Hypothalamic Hamartoma Treatment: Surgical Resection With the Transcallosal Approach

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Multiple treatment options are available for patients with hypothalamic hamartoma (HH) including the frontotemporal approaches, the anterior transcallosal transseptal interforrnical approach, the transventricular endoscopic approach, and stereotactic radiosurgery. Relatively large patient series of the transcallosal resection/disconnection from Royal Children’s Hospital in Melbourne and the Barrow Neurological Institute in Phoenix, AZ, show, respectively, that 52% to 54% are 100% seizure free, and 24% to 35% have >90% seizure reduction. However, there appears to be an 8% to 14% risk of persisting memory problems. The surgery should ideally be performed in the early years of childhood before secondary generalized epilepsy develops and developmental delay and behavioral problems are established. Radiosurgery may be a preferable option for higher-functioning adolescent or adult patients with HH. The choice of treatment must be individualized depending on the age and clinical circumstances of the patient and the size and anatomic relationships of the hamartoma. The transcallosal resection of HH is an effective and safe treatment, but there is a small risk of short-term memory impairment. The endoscopic approach is an alternative to the transcallosal approach for smaller HH.

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Hypothalamic hamartoma (HH) is a rare developmental abnormality of the hypothalamus that occurs either as a small pedunculated lesion attached to the tuber cinereum or more commonly as a sessile mass lesion that is intimately attached to the hypothalamus on 1 or both sides and bulges into the third ventricular cavity and in some cases the suprassellar and preopticine cisterns. The true incidence is unknown. We have estimated a frequency of roughly 1 case per million based on the number of HH patients from Australia that we had seen as a central reference center. HH is probably more frequent than previously appreciated because of increased awareness of the condition by clinicians and improved imaging with magnetic resonance imaging (MRI). We have also encountered a number of failed temporal lobectomy and frontal corticectomy patients who had a small HH that was missed at the original epilepsy workup. Brandberg and coworkers estimated an incidence of one in 200,000 children and adolescents for HH and epilepsy.

HH vary in size considerably ranging from a few millimeters to several centimeters in diameter. The structural relationships of HH are best appreciated on MRI, and the radiologic features of HH have recently been described in a detailed review of 72 cases. The larger of these lesions may extend into the preoptic cistern and be associated with cystic components. The pedunculated lesion may cause precocious puberty, and the sessile intrahypothalamic lesions cause combinations of gelastic epilepsy and precocious puberty. Most cases of HH are sporadic, but about 5% of cases have the Pallister-Hall syndrome, which is associated with a mutation in the GLI3 gene and manifests with multiple dysmorphic features, including postradial polydactyly, bifid epiglottis, and imperforate anus.

HH are now known to be intrinsically epileptogenic and are the site of origin of gelastic seizures. There is a wide variation in the initial presentation and clinical course of the seizures in patients with HH. The spectrum of epilepsy in patients with HH ranges from a benign static course of infrequent gelastic seizures causing minimal interference to the daily life of the affected individual to a progressive epilepsy with multiple seizure types, secondary generalized epilepsy,
and in the most severe form, seizures every few minutes and resultant epileptic encephalopathy. The seizures may occur from day 1 of life. Developmental delay, behavioral disorders with aggression and temper tantrums, intellectual disability, and in some cases autistic features occur in the more severely affected patients. The epilepsy caused by hypothalamic hamartomas tends to be resistant to antiepileptic drugs, and it is very burdensome for the parents to care for a severely affected child. Adults may present with nongelastic seizures and have a milder course with less behavioral problems.

We identified 27 publications reporting outcome of HH surgery from 1967 to 2000, most consisting of small case series, showing variable success, relatively short follow-up intervals, and some serious complications. There has been an increasing number of reports of successful surgical approaches for HH over the last decade. The pedunculated HH causing precocious puberty should be managed medically. Surgical extirpation of intrahypothalamic HH has been performed since the 1960s by using the classical subfrontal or trans-sylvian approach. However, the results of these approaches have generally been poor with serious complications such as hemiplegia, blindness, and death being reported in the literature and by families. Until it was shown that gelastic seizures were originating from the HH, some children had temporal and frontal lobe resections without any success. Surgical extirpation of intrahypothalamic HH has been performed since the 1960s by using the classical subfrontal or trans-sylvian approach. However, the results of these approaches have generally been poor with serious complications such as hemiplegia, blindness, and death being reported in the literature and by families. Until it was shown that gelastic seizures were originating from the HH, some children had temporal and frontal lobe resections without any success.

Palmini and coworkers reported 13 patients from 3 centers in 2002, 12 with a frontotemporal and 1 an endoscopic approach. Two of 13 (15.4%) were seizure free, and 11 of 13 (84.6%) had >90% reduction of drop attacks and generalized tonic-clonic seizures. However, gelastic, complex partial, and atypical absence seizures persisted in 11 patients with a mean follow-up of 2.8 years (1-5.5 years).

Delalande and Fohlen reported 17 patients in 2003. Sixteen had disconnection and 1 total removal. There were 14 open and 9 endoscopic procedures. Eight of 17 (47%) patients were seizure free, 1 patient had only brief gelastic seizures, and 8 of 17 (47%) patients were improved with a mean follow-up of 18.6 months (8 days-43 months). Eight of 17 patients (47%) required a second (endoscopic) procedure to enhance the disconnection of the HH.

Surgery within the hypothalamus is treated with great caution, respect, and trepidation by neurosurgeons, and until recently neurologists have been reluctant to refer patients with HH for surgery. We were driven to attempt surgery on the affected children because the effects of the HH were so devastating for the child, and the family and surgery had become a last resort. However, we found that we were not able to adequately resect the intraventricular component of the HH by using a trans-sylvian subfrontal approach, and the epilepsy control was incomplete. Therefore, a different approach was conceived to optimize HH resection. Rosenfeld and coworkers first described the transcallosal approach for HH in 2001. Nguyen and coworkers did a review of 71 surgical cases in the literature and found the best results were seen in the 15 patients with complete or near-complete HH resection, with 10 (66%) seizure free and 5 (33%) with “significant improvement.”

Patients with a HH and medically intractable epilepsy are potential candidates for surgery particularly if they are in early childhood years (2-6 years) and have developed behavioral problems and cognitive impairment. We recommend that all patients require detailed assessment in a Comprehensive Epilepsy Program and that each individual case be judged on its merits. We suggest a more cautious approach when considering surgery for severely retarded children or adults with HH and severe epilepsy. Although surgery will not reverse developmental disability, even a marginal improvement in the epilepsy may be important to the family and caregivers.

The “Classic” Transcallosal Interforniceal Approach

The midline transcallosal approach to the third ventricle via a transeptal interforniceal trajectory has been well described. This is an extensile exposure done through a callosotomy across the body of the corpus callosum with a separation of the fornices where the arching fibers are splaying apart and both sides are fused at the fornical commissure or raphe. Beneath the fornices is the tela choroidea of the third ventricle with the 2 internal cerebral veins passing posteriorly from the confluence of the thalamostriate and septal veins. Although this approach gives a wide exposure of the third ventricle, there is a risk of bridging vein injury and consequent cerebral hemisphere swelling; pericallosal artery injury; callosal disconnection syndrome; bilateral fornical retraction injury, which may cause permanent short-term memory impairment; and deep cerebral venous injury, which may cause cerebral swelling, infarction and death. The more posterior the callosotomy, the more chance there is of causing injury to the fornix at the level of the fornical and hippocampal commissures or to the motor cortex.

The potential for short-term episodic memory disturbance because of fornical trauma is a major disincentive to the transcallosal interforniceal approach. Memory disturbance caused by fornical or mammillary body injury may be permanent. A transient short-term memory loss was reported in 30% of patients in the series of Apuzzo and Amar by using the interforniceal approach. The memory disturbance was maximal for the first 24 to 72 hours and gradually settled; 75% resolved over 7 days and all resolved or returned to preoperative status by 3 months.

Winkler and coworkers used the transcallosal and transforaminal approaches in 30 patients with mass lesions in the third ventricle. In the transforaminal approach, the lateral ventricle is entered through the septum pellucidum for tumors presenting at the foramen. Thirteen of the cases had colloid cysts. Winkler et al emphasizes that the callosotomy should not be more than 15 to 20 mm in length. Twenty-three of 30 patients (77%) experienced an excellent clinical outcome. Detailed neuropsychological testing was performed, and verbal memory and attentional deficits were not observed at retesting.
Other variations of the transcallosal approach are the subchoroidal, transchoroidal transvelum, and suprachoroidal,24,25 but these all carry the risk of deep venous injury and may injure the fornix on the side of the approach and the mammillary body on the side of the HH. The transforaminal approach is not suitable for the HH unless an endoscopic approach is being used (see later).

The Anterior Transcallosal Transseptal Interforniceal Approach

The first 5 HH cases using this approach were reported in 2001.11 This series was expanded to 29 cases and was reported in 2003.10 There are now a total of 35 patients in the first author’s personal series. The anatomy of the anterior transcallosal transeptal interforniceal approach has been described in detail using injected cadaver specimens by Siwanuwatn and coworkers,26 and the clinical operative anatomy was described by Rosenfeld and coworkers.27 This approach is a midline interhemispheric approach with a small corpus callosotomy (1.5-2 cm) just behind the genu, a midline transeptal dissection (between the leaves of the septum pellucidum), and an interforniceal approach between the uppermost section of the columns before they converge to form the arches of the fornix, entering the anterior end of the roof of the third ventricle and removing the hamartoma using the long curved microtip of the ultrasonic aspirator. Various aspects of the operative approach are presented in Figure 1.

The advantages of this approach compared with the approaches from below are the excellent view of the HH obtained from above. Second, being able to debulk and/or disconnect the HH and spare the mammillary bodies if they can be identified, and preservation of the pituitary stalk and the optic chiasm. Third, the avoidance of the blood vessels and cranial nerves that are encountered in the trans-sylvian approach may reduce the risk of stroke and oculomotor nerve palsy. It is also possible to partially debulk and disconnect HH extending into the interpeduncular fossa and the preoptic cistern using the transcallosal approach.

There is a risk to short-term memory because of mammillary body or fornical injury. There is also a risk of stroke from trauma to the thalamic perforators. If the perforating arteries are injured or diathermed, a stroke with hemiparesis may result. A further disadvantage of this approach is the inaccessibility to resect the lateral one third posterior to the coronal suture and the anterior one third anterior and one third posterior to the coronal suture. The craniotomy is based on the frameless stereotaxy trajectory to the anterior segment of the body of the corpus callosum. The craniotomy crosses the midline. We do not plan the craniotomy according to the position of the cortical bridging veins. Sacrificing a bridging vein in this region usually does not result in any problem. It is more important to achieve the optimal trajectory.

A small (1.5-cm) callosotomy is made immediately behind the genu of the corpus callosum. The advantage of this approach is that the trajectory is anterior to or passing through the foramina of Monro and then passing between the leaves of the septum between the columns of the fornices and therefore remaining strictly in the midline. A gush of cerebrospinal fluid is seen as the third ventricle is entered. This approach provides a panoramic view of the anterior and mid segment and floor of the third ventricle, which is adequate to resect or disconnect an HH. The choroid plexus, thalamostriate, and internal cerebral veins are avoided altogether, and the fornical retraction is minimized because the fornices are separated in this trajectory. Although the nuances of this approach compared with the more extensive standard approach are subtle, this approach is different in trajectory, site, extent of opening, and in the structures encountered compared with the standard description and practice of the transcallosal interforniceal approach as described by Appuzo et al.20,21

All of the HH we have encountered have been attached to 1 or both mammillary bodies, and we believe that this is a likely route for spread of the seizures from the HH.4,29 The HH is relatively avascular, and there is usually a subtle demarcation between the HH, which has a firmer consistency
Figure 1 Operative photographs of the anterior transcallosal transseptal interforniceal approach to an HH. (A) Interhemispheric dissection showing the right hemisphere retracted from the falk (black arrow). The left callosomarginal artery and gyri of the left hemisphere are exposed. (B) The corpus callosum is exposed with dissection and displacement of the pericallosal arteries laterally on each side. (C) Midline transeptal dissection with spreading of the leaves of the septum pellucidum. Arrow on the transeptal plane. (D) The ovoid smooth surfaced HH protruding into the cavity of the third ventricle. (E) Translucent pia/arachnoid floor of the third ventricle partially exposed following partial resection of the HH.
with a somewhat granular texture and is a light brown color, in comparison to the softer adjacent normal brain which has a white color. Frameless stereotactic navigation is helpful to choose the ideal trajectory and define the margins of the resection.27

We have found the Cavitron ultrasonic aspirator on its lowest settings to be the most gentle and sensitive instrument to resect and disconnect the HH. Disconnection of the HH from the adjacent hypothalamus, rather than excision, may be sufficient to ensure control of seizures and the surgeon should try to disconnect the HH from the mammillary body. The lateral margins of the HH can usually be disconnected except when the lateral margin is oblique and the micro-Cavitron Ultrasonic Aspirator cannot reach this edge. For some large HH, the optic chiasm demarcates the most anterior extent of the resection. Using the frameless stereotaxy to determine the plane of disconnection or resection should be seen as an adjunct to the surgeon’s vision and tactile sense, not as a replacement. The arachnoid at the base of the third ventricle will be seen as the hamartoma is removed from the floor of the third ventricle.

The anterior commissure may require gentle anterior retraction to resect or disconnect the most anterior component of the hamartoma. In some of our cases, the anterior commissure has been transected. The surgeon should not interfere with the blood vessels laterally and posteriorly in the resection bed. These are deep perforating branches of the basilar artery apex. They are a guide to the margins of the hamartoma especially posteriorly. Interference with these vessels will likely result in hemiparesis. Any diathermy of these vessels is to be avoided. The HH is relatively avascular, and hemorrhage usually stops with Surgicel (Ethicon Inc, Johnson & Johnson, Somerville, NJ) and time.

We do not place a ventricular drain at the end of the procedure because the subarachnoid space is widely open. None of our patients have developed hydrocephalus; however, we acknowledge that some surgeons will wish to use a drain to prevent acute obstructive hydrocephalus in the early postoperative period.

**Prevention of Short-Term Memory Loss**

Retraction of the brain especially of the fornices and the walls of the third ventricle should be minimized as much as possible. The risk of memory loss is probably higher when there is bilateral attachment of the HH particularly to the mammillary bodies. This can be assessed on the preoperative imaging. The neurosurgeon should take extreme caution when dissecting the HH off the mammillary bodies and should try and preserve them at the same time considering that a residual element of the hamartoma left attached to a mammillary body or the adjacent hypothalamus will probably result in incomplete control of the epilepsy. We have shown that mammillary bodies can be preserved when there is a delicate dissection even when the mammillary bodies are distorted and displaced10 (Fig 2).

It has been stated that it is damage to the fornices that cause the short-term memory loss in the transcallosal approach and that this is a reason to avoid the approach.27 Although this is a major factor, injury to the mammillary bodies or mammillothalamic tracts may be just as important, and great care should be taken to avoid damaging these structures (which are also at risk in the other surgical approaches). Retraction or manipulation of the third ventricular walls should therefore be avoided. Memory disturbance may occur after any type of intervention to an HH. For instance, 1 patient in the Barrow series had significant long-term memory disturbance after a frontotemporal orbitozygomatic approach.30 We agree with Rekate and coworkers31 who point out that the septal leaves are more adherent in the older patients rendering the interforniceal approach more difficult, requiring more manipulation of the fornices and therefore increasing the chance of memory disturbance. Thus, endoscopic resection or radiosurgery may be preferable to the anterior transeptal interforniceal approach in the older patient.

**Endoscope-Assisted Craniotomy**

Endoscopy is also helpful as an adjunct to the open operation to inspect the region of the resection for completeness of the disconnection. We have found the use of the endoscopic bipolar diathermy probe useful in the open transcallosal approach because it can be passed through the narrow corridor for this approach without restricting the surgeon’s view.

**Outcome of Transcallosal Surgery for Hypothalamic Hamartoma**

**Seizure Outcome**

Early postoperative generalized seizures are encountered occasionally and probably relate to the postoperative irritability caused by the surgery. We recommend boosting the epileptic medication with perioperative intravenous fosphenytoin, which we discontinue when the patient’s regular seizure medications are resumed.

The medium-term seizure outcome of HH resection via the transcallosal approach in 29 patients with a mean follow-up of 30 months (range, 12-70 months) was as follows: 15 patients were seizure free (9 were off all antiepileptic medication), 7 patients had >90% reduction in seizure frequency, 3 patients had 55% to 80% reduction in seizure frequency, and 4 patients had <40% reduction in seizure frequency.16 Ng and coworkers31 recently reported their transcallosal series of HH patients from the Barrow Neurological Institute in Phoenix, AZ. A total of 26 patients (mean age, 10.0 years; range, 2.1-24.2 years) had an interforniceal transcallosal approach to remove and/or disconnect the hamartoma. Fourteen (54%) were seizure free, and 9 (35%) had ≥90% improvement in total seizure frequency. The likelihood of seizure freedom correlated with younger age, shorter lifetime duration of epilepsy, smaller preoperative HH volume, and 100% HH resection. Presence or absence of developmental
Figure 2 Pre- and postoperative MRI of a patient with an HH. (A) Preoperative coronal MRI with an arrow on an intraventricular component of a HH. (B) Preoperative sagittal MRI with an arrow on the HH. Note the attachment of the HH to the mammillary body. (C) Postoperative coronal MRI showing the resection of the HH with preservation of the mammillary bodies (arrow on the left mammillary body). (D) Postoperative sagittal MRI showing the small callosotomy (arrow) just posterior to the genu of the corpus callosum. (E) Postoperative sagittal MRI showing the resection of the HH with preservation of the mammillary body.
retardation and the seizure type (gelastic only v multiple seizure types) did not correlate with seizure freedom.

**Extent of HH Resection:**

**Disconnection Versus Resection**

The extent of resection that the surgeon achieves depends on the size and position of the HH, the surgical approach, and the degree of disconnection as opposed to excision that the surgeon is planning. In the transcallosal series of Harvey and coworkers, there was a near complete excision (95%–100%) in 18 of 29 patients, 75% to 95% resection achieved in 7 patients (4 of these had near complete disconnection of residual HH), and less than 50% resection was achieved in 4. Delalande and Fohlen have advocated disconnection of the HH but stated that the plane for disconnection was ill-defined. In the series of Delalande and Fohlen, there was total removal in 1 of 17 patients and disconnection in 16 of 17. Excision and/or disconnection of the intraventricular HH is the goal of surgery, but attempts at complete excision may increase morbidity without improving seizure control unless the HH is small.

Seizure control was not correlated with the extent of resection, and seizure freedom was seen in patients with incomplete resection in our series. This may have been because the critical disconnection, particularly with the mammillary bodies, was achieved. However, in contradistinction, Ng and coworkers found seizure-free patients had a mean volume of HH at 2.4 cm³ compared with the non–seizure-free patients with a mean volume of HH of 5.8 cm³, and the percent of resection correlated with the likelihood of being 100% seizure free. In those patients with remaining HH tissue, the percent of disconnection (surface area of attachment before and after surgery) did not correlate with seizure outcome. These data should not be used as a valid comparison of resection versus disconnection because the surgical strategy was resection in almost all cases. Clarification of these relationships will require further clinical research. A secondary finding was that the likelihood of 100% resection correlated strongly with HH lesion volume. Lesions that were 100% resected had a mean volume of 1.2 cm³ compared with a mean volume of 5.5 cm³ for those lesions incompletely resected.

**Surgical Complications**

The main surgical complications of HH resection relate to hypothalamic disturbance (see later) including third nerve paresis, which occurred in 1 of 17, transient in 1 of 29, and 4 of 13 (3 resolved fully); and hemiparesis or hemiplegia caused by perforator artery injury or internal carotid, anterior or middle cerebral artery injury, or vasospasm. This results in thalamic, capsular or cortical ischemia, or infarction. Harvey and coworkers reported 2 of 29 cases of temporary hemiparesis caused by anterior thalamic infarcts.

**Behavioral and Cognitive Improvements**

There are often dramatic improvements in behavior after surgery, with decreased aggression, increased concentration and involvement in tasks, elevated mood, and greater speech output in many patients, which is often seen in the first few weeks postoperatively. These improvements require further careful evaluation to confirm. The improvement is generally associated with a reduction in interictal spike-wave activity and may relate to a reversal of the epileptic encephalopathy in some of these children. Short-term memory disturbance occurred in 14 of 29 patients, and this resolved in all but 4 patients. The disadvantage of the ongoing memory disturbance may be outweighed by the improvements in seizures and behavior.

Ng and coworkers found an improvement in behavior in 23 (88%) and in cognition in 15 (58%) as reported by parents. There was transient postoperative memory disturbance in 15 (58%) patients, which persisted in only 2 (8%).

**Endocrine Complications**

Precocious puberty in patients with intrahypothalamic HH and gelastic epilepsy is not usually altered by HH surgery probably because the hypothalamus once primed remains switched on. Transient hypsomnolence and hyperthermia may occur in the early postoperative period. Free thyroxine commonly falls after surgery, and some patients may require replacement therapy. Low-growth hormone occurred in 6 of 29 (21%) patients after transcallosal surgery at our center. Ng and coworkers reported that 2 of 26 (8%) patients had persisting endocrine disturbance requiring treatment for hypothyroidism and diabetes insipidus in 1 each.

Hypernatraemia developed in most patients postoperatively with sodium >150 mmol/L seen in 16 of 29 (55%) patients at our center; however, this was asymptomatic and not often associated with polyuria. Four of 29 (14%) developed transient diabetes insipidus, and no patient required ongoing antidiuretic hormone replacement. Except for appetite stimulation and weight gain in some patients (see later), postoperative endocrine disturbances appear to be transient, mild, or asymptomatic and easily treated where necessary. Long-term follow-up of growth and sexual development in a larger series of patients is required.

**Weight and Appetite**

Appetite stimulation and early postoperative weight gain occurred in 45% of our patients having transcallosal surgery. This risk may be different in other surgical approaches. The weight gain tends to plateau, but some dietary control is required. The causation of the weight gain is variable and multifactorial and may relate to ventromedial nucleus hypothalamic injury; dexamethasone therapy; physical inactivity in convalescence; psychosocial factors; psychiatric comorbidity with autism, depression, or anxiety; parental nurturing instinct; postoperative hypothyroidism; preoperative genetic/environmental effects; and antiepileptic drugs.

**Follow-Up/Specific Problems and Measures**

Regular neurologic and endocrine follow-up of the patient is recommended. After hypothalamic surgery, the patient must
be observed closely over several weeks to detect hypernatremia, diabetes insipidus, and thirst dysregulation, which may be delayed in onset. Ensuring a set daily volume of fluid intake should prevent the hypernatremia and dehydration. As with any epilepsy surgery, it is advisable to continue antiepileptic drugs for 18 months to 2 years. The patient’s weight must be closely monitored and a diet introduced if weight gain is a problem. Neuropsychology review should be continued postoperatively with an assessment of cognitive function including memory. Postoperative communicating hydrocephalus is unlikely but should be considered if there is a late cognitive decline.

Pterional or Frontotemporal Approach With the Option of Orbitozygomatic Osteotomy

This approach was the standard surgical approach before the development of the transcallosal and endoscopic approaches. The surgeon may choose varying combinations of subfrontal, trans-sylvian, or subtemporal approaches depending on the individual anatomy. For pedunculated lesions, projecting below the hypothalamus and hamartomas with a large attachment on the base of the hypothalamus extending laterally with minimal or no intraventricular component the surgical approach from below is preferred. There is good access to the suprasellar cistern, but there is restricted access into the third ventricle and the intraventricular component of the HH. It is feasible to debulk the portion of the HH that is protruding below the third ventricle and to disconnect it from the intraventricular component. However, we believe that it is more difficult to dissect the HH tissue off the mammillary body from below compared with the transcallosal approach. The third cranial nerve and the internal carotid artery and its branches including perforating vessels are at risk if there is extensive dissection and retraction in this region. The addition of an orbitalzygomatic craniotomy may provide improved access to the subventricular HH with reduced brain retraction.

Delalande and Fohlen18 reported only 2 patients of 14 who are seizure free after a single disconnection through a pterional approach. We believe that this poor control of the epilepsy is probably because the lesion cannot be adequately disconnected when using this trajectory. A significant component of intrahypothalamic lesion would remain, and there is also more chance of injuring the mammillary bodies with this approach. Prepontine extensions of the HH can be disconnected from above. Lateral extensions of the HH that cannot be disconnected from above could be disconnected via a pterional approach as a second-stage procedure, but these could also be treated with radiosurgery.

Feiz-Erfan and coworkers33 reported 10 children with 9 sessile and 1 pedunculated HH and used a superior trajectory in 7 (transcallosal interforniceal approach on 6 and a transventricular endoscopic approach in 1) and a ventral trajectory (frontotemporal craniotomy with orbitozygomatic osteotomy) in 3. The superior trajectory allowed excellent exposure and visualization of local structures during resection. Five were seizure free, and 2 had >95% reduction in seizures. In those 3 having the approach from below, 1 was seizure free after 2 operations, 1 had a 75% reduction in seizure frequency, and 1 (the single patient with a pedunculated HH) was not improved. For the 2 sessile lesions approached from below, the surgical exposure was adequate and critical tissue borders were not apparent. The third patient had a pedunculated lesion where the exposure was adequate, but the epilepsy persisted despite complete resection. The conclusions of this limited study were that sessile lesions were best approached from above and pedunculated lesions from below and suggested that the likelihood of curing seizures was higher when lesions were approached from above rather than below.

The resection of a giant HH was recently reported by using a subfrontal approach with orbital rim osteotomy, but only a partial resection was obtained and only a 50% improvement in the epilepsy occurred.34 We suggest that this type of HH is better approached from above because disconnection may be more complete compared with the approach from below and better epilepsy control may be obtained.

Trans-Lamina Terminalis Approach

This approach has been used for HH4 and is sometimes used to remove the intraventricular component of a craniopharyngioma or other intraventricular tumors.27 There are a number of disadvantages to this approach for resection of a HH. The approach requires a subfrontal or bifrontal interhemispheric approach, which involves retraction and possible injury to 1 or both frontal lobes, olfactory tract and bulb, and optic chiasm. The anterior communicating artery complex is also in the line of the approach. It would be difficult to obtain as complete a clearance of a moderate- or larger-sized lesion through this approach, and the view of the posterior aspect of the lesion would also be obscured.

Endoscopic Disconnection/Resection

The endoscopic approach is separately reviewed in this issue35 and has been reported by others.18,36-38 The endoscope is passed transcortically via the lateral ventricle and the Foramen of Monro to the HH. The Barrow group described the endoscopic resection of HH using a newly developed variable aspiration tissue resector in 2 patients.39 The hamartoma was disconnected in 1 patient and completely resected in the other. The use of this device will likely improve the technical aspects of the surgery through the narrow working channel of the endoscope, which has been a limitation of the endoscopic approach. Rekate and coworkers30 have recently extended the numbers of endoscopic cases to 44 using frameless stereotaxy and a micromanipulator. Fourteen
of these had a complete resection of which 13 were seizure free with brief follow-up. Complications consisted of 3 patients with ongoing short-term memory loss and 1 patient with residual hemiparesis. In this series, the HH lesions selected for endoscopic resection were relatively small; 32 of 44 (73%) of the HH were less than 1 cm³ in volume. Rekate and coworkers state that the ideal patient for endoscopic HH resection has a lesion <1.5 cm in diameter and that >6-mm clearance is present to the top of the third ventricle for the larger lesions so that the operator can see the tips of the instruments.

The capacity to do the disconnection or the resection of a larger lesion in 1 procedure is not always possible by using the endoscopic approach. The advantage of the transcallosal transeptal interforniceal approach compared with endoscopy is the extensive direct access to the HH except for the extremes of lateral extent. The frameless stereotaxy navigation becomes more unreliable as the operation proceeds because of shift of the tissues. The surgeon’s orientation and vision within the third ventricle and the tactile feedback of the instruments especially at the transition zone between the hypothalamus and the adjacent normal tissue, particularly the mamillary body, may be suboptimal with the endoscopic approach. A narrow third ventricle, a large HH with disturbance of the anatomical landmarks, an HH passing beneath the optic tract, or a bilateral attachment of the HH render endoscopic disconnection/resection more difficult and risky. We still recommend the transcallosal transeptal interforniceal approach for these situations.

The advantage of the endoscopic approach compared with the transcallosal transeptal interforniceal approach is that the fornix is retracted or manipulated only on 1 side compared with the potential for bilateral manipulation with the open approach. However, the endoscope is usually introduced on the contralateral side to the HH if it has a mainly unilateral attachment because an ipsilateral trajectory through the foramen of Monro on the side of the HH does not allow a satisfactory angle for the resection of the lesion. During the endoscopic resection, the mammillary body, adjacent fornix column, and possibly the mammillothalamic tract is being manipulated or possibly injured on the contralateral side to the fornical retraction at the level of the Foramen of Monro through which the endoscope passes. Therefore, memory disturbance remains a serious potential problem (just as it does for the transcallosal approach), particularly if the endoscope movement is large at the level of the Foramen of Monro and the cognitive function of the patient is already impaired. Whether epilepsy control and cognitive outcome and memory impairment are superior with the endoscopic approach compared with the transcallosal approach remains to be determined.

Gore and coworkers have recently described the novel approach of synchronous endoscopy from above and microsurgery via a supraorbital craniotomy for a patient with a large HH and also used this 2 corridor approach for other patients with complex ventricular lesions.

**Radiosurgery**

Regis and coworkers enrolled 60 patients with HH between 1999 and 2005 for gamma knife radiosurgery in a prospective multicenter trial. Twenty-seven patients had a follow-up greater than 3 years; 59.2% are reported to have an excellent result with cognitive and behavioral improvements, 37% are seizure free, and 22.2% have only rare nondisabling seizures. There was no neurologic or endocrine morbidity reported. There was no report of memory disturbance or cognitive ability, but formal testing was not provided. Care was taken to avoid or minimize irradiation of the surrounding structures in the dosimetry planning, but the long-term effects of the radiosurgery on these structures is unknown.

Regis and coworkers recommend repeat radiosurgery for a small well-defined HH if the first radiosurgery treatment fails but have recommended a delay of 36 months before administering the second treatment to fully observe the therapeutic effect of the initial course of radiosurgery. The disadvantage of radiosurgery is the delayed efficacy. Seizures start to decrease around the sixth month postradiosurgery, but there is a great deal of variability in the timing of the therapeutic response. For this reason, a patient with severe epilepsy and behavior disorder, particularly those with a progressive epileptic encephalopathy, may be better suited for open surgery. In summary, the disadvantages of radiosurgery are delay in the therapeutic response, a lower likelihood of a seizure-free outcome (in comparison to transcallosal resection), and the possibility of delayed radiation injury to the surrounding hypothalamus and adjacent visual pathways. The risk of radiation-induced tumors later in life is probably low. Conversely, the risk of perioperative complications from gamma knife treatment is clearly favorable in comparison to resective surgery.

Some patients with residual HH lesions after surgery who have incompletely controlled epilepsy may be suitable for radiosurgery. Regis and coworkers recommend this to be done 3 months after the surgery. Adolescents and adults with HH who have a milder form of epilepsy and have normal or near normal cognitive function and are in school or employed are at risk for a greater degree of social disability in the event of a residual episodic memory deficit resulting from surgical resection, and radiosurgery may be a preferable option. We believe that bilateral attachment to the mammillary bodies carries a higher risk to memory with surgery than unilateral attachment. Patients with smaller HH and bilateral attachment may be more suited to radiosurgery. However, larger HH with bilateral attachment to the mammillary bodies are more suitable for transcallosal surgery.

**Other Surgical Treatments**

Stereotactic radiofrequency thermoablation has been performed on a limited number of patients. Kuusniecoky and Guthrie reported 12 patients treated with stereotactic thermoablation, 8 with this alone and 4 combined with endoscopic resection. A lower success rate of seizure control was reported for thermoablation alone, and there was 1 death in
the series. The application of interstitial radiosurgery (\(^{125}\)I seeds) has also been reported in an HH cohort with refractory epilepsy\(^{42}\) and is discussed in detail elsewhere in this issue.\(^ {43}\) However, interstitial radiosurgery and stereotactic thermablation are not widely available in pediatric epilepsy centers.

**Discussion**

As more experience is gained with the various treatment modalities, the selection of a treatment regimen will become clearer and more predictable for a particular patient with a particular type of HH. The ideal age for surgery is not yet well defined, but it is probably better to operate earlier in the course of the epilepsy before the irreversible changes of secondary generalized epilepsy have become established and before intellectual development becomes irreversibly stunted (presumably by the effects of the frequent seizures). Which HH patients are suitable for surgery versus radiosurgery or radiofrequency lesioning needs further clarification and has been discussed earlier. The long-term follow-up of seizures, cognitive function, behavior, growth, and development is required to better judge the role of the various treatments. This applies particularly in regard to seizure recurrence, which should be assessed with follow-up of at least 5 years. More research is needed on the cognitive outcome after HH surgery with particular attention to short-term memory function. It is unknown what proportion of the memory disturbance is caused by fornical retraction as opposed to injury to mammillary bodies or mammillothalamic tracts. Any series of HH treatment reported in the literature should include a before and after neuropsychological assessment if it is possible to do so. There is criticism of the transcallosal approach because of the potential effects on short-term memory, but detailed neuropsychological testing on patients who have had alternate approaches of HH treatment are not yet reported in the literature. Moreover, many patients have cognitive impairment and psychiatric comorbidity before any surgery.\(^ {44, 45}\) Quiske and coworkers\(^ {44}\) reported in a series of 13 juvenile and adult patients that memory functions were impaired for both visual (77%) and verbal learning (62%). There is a high prevalence of mood and anxiety disorders in patients with HH.\(^ {45}\)

The neurosurgeon should be flexible in the selection of a treatment modality for an individual patient with HH because of the wide variability of the anatomy and the clinical features. The crucial factors are the age of the patient; the severity, duration, and tempo of progression of the clinical condition; and the anatomy, location, and size of the HH. The surgeon should be skilled in approaches to the third ventricle before performing the transcallosal approach and should also be able to offer endoscopic and frontotemporal approaches and should work closely with the radiotherapists to also consider the role of radiosurgery as an alternative. The parents (and the patient if old enough) should be fully informed of all the approaches and the preferred therapeutic option for the individual case and the predicted success rate and attendant risks. We certainly agree with Regis and coworkers\(^ {17}\) that dogmatism in the approach to HH is to be abhorred. Combinations of surgery and radiosurgery should become more common to optimize the control of the epilepsy and behavioral disorder.

If reoperation is planned for the treatment of a residual HH that remains symptomatic, the neurosurgeon should plan to use a different corridor such as the endoscopic route when the transcallosal route was used for the first procedure.

**Conclusions**

Refractory epilepsy associated with HH can be safely and effectively treated with the transcallosal interforniceal approach. The short-term memory deficits appear to be transient for most patients. Effects on behavior and cognitive function are favorable. The relationship of epilepsy control to size of HH resected or disconnected is not clear cut. A patient with severe epilepsy or epileptic encephalopathy is better suited to surgery than radiosurgery. The findings of Ng and coworkers\(^ {32}\) are very similar to those of the Royal Children's Hospital series\(^ {10}\) and therefore provide independent corroboration of our findings, and there can now be a greater confidence in the claims made for this surgical approach particularly in relation to the risk of persistent short term memory disturbance.

A patient with a large HH is better suited to open surgery. For HH lesions <1.5 cm in diameter and where >6-mm clearance is present to the top of the third ventricle, the endoscopic resection and/or disconnection is the preferred option provided the operator is experienced with endoscopy and has the requisite equipment. An adolescent or adult HH patient with milder epilepsy and intact cognition would be better suited to gamma knife surgery. A patient with a residual HH after resective surgery and ongoing epilepsy may be suited to the gamma knife. Bilateral attachment to the mammillary bodies may favor radiosurgery in the patient who has good cognitive function. Unilateral attachment to the mammillary bodies is more suited to disconnection surgery.

If the HH is sessile and intrahypothalamic/intraventricular in location, we recommend the anterior transcallosal interforniceal approach or the foramen of Monro endoscopic approach. If the HH is pedunculated or protruding inferiorly from the hypothalamus with minimal intraventricular component and particularly if the HH has an attachment lateral to the midline, we recommend an approach from below. This is via a subfrontal/transylvian approach via a frontotemporal craniotomy. The addition of an orbitozygomatic osteotomy provides a more inferior trajectory with minimization of cerebral retraction.

In the last decade, there have been major improvements in the outcome for patients with HH with some dramatic improvements in epilepsy control and behavioral and cognitive function. The control of postoperative seizures is variable and depends on the technique used and length of follow-up. Results of the transcallosal approach are that 52% to 54% are seizure free, and 24% to 35% have >90% seizure reduction. There is an 8% risk of persisting memory problems.\(^ {27, 32}\) Improvements in quality of life, behavior, and general functioning are common. The endocrine risks are small, but there is a potential for appetite stimulation. There is a small risk of stroke and cranial nerve palsies. The quality of life has been transformed in many patients after HH surgery or radiosurgery.
References


