

Discussion

This is the first reported epidemiological investigation within a US state based entirely on autopsy-confirmed cases, thereby allowing estimation of prion disease death rate in Washington. Although there were no additional reported cases of confirmed prion disease in Washington during this period, our calculated death rate may represent a lower estimate because some cases of prion disease may not have been recognized clinically, some clinically compatible cases may not have been autopsied, and some cases may not have been reported. Despite these potential limitations, our death rate estimate from autopsies closely aligns with the estimated national rate of 1.2 cases per 1 million population annually calculated from death certificate data.⁵ Although the incubation period of 6 to 12 years for vCJD has to be considered, it is not at all clear that timing should begin with the first recognized case of BSE in the United States, because no comprehensive screening program was in place. Nevertheless, our results do not support the hypotheses that vCJD is an emerging illness in Washington, or that sCJD is more common in this state than in other regions of the world.⁶ Although our findings and lack of evidence for epidemic BSE in the United States is encouraging, continued enhanced surveillance for prion diseases is needed because our knowledge about emergence and transmission is inadequate, and because an endemic prion disease of North American elk and deer (chronic wasting disease) is spreading.⁷ Our program may serve as an example to other states that wish to enhance surveillance of prion diseases.

This work was supported by the National Prion Disease Pathology Surveillance Center, the Centers for Disease Control, and the NIH (NIA, AG05136, T.J.M.).

References

1. Zeidler M, Ironside JW. The new variant of Creutzfeldt-Jakob disease. *Rev Sci Tech* 2000;19:98–120.
2. Cali I, Castellani R, Yuan J, et al. Classification of sporadic Creutzfeldt-Jakob disease revisited. *Brain* 2006;129:2266–2277.
3. Markesbery WR, ed. *Neuropathology of dementing disorders*. London: Arnold Publishers, 1998.
4. Parchi P, Giese A, Capellari S, et al. Classification of sporadic Creutzfeldt-Jakob disease based on molecular and phenotypic analysis of 300 subjects. *Ann Neurol* 1999;46:224–233.
5. Centers for Disease Control and Prevention (CDC). Surveillance for Creutzfeldt-Jakob disease—United States. *MMWR Morb Mortal Wkly Rev* 1996;45:665–668.
6. Ladogana A, Puopolo M, Croes EA, et al. Mortality from Creutzfeldt-Jakob disease and related disorders in Europe, Australia, and Canada. *Neurology* 2005;64:1586–1591.
7. Williams ES. Chronic wasting disease. *Vet Pathol* 2005;42:530–549.

Hemispherectomy for Intractable Epilepsy in Adults: The First Reported Series

Shearwood McClelland III, MD,
and Robert E. Maxwell, MD, PhD

Hemispherectomy for intractable unihemispheric epilepsy (IUE) has long been established in pediatric patients. This study reports the first series examining hemispherectomy exclusively in adult patients (>18 years old). Nine adults with IUE underwent hemispherectomy at the University of Minnesota. All patients had unilateral hemiplegia and visual field loss. Seven patients (77.8%) were Engel class I/II at last follow-up. Five (83.3%) of the six patients with >30 years of follow-up were seizure free. No surgery-related mortality, hydrocephalus, or superficial cerebral hemosiderosis occurred. Hemispherectomy is an effective procedure in appropriately selected adult patients, resulting in excellent long-term seizure control and no mortality.

Ann Neurol 2007;61:372–376

The removal of an entire cortical hemisphere, known as a classic anatomic hemispherectomy, was initially utilized in 1928 for the treatment of diffuse malignant gliomas of the nondominant cerebral hemisphere.^{1,2} Despite disappointing results, the radical novelty of the technique led to its initial utilization for treatment of intractable seizures just 10 years later.³ However, it was not until 1950, when utilization of the procedure to treat infantile hemiplegia associated with intractable epilepsy resulted in excellent short-term seizure control, that hemispherectomy became widely used for treating intractable epilepsy associated with unilateral hemisphere damage.⁴ Multiple subsequent reports involving classic and modified (functional) hemispherectomies have confirmed the efficacy of the approach in the pediatric population for intractable epilepsy for many conditions, including hemimeganencephaly, infantile hemiplegia seizures, Lennox–Gastaut syndrome, Ras-

From the Department of Neurosurgery, University of Minnesota Medical School, Minneapolis, MN.

Received Sep 13, 2007, and in revised form Dec 20. Accepted for publication Dec 22, 2007.

Published online Feb 23, 2007, in Wiley InterScience (www.interscience.wiley.com). DOI: 10.1002/ana.21084

Address correspondence to Dr McClelland, Department of Neurosurgery, University of Minnesota, Mayo Mail Code 96, 420 Delaware Street SE, Minneapolis, MN 55455. E-mail: mccl0285@umn.edu

mussen's encephalitis, Sturge-Weber syndrome, and infantile spasms.⁵⁻¹⁶

Despite the well-established efficacy of hemispherectomy for treating intractable epilepsy in pediatric patients, only a limited number of case reports on hemispherectomy for adults have been published.¹⁷⁻¹⁹ To address this void, we present the following hemispherectomy series, the first to focus exclusively on adult patients.

Patients and Methods

Patient Demographics

All hemispherectomies were performed by one of two surgeons (Robert E. Maxwell, Lyle A. French). Patients were selected by the operating surgeon and a neurology team specializing in the treatment of epilepsy by long-standing intractable seizures despite optimal medication adjustment. In addition, eligible patients had to have demonstrated previous hemispheric damage, homonymous hemianopsia, and hemiparesis contralateral to the side of hemispheric damage, with no other evidence of neurological deficits. Intracarotid amobarbital (Amytal) testing was performed on all patients subsequent to the initial two of this series. Over a 49-year period, nine adults (six women and three men) with medically intractable epilepsy underwent hemispherectomy at the University of Minnesota Hospitals (eight anatomic, one functional) (Table 1). Mean age at surgery was 28.1 (range, 19-38) years. Five procedures were right-sided and four were left-sided procedures. The most common seizure cause was birth trauma (four patients); two patients had encephalitis, two patients had prior glioma resections, and one patient had a large hemispheric arteriovenous malformation (see Table 1). The mean duration of seizures was 22.2 (range, 12-34) years (see Table 1).

Operative Techniques

Classic anatomic and functional hemispherectomies were performed as detailed previously.^{14,20,21} In brief, for anatomic hemispherectomies, a large craniotomy flap was

turned, and once the opposite anterior cerebral artery was deemed competent, the ipsilateral middle cerebral and anterior cerebral arteries were ligated. The posterior cerebral artery was ligated approximately 1cm from its origin, after which the veins entering the dural venous sinuses were divided and the corpus callosum transected. The lateral ventricle was then entered and the stria terminalis was visualized and incised to enable the caudate nucleus to be separated from the thalamus. This dissection was then taken down to the internal capsule. An area of the cerebellum was then exposed via removal of a wedge of the tentorium cerebelli, which served to enlarge the incisura and facilitate drainage from the cavity. The choroid plexus was then coagulated and destroyed. Although the precise extent of basal ganglia resection varied slightly in different patients, the entire cortex was removed in all patients, including the inferior orbital gyri, insula, hippocampus, and lateral amygdala. The head and tail of the caudate nucleus and the thalamus were spared in all patients, and the foramen of Monro was left patent. Regardless of technique, particular attention was paid to hemostasis at the time of surgery, and a drain was left in the hemispherectomy cavity.

Postoperative Care

After surgery, the hemispherectomy cavity drains were left in place until the drainage cleared to ensure minimal collection of blood products within the hemispherectomy cavity. Typically, patients were discharged from the neurosurgery service 7 to 14 days after surgery, were seen for outpatient visits several times during the first few months, and then annually thereafter if seizure free (more often if not). Postoperative imaging was routinely obtained after surgery. Antiepileptic medications were managed by the treating neurologist, but generally were not substantially changed during the first year after surgery.

Results

Clinical Outcome

Mean follow-up time was 21 (range, 0.8-38) years. Using a modified Engel outcome scale, we designated 5

Table 1. Demographics of Adult Patients Receiving Hemispherectomy for Intractable Epilepsy

Patient No.	Age at Surgery (yr)	Sex	Seizure Duration (yr)	Surgery Side	Type of Operation	Causative Factors of Seizures
1	38	M	12	L	Complete	Previous glioma resection
2	34	F	29	R	Complete	Encephalitis at age 2
3	19	F	19	L	Complete	Meningoencephalitis at 5 weeks
4	35	F	34	R	Complete	Birth trauma
5	30	M	30	R	Complete	Birth trauma
6	26	F	18	L	Complete	Large hemispheric AVM
7	23	M	23	L	Complete	Birth trauma
8	22	F	16	R	Complete	Previous astrocytoma resection
9	26	F	19	R	Functional	Birth trauma

L = left; R = right; AVM = arteriovenous malformation.

patients (55.6%) as class I (seizure free), 2 (22.2%) as class II (rare seizures), none as class III ($\geq 75\%$ seizure reduction), and 2 (22.2%) as class IV ($< 75\%$ improvement) at last follow-up (Table 2).²² Six patients had at least 10 years of follow-up, all of whom were either class I or II, with five (83.3%) being class IA (see Table 2). Five patients had at least 30 years of follow-up, four (80%) of whom were class IA (see Table 2). Six patients were still requiring antiepileptic medication at the time of latest follow-up. Three patients have become employable since surgery, with three leading independent lives and one semi-independent (living in a community home) (see Table 2).

Postoperative Course

There were no cases of compromised ambulation, blood losses requiring transfusion, hydrocephalus, thromboplastin reactions, or surgery-related mortality among the nine patients. Two patients experienced perioperative morbidity. One patient with a large arteriovenous malformation developed an epidural abscess with subsequent bone flap infection resulting in a permanent dysphasia. Another patient had an exacerbation of pre-existing hemiparesis (see Table 2). The patient with permanent dysphasia (Case 6; left-sided resection) was the only patient receiving intracarotid Amytal testing to have mixed language dominance. All other left-sided resection candidates tested were shown to have right-sided hemisphere dominance for language, with no other patient having language compromise after. There were no cases of late perioperative morbidity (defined as morbidity greater than 10 years after surgery), including superficial cerebral hemosiderosis, recurrent bleeding into the cerebrospinal fluid (CSF), subdural hematomas, or increased intracranial pressure

associated with lateral ventricle enlargement. The perioperative complication rate was 22.2%, with no delayed complications occurring in this adult series.

Discussion

Despite the extensive amount of brain resected, hemispherectomy is an accepted treatment for appropriately chosen epilepsy patients because of its well-established efficacy in eliminating or significantly reducing intractable seizures in the pediatric population. More than 90% of children have reduced seizures after surgery, with seizure freedom rates after surgery ranging from 40 to 100%.^{9,13-15,21,23,24}

Unfortunately, the published experience with hemispherectomy in adult patients is lacking. This may be due to concern that the relatively high morbidity (reported as high as 50%) and/or perioperative mortality rates (reported as high as 6% in the mid-1990s) of hemispherectomy in children would be significantly greater after extensive resection of adult brain, which is not as plastic as the pediatric brain.^{13,21,25} This retrospective analysis of outcomes after hemispherectomy in adult epilepsy patients addresses this void.

Before surgery, all patients in this series had severe hemiparesis consistent with unihemispheric damage, together with a nonfunctional "helper" hand and homonymous hemianopsia. No other neurological deficit was present in these patients either before or after surgery. After hemispherectomy, the neurological improvement concomitant with excellent seizure control in the majority of the patients in this series can be attributed to two main factors. First, the absence of the diseased hemisphere enables the remaining hemisphere to function with improved efficacy without being contaminated by seizure propagation. Second, the reduced

Table 2. Outcomes of Adult Patients after Hemispherectomy

Patient No.	Follow-up	Engel Class	AED Needed	Employment	Living Situation	Morbidity
1	10 yr	IA	N	N	Family home	None
2	38 yr	IA	Y	N	Family home	None
3	1 yr	IVA	N/A	N/A	N/A	None (died of diphtheria 13 months after surgery)
4	36 yr	IA	Y	Y	Community home	None
5	37 yr	IIA	N	N	Independent	None
6	33 yr	IA	Y	N	Family home	Epidural abscess, bone flap infection, permanent new-onset dysphasia
7	32 yr	IA	Y	Y	Independent	None
8	1 yr	IVB	Y	N	Family home	Worsening of preoperative hemiparesis
9	10 mo	IID	Y	Y	Independent	None

AED = antiepileptic drug; IA = completely free of disabling seizures; IVA = less than 75% seizure reduction, but with significant reduction of seizures; N/A = not applicable; IIA = initially seizure free, now with rare disabling seizures; IVB = no significant change in seizures; IID = nocturnal seizures only.

antiepileptic medication requirements after surgery decrease the likelihood of patients suffering potentially toxic medication-related side effects. In the two patients with less than 75% reduction of preoperative seizures (Patients 3 and 8, class IVA and IVB, respectively; see Table 2), each was found to have contralateral seizure foci after surgery, which although much less prevalent than in the hemisphere resected, was sufficient to result in seizures after surgery. The most prevalent risk factor for this occurrence is the preoperative seizure duration, which may predispose to small seizure foci in the contralateral hemisphere, although in this series, the seizure duration of these two patients was not significantly different from that of the remaining seven patients (see Table 1).

This series shows that adult hemispherectomy is associated with greater than 55% seizure freedom at last follow-up, with nearly 80% of patients being Engel class I or II at 1 year after surgery and 100% being Engel class I or II at both 10 and 30 years after surgery. These findings are consistent with a previous pediatric hemispherectomy study, which notes a positive correlation between increasing age at surgery and postoperative seizure freedom.²⁵ Equally, if not more, important, the morbidity was low in this series with no surgery-related mortality, particularly encouraging because the predominant surgical technique, the classic anatomic hemispherectomy, has historically been associated with the greatest morbidity rate among hemispherectomy modalities.^{26–29}

The low morbidity rate in this series is believed to be because of several factors. Meticulous attention to hemostasis throughout surgery, particularly before dural closure, reduces the deposition of blood products that when present result in membrane formation and the eventual development of hydrocephalus or superficial cerebral hemosiderosis, or both. Prophylactic drainage of the hemispherectomy cavity also prevented postoperative collection of blood products that could otherwise predispose to membrane formation and superficial cerebral hemosiderosis.^{10,11,26,27,30} These drains were left in place until there was no visible evidence of blood product remnants.

Care was taken during the operation to establish free communication between the supratentorial and infratentorial spaces by fenestration of the tentorium cerebelli at the incisura. This further served to promote CSF circulation and toiletry of the supratentorial spaces. Finally, the intraoperative coagulation of the choroid plexus where visualized was performed with the intent of reducing CSF production, thereby offsetting any reduction of CSF absorption caused by aseptic meningitis and membrane formation.

The results from this study indicate that for appropriately chosen patients, hemispherectomy can be as efficacious in adults as it is in children, with seizure con-

trol sustainable over multiple decades. The additional benefit of increased postoperative employability for these adult patients should not be overlooked, because it underscores the potential for hemispherectomy to contribute toward reducing the overall socioeconomic burden imposed by severe, intractable, unihemispheric epilepsy.

Conclusions

This long-term follow-up study suggests that hemispherectomy is an effective procedure in appropriately selected adult patients, resulting in greater than 55% seizure freedom and 78% seizure control (Engel class I or II). The seizure control after hemispherectomy remains stable over the long term, as all patients with more than 30 years of follow-up experienced seizure control, 80% of whom were seizure free. The minimal morbidity and absence of delayed complications with this technique in adults suggests that the incidence and severity of hemorrhagic complications after anatomic hemispherectomy are not a contraindication for this surgical option in adults. Hemispherectomy can be a safe and effective adjunctive treatment for appropriately selected adult patients with medically intractable epilepsy.

We thank Dr L. A. French, Dr K. G. Davies, and J. Odegard for invaluable assistance.

References

1. Dandy WE. Removal of right cerebral hemisphere for certain tumors with hemiplegia. Preliminary report. *JAMA* 1928;90:823–825.
2. L'Hermite J. L'ablation complete de l'hémisphère droit dans les cas de tumeur cérébrale localisée compliquée d'hémiplégie. La décebration supra-thalamique unilatérale chez l'homme. *Encephale* 1928;23:314–323.
3. McKenzie KG. The present status of a patient who had the right cerebral hemisphere removed. *JAMA* 1938;111:168.
4. Krynauw RA. Infantile hemiplegia treated by removing one cerebral hemisphere. *J Neurol Neurosurg Psychiatry* 1950;13:243–267.
5. French LA, Johnson DR, Brown IA, Van Bergen FB. Cerebral hemispherectomy for control of intractable convulsive seizures. *J Neurosurg* 1955;12:154–164.
6. Griffith HB. Cerebral hemispherectomy for infantile hemiplegia in the light of the late results. *Ann R Coll Surg Engl* 1987;41:183–201.
7. Ignelzi RJ, Bucy PC. Cerebral hemidecortication in the treatment of infantile cerebral hemiatrophy. *J Nerv Ment Dis* 1968;147:14–30.
8. Lindsay J, Ounsted C, Richards P. Hemispherectomy for childhood epilepsy: a 36 year study. *Dev Med Child Neurol* 1987;29:592–600.
9. Rasmussen T. Hemispherectomy for seizures revisited. *Can J Neurol Sci* 1983;10:71–78.
10. Adams CBT. Hemispherectomy—a modification. *J Neurol Neurosurg Psychiatry* 1983;46:617–619.

11. Beardsworth ED, Adams CBT. Modified hemispherectomy for epilepsy: early results in 10 cases. *Br J Neurosurg* 1988;2:73–84.
12. Peacock WJ. Hemispherectomy for the treatment of intractable seizures in childhood. *Neurosurg Clin N Am* 1995;6:549–556.
13. Carson BS, Javedan SP, Freeman JM, et al. Hemispherectomy: a hemidecortication approach and review of 52 cases. *J Neurosurg* 1996;84:903–911.
14. Tubbs RS, Nimjee SM, Oakes WJ. Long-term follow-up in children with functional hemispherectomy for Rasmussen's encephalitis. *Childs Nerv Syst* 2005;21:461–465.
15. Gonzalez-Martinez JA, Gupta A, Kotagal P, et al. Hemispherectomy for catastrophic epilepsy in infants. *Epilepsia*. 2005;46:1518–1525.
16. O'Brien DF, Basu S, Williams DH, May PL. Anatomical hemispherectomy for intractable seizures: excellent seizure control, low morbidity and no superficial cerebral haemosiderosis. *Childs Nerv Syst* 2006;22:489–498.
17. Muller F, Kunesch E, Binkofski F, Freund HJ. Residual sensorimotor functions in a patient after right-sided hemispherectomy. *Neuropsychologia* 1991;29:125–145.
18. Bates AL, Zadai CC. Acute care physical therapist evaluation and intervention for an adult after right hemispherectomy. *Phys Ther* 2003;83:567–580.
19. Loddenkemper T, Dinner DS, Kubu C, et al. Aphasia after hemispherectomy in an adult with early onset epilepsy and hemiplegia. *J Neurol Neurosurg Psychiatry* 2004;75:149–151.
20. French LA, Johnson DR, Adkins GH. Cerebral hemispherectomy for intractable seizures—a long-term follow-up. *J Lancet* 1961;2:58–65.
21. Davies KG, Maxwell RE, French LA. Hemispherectomy for intractable seizures: long-term results in 17 patients followed for up to 38 years. *J Neurosurg* 1993;78:733–740.
22. 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*. 2nd ed. New York: Raven Press, 1993;609–621.
23. Devlin AM, Cross JH, Harkness W, et al. Clinical outcomes of hemispherectomy for epilepsy in childhood and adolescence. *Brain* 2003;126:556–566.
24. Kanev PM, Foley CM, Miles D. Ultrasound-tailored functional hemispherectomy for surgical control of seizures in children. *J Neurosurg* 1997;86:762–767.
25. Kossoff EH, Buck C, Freeman JM. Outcomes of 32 hemispherectomies for Sturge-Weber syndrome worldwide. *Neurology* 2002;59:1735–1738.
26. Hughes JT, Oppenheimer DR. Superficial siderosis of the central nervous system. A report of nine cases with autopsy. *Acta Neuropathol* 1969;13:56–74.
27. Oppenheimer DR, Griffith HB. Persistent intracranial bleeding as a complication of hemispherectomy. *J Neurol Neurosurg Psychiatry* 1966;29:229–240.
28. White HH. Cerebral hemispherectomy in the treatment of infantile hemiplegia. Review of the literature and report of two cases. *Confin Neurol* 1961;21:1–50.
29. Wilson PJE. Cerebral hemispherectomy for infantile hemiplegia. A report of 50 cases. *Brain* 1970;93:147–180.
30. Goodman R. Hemispherectomy and its alternatives in the treatment of intractable epilepsy in patients with infantile hemiplegia. *Dev Med Child Neurol* 1986;28:251–258.