Hemispherectomy for treatment of refractory epilepsy in the pediatric age group: a systematic review

Christoph J. Griessenauer, MD,¹ Smeer Salam, MD,¹ Philipp Hendrix, MD,² Daxa M. Patel, MD,¹ R. Shane Tubbs, MS, PA-C, PhD,¹ Jeffrey P. Blount, MD,¹ and Peter A. Winkler, MD, PhD³

¹Division of Pediatric Neurosurgery, Department of Neurosurgery, University of Alabama at Birmingham, Alabama; ²Department of Neurosurgery, Saarland University Hospital, Homburg/Saar, Germany; and ³Department of Neurosurgery, Paracelsus Medical University, Salzburg, Austria

OBJECT Evidence in support of hemispherectomy stems from a multitude of retrospective studies illustrating individual institutions' experience. A systematic review of this topic, however, is lacking in the literature.

METHODS A systematic review of hemispherectomy for the treatment of refractory epilepsy available up to October 2013 was performed using the following inclusion criteria: reports of a total of 10 or more patients in the pediatric age group (≤ 20 years) undergoing hemispherectomy, seizure outcome reported after a minimum follow-up of 1 year after the initial procedure, and description of the type of hemispherectomy. Only the most recent paper from institutions that published multiple papers with overlapping study periods was included. Two reviewers independently applied the inclusion criteria and extracted all the data.

RESULTS Twenty-nine studies with a total of 1161 patients met the inclusion criteria. Seizure outcome was available for 1102 patients, and the overall rate of seizure freedom at the last follow-up was 73.4%. Sixteen studies (55.2%) exclusively reported seizure outcomes of a single type of hemispherectomy. There was no statistically significant difference in seizure outcome and type of hemispherectomy ($p = 0.737$). Underlying etiology was reported for 85.4% of patients with documented seizure outcome, and the overall distribution of acquired, developmental, and progressive etiologies was 30.5%, 40.7%, and 28.8%, respectively. Acquired and progressive etiologies were associated with significantly higher seizure-free rates than developmental etiologies ($p < 0.001$). Twenty of the 29 studies (69%) reported complications. The overall rate of hydrocephalus requiring CSF diversion was 14%. Mortality within 30 days was 2.2% and was not statistically different between types of hemispherectomy ($p = 0.787$).

CONCLUSIONS Hemispherectomy is highly effective for treating refractory epilepsy in the pediatric age group, particularly for acquired and progressive etiologies. While the type of hemispherectomy does not have any influence on seizure outcome, hemispherotomy procedures are associated with a more favorable complication profile.

<http://thejns.org/doi/abs/10.3171/2014.10.PEDS14155>

KEY WORDS hemispherectomy; epilepsy; pediatric; systematic review

HEMISPHERECTOMY for the treatment of refractory epilepsy was first performed in the first half of the 20th century.²⁰ Anatomical hemispherectomy, the resection of an entire hemisphere frequently done in the 1950s and 1960s that was associated with high complication rates from hydrocephalus and superficial cerebral hemosiderosis, has been replaced with less invasive procedures that accomplish a functional equivalent by disconnection of the epileptogenic cortex of one hemisphere from

the contralateral hemisphere and deeper brain structures or removal of the epileptogenic cortex. These procedures are associated with comparable seizure control rates but a lower incidence of the aforementioned complications. This transition began with the development of functional hemispherectomy²⁸ and hemidecortication¹⁶ in the 1970s and 1980s and evolved in the 1990s with the introduction of several different approaches, collectively referred to as hemispherotomy. These procedures were developed almost

SUBMITTED March 21, 2014. **ACCEPTED** October 6, 2014.

INCLUDE WHEN CITING Published online November 7, 2014; DOI: 10.3171/2014.10.PEDS14155.

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

simultaneously, rely mostly on disconnection, and require only minimal brain resection.^{10,30,33,44} Conditions amenable to these procedures are characterized by diffuse damage to one hemisphere resulting in medically resistant epilepsy and are frequently grouped into acquired (e.g., perinatal cerebral infarction or intracranial hemorrhage, hemiconvulsion-hemiplegia-epilepsy syndrome, and other sequelae of brain trauma and infection), developmental (e.g., cortical dysplasia, hemimegalencephaly, and migration disorders), and progressive (e.g., Rasmussen's encephalitis and Sturge-Weber syndrome) etiologies.^{11,27,41} The aim of this study was to systematically review the literature on hemispherectomy with emphasis on seizure outcome stratified by type of hemispherectomy and underlying etiology.

Methods

A PubMed search was performed, of the literature until October 2013, with the search terms "hemispherectomy" and "outcome" limited to papers written in the English language with a focus on the pediatric age group. Additionally, papers retrieved from the references listed in the papers found in the PubMed search were also evaluated. Two reviewers independently applied the following inclusion criteria: reports of a total of 10 or more patients in the pediatric age group (≤ 20 years) undergoing hemispherectomy, seizure outcome reported after a minimum follow-up of 1 year after the initial procedure, and description of the type of hemispherectomy. To account only once for each patient, only the most recent paper from institutions that published multiple papers with overlapping study periods was included. Studies reporting outcome after repeat hemispherectomy with failure of the initial procedure were excluded. Studies were categorized by the type of hemispherectomy (Fig. 1) into anatomical hemispherectomy, functional hemispherectomy (Fig. 1B),^{6,28} hemispherotomy including trans- and perisylvian (Fig. 1C)^{30,31,33,44} and vertical parasagittal techniques (Fig. 1D),⁹ and hemidecortication.¹⁶ Indications for hemispherectomy were grouped into acquired, developmental, and progressive etiologies. Two reviewers independently extracted all the data and resolved any disagreements through discussions. Descriptive and statistical analyses were performed using commercially available software (version 21, SPSS, IBM). A comparison of groups of 3 or more studies was conducted using ANOVA and Fisher's least significant difference post hoc analysis, where appropriate. This systematic review was prepared according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.²⁴

Results

Descriptive Analysis

The literature search yielded 186 references, of which 85 (45.7%) were excluded based on the abstract. One hundred one potentially eligible studies underwent a full-text review, and 29 studies (15.6%) met the inclusion criteria and constituted the data set. The search strategy is outlined in detail in Fig. 2. Two reviewers independently performed assessment at each step. All 29 studies identified

were retrospective in nature. The cumulative number of patients from all 29 studies was 1161. The number of patients per study ranged from 10 to 186. All 29 studies reported seizure outcome, and 21 (72.4%) reported complete Engel scores.¹³ One study used the International League Against Epilepsy classification.³² Seizure outcome was available for 1102 patients, and the overall rate of seizure freedom at last follow-up was 73.4%. Of the 29 studies, 16 (55.2%) exclusively reported seizure outcomes of a single type of hemispherectomy. Eight studies (27.6%) reported only hemispherotomy results, while 6 (20.1%) and 2 (6.9%) studies reported results of functional and anatomical hemispherectomy, respectively. No study exclusively studied hemidecortication. The underlying etiology was reported for 85.4% of patients with documented seizure outcome. The overall distribution of acquired, developmental, and progressive etiologies was 30.5%, 40.7%, and 28.8%, respectively (Table 1).

Seizure Outcome, Type of Hemispherectomy, and Underlying Etiology

In addition to the 16 studies that reported solely one type of hemispherectomy, another 6 studies^{2,6,11,21,32,38} from the mixed study pool provided detailed enough information allowing for extraction of seizure outcome as a function of the type of hemispherectomy. One additional study was analyzed as if all patients had hemidecortication since the vast majority (98%) of patients in this study underwent hemidecortication.¹⁹ Thus, seizure outcome was available for 406 (56.7%), 132 (18.4%), 61 (8.5%), and 117 (16.3%) patients who underwent hemispherotomy, functional hemispherectomy, anatomical hemispherectomy, and hemidecortication, respectively. The seizure-free rate was highest for anatomical hemispherectomy and lowest for hemidecortication without any statistically significant differences between types of hemispherectomy ($p = 0.737$) (Table 2; Fig. 3).

Information on underlying etiology was available from 17 studies with a total of 667 patients. Of these patients, 211 (31.6%) had acquired, 269 (40.3%) developmental, and 187 (28%) progressive etiologies. The mean seizure-free rates for acquired, progressive, and developmental etiologies were 82.4%, 82.8%, and 61.4%, respectively. Both acquired and progressive etiologies were associated with significantly higher seizure-free rates than developmental etiologies ($p < 0.001$). There was, however, no difference in seizure-free rates between acquired and progressive etiologies ($p = 0.945$) (Table 3; Fig. 4).

A comparison of seizure outcome for different etiologies dependent on the type of hemispherectomy was feasible for hemispherotomy and functional hemispherectomy only. For anatomical hemispherectomy and hemidecortication there were fewer than 3 studies each, thereby precluding them from inclusion in the analysis. There was no difference in seizure-free rates for the 3 etiologies between hemispherectomy and functional hemispherectomy. While developmental etiologies had the lowest rates of seizure freedom, seizure-free rates among patients undergoing functional hemispherectomy were significantly higher in those who suffered from an acquired or progressive etiology in contrast to those suffering from a developmental etiology.

FIG. 1. Schematic drawings of the types of hemispherectomy illustrated by the senior author (P.A.W.). **A:** Coronal view of the brain at the level of mammillary bodies. **B:** Functional hemispherectomy (Rasmussen). **C:** Trans- and perisylvian technique (Villemure, Mascott, and Schramm). **D:** Vertical parasagittal technique (Delalande). Copyright Peter Winkler. Published with permission. Figure is available in color online only.

FIG. 2. Outline of search strategy.

ology ($p < 0.05$). Seizure-free rates in patients undergoing hemispherotomy for a developmental etiology did not significantly differ from seizure-free rates for acquired ($p = 0.063$) or progressive ($p = 0.106$) etiology (Table 4; Fig. 5).

Hydrocephalus, Complications, and Mortality

Twenty of the 29 studies (69%) reported complications. Data from 20 studies (69%) that reported postoperative CSF diversion rates revealed a cumulative overall shunt rate of 14% following hemispherectomy. Fifteen studies (52%) provided detailed enough information to compare shunt rates for hemispherotomy, functional hemispherectomy, and anatomical hemispherectomy. For hemidecortication there were fewer than 3 studies, thus precluding them from inclusion in the analysis. Anatomical hemispherectomy was associated with a significantly higher shunt rate than functional hemispherectomy ($p < 0.05$) and hemispherotomy ($p < 0.01$). One of the 4 studies in the anatomical hemispherectomy group had a shunt rate of 78%,⁶ which was considerably higher than the shunt rate in the other 3 studies. The study, however, was included because it contributed 37 patients and was the single largest contributor to this group (54.4%) (Table 5; Fig. 6).

The rate of wound complications requiring surgical revision was 2%. The rate for other surgical complications, such as epidural, subdural, or intraparenchymal hemorrhages, and intracranial abscesses, was 3.5%. The rate of nonsurgical, medical complications was 10.6% and included, but was not limited to, meningitis, ventriculitis, venous thrombosis, and others. Neurological deficits affecting motor and sensory function or visual fields are expected following hemispherectomy and were not considered complications. The need for additional epilepsy surgery was reported in 18 studies with a cumulative rate of 4.5%. Complications other than hydrocephalus were all reported inconsistently, thereby not allowing for further statistical analysis.

The overall mortality was 2.2% (25 patients), with 15

patients (1.3%) dying within 30 days after surgery. Fifteen studies (52%) provided detailed enough information to compare mortality rates for hemispherotomy, functional hemispherectomy, and anatomical hemispherectomy. For hemidecortication there were fewer than 3 studies, thus precluding them from inclusion in the analysis. There were no significant differences between mortality rates from the 3 types of hemispherectomy ($p = 0.787$) (Table 6; Fig. 7).

Discussion

Hemispherectomy refers to a group of surgical interventions for treatment-refractory epilepsy that is due to a diffusely damaged hemisphere. The evidence supporting this procedure is largely based on a multitude of retrospective studies illustrating individual institutions' experience with a few notable exceptions. One such important study is a retrospective multicenter study led by Holthausen et al. that gathered information concerning hemispherectomy from 333 patients at 11 participating centers.¹⁵ However, more than a decade has passed since Holthausen and colleagues' report was published, significant advances have been made, and many centers have subsequently reported their experience. Therefore, the aim of this study was to systematically review the literature available on hemispherectomy with emphasis on seizure outcome stratified by type of hemispherectomy and underlying etiologies.

Seizure Outcome, Type of Procedure, and Underlying Etiology

Twenty-nine studies comprising 1161 patients were identified and met inclusion criteria. The overall rate of seizure freedom was 73.4%, which is slightly higher than the rate of seizure freedom found by Holthausen et al.¹⁵ and comparable to other large, more recent series.^{6,9,19,25,27,32,43} Long-term sustainability of seizure freedom is absolutely critical to justify surgery for epilepsy, which is

TABLE 1. Studies included in the systematic review

Authors & Year	Study Period	Institution	Journal	Outcome Assessment	No. of Pts	No. of Pts w/ Sz Outcome Information			Mortality		No. of Patients (%)		
						No.	No. Free (%)	No. Sz	30 Days	w/in FU	Acquired	Developmental	Progressive
Anatomical hemispherectomy													
Beardsworth & Adams, 1988	1979–NR	Radcliffe Infirmary	Br J Neurosurg	Sz, yes/no	10	10	7 (70)	0	0				
Davies et al., 1993	1950–1971	University of Minnesota	J Neurosurg	Sz, yes/no	10	10	4 (40)	0	2	2 (20)			1 (10)
Functional hemispherectomy													
Smith et al., 1991	1976–1988	Montreal Neurological Institute & Hospital	Neurology	Sz, yes/no	20	19	15 (79)	1	0				
Duchowny et al., 1998	1979–1996	Miami Children's Hospital	Epilepsia	Engel	14	12	9 (75)	1	1	1 (7)	10 (71)		2 (14)
Sugimoto et al., 1999	1991–1996	Hospital for Sick Children	Epilepsia	Engel	11	11	8 (73)	0	0	2 (18)	4 (36)		5 (45)
Shimizu & Maehara, 2000 ³⁴	1983–1998	Tokyo Metropolitan Neurological Hospital	Epilepsia	Engel	24	18	8 (44)	0	0	2 (8)	18 (75)		
Aaberg et al., 2012	1995–2004	Oslo University Hospital	Acta Paediatr	Engel	10	10	9 (90)	0	0				
Villarejo-Ortega et al., 2013	2001–2009	Hospital Infantil Universitario Niño Jesús	Childs Nerv Syst	Engel	17	17	10 (59)	0	0	9 (53)	5 (29)		3 (18)
Hemispherotomy													
Villemure & Daniel, 2006	NR	Christian Medical College, Centre Hospitalier Universitaire Vaudois	Childs Nerv Syst	Engel	43	37	34 (92)	1	0	17 (40)	5 (12)		12 (28)
Delalande et al., 2007	1990–2000	Fondation Ophtalmologique	Neurosurgery	Engel	78	75	57 (76)	3	0	16 (21)	28 (36)		31 (40)
Marras et al., 2010	2000–2007	Carlo Besta Neurological Institute	Epilepsy Res	Engel	13	13	8 (62)	0	0	2 (15)	5 (38)		6 (46)
Thomas et al., 2010	2005–2009	Christian Medical College	Childs Nerv Syst	Engel	16	16	15 (94)	0	0		2 (13)		12 (75)
Dagar et al., 2011	2000–2011	All India Institute of Medical Sciences	Pediatr Neurosurg	Engel	35	35	30 (86)	0	0				
Torres et al., 2011	2002–2007	Hospital for Sick Children	J Neurosurg Pediatr	Engel	13	13	10 (77)	0	0		7 (54)		6 (46)
Ramantani et al., 2013	2002–2011	University Hospital Freiburg	Epilepsia	Engel	52	52	43 (83)	0	0	24 (46)	22 (42)		6 (12)
van der Kolk et al., 2013	1996–2007	Wilhelmina Children's Hospital	Epilepsy Res	Engel	35	35	30 (86)	0	0	13 (37)	13 (37)		9 (26)
Hemidecortication													
Kossoff et al., 2003*	1975–2001	Johns Hopkins University	Neurology	Sz, yes/no	111	105	68 (65)	3	2	16 (14)	33 (30)		51 (46)
(continued)													

(continued)

TABLE 1. Studies included in the systematic review (*continued*)

Authors & Year	Study Period	Institution	Journal	Outcome Assessment	No. of Pts	No. of Pts w/ Sz Outcome Information			Mortality		No. of Patients (%)		
						No.	No. Free (%)	No. Sz	30 Days	w/in FU	Acquired	Developmental	Progressive
Mixed surgery type													
Carmant et al., 1995	1963–1992	Boston Children's Hospital	<i>Electroencephalogr Clin Neurophysiol</i>	Engel	12	12	8 (67)	0	0	0	6 (50)	3 (25)	3 (25)
Villemure et al., 2003	NR	Lausanne University Hospital	<i>Epileptic Disord</i>	Engel	12	11	8 (73)	1	0	0		11 (92)	
Devlin et al., 2003	1991–1997	Great Ormond Street Hospital	<i>Brain</i>	Engel	33	33	17 (52)	0	0	0	7 (21)	16 (48)	6 (18)
Cook et al., 2004	1986–2002	University of California, Los Angeles	<i>J Neurosurg Pediatr</i>	Sz, yes/no	115	103	79 (77)	2	0	0	27 (23)	55 (48)	21 (18)
Basheer et al., 2007	1993–2004	British Columbia's Children's Hospital	<i>Epilepsia</i>	Engel	24	24	19 (79)	0	0	0	7 (29)	7 (29)	10 (42)
Terra-Bustamante et al., 2007	1996–2005	Ribeirão Preto, Brazil	<i>Childs Nerv Syst</i>	Engel	39	38	21 (55)	1	2	0		9 (23)	14 (36)
Lettori et al., 2008	1980–2003	Università Cattolica del Sacro Cuore	<i>Seizure</i>	Engel	19	19	14 (74)	0	0	0	2 (11)	13 (68)	4 (21)
Limbrick et al., 2009	1995–2008	University of Washington, St. Louis	<i>J Neurosurg Pediatr</i>	Engel	49	49	38 (78)	0	0	0	13 (27)	16 (33)	8 (16)
Caraballo et al., 2011	1990–2010	Hospital Nacional de Pediatría, Buenos Aires	<i>Childs Nerv Syst</i>	Engel	45	45	33 (73)	0	1	0		18 (40)	14 (31)
Schramm et al., 2012	1990–2009	Bonn University Medical Center	<i>Acta Neurochir</i>	ILAE	96	92	78 (85)	1	2	2	42 (44)	20 (21)	19 (20)
Yu et al., 2012	2001–2009	Capital Medical University	<i>Seizure</i>	Sz, yes/no	19	18	17 (94)	1	0	0			
Moosa et al., 2013	1997–2009	Cleveland Clinic	<i>Neurology</i>	Sz, yes/no	186	170	112 (66)	0	0	0	79 (42)	63 (34)	28 (15)
Overall					1161	1102	809 (73.4)	15	10	10	287 (30.5)	383 (40.7)	271 (28.8)

FU = follow-up; ILAE = International League Against Epilepsy; NR = not reported; pt = patient; Sz = seizure.

* Two of 111 patients did not undergo hemidecortication.

TABLE 2. Seizure outcome and type of hemispherectomy*

Type of Hemispherectomy & Study	No. of Studies	No. of Pts	Sz-Free Rate (%)	
			Mean $\pm$ SD	95% CI
Hemispherotomy Cook 2004, Villemure 2006, Basheer 2007, Delalande 2007, Terra-Bustamante 2007, Marras 2010, Torres 2011, Schramm 2012, van der Kolk 2013, Ramantani 2013	10	406	76.0 $\pm$ 16.7	69.4–82.6
Functional hemispherectomy Duchowny 1998, Sugimoto 1999, Shimizu 2000, ³⁴ Devlin 2003, Cook 2004, Lettori 2008, Villarejo-Ortega 2013	7	132	71.9 $\pm$ 26.7	58.1–85.6
Anatomical hemispherectomy Davies 1993, Devlin 2003, Cook 2004, Lettori 2008	4	61	80.7 $\pm$ 21.0	63.1–98.2
Hemidecortication Kossof 2003, Basheer 2007, Lettori 2008	3	117	71.2 $\pm$ 20.9	53.8–88.7

* There was no statistically significant difference in seizure outcome and type of hemispherectomy ($p = 0.737$).

FIG. 3. Seizure-free rates and type of hemispherectomy ($p = 0.737$).**TABLE 3. Seizure outcome and underlying etiology***

Underlying Etiology & Study	No. of Studies	No. of Pts	Sz-Free Rate (%)	
			Mean $\pm$ SD	95% CI
Acquired Davies 1993, Duchowny 1998, Sugimoto 1999, Devlin 2003, Kossof 2003, Cook 2004, Villemure 2006, Basheer 2007, Delalande 2007, Lettori 2008, Marras 2010, Schramm 2012, Ramantani 2013, van der Kolk 2013, Villarejo-Ortega 2013	15	211	82.4 $\pm$ 15.9	74.7–90.0
Developmental Duchowny 1998, Sugimoto 1999, Devlin 2003, Kossof 2003, Cook 2004, Villemure 2006, Basheer 2007, Delalande 2007, Terra-Bustamante 2007, Lettori 2008, Marras 2010, Torres 2011, Schramm 2012, Ramanti 2013, van der Kolk 2013, Villarejo-Ortega 2013	16	269	61.4 $\pm$ 20.8	52.2–70.7
Progressive Duchowny 1998, Sugimoto 1999, Devlin 2003, Kossof 2003, Cook 2004, Villemure 2006, Basheer 2007, Delalande 2007, Terra-Bustamante 2007, Lettori 2008, Marras 2010, Torres 2011, Schramm 2012, Ramantani 2013, van der Kolk 2013, Villarejo-Ortega 2013	16	187	82.8 $\pm$ 17.5	74.3–91.2

* Acquired and progressive etiologies were associated with significantly higher seizure-free rates than developmental etiologies ($p < 0.001$).

FIG. 4. Seizure-free rates and underlying etiology. Post hoc analysis using Fisher's least significant difference. *** $p < 0.001$.

an irreversible intervention. Long-term seizure-free rates (≥ 5 years) following surgery for temporal lobe epilepsy are comparable to those reported in shorter-term studies. The rates of seizure freedom after surgery for extratemporal epilepsy, however, decline over time.^{14,37,46} Existing evidence shows that the benefit of hemispherectomy is maintained over time and seizure-free rates drop only slightly in the long term.^{26,37} For the purpose of this review, only studies with at least 1 year of follow-up were considered in an attempt to compensate for the initial decrease in seizure-free rates after hemispherectomy.¹⁷ Insufficient data on long-term outcome were available to perform any meaningful statistical analysis. Also, to account only once for each patient, only the most recent paper from institutions that published multiple papers with overlapping study periods was considered. This predomi-

FIG. 5. Seizure-free rates, underlying etiology, and type of hemispherectomy. Post hoc analysis using Fisher's least significant difference. * $p < 0.05$. ns = not significant.

nantly affected institutions that published a sequential series of papers on outcomes.

There was no significant difference in the rate of seizure freedom between different types of hemispherectomy in this study, which is plausible as they all follow the same underlying principle. Holthausen et al., however, found that hemispherotomy is superior to anatomical and functional hemispherectomies as well as hemidecortication.¹⁵ However, other studies did not make such an observation.^{6,32}

The underlying etiology warranting hemispherectomy is by contrast an important determinant for seizure outcome. To assess this effect, indications for hemispherectomy were grouped similarly to those in prior studies into acquired, developmental, and progressive etiologies.^{11,27,41} Patients suffering from acquired and progressive condi-

TABLE 4. Seizure outcome, type of hemispherectomy, and underlying etiology*

Variables & Study	No. of Studies	No. of Pts	Sz-Free Rate (%)	
			Mean $\pm$ SD	95% CI
Hemispherotomy				
Acquired Cook 2004, Villemure 2006, Delalande 2007, Basheer 2007, Marras 2010, Schramm 2012, Ramantani 2013, van der Kolk 2013	8	140	83.3 $\pm$ 11.5	73.7–92.9
Developmental Cook 2004, Villemure 2006, Delalande 2007, Terra-Bustamante 2007, Basheer 2007, Marras 2010, Torres 2011, Schramm 2012, Ramantani 2013, van der Kolk 2013	10	152	66.1 $\pm$ 15.8	54.8–77.4
Progressive Cook 2004, Villemure 2006, Delalande 2007, Terra-Bustamante 2007, Marras 2010, Torres 2011, Schramm 2012, Ramantani 2013, van der Kolk 2013	9	93	80.5 $\pm$ 17.7	66.9–94.1
Functional hemispherectomy				
Acquired Duchowny 1998, Sugimoto 1999, Devlin 2003, Cook 2004, Lettori 2008, Villarejo-Ortega 2013	6	32	82.8 $\pm$ 21.1	60.6–104.9
Developmental Duchowny 1998, Sugimoto 1999, Devlin 2003, Cook 2004, Lettori 2008, Villarejo-Ortega 2013	6	50	53.9 $\pm$ 29.6	22.8–85.0
Progressive Duchowny 1998, Sugimoto 1999, Devlin 2003, Cook 2004, Villarejo-Ortega 2013	5	23	80.3 $\pm$ 21.1	54.1–106.4

* $p = 0.048$.

TABLE 5. Shunted hydrocephalus and type of hemispherectomy*

Type of Hemispherectomy & Study	No. of Studies	No. of Pts	Shunt Rate (%)	
			Mean $\pm$ SD	95% CI
Hemispherotomy Cook 2004, Villemure 2006, Delalande 2007, Terra-Bustamante 2007, Marras 2010, Dagar 2011, Torres 2011, Schramm 2012, Ramantani 2013	9	388	8.3 $\pm$ 7.9	2.2 to 14.4
Functional hemispherectomy Duchowny 1998, Shimizu 2000, ³⁴ Cook 2004, Lettori 2008, Schramm 2012, Villarejo-Ortega 2013	6	105	12.9 $\pm$ 8.2	4.3 to 21.4
Anatomical hemispherectomy Beardsworth & Adams 1988, Davies 1993, Cook 2004, Lettori 2008	4	68	36.4 $\pm$ 29.3	-10.3 to 83.1

* $p = 0.017$.

tions generally do better than patients with developmental disorders,^{11,18,19,21} and this observation is supported by the findings of the present study. Due to the small number of available studies for anatomical hemispherectomy and hemidecortication, seizure outcome for different etiologies dependent on the type of hemispherectomy was only feasible for hemispherotomy and functional hemispherectomy. The highest rate of seizure freedom was achieved with hemispherotomy and functional hemispherectomy for acquired lesions (83.3% and 82.8% seizure free, respectively). Functional hemispherectomy of developmental conditions was least successful (53.9% seizure free). The lower success rate for developmental etiologies was statistically significant for functional hemispherectomy but not for hemispherotomy. A higher hemispherectomy failure rate for developmental etiologies has been associated with epileptogenesis in the contralateral hemisphere and higher rates of incomplete disconnection, particularly in hemimegalencephaly.¹⁵ In the present study, the influence of epileptiform discharges over the normal hemisphere could not be assessed as these data were inconsistently reported.

Hydrocephalus, Complications, and Mortality

The most common complication reported was hydrocephalus requiring CSF diversion with an overall rate across all studies of 14%. Anatomical hemispherectomy resulted in the highest rate of shunted hydrocephalus

FIG. 6. Shunted hydrocephalus rates and type of hemispherectomy. Post hoc analysis using Fisher's least significant difference. * $p < 0.05$; ** $p < 0.01$.

with rates for functional hemispherectomy and hemispherotomy comparable and significantly lower. Shunt rates of 8%–23% have been previously reported and seem to be directly proportional to the amount of brain tissue removed.²⁹ Approximately 5% of patients underwent additional epilepsy surgery, most commonly for completion of incomplete disconnection. Incomplete disconnection has been reported as a cause of persistent seizures in up to 30% of patients who do not become seizure free after the initial intervention.²⁹ The overall number of patients requiring additional epilepsy surgery found in the present study appears somewhat low. This may, however, be explained by the greater experience high-volume centers that published their outcomes have with these procedures. Mortality was generally low at 2% and was similar for all types of hemispherectomy.²⁹

Limitations

The categorization of studies based on the type of hemispherectomy applied here presents a challenge as there are surgical modifications and nuances that may go beyond these basic categories that are not accounted for. Multiple variations of functional hemispherectomy have been reported.^{6,28} Hemispherotomy is a collective term encompassing trans- and perisylvian^{30,31,33,44} as well as vertical parasagittal techniques.⁹ However, to accumulate numbers large enough to perform any meaningful statistical analysis, a common denominator has to be agreed upon.

FIG. 7. Mortality rates and type of hemispherectomy ($p = 0.787$).

TABLE 6. Mortality and type of hemispherectomy*

Type of Hemispherectomy	No. of Studies	No. of Pts	Mortality Rate (%)	
			Mean $\pm$ SD	95% CI
Hemispherotomy	9	388	1.1 $\pm$ 1.6	-0.2 to 2.3
Cook 2004, Villemure 2006, Delalande 2007, Terra-Bustamante 2007, Marras 2010, Dagar 2011, Torres 2011, Schramm 2012, Ramantani 2013				
Functional hemispherectomy	6	105	2.4 $\pm$ 5.8	-3.7 to 8.5
Duchowny 1998, Shimizu 2000, ³⁴ Cook 2004, Lettori 2008, Schramm 2012, Villarejo-Ortega 2013				
Anatomic hemispherectomy	4	68	1.4 $\pm$ 2.7	-2.9 to 5.7
Beardsworth & Adams 1988, Davies 1993, Cook 2004, Lettori 2008				

* Mortality within 30 days was not statistically different between types of hemispherectomy ($p = 0.787$).

Conclusions

Hemispherectomy is highly effective for the treatment of refractory epilepsy in the pediatric age group, particularly for acquired and progressive etiologies. While the type of hemispherectomy does not have any influence on seizure outcome, hemispherotomy procedures are associated with a more favorable complication profile. Developmental etiologies have worse outcomes than acquired or progressive etiologies regardless of hemispherectomy technique.

References

1. Aaberg KM, Eriksson AS, Ramm-Petersen J, Nakken KO: Long-term outcome of resective epilepsy surgery in Norwegian children. *Acta Paediatr* **101**:e557–e560, 2012
2. Basheer SN, Connolly MB, Lautzenhiser A, Sherman EM, Henderson G, Steinbok P: Hemispheric surgery in children with refractory epilepsy: seizure outcome, complications, and adaptive function. *Epilepsia* **48**:133–140, 2007
3. Beardsworth ED, Adams CB: Modified hemispherectomy for epilepsy: early results in 10 cases. *Br J Neurosurg* **2**:73–84, 1988
4. Caraballo R, Bartuluchi M, Cersósimo R, Soraru A, Pomata H: Hemispherectomy in pediatric patients with epilepsy: a study of 45 cases with special emphasis on epileptic syndromes. *Childs Nerv Syst* **27**:2131–2136, 2011
5. Carmant L, Kramer U, Riviello JJ, Helmers SL, Mikati MA, Madsen JR, et al: EEG prior to hemispherectomy: correlation with outcome and pathology. *Electroencephalogr Clin Neurophysiol* **94**:265–270, 1995
6. Cook SW, Nguyen ST, Hu B, Yudovin S, Shields WD, Vinters HV, et al: Cerebral hemispherectomy in pediatric patients with epilepsy: comparison of three techniques by pathological substrate in 115 patients. *J Neurosurg* **100** (2 Suppl Pediatrics):125–141, 2004
7. Dagar A, Chandra PS, Chaudhary K, Avnish C, Bal CS, Gai-kwad S, et al: Epilepsy surgery in a pediatric population: a retrospective study of 129 children from a tertiary care hospital in a developing country along with assessment of quality of life. *Pediatr Neurosurg* **47**:186–193, 2011
8. Davies KG, Maxwell RE, French LA: Hemispherectomy for intractable seizures: long-term results in 17 patients followed for up to 38 years. *J Neurosurg* **78**:733–740, 1993
9. Delalande O, Bulteau C, Dellatolas G, Fohlen M, Jalin C, Buret V, et al: Vertical parasagittal hemispherotomy: surgical procedures and clinical long-term outcomes in a population of 83 children. *Neurosurgery* **60** (2 Suppl 1):ONS19–ONS32, 2007
10. Delalande O, Pinard JM, Basdevant C, Gauthe M, Plouin P, Dulac O: Hemispherotomy: a new procedure for central disconnection. *Epilepsia* **33** (Suppl 3):99–100, 1992
11. Devlin AM, Cross JH, Harkness W, Chong WK, Harding B, Vargha-Khadem F, et al: Clinical outcomes of hemispherectomy for epilepsy in childhood and adolescence. *Brain* **126**:556–566, 2003
12. Duchowny M, Jayakar P, Resnick T, Harvey AS, Alvarez L, Dean P, et al: Epilepsy surgery in the first three years of life. *Epilepsia* **39**:737–743, 1998
13. Engel J Jr, Van Ness PC, Rasmussen TB, Ojemann LM: Outcome with respect to epileptic seizures, in Engel J Jr (ed): *Surgical Treatment of the Epilepsies*, ed 2. New York: Raven Press, 1993, pp 609–621
14. Engel J Jr, Wiebe S, French J, Sperling M, Williamson P, Spencer D, et al: Practice parameter: temporal lobe and localized neocortical resections for epilepsy: report of the Quality Standards Subcommittee of the American Academy of Neurology, in association with the American Epilepsy Society and the American Association of Neurological Surgeons. *Neurology* **60**:538–547, 2003
15. Holthausen H, May TW, Adams CT, Andermann F, Comair Y, Delalande O: Seizures post hemispherectomy, in Tuxhorn I, Holthausen H, Boenigk H (eds): *Paediatric Epilepsy Syndromes and Their Surgical Treatment*. London: John Libbey, 1997, pp 749–773
16. Ignelzi RJ, Bucy PC: Cerebral hemidecortication in the treatment of infantile cerebral hemiatrophy. *J Nerv Ment Dis* **147**:14–30, 1968
17. Jonas R, Nguyen S, Hu B, Asarnow RF, LoPresti C, Curtiss S, et al: Cerebral hemispherectomy: hospital course, seizure, developmental, language, and motor outcomes. *Neurology* **62**:1712–1721, 2004
18. Kossoff EH, Buck C, Freeman JM: Outcomes of 32 hemispherectomies for Sturge-Weber syndrome worldwide. *Neurology* **59**:1735–1738, 2002
19. Kossoff EH, Vining EP, Pillas DJ, Pyzik PL, Avellino AM, Carson BS, et al: Hemispherectomy for intractable unihemispheric epilepsy etiology vs outcome. *Neurology* **61**:887–890, 2003
20. Krynauw RA: Infantile hemiplegia treated by removing one cerebral hemisphere. *J Neurol Neurosurg Psychiatry* **13**:243–267, 1950
21. Lettori D, Battaglia D, Sacco A, Veredice C, Chieffo D, Massimi L, et al: Early hemispherectomy in catastrophic epilepsy: a neuro-cognitive and epileptic long-term follow-up. *Seizure* **17**:49–63, 2008
22. Limbrick DD, Narayan P, Powers AK, Ojemann JG, Park TS, Bertrand M, et al: Hemispherotomy: efficacy and analysis of seizure recurrence. Clinical article. *J Neurosurg Pediatr* **4**:323–332, 2009
23. Marras CE, Granata T, Franzini A, Freri E, Villani F, Casazza M, et al: Hemispherotomy and functional hemispherectomy.

- tomy: indications and outcome. **Epilepsy Res** 89:104–112, 2010
24. Moher D, Liberati A, Tetzlaff J, Altman DG: Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. **PLoS Med** 6:e1000097, 2009
 25. Moosa AN, Gupta A, Jehi L, Marashly A, Cosmo G, Lachhwani D, et al: Longitudinal seizure outcome and prognostic predictors after hemispherectomy in 170 children. **Neurology** 80:253–260, 2013
 26. Pulsifer MB, Brandt J, Salorio CF, Vining EP, Carson BS, Freeman JM: The cognitive outcome of hemispherectomy in 71 children. **Epilepsia** 45:243–254, 2004
 27. Ramantani G, Kadish NE, Brandt A, Strobl K, Stathi A, Wiegang G, et al: Seizure control and developmental trajectories after hemispherotomy for refractory epilepsy in childhood and adolescence. **Epilepsia** 54:1046–1055, 2013
 28. Rasmussen T: Hemispherectomy for seizures revisited. **Can J Neurol Sci** 10:71–78, 1983
 29. Schramm J: Hemispheric disconnection procedures, in Winn HR (ed): **Youmans Neurological Surgery**, ed 6. Philadelphia: Elsevier/Saunders, 2011, Vol 1, pp 796–806
 30. Schramm J, Behrens E, Entzian W: Hemispherical deafferentation: an alternative to functional hemispherectomy. **Neurosurgery** 36:509–516, 1995
 31. Schramm J, Kral T, Clusmann H: Transylvian keyhole functional hemispherectomy. **Neurosurgery** 49:891–901, 2001
 32. Schramm J, Kuczaty S, Sassen R, Elger CE, von Lehe M: Pediatric functional hemispherectomy: outcome in 92 patients. **Acta Neurochir (Wien)** 154:2017–2028, 2012
 33. Shimizu H, Maehara T: Modification of peri-insular hemispherotomy and surgical results. **Neurosurgery** 47:367–373, 2000
 34. Shimizu H, Maehara T: Neuronal disconnection for the surgical treatment of pediatric epilepsy. **Epilepsia** 41 (Suppl 9): 28–30, 2000
 35. Smith SJ, Andermann F, Villemure JG, Rasmussen TB, Quesney LF: Functional hemispherectomy: EEG findings, spiking from isolated brain postoperatively, and prediction of outcome. **Neurology** 41:1790–1794, 1991
 36. Sugimoto T, Otsubo H, Hwang PA, Hoffman HJ, Jay V, Snead OC III: Outcome of epilepsy surgery in the first three years of life. **Epilepsia** 40:560–565, 1999
 37. Téllez-Zenteno JF, Dhar R, Wiebe S: Long-term seizure outcomes following epilepsy surgery: a systematic review and meta-analysis. **Brain** 128:1188–1198, 2005
 38. Terra-Bustamante VC, Inuzuka LM, Fernandes RM, Escorsi-Rosset S, Wichert-Ana L, Alexandre V Jr, et al: Outcome of hemispheric surgeries for refractory epilepsy in pediatric patients. **Childs Nerv Syst** 23:321–326, 2007
 39. Thomas SG, Daniel RT, Chacko AG, Thomas M, Russell PS: Cognitive changes following surgery in intractable hemispheric and sub-hemispheric pediatric epilepsy. **Childs Nerv Syst** 26:1067–1073, 2010
 40. Torres CV, Fallah A, Ibrahim GM, Cheshier S, Otsubo H, Ochi A, et al: The role of magnetoencephalography in children undergoing hemispherectomy. Clinical article. **J Neurosurg Pediatr** 8:575–583, 2011
 41. van der Kolk NM, Boshuisen K, van Empelen R, Koudijs SM, Staudt M, van Rijen PC, et al: Etiology-specific differences in motor function after hemispherectomy. **Epilepsy Res** 103:221–230, 2013
 42. Villarejo-Ortega F, García-Fernández M, Fournier-Del Castillo C, Fabregate-Fuente M, Álvarez-Linera J, De Prada-Vicente I, et al: Seizure and developmental outcomes after hemispherectomy in children and adolescents with intractable epilepsy. **Childs Nerv Syst** 29:475–488, 2013
 43. Villemure JG, Daniel RT: Peri-insular hemispherotomy in paediatric epilepsy. **Childs Nerv Syst** 22:967–981, 2006
 44. Villemure JG, Mascott CR: Peri-insular hemispherotomy: surgical principles and anatomy. **Neurosurgery** 37:975–981, 1995
 45. Villemure JG, Meagher-Villemure K, Montes JL, Farmer JP, Broggi G: Disconnective hemispherectomy for hemispheric dysplasia. **Epileptic Disord** 5 (Suppl 2):S125–S130, 2003
 46. Wiebe S, Blume WT, Girvin JP, Eliasziw M: A randomized, controlled trial of surgery for temporal-lobe epilepsy. **N Engl J Med** 345:311–318, 2001
 47. Yu T, Zhang G, Kohrman MH, Wang Y, Cai L, Shu W, et al: A retrospective study comparing preoperative evaluations and postoperative outcomes in paediatric and adult patients undergoing surgical resection for refractory epilepsy. **Seizure** 21:444–449, 2012

Author Contributions

Conception and design: Griessenauer, Blount, Winkler.
 Acquisition of data: Griessenauer, Salam, Hendrix, Patel.
 Analysis and interpretation of data: Griessenauer, Salam, Hendrix, Patel. Drafting the article: Griessenauer. Critically revising the article: Griessenauer, Hendrix, Tubbs, Blount, Winkler.
 Reviewed submitted version of manuscript: Griessenauer, Tubbs, Blount, Winkler. Approved the final version of the manuscript on behalf of all authors: Griessenauer. Statistical analysis: Griessenauer, Hendrix. Administrative/technical/material support: Griessenauer, Tubbs. Study supervision: Griessenauer, Blount, Winkler.

Correspondence

Christoph J. Griessenauer, 1530 3rd Ave. S, Birmingham, AL 35294. email: cgriessenauer@uabmc.edu.