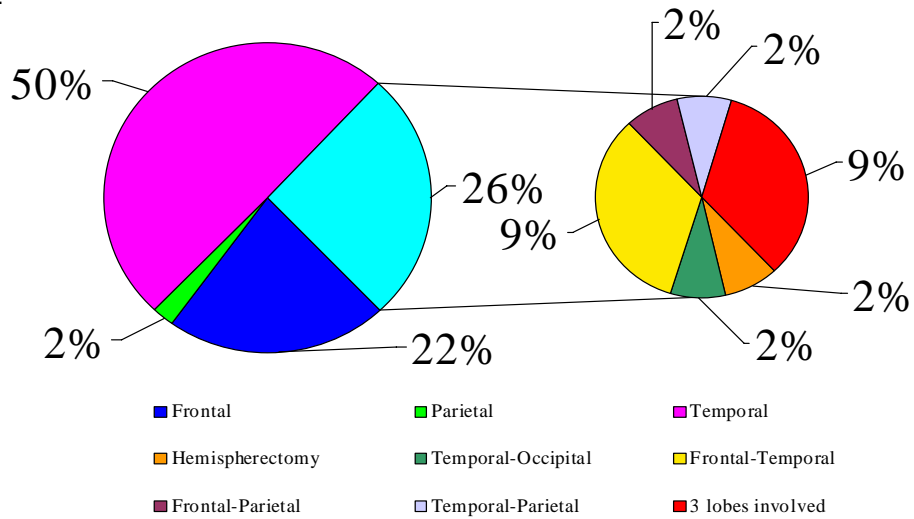
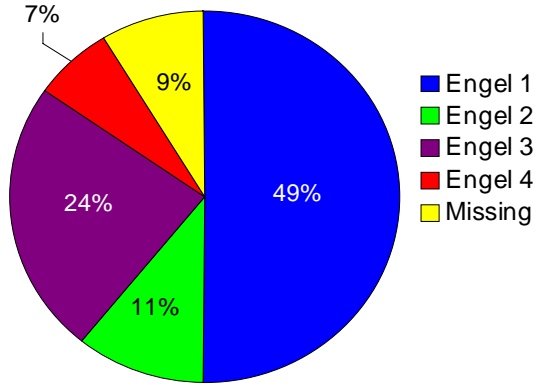


Table 2. 24 Month Engel Class: clinical variables of epilepsy patients

		Epilepsy Duration (y)	Age of Epilepsy Onset (y)	Seizure Frequency (#/mn)	# AED Prior to Surgery	# AED Following Surgery
Engel 1	Mean	7.268	3.8700	29.5789	3.79	1.95
	N	19	19	19	19	19
	Std. Deviation	6.966	4.2692	38.0720	2.30	.62
Engel 2	Mean	7.400	4.6500	73.7000	4.40	2.20
	N	5	5	5	5	5
	Std. Deviation	5.550	1.9969	127.3615	3.91	1.10
Engel 3	Mean	4.813	2.8569	284.3750	7.38	2.25
	N	8	8	8	8	8
	Std. Deviation	1.668	2.9536	510.8284	2.20	.89
Engel 4	Mean	12.250	1.2500	515.0000	10.00	4.50
	N	2	2	2	2	2
	Std. Deviation	6.718	1.0607	685.8936	1.41	.71
Total	Mean	7.003	3.5922	124.5735	5.09	2.21
	N	34	34	34	34	34
	Std. Deviation	5.921	3.6038	305.5843	3.10	.95

Figure 3

12 Month: Engel Class

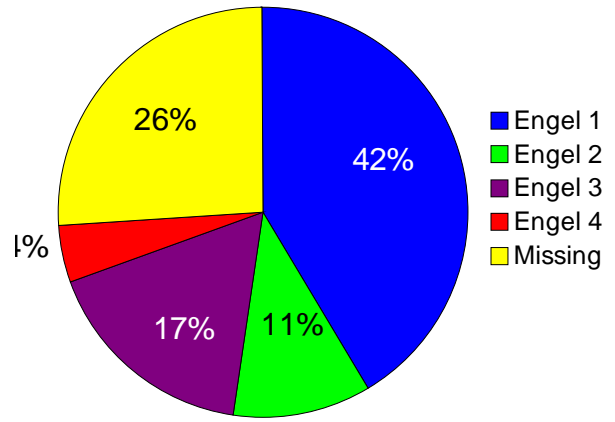


12-Month Outcome: Engel class v. Region of Resection & Etiology

Count			ENGEL12				Total
			Engel I	Engel 2	Engel 3	Engel 4	
Temporal	AXIS4ETI	Congenital	1				1
		Genetic/metabolic/degenerative	1				1
		Tumor	6	1			7
		Mesial Temporal Sclerosis	5	3	3		11
		Undetermined			1		1
Total			13	4	4	21	
Frontal	AXIS4ETI	Congenital	2			1	3
		Tumor	1				1
		Vascular Malformation	1				1
		Undetermined	1		3	1	5
Total			5		3	2	10
Parietal	AXIS4ETI	Encephalomalacia (extra-temporal gliosis)		1			1
Total				1			1
Multi-lobar	AXIS4ETI	Congenital			2		2
		Tumor	1				1
		Traumatic	1				1
		Encephalomalacia (extra-temporal gliosis)	1		1		2
		Mesial Temporal Sclerosis	1			1	2
		Undetermined	1		1		2
Total			5		4	1	10

Figure 4

24 Month: Engel Class



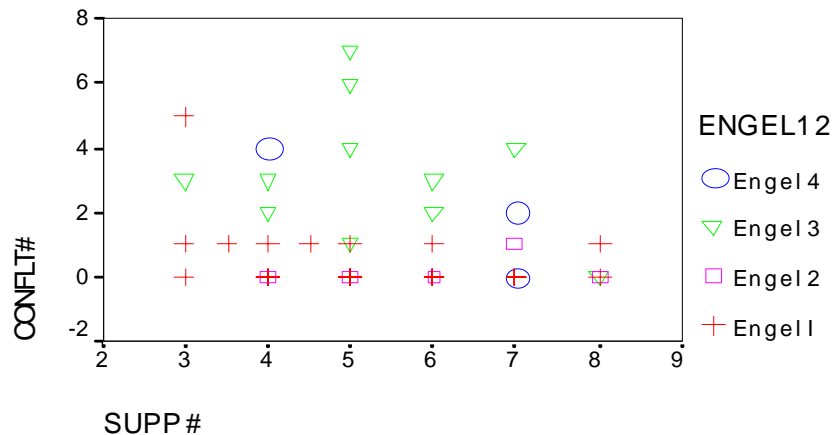
24-Month Outcome: Engel Class v. Region of Resection & Etiology

Count			ENGEL24				Total
			Engel I	Engel 2	Engel 3	Engel 4	
Temporal	AXIS4ETI	Congenital	1				1
		Genetic/metabolic/degenerative	1				1
		Tumor	6				6
		Mesial Temporal Sclerosis	4	3	2		9
		Undetermined					1
Total			12	3	2	17	
Frontal	AXIS4ETI	Congenital	2			1	3
		Tumor	1				1
		Vascular Malformation	1				1
		Undetermined			2	1	3
Total			4		2	2	8
Parietal	AXIS4ETI	Encephalomalacia (extra-temporal gliosis)		1			1
Total				1			1
Multi-lobar	AXIS4ETI	Congenital			2		2
		Tumor		1			1
		Encephalomalacia (extra-temporal gliosis)	1		1		2
		Mesial Temporal Sclerosis	1				1
		Undetermined	1			1	2
Total			3	1	4	1	8

12-Month Outcome: Engel Class

Presurgical Conflict in v. Supporting Variables

Figure 5



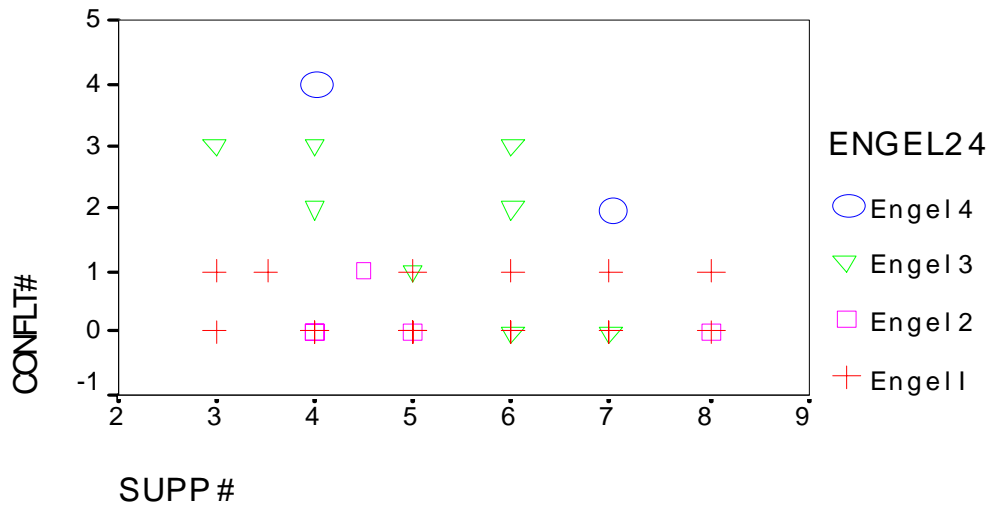
12-Month Outcome: Less than 2 conflicting diagnostic variables associated with beneficial outcome. (Fisher's Exact Test p<0.001)

Count		BENF12		Total
		Engel I or II	Engel III or IV	
SIGCONF	1 or fewer variables conflicting	27	3	30
	2 or more variables conflicting	1	11	12
Total		28	14	42

24-Month Outcome: Engel Class

Presurgical Conflict in g v. Supporting Variables

Figure 6



SUPP #
24-Month Outcome: Less than 2 conflicting diagnostic variables associated with beneficial outcome. (Fisher's Exact Test p<0.001)

Count		BENF24		Total
		Engel I or II	Engel III or IV	
SIGCONF	1 or fewer variables conflicting	24	3	27
	2 or more variables conflicting		7	7
Total		24	10	34