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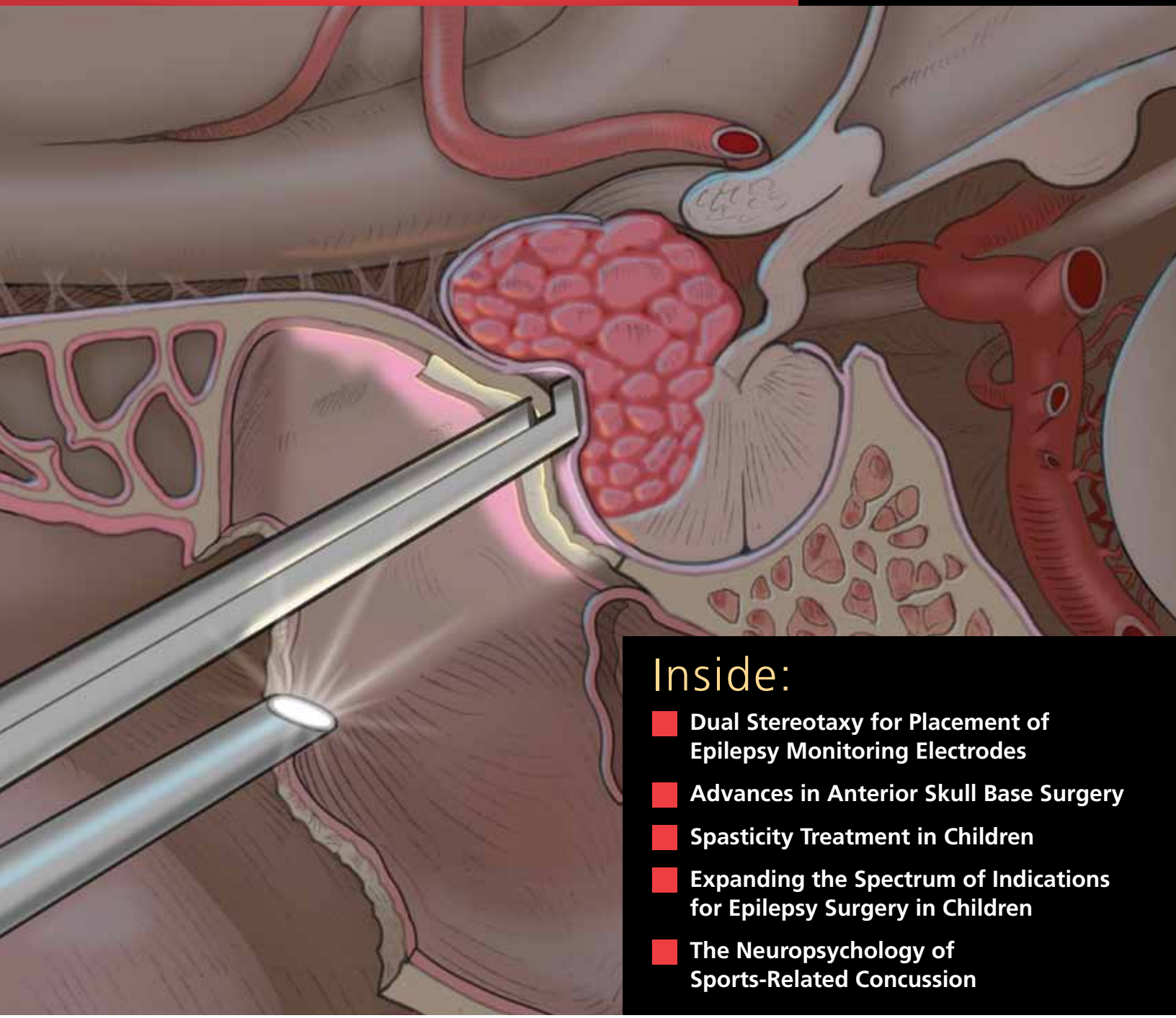
Volume 4 • Number 1 • Spring 2011

UH Neurological Institute Journal



Inside:

- Dual Stereotaxy for Placement of Epilepsy Monitoring Electrodes
- Advances in Anterior Skull Base Surgery
- Spasticity Treatment in Children
- Expanding the Spectrum of Indications for Epilepsy Surgery in Children
- The Neuropsychology of Sports-Related Concussion

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UH Neurological Institute Journal

FROM THE EDITOR

Dear Colleague,

I am pleased to bring you the Spring 2011 issue of the UH Neurological Institute Journal.

Through continuing collaboration with scientists at Case Western Reserve University School of Medicine, physicians at the UH Neurological Institute test and refine the latest advances in treatment for patients with disabling neurological disorders. The NI Journal highlights these advances and demonstrates our interdisciplinary strengths. As an added benefit for our readers, CME credit is readily available in each issue for the busy practitioner interested in receiving *AMA PRA Category 1 Credits*™.

In this issue, Jonathan Miller, MD, describes a novel technique using concomitant frame-based and frameless techniques for precise electrode placement in patients who require both surface electrodes and deep electrodes to evaluate whether they will benefit from epilepsy surgery.

Chad Zender, MD, and colleagues review how their increasing experience with endoscopic approaches of the anterior skull base has allowed them to resect tumors without compromising surgical outcomes at University Hospitals.

Dararat Mingbunjerdsuk, MD, and Shenandoah Robinson, MD, discuss spasticity treatment in children. The multidisciplinary team of University Hospitals Rainbow Babies & Children's Hospital's Spasticity Program uses individualized strategies to best tailor treatment options and help children optimize their development, comfort and independence. Read about it in this issue.

Ingrid Tuxhorn, MD, looks at epilepsy surgery for pediatric patients and explains how referring children with surgical epilepsy syndromes to a specialized pediatric epilepsy unit early can optimize seizure and psychosocial outcome.

Christopher Bailey, PhD, presents an article on sports-related concussion, a common but challenging and complex clinical phenomenon. Though the basic and clinical science of the injury is still only partially understood, the high level of recent public interest is resulting in an influx of research and leading to better management of this head injury.

Thanks to our authors for contributing their valuable research and insight to our journal, and thanks to our readers for joining us this issue. Your comments and suggestions are always welcomed. From all of us at the NI Journal, have a safe and enjoyable summer.

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University Hospitals Neurological Institute

University Hospitals Neurological Institute is Northeast Ohio's first designated institute for the comprehensive care of patients with diseases affecting the nervous system. The institute comprises 16 Centers of Excellence, which bring together some of the country's foremost experts in neurology, neurosurgery, neuroradiology, neuro-oncology, neuro-ophthalmology, neurotology, neuropathology, neuropsychology, neuropsychiatry and related specialties.

The UH Neurological Institute offers an interdisciplinary approach to highly individualized therapies and offers leading-edge care, including stereotactic radiosurgery, endovascular stroke and aneurysm treatments, neurostimulation and artificial disc replacement.

On the cover: Endoscopic visualization of the pituitary region with conceptualized drawing of removal of intradural tumor from the frontal fossa floor. (Illustration by Ravin Art & Design.)

Kim Duvall, *Editorial Manager*
Bryan Kokish, *Marketing Manager*
Susan Miazga, *Senior Graphic Designer*

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When Close Enough Isn't Close Enough: Dual Stereotaxy for Placement of Epilepsy Monitoring Electrodes

By
Jonathan Miller, MD

Epilepsy monitoring using intracranial electrodes is sometimes required to determine whether patients are candidates for further surgery. As techniques improve and indications for surgery expand, there is a need for increased precision in electrode placement. These techniques have evolved along with the specialty of neurological surgery, from early frame-based localization based on anatomic approximations to sophisticated computerized frameless systems capable of real-time identification of location of surgical instruments projected onto preoperative scans. For certain applications, frame-based stereotaxy is still required because no frameless system can rival the accuracy obtained using a rigid stereotactic frame. In this article, we outline the history of stereotaxy and describe a novel technique using concomitant frame-based and frameless techniques for precise electrode placement in patients who require both surface electrodes and deep electrodes to evaluate whether they will benefit from epilepsy surgery.

Introduction: The Clinical Problem

One in 10 Americans have had or will have a seizure at some point in their lives, and three million have some form of epilepsy. Almost 500 new cases of epilepsy are diagnosed every day in the United States, more than multiple sclerosis, cerebral palsy, muscular dystrophy, and Parkinson's disease combined.[1] For patients who are candidates for surgical resection, prognosis can be quite good: one randomized controlled trial of surgery for temporal lobe epilepsy demonstrated a tenfold increased rate of freedom from seizure with surgery compared with the use of medications alone.[2] Successful surgery for epilepsy requires precise delineation of the region of onset and early spread of seizures and is usually accomplished using a combination of clinical, electrophysiological (electroencephalography), and imaging (magnetic resonance) data. However, sometimes the seizure onset zone is not readily identified using these techniques, and patients require sampling of electrical signals from the brain itself, with the use of surface electrodes in the subdural space[3] or depth electrodes passed into deep structures of the brain.[4,5] There are limitations to both techniques, and when the seizure onset zone could be from either surface or deep tissue or when it is necessary to map the brain surface to determine the location of motor or speech areas, both electrode types must be used concurrently. To do so, it is necessary to use stereotaxy techniques, which fall into two basic categories: (1) frame-based, which utilizes a rigid frame attached to the patient's head that is used to guide surgical instruments and (2) frameless, which uses optical techniques to triangulate the real-time position of surgical instruments relative to preoperative imaging.[6]

Early Stereotaxy: The Stereotactic Frame

The history of stereotaxy as a tool to assist neurosurgeons in intracranial navigation largely parallels developments in neuroimaging, but the concept of a localizing apparatus attached to the head dates from far earlier. In 1899, an anatomy professor in Moscow named D. N. Zernov developed the "encephalometer," an aluminum ring surrounding the head mounted with two arcs that could identify any point above the ring using polar coordinates.[7] It was used intraoperatively on at least one occasion to define the motor cortex to drain an abscess in a patient with Jacksonian epilepsy. Shortly thereafter, Robert Clarke and Sir Victor Horsley developed another frame using a three-dimensional coordinate system based on external skull landmarks and used it for neurophysiological experiments on animals.[8] Though the new term "stereotaxy" and the use of Cartesian coordinates to identify points in the head survive to the present, the Horsley-Clarke apparatus had limited clinical use.

This lack of utility changed dramatically with the evolution of imaging techniques. In the 1940s, X-ray technology could be used to define the anatomy of the cerebral ventricles, which have a defined relationship to other intracranial structures. Using this technique, Ernest Spiegel and Henry Wycis in 1947 developed the "encephalatome," a rigidly attached frame with reference marks that could be seen on imaging and subsequently used to guide manipulation of surgical instruments.[9] This technique led to a proliferation of stereotactic frames and other techniques such as lesioning of deep brain structures to biopsy deep tissue for tumor diagnosis, implant radioisotopes and electrodes, and treat movement disorders, pain, and epilepsy. Frame-based stereotaxy offered accuracy within 1 millimeter but was associated with the inconvenience and expense of additional imaging as well as restricted access to the surgical field, so it has been used primarily for minimally invasive surgical procedures.

An example of a modern arc-centered frame is shown in Figure 1. Frame-based stereotaxy uses a series of five numbers to define an approach to a target. The target itself is identified based on distance from an arbitrary reference point above, behind, and to the right of the patient's head using Cartesian coordinates: x is used for the lateral dimension, y for the anterior-posterior, and z for the vertical. Two additional numbers, the arc and ring, define the angle from the plane of the frame in the left–right and anterior–posterior directions. The frame itself has a series of slides that allow precise navigation to any desired target using a precise trajectory.

Figure 1: Leksell stereotactic frame. (A) Front view. (B) Side view. The pins for rigid fixation onto the head are visible. (C) The indicator apparatus is attached to the frame during imaging to allow the software to determine the spatial relationship of the head to the frame. (D) The arc system is added intraoperatively to allow for precise targeting of any intracranial location using a predefined trajectory.

Development of Frameless Stereotactic Systems

In the 1980s, increased computing power coupled with improved image resolution led to the development of a number of techniques for intracranial navigation that required neither a frame nor a dedicated image on the day of surgery. The first such system was reported in 1986 and consisted of several ultrasonic sound sources and microphones that triangulated the position of surgical instruments based on the relative delay of the sounds to each microphone.[10] Though highly accurate under testing conditions, the system was found to be somewhat troublesome in clinical settings due to its sensitivity to air temperature, humidity, turbulence, extraneous noise, and echo.[11] Another system called the "neuronavigator" consisted of a multi-jointed arm with potentiometers at each joint that determined the location of the end based on the distance and angle of each segment of the arm.[12] This system was highly accurate but large and cumbersome. It never entered widespread use. Electromagnetic systems that could determine the position and orientation of small magnetic sensors within a low-frequency electromagnetic reference field were developed.[13] Interference with metal objects led to problems in practical use.

Developed in the early 1990s, optical systems consist of an array of cameras that localize the position of infrared light sources or reflecting spheres mounted on surgical instruments and compare them to a reference star attached to the patient.[14,15] By registering the patient's external anatomy to the preoperative scan, a computer uses the relative geometric orientation of the light sources to calculate the exact position and orientation of surgical instruments relative to the scans. In operating rooms with intraoperative computed tomography or magnetic resonance imaging capabilities, it is possible to obtain scans during the operation and re-register the new scan based on updated anatomy. Most frameless platforms in current use are based on optical technology. These systems are user-friendly and have become ubiquitous for intraoperative navigation.

Back to Basics: Framed Stereotaxy in a Frameless Era

Though frameless techniques are considerably more efficient and cost-effective than frame-based techniques,[16,17] direct comparison of frame-based to frameless stereotaxy has repeatedly demonstrated superior accuracy using a frame. One study compared the two techniques during implantation

of deep brain stimulator leads, using frameless stereotaxy for one side and frame-based stereotaxy for the other, and found significantly lower rates of error in the group implanted using frame-based stereotaxy (1.2 +/- 0.6 mm vs. 2.5 +/- 1.4 mm, P <0.05).[18] Similar results have been reported in multiple other studies.[19-21] Overall, accuracy using a frame appears to be about twice as good as frameless systems in real-world applications. As a result, frame-based stereotaxy is still used when extraordinary accuracy is required, including gamma knife radiosurgery, biopsy of deep lesions very close to vital structures, and implantation of deep brain stimulator electrodes.

Dual Stereotaxy: A Novel Approach

Frame-based stereotaxy is often used to implant depth electrodes for epilepsy monitoring, especially when electrodes need to be placed in deep targets adjacent to vital structures. Sometimes a craniotomy is required to place subdural electrodes as well, either to sample surface cortical tissue to determine the evolution of seizures or to map eloquent cortex used for speech or movement, and it can lead to unique challenges. When both electrode types need to be placed concurrently, it has traditionally been necessary either to place the depth electrodes first using the frame and then performing the craniotomy in a separate step or to use frameless stereotaxy and accept slightly lower accuracy in electrode placement.[6]

To solve this problem, we postulated that it would be possible to perform a craniotomy while in the stereotactic frame, placing the depth electrodes using framed stereotaxy and surface electrodes using frameless stereotaxy.[22] An example of the operative setup is shown in Figure 2. This combined approach works to the advantages of both techniques. Modern software makes it possible to reformat images in the standard projections so that the same preoperative images used for frame-based stereotaxy can be registered to a frameless system. Real-time X-ray can be used to verify placement of depth electrodes in the frame (Figure 3), and the frame-based instruments can be registered to the frameless system, allowing for yet another level of verification that the electrodes are in the correct place. The trajectory for the electrodes can be precisely planned ahead of surgery to avoid blood vessels and cerebral ventricles. Finally, electrodes can be placed either before the craniotomy from points outside the bone flap or afterwards through the cranial defect itself. One potential disadvantage of performing a craniotomy in the frame is limitation of access to the surgical field produced by the fixation posts and frame base. However, with some foresight, it is possible to carefully position the frame slightly tilted and rotated to place the center of the intended cranial flap equidistant from the fixation posts, making virtually any craniotomy possible.

Detailed postoperative analysis of patients who underwent this procedure demonstrated an average error from preoperative plan of less than 1 millimeter, similar to most other studies of frame-based stereotaxy (Figures 4 and 5). Since 2008, 22 patients with epilepsy, but without lesions found with magnetic resonance imaging, have been studied at University Hospitals Case Medical Center using this technique, and all but six were found to have a seizure onset zone amenable to subsequent resection. All patients undergoing resection experienced significant decrease or elimination of seizures postoperatively. Without the precision of the stereotactic frame and the versatility of the frameless system, the degree of accuracy required might not have been possible, and these patients might not have been identified as candidates for surgical resection of epileptic tissue. The combined approach is not appropriate for every case, but it is very useful when targeting sensitive structures deep in the brain is necessary. With this technique, it is possible to implant all electrodes in a single step and obtain the level of precision possible with a stereotactic frame without sacrificing subdural recordings.

Conclusions

Stereotactic techniques have changed significantly in the past 100 years, but the goal has always been the same: to allow precise navigation within the cranial cavity. Early frame-based systems have largely been supplanted by newer frameless techniques, but the accuracy possible using a frame has not been surpassed. If necessary, both techniques can be combined to expand the versatility of the approach. This combination is especially useful for epilepsy evaluation and has allowed for sampling of tissue in locations that otherwise would not be accessible for monitoring.

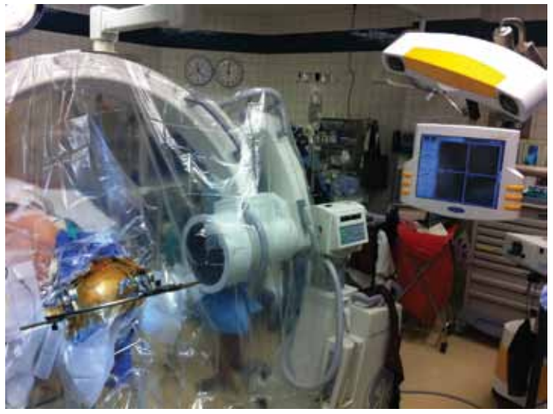

Figure 2: Operative setup. The patient's head is fixed in a stereotactic frame, but the frameless system is also used. The large "eyes" in the top right corner shine and detect infrared light that is reflected off spheres attached to surgical instruments. The reference star holding three of these spheres is visible just below the patient's head.

Figure 3: Fluoroscopic view. The target of the frame is located at the crosshairs so that X-ray can be used to verify that the electrode has been precisely placed.

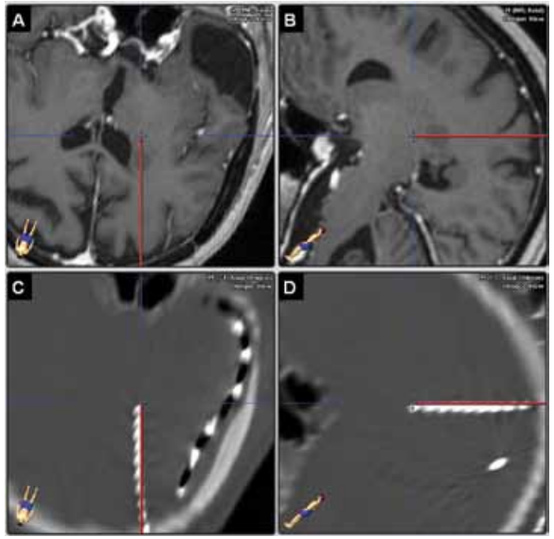

Figure 4: Example of comparison of preoperative planned trajectory (red line) to a deep heterotopia on (A, B) preoperative magnetic resonance imaging and (C, D) postoperative computed tomography. Electrode placement was accurate to within 1 millimeter of the preoperative plan.

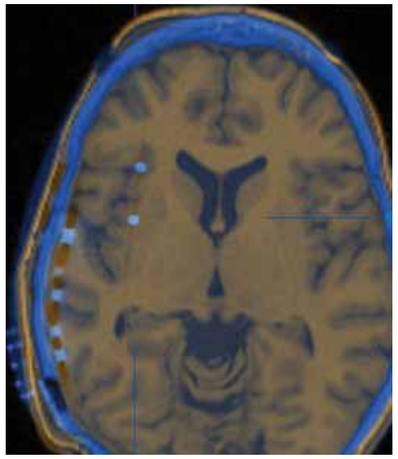

Figure 5: Example of fused postoperative computed tomography and preoperative magnetic resonance imaging demonstrates depth electrode placed in the insula, a sensitive structure because the Sylvian fissure with the middle cerebral artery branches is merely millimeters away. The subdural grid is also visible.

Jonathan Miller, MD, reports no financial relationships with commercial interests relevant to the content of this article.

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Advances in Anterior Skull Base Surgery

By
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Introduction

Anterior skull base tumors represent a rare subset of neoplasms whose treatment has evolved tremendously over the past 20 years. Traditional treatments require a craniotomy and a transfacial approach. This classic approach carries significant morbidity ranging from 15% to 40%,[1,2] frequently in the form of frontal lobe injuries, pneumocephalus, meningitis, and leaking cerebrospinal fluid (CSF). Endoscopic approaches allow for excellent visualization and the potential for a less invasive approach to areas like the clivus, cavernous sinus, and petrous apex. Also, frontal lobe retraction is unnecessary. Our increasing experience with endoscopic approaches has allowed us to expand our paradigm and resect benign and select malignant tumors without compromising surgical outcomes.[3] In this article, we discuss advantages and disadvantages of each approach, advances in stereotactic image guidance, and the endoscopic repair of the anterior skull base.[4]

Anterior Skull Base Neoplasms

Neoplasms of the anterior skull base have always been challenging to treat. Pioneers in treating these tumors gave hope to patients who historically had limited treatment options. Because of the rarity of these neoplasms, the complex anatomy, and the resultant communication between the bacteria ridden nasal cavity and cranial vault, complications were frequent. Over the past 30 years, techniques have been refined and methods developed to decrease peri-operative morbidity and improve survival for these patients.[5] Many open approaches have been described for the treatment of anterior skull base tumors; most require a transcranial approach and a transfacial approach. A two-team method that includes both a neurosurgeon and an otolaryngologist brings the expertise of both specialties to the patient and optimizes care and outcome.

Craniofacial Approach

We use a similar approach as described by Ketcham and others.[6,7] The procedure begins with a bicoronal skin flap elevation and an anterior craniotomy with removal of the frontal bar when necessary, allowing exposure of the frontal lobes/dura, the cribriform, and entire anterior skull base back to the planum sphenoidale. Traction on the frontal lobes must be minimized and can be accomplished by removal of the frontal bar to gain sufficient inferior exposure. This "top down" approach allows the neurosurgeon to identify the superior limits of the tumor and resect tumor, dura, and involved tissues from above. A transfacial incision is then added to allow a "bottom up" approach. The otolaryngologist removes the intranasal and paranasal sinus component of the tumor. Various incisions can be utilized for exposure and access of the anterior skull base from below. A lateral rhinotomy, Weber-Ferguson, or facial degloving

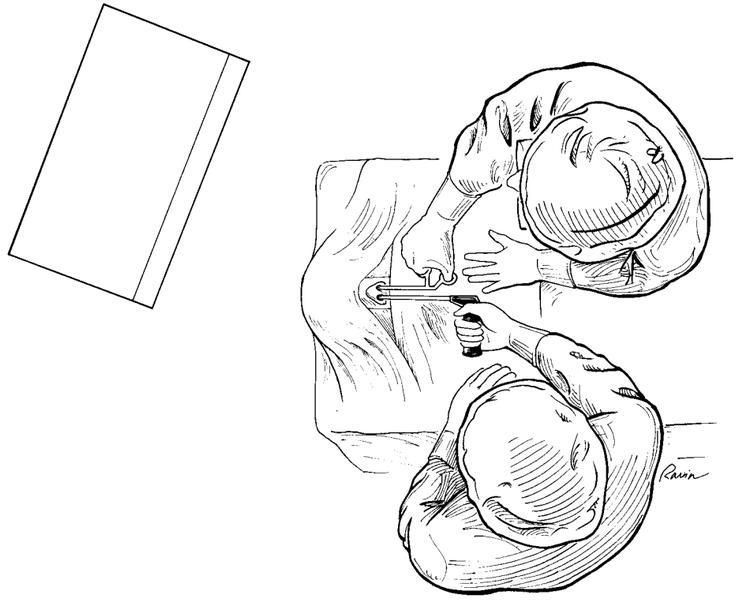

Figure 1: Illustration demonstrates positioning of the patient and surgical team. The anesthesiologist is located near the foot of the operating table so that bilateral access to the face can be obtained by the surgical team members. The endoscopic tower with monitor is positioned at the head of the table. Image courtesy of Ravin Art and Design.

approach may be appropriate depending on the inferior extent of the tumor. Once adequate exposure of the tumor is achieved, the inferior component can be resected with clear margins. This approach allows for an en bloc resection, but portions of the tumor frequently must be removed separately, especially posteriorly in and around the sphenoid sinus.[8]

After the resection is complete, reconstruction of the floor of the anterior cranial fossa is performed, which begins by cranializing the frontal sinuses and obliterating the nasofrontal duct.[9] Local tissues such as the pericranial flap based on the supraorbital vessels can be used. The pericranial flap is harvested at the beginning of the case and elevated off of the skull separately from the bicoronal skin flap, or it is raised with the skin flap and can be separated at the end of the procedure. The pericranial flap is draped over the frontal bar and secured to the orbits laterally and the planum posteriorly. In previously treated patients, there may be a paucity of local tissues for adequate reconstruction. One of the major advances in the reconstruction of skull base defects has been the advent of microvascular free tissue transfer. Extensive tumor resection in previously treated patients requires that healthy vascularized tissue be brought in from remote sites. Coordinating these cases with a microvascular surgeon ensures that the necessary tissue is available for skull base repair.[10]

These open approaches revolutionized treatment of malignant lesions of the anterior skull base. Before these surgical approaches were available, patients had few options and little chance of a cure. Even with the various advances in skull base surgery, complication rates from these procedures can be as high as 30% to 40%. Meningitis, CSF leaks, intracranial hematomas, frontal lobe injuries, and tension pneumocephalus can all result from this kind of approach. Because of these complications, both otolaryngologist and neurosurgeons have been pursuing ways to remove these tumors with less morbidity to the patient.

Endoscopic Approaches

Endoscopic approaches differ significantly from their open counterparts. These approaches are endonasal and utilize a telescope with a camera and monitor (Figure 1). New units are available in high definition, and the quality of images is outstanding. The images can be magnified for the surgeon, and multiple monitors can be used. An endoscopic approach allows for surgical resection of various benign and select malignant tumors of the skull base, avoiding a craniotomy and requiring no retraction of the frontal lobes. The amount of literature showing less morbidity, without a sacrifice in surgical outcomes in appropriately selected patients, is growing.[11,12]

The endoscopic approach requires that the traditional Halstead principle of en bloc resection be violated. Complete tumor resection can be achieved as long as margins are sent after each area is resected. This approach requires that tumor resection be employed in a systematic fashion. First, the tumor is debulked, allowing the surgeon to remove enough of the lesion to adequately see the key landmarks that were identified on preoperative imaging. Next, in a stepwise fashion, areas of tumor involvement are cleared out and appropriate margins sent, making a very important point about endoscopic surgery. Significant tumor bulk, expansion, and destruction can distort landmarks and make it difficult to know lateral and superior limits. Preoperative magnetic resonance imaging (MRI) and computed tomography (CT) are paramount in helping the surgeon outline his or her surgical plan. An intact clivus, pterygoid plate, and cribriform plate can all help the surgeon navigate around the tumor and utilize preserved landmarks to avoid critical structures and significant morbidity.[13]

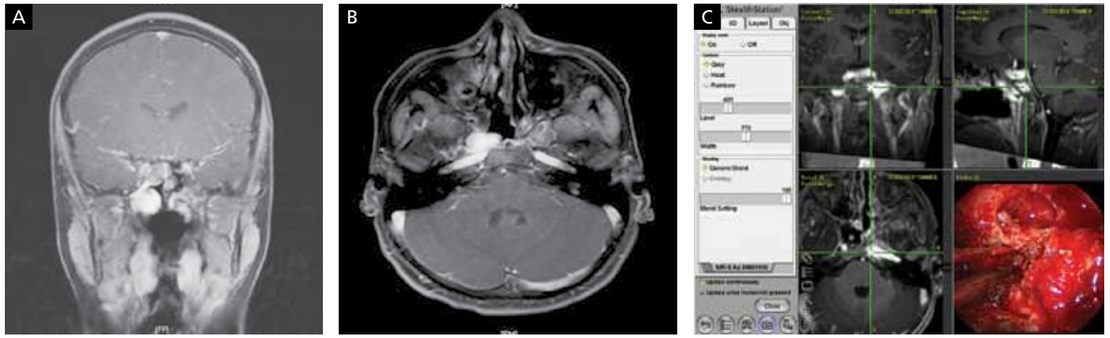

Figure 2: (A) Coronal and (B) axial T1-weighted contrast magnetic resonance images in a 12-year-old with a recurrent juvenile angiofibroma presenting with a local recurrence, previously treated with midface degloving. Following endoscopic medial maxillectomy and inferior turbinectomy, (C) the tumor was resected off the inferior clivus and floor of the sphenoid sinus.

The endoscopic approach is useful in treating primary tumors of the nasal cavity and paranasal sinuses with limited extension into the skull base and anterior cranial fossa (Figure 2). An extensive resection of the paranasal sinuses, septum, and cribriform plate is possible when indicated. Frequently, a solely endoscopic approach can be used when tumors are appropriately selected. Even when tumors extend into the orbital contents or have significant extension into the brain parenchyma, a combination of endoscopic and open approaches can be utilized.[11] An endoscopic approach in conjunction with a traditional craniofacial approach allows for a safe and oncologic resection of larger and more advanced tumors. Combining the two approaches allows for complete tumor resection and avoids incisions on the face, providing better cosmesis.

Central lesions like pituitary adenomas and craniopharyngiomas can also be treated via an endoscopic approach (Figures 3 and 4).[14] Cooperation between the neurosurgeon and the head and neck surgeon is paramount. The endoscopic approach requires the otolaryngologist perform limited endoscopic sinus surgery. Bilateral sphenoidotomies, a posterior septectomy with removal of the sphenoid rostrum and keel, are performed. Surgical resection of the middle turbinate does not need to be done routinely.[15] Once a common sphenoid sinus is created, it is usually necessary to take down the entire intersinus septum. The carotid arteries laterally and the optic nerves superiorly and laterally are identified while remembering that the intersinus septum will direct the surgeon to one of the carotid arteries posteriorly. Care must be taken in the sinus not to fracture this septum, injuring the associated carotid. A wide anterior sphenoidotomy is performed to allow the neurosurgeon to make the dural opening and work low in the sella. If the inferior tumor is removed first, it will allow the diaphragma to "push" the remaining tumor down low in the surgeon's view. A scope holder may be utilized during tumor resection, but both surgeons working simultaneously allows for dynamic visualization and movement of the scope to avoid collisions with instrumentation. Once the tumor has been removed, another benefit of utilizing the endoscope is apparent; the scope can be placed into the sella to confirm complete tumor removal. This inspection is not possible with traditional approaches that use the operating microscope.

Image Guidance and Skull Base Repair

Stereotactic image guidance is frequently used as a supplement in endoscopic cases.[16,17] It is not a substitute for surgeon experience or knowing the anatomy of the paranasal sinuses and anterior skull base but is a useful adjunct. Both volumetric MRI and CT can aid the surgeon, helping to delineate distorted landmarks and map out tumor locations. MRI does an excellent job of helping to differentiate between normal soft tissue and tumor. CT scanning is best at helping identify bony landmarks and is very useful in revision cases in which the common bony landmarks are distorted or gone. Another tool frequently used is the vascular Doppler. This tool is useful when drilling out the petrous carotid and mapping out its course. It allows the surgeon to identify its path, even when it is still covered by bone.

Both endoscopic and open approaches require that the cranial vault is separated from the nasal cavity at the end of the resection. The open approach has traditionally used the pericranial flap as a vascularized reconstruction. Endoscopic harvesting of this flap has been described, but the vascularized septal flap is easier to harvest and very versatile. Prior to the development of a reliable vascularized flap, endoscopic skull base resections had a high rate of CSF leaks, ranging from 10% to 20%. The Hadad-Bassagasteguy flap has helped revolutionize endoscopic skull base repair.[18]

This vascularized flap is based off of the posterior septal artery as it runs below the sphenoid ostium. When tumor resection doesn't require resection of the septal mucosa, this flap can be harvested at the beginning of the case. Once the sphenoid ostium is identified, the mucosa above the ostia is cut and is carried onto the septum high in the nasal vault. The incision is brought anteriorly and then inferiorly and posteriorly back to the choana. A mucoperichondrial flap is then elevated, leaving it pedicled on the mucosa running below the sphenoid ostia, where the posterior septal artery runs into the flap. With careful planning, this vascularized flap can cover skull base defects that span from the planum to the nasal frontal ducts.

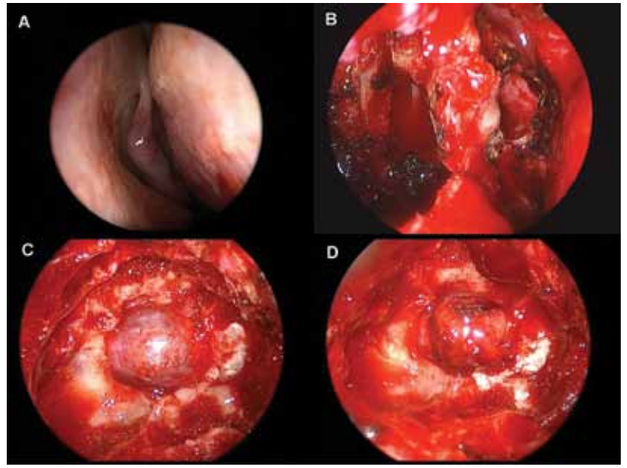

Figure 3: (A) Neuroendoscopic approach to the sella showing the initial endoscopic view of the nasal cavity. (B) Image after bilateral sphenoidotomies just prior to removal of the rostrum of the sphenoid. (C) A view of the sella after removal of the intersinus septum and the posterior wall of the sphenoid. (D) A view of the sella during tumor removal.

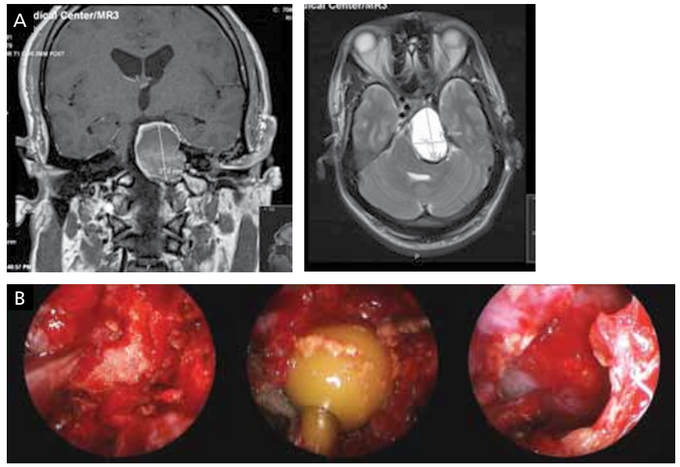

Figure 4: (A, left) Coronal T1-weighted and (A, right) axial T2-weighted magnetic resonance images of a 50-year-old man with a history of diplopia and severe headaches, demonstrating a large petrous apex cholesterol granuloma. Previous drainage attempts via a transtemporal approach were unsuccessful in adequately draining the lesion. (B, left) After removal of the upper clivus and posterior wall of the sella (B, center), excellent visualization of the cyst and drainage of its contents can be performed through a transnasal endoscopic approach. (B, right) After the cyst is drained, the posterior wall of the lesion comes into view with the dural margins.

Conclusion

As our experience with an endoscopic approach has increased, its utility in treating both benign and malignant tumors of the anterior skull base has expanded. It can be used as an adjunct with open approaches, avoiding incisions on the face, or used alone, allowing the otolaryngologist and neurosurgeon to work endonasally to resect select tumors. Stereotactic image guidance has expanded our ability to navigate across the skull base, even when normal structures are distorted or destroyed by neoplasms. New endoscopic techniques in skull base reconstruction have allowed us to perform more extensive resections and decrease morbidity to the patient.

Nicholas C. Bambakidis, MD, is a consultant for Medtronic Sofamor Danek, and Warren R. Selman, MD, is a consultant for Stryker and Anspach, though these relationships have not affected the content of this article. The other authors report no financial relationships with commercial interests relevant to the content of this article.

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Cerebrovascular and Skull Base Surgery Program

Nicholas C. Bambakidis, MD, Director

The Cerebrovascular and Skull Base Surgery Program provides a multidisciplinary team of specially trained and experienced surgeons to treat cerebrovascular and skull base disorders using minimally invasive, image-guided and radiosurgical techniques. Specialists from neurosurgery, radiology, otolaryngology, ophthalmology, radiology, endocrinology, neurology, oncology and radiation therapy have joined together to provide comprehensive care for complex clinical conditions, such as meningiomas, arteriovenous malformations, pituitary tumors and acoustic neuromas.

The skull base surgery team meets regularly to review new cases and determine the appropriate course of treatment for every patient. Each new case is discussed by members of the team, and care is tailored to the needs of the individual patient. Clinical and basic science research efforts are underway to advance the understanding of the cause, prevention, detection and treatment of these diseases and disorders.

Spasticity Treatment in Children

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By
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Spasticity is a motor disorder characterized by a velocity-dependent increase in tonic stretch reflexes (muscle tone) with exaggerated tendon jerks, resulting from hyperexcitability of the stretch reflex.[1] Progress in understanding the molecular basis of spasticity is underway,[2-4] and novel therapeutic strategies to minimize the injury that leads to spasticity are in the pipeline. Currently, the diagnosis of motor disorders in children is often associated with angst in families, particularly the term "cerebral palsy." A thorough assessment by an experienced multispecialty team can offer parents and caregivers definitive information that can relieve unfounded concerns and provide hope and empowerment. For many children, spasticity is just one component of an array of neurological impairments. Thus, the impact of spasticity on a child's development can vary tremendously. The impact of spasticity can also change over time as the child ages. Teenagers and young adults are much more likely to experience significant discomfort from untreated muscle spasms.

Injury at one or several sites along the pathway from the primary motor and pre-motor cortex to spinal circuitry can result in spasticity. In children, spasticity can be seen commonly in neurological disorders such as cerebral palsy, spinal cord injury, and stroke as well in a subset of childhood-onset neurodegenerative diseases with central white matter destruction, such as X-link adrenal leukodystrophy, metachromatic leukodystrophy, and Pelizaeus-Merzbacher disease. The pattern of muscle involvement typically affects certain muscle groups more than others. For example, flexors, adductors, and other internal rotators are affected more than their antagonists. Spasticity is often evident by 1 year of age and may improve or resolve during early childhood. In addition to recognizing the presence of spasticity, it is important to identify other types of motor disorders. For example, dystonia is commonly present in combination with spasticity in patients with cerebral palsy.

The decision to treat spasticity is based on the severity of tone abnormality and the impact it has on the child's comfort, function, cosmesis, and ease of care. Chronic spasticity may have negative effects on a child's growth and development. Prolonged involuntary muscle contraction results in permanent shortening in the muscle and tendon, restricting the range of motion in the affected joints, which may cause progressive dislocation of hip joints, bone and joint deformities, and discomfort. Generally, spasticity is treated if it interferes with mobility such as crawling, standing, and walking or with activities of daily living such as feeding, dressing, bathing, and orthopaedic alignment. If these activities are not affected, no treatment is necessary. On the other hand, a certain degree of spasticity can aid the child's function. For example, some children use lower extremity spasticity to compensate for muscle weakness during ambulation or transfers. In such a situation, reduction of useful spasticity may be counter-productive.

Multidisciplinary Team Provides Individualized Approach

The treatment team for spasticity management consists of the child and caregivers, primary care physicians, physical and occupational therapists, nurses, neurologists, physiatrists, neurosurgeons, orthopaedic surgeons, orthotists, social workers, and psychologists. The goal of spasticity management is not to cure but to increase

functionality, sustain locomotion, improve ease of care, and prevent secondary complications such as pain, subluxation, and contracture. It is crucial to obtain information from the caregiver with regards to how the child is currently functioning at home and school and how the child's interests may be affected by potential treatments. Several factors play important roles in determining the treatment plan, such as the age of the child, the presence of co-morbidities (seizures or cognitive impairment), the ability of the family to carry out home treatments or return for regular follow-up appointments, and financial concerns. The types of treatment for spasticity range from physical therapy, occupational therapy, orthosis, oral medications, and neuromuscular blockade to surgeries, including selective dorsal rhizotomy, intrathecal baclofen, and orthopedic procedures. Ideally, treatments are considered early in childhood to optimize a child's function and independence prior to beginning kindergarten.

Physical Therapy and Occupational Therapy

Physical therapy and occupational therapy remain the mainstay intervention for spasticity. A stretching and strengthening exercise program may help prevent musculoskeletal complications and enhance potential benefits of other treatment modalities. Infants are often enrolled in Help Me Grow programs and, at 3 years, toddlers transfer to pre-school programs that continue to include therapy. Sustained therapy programs combined with daily stretching exercises performed by caregivers are essential to the success of any of the more invasive treatment options discussed below.

Oral Medications

The advantage of oral medications is the ease of use. However, the systemic side effects are often problematic. Oral medications are most appropriate for children who need mild tone reduction or who have diffuse involvement in most extremities. Similar to other areas of pediatric medicine, most anti-spasticity medication trials have been conducted in adults and relatively few trials have been carried out in children. Therefore, the choice of agent is often based on personal experience and trial and error rather than rigorous, evidence-based medicine.

Baclofen

Baclofen is a GABA-B (gamma-amino butyric acid) agonist and oral baclofen is often used for spasticity of spinal cord origin in adults. It may be useful in selected pediatric patients. Similar to most medications routinely used in children, baclofen does not have approval from the United States Food and Drug Administration for use in cerebral palsy. The tendency of oral baclofen to cause confusion and sedation due to central effects limits the dose most children tolerate. These side effects may diminish after several weeks of treatment. This medication is usually considered in patients older than 2 years. A typical starting dose is 2.5 mg/day, and the dose can be titrated slowly to a maximum of 20–60 mg divided three times a day, depending on the patient's weight.[5] Weaning off this medication must be done gradually to avoid withdrawal symptoms such as high fever, increased spasticity, altered mental status, seizure, and death in rare cases.

Tizanidine

Tizanidine is a centrally acting alpha-2 noradrenergic agonist that has been shown to reduce tonic stretch reflexes and to enhance pre-synaptic inhibition in animals. To date, no clinical trials of this agent in children have been published in the English-language literature. Sedation and the requirement for frequent dosing throughout the day often limit tizanidine use in children. Some children with spasticity experience difficulty sleeping due to painful spasms. Tizanidine's sedative quality can be advantageous when the medication is given at bedtime. Improved initiation of sleep and reduced tone throughout the night are potential benefits.

Diazepam

Diazepam is a benzodiazepine that facilitates the postsynaptic action of GABA. A series of trials in the 1960s demonstrated its ability to reduce spasticity in children with cerebral palsy.[6-10] More recently, Mathew and colleagues showed that diazepam reduced muscle overactivity compared with placebo in a randomized trial of 180 children.[11] The daily dose of diazepam is usually 0.12–0.8 mg/kg, divided into three to four doses. The known sedation profile of this class of medications must be considered. Diazepam at bedtime may aid sleep without daytime sedation. Similar to the other medications discussed here, diazepam should not be discontinued abruptly.

Dantrolene Sodium

Dantrolene sodium acts at the muscle level by inhibiting calcium release from the sarcoplasmic reticulum, causing muscle weakness. In double-blind crossover studies, it has been shown to reduce spasticity in children with cerebral palsy.[12,13] It can cause global weakness and sedation, and hepatotoxicity is found in approximately 1% of patients.

In general, the cognitive and sedative side effects of oral medications can overshadow any improvement in spasticity, leaving the patient with minimal global gain in function. Thus, other types of treatments often play a more important role in tone management in the child with spasticity.

Neuromuscular Blockade

Currently, there are two methods of neuromuscular blockade in use: perineural injection of phenol or ethyl alcohol and intramuscular injection of botulinum toxin (BoNT). They are appropriate for focal spasticity or for targeting specific problem muscles in the setting of more generalized spasticity.

Phenol and Alcohol

Phenol and alcohol have been used in children with cerebral palsy, though neither has been widely used or rigorously tested. Phenol is typically injected at a concentration of 3–6% aqueous solution, whereas absolute alcohol is diluted to 30–50%. The target nerve is identified with electrical stimulation, which is poorly tolerated in children, making sedation or anesthesia necessary. The agent is injected perineurally, where it promotes denervation via axonal degeneration. The effect is transient with functional reinnervation occurring over months to years. The period of benefit typically ranges from a few weeks to two years. Adverse effects of both agents include a significant risk of pain or paresthesia when targeting a mixed nerve, which may persist. This risk, combined with the high degree of skill required to target the nerve and the availability of BoNT as an alternative, has kept phenol and alcohol from assuming a larger role in focal spasticity management. However, the absence of immunogenicity and the lower cost compared to BoNT make these agents more attractive in selected settings.[14]

Botulinum Toxin

BoNT is an exotoxin produced by Clostridium botulinum. There are seven naturally occurring serotypes of the toxin, A–G, all of which are zinc proteases that target the synaptic vesicle fusion machinery at the neuromuscular junction. Denervation occurs secondary to the blockade of the release of acetylcholine at the neuromuscular junction and results in flaccid muscle paralysis. The seven serotypes differ in the specific component of the fusion machinery that they target, their duration of action, their unit potency, and their immunogenic potential. Two serotypes, A and B, are commercially available. At effective anti-spasticity doses, they have roughly the same duration of clinical action (approximately three months). Potency is expressed in mouse units, the amount of toxin required to kill 50% of mice in a standardized assay. Because of differences in molecular formulation and other variables, the potency of a single unit varies greatly among the commercial types. On average, BoNT has a clinical onset of action approximately 12 to 72 hours after the injection, with the peak effect at one to three weeks. The lowest effective dose with an injection interval of at least three months or more should be used to minimize the risk of antibody development. For comfort, children may need a topical anesthetic or light sedation during injection. Electromyography or electrical stimulation is sometimes used to help target muscles that are difficult to localize, such as in the upper extremities, though clinical examination is sufficient for determining affected muscles in most situations. Adverse effects of BoNT injection are usually mild and transient and consist of pain on injection, a flulike syndrome, and excess weakness.[15,16] The botulinum neurotoxin complex is immunogenic, and repeated exposure can lead to immuno-resistance and decreased efficacy with repeated injections. These injections are often quite useful in children who experience worsening of their spasticity during a growth spurt but are less effective as a primary long-term solution for children with severe spasticity.

Selective Dorsal Rhizotomy

Although the nonsurgical treatments described above are effective for many children, other children continue to have problems walking normally due to spasticity. These children, especially those with spastic diplegia secondary to preterm birth, may benefit from selective dorsal rhizotomy. The term dorsal rhizotomy is used to describe cutting of the posterior sensory nerve roots after they exit the spinal cord. Selective refers to the use of electrophysiological monitoring during the procedure to identify and cut only those nerve rootlets that are most abnormal.

The goal of selective dorsal rhizotomy is to help normalize the feedback loop that causes increased muscle tone. Normally, muscle tone is determined by a spinal cord feedback loop between the motor and sensory nerves to each muscle. Descending inhibitory input from the brain modulates the spinal cord feedback loop and suppresses muscle tone. Children who have cerebral palsy from preterm birth have limited descending inhibitory input from the brain and thus experience excessive muscle tone in the extremities. In addition, children with cerebral palsy from preterm birth have difficulty generating isolated muscle movements and experience increased spread of muscle tone to adjacent muscle groups and limited isolated movements. The selective dorsal rhizotomy procedure normalizes the spinal cord feedback loop by cutting a portion of the sensory roots at each spinal level in the lumbar and upper sacral areas. The decreased sensory portion of the feedback loop selectively reduces abnormal muscle tone without affecting sensation.

The multidisciplinary Spasticity Team at University Hospitals Rainbow Babies & Children's Hospital evaluates children who are possible candidates for selective dorsal rhizotomy on an individualized basis. The ideal candidate for selective dorsal rhizotomy has primarily lower extremity spasticity due to preterm birth. In addition, the child must be able to cooperate with an intensive post-operative course of physical therapy to optimize the improvement in muscle tone after surgery. In general, the best candidates are those children who have the potential to walk independently or with assistance from a device. The ideal time for selective dorsal rhizotomy is after less invasive options have been tried and after the child has developed the cognitive skills and stamina to complete the intensive post-operative course of physical therapy but before the child starts kindergarten and is frustrated by his or her relative immobility. Children with spastic hemiparesis also benefit from this surgery.[17] The operation can also help non-ambulators who are significantly impaired by spasticity. Children who use their increased tone to substitute for muscle strength are not the best candidates for this surgery.

Selective dorsal rhizotomy typically requires a four to five day hospital stay, and families may stay with their child the entire time except during the surgery itself. After the child is asleep under general anesthesia, a small incision is made in the upper lumbar spine centered over the lower conus, and a 1 to 1.5 level laminectomy is performed. The small incision and limited bone removal minimizes the amount of post-operative pain and recovery time and decreases the chance that the child will develop spine problems later. UH Rainbow Babies & Children's Hospital is the only children's hospital in the multistate region to offer this surgery using a minimally invasive approach. After the dura is opened under the operating microscope, the dorsal spinal roots are identified, tested, and divided into rootlets (Figure 1). A specially trained electrophysiology team monitors the response of each nerve rootlet as it is tested. The surgeon evaluates the information found by the electrophysiology team and selects the rootlets to cut. The location and percentage of rootlets that are cut are individualized for each child. The wound is closed, and the child is awakened from surgery.

The first night after surgery, the child is typically monitored in the Pediatric Intensive Care Unit while receiving continuous intravenous pain medicine. The day after surgery, the child moves to a room on a regular floor and begins oral pain medicine and physical therapy. Children lie flat in bed for three days post-operatively to minimize the risk of cerebrospinal fluid leakage. An intensive course of physical therapy (four to five sessions a week) is continued for at least six weeks after the surgery. This intensive therapy will greatly help the child's improvement after surgery. The only restrictions on the child's

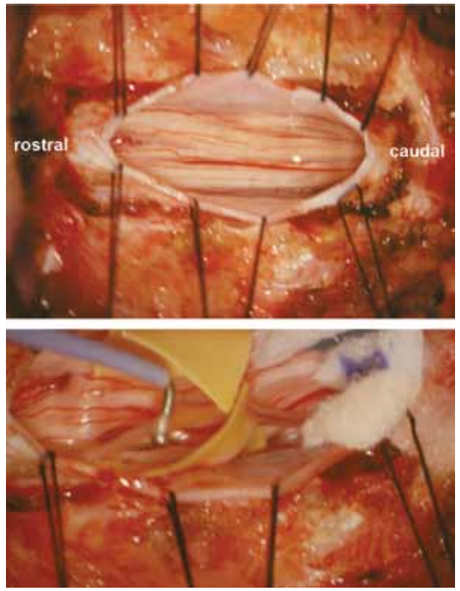

Figure 1: Intraoperative images of the surgical field during a selective dorsal rhizotomy. In the upper image, the dorsal roots overlie the conus (*). In the lower image, the left L3 dorsal root has been separated into multiple rootlets, and the response of the rootlet to stimulation will be tested.

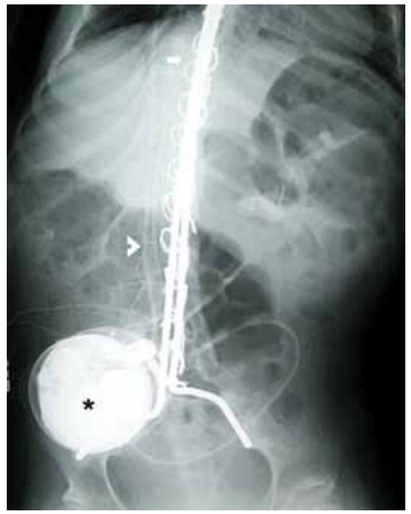

Figure 2: A radiograph demonstrating the integration of an intrathecal baclofen pump (*) and catheter (arrow) with other interventions. In addition to spastic quadriplegia, this patient had multiple other difficulties secondary to preterm birth, including shunted hydrocephalus (arrowhead), scoliosis requiring a spinal fusion, and a gastrostomy tube. Comprehensive coordination of care is essential to optimizing this child's quality of life.

activity are sponge baths for one week after surgery and no swimming for two weeks to help prevent wound infection. Overall, selective dorsal rhizotomy has a very low complication rate.

Benefits of Selective Dorsal Rhizotomy

Children who undergo a selective dorsal rhizotomy experience life-long benefits after a single procedure. They usually can expect to decrease their dependence on devices to assist ambulation. It is an effective procedure that has been shown to produce long-term improvement in muscle tone in research studies with 20-year follow-up.[18,19] Overall, children who have had selective dorsal rhizotomy often have a decreased need for other surgical procedures for spasticity, such as orthopaedic procedures.[20] Many children also note improved use of their arms and improved school performance. These added benefits are related to reducing the spasticity and have been found with other treatments that reduce spasticity, such as intrathecal baclofen medication pumps.

Intrathecal Baclofen Pump

Although nonsurgical treatments are effective for selected children with spasticity, others still suffer from immobility and discomfort. Many children with spasticity or other movement disorders have limited potential to ambulate. They also suffer muscle spasms, have difficulty maintaining adequate nutrition, and are difficult to position for personal hygiene. These children, who typically are not ideal candidates for selective dorsal rhizotomy, may benefit from an intrathecal baclofen pump. The pump is surgically inserted in the abdominal wall, and it pumps baclofen into the spinal fluid through a small catheter (Figure 2). By delivering baclofen directly to the cerebrospinal fluid, many of the unwanted central effects of oral baclofen, such as sedation, are avoided. Intrathecal baclofen is 1000-fold more potent than oral baclofen.

With increased flexibility and comfort from intrathecal baclofen, children can experience a significant improvement in their quality of life. The Spasticity Team at UH Rainbow Babies & Children's Hospital evaluates all children who are potential candidates for an intrathecal baclofen pump on an individualized basis. Children with severe spasticity from almost any cause, such as meningitis, stroke, trauma, or preterm birth, can benefit from a pump. Ideally, the child can cooperate with the physical therapist to make the most of the improvement in muscle tone after surgery, but cooperation is not imperative as it is for a selective dorsal rhizotomy.

At UH Rainbow Babies & Children's Hospital, children who are potential candidates for the pump undergo a test dose of intrathecal baclofen via a lumbar puncture under sedation. The test dose provides a glimpse of the impact of decreased muscle tone for the child and checks for an adverse reaction. A physical therapist evaluates the child before the test dose and then multiple times during the several hours after the dose to quantify the changes that the child experiences. The effect from the test dose typically lasts six to eight hours. Many families prefer to have the test dose performed on the day prior to surgery as they find one trip to the hospital less burdensome. For children who have previously had a spinal fusion, a two-part surgery may be required. During the first surgery, the intrathecal catheter is inserted and attached to a small reservoir. After the child has fully recovered from the first surgery, the test dose is administered into the reservoir. If the child experiences a favorable response, he or she returns to surgery to have the pump inserted.

A small incision is made in the lower spine, and the intrathecal catheter is inserted using fluoroscopic guidance. Space is made for the pump in the abdominal wall, and the catheter is connected to the pump. After the surgery is completed, the pump is programmed to deliver a relatively low dose similar to the test dose. Programming the pump is painfree and takes only a few minutes. The child typically recovers in a regular hospital room for a few days. Post-operative pain is treated with intravenous or oral pain medicine as needed. Physical therapy begins during hospitalization, and some children and young adults benefit from an inpatient rehabilitation stay. The pump dose is increased about 10% every two to three weeks for outpatients and more rapidly for inpatients. When the volume of drug in the pump is low, the pump is refilled by inserting a needle sterilely through the skin into the pump. The timeframe for refills depends on the size of the pump (20 or 40 milliliters) and the dose the child receives and typically occurs a few times a year. There are several options for obtaining the refills, including having a specially trained nurse visit the home or school. The pump battery is depleted of energy after about five to seven years. Surgery is required to replace the pump, but the pump replacement surgery is a relatively minor surgery. Some children have the replacement as an outpatient, and others stay in the hospital one night. The pump includes alarms for both low drug volume and low battery strength. Acute untreated withdrawal from the intrathecal baclofen can cause severe medical problems and, rarely, death. The withdrawal can be easily controlled by administering intravenous medications, and families are educated about warning signs and how to seek emergency care for possible withdrawal.

Benefits of Intrathecal Baclofen Therapy

The intrathecal pump offers several benefits and is an effective procedure that has been shown to produce sustained long-term improvement in muscle tone. Overall, children who have a pump have fewer complications related to immobility.[21] Added potential benefits for children include improved use of their arms and improved school performance. Many parents report that the children with intrathecal baclofen therapy are much more comfortable and can better maintain their weight than without the pump.

While the pumps themselves rarely malfunction, there can be complications related to the catheter breaking, occluding, or migrating that typically require surgery to correct the problem. The pump and catheter can be a nidus for infection. At UH Rainbow Babies & Children's Hospital, the infection rate for baclofen pumps during the past three years has been 2.04% per procedure. Infections can require removal of the pump and typically require extended treatment with intravenous antibiotics. If the baclofen dose is increased too quickly, the child may experience an overdose, typically requiring supportive care in the hospital. Despite these potential complications, most families feel the benefits far outweigh the risks. The team at UH Rainbow Babies & Children's Hospital is used to caring for children with cerebral palsy who have other complex medical conditions, such as pulmonary problems, epilepsy, and impaired cognitive development. UH Rainbow Babies & Children's Hospital is known for its family-centered care.

Conclusion

Spasticity and related motor problems can limit a child's mobility and cause discomfort. Current therapy regimens and treatments offer a spectrum of effective options for children. The multidisciplinary team of UH Rainbow Babies & Children's Hospital's Spasticity Program uses individualized strategies to best tailor treatment options and help children optimize their development, comfort, and independence.

Dararat Mingbunjerdsuk, MD, and Shenandoah Robinson, MD, report no financial relationships with commercial interests relevant to the content of this article.

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Expanding the Spectrum of Indications for Epilepsy Surgery in Children

By
Ingrid Tuxhorn, MD

Introduction

The incidence of epilepsy peaks in children and the elderly, and a number of well-defined syndromes may be amenable to surgical management, resulting in a cure with complete seizure control or palliation with significantly improved seizure control. Surgery for epilepsy is no longer a treatment of last resort. Early onset of seizure, a high frequency of seizure, and intractability are significant risk factors for overall poor developmental and social outcome in children. Therefore, children with surgical epilepsy syndromes should be referred to a specialized pediatric epilepsy unit early and selected early for operation to optimize seizure and psychosocial outcome.[1] Indeed, early epilepsy surgery may be considered a disease-modifying approach to management of refractory seizures.

Unique Aspects of Epilepsy Surgery in Children

Unique neurobiological aspects of epilepsy in children, especially young children, have been recently recognized and require specific pediatric epilepsy expertise in a multidisciplinary tertiary care center with high-level services in pediatric epilepsy, imaging, surgery, cognition, mental health, and behavioral medicine. A uniquely pediatric approach is required for referral, diagnosis, and management. The recent recommendations of the subcommission for pediatric epilepsy surgery have highlighted the following aspects.[2]

Neurobiological aspects: Brain maturation in infancy and childhood affects the clinical manifestation of seizure semiology, the electroencephalography (EEG) signature, and neuroimaging findings. Generalized seizure semiology, including spasms as well as myoclonic and tonic seizures, is noted frequently in young children with focal epilepsies arising from the temporal lobe and extratemporal neocortex.[3,4] In addition, the interictal and ictal EEG may be less localizing and show generalized features.[5]

Comorbidities are common in pediatric patients of epilepsy surgery and include epileptic encephalopathy, mental retardation, and behavioral and psychiatric disturbances. Increasing evidence from a number of studies suggests that early surgical intervention is critical in infants with catastrophic epilepsy to prevent mortality and deleterious secondary brain damage leading to developmental arrest and regression. There is compelling evidence that adequate timing of surgery leads to the restart of development and may result in a higher long-term cognitive level of functioning.[6] As there is little evidence at this point for postoperative catch-up or normalization of deficits, there may be a narrow time window to allow best recovery in infantile catastrophic surgical syndromes.[7]

Psychosocial aspects: Chronic epilepsy poses a significant burden on patients and their families, and an earlier reduction of this burden will improve quality of life. Therefore, every attempt should be made to make surgery available early to children that are good surgical candidates to confer psychosocial benefits on these patients.

Surgical Epilepsy Syndromes

Compared with adult patients, the etiologies of surgical epilepsies in children generally more extensively involve the brain and cerebral cortex and are more diverse; however, there are few studies documenting the exact incidence of these conditions. In addition to well-defined etiologies that are well-recognized as surgical epilepsy substrates by pediatric epilepsy experts, the spectrum of surgical epilepsies is expanding based on reports from a number of pediatric centers around the world. The following etiologies and syndromes are commonly recognized.

Hemispheric syndromes: Children with refractory epilepsy due to a unilateral epileptogenic zone that lateralizes with a unilateral brain pathology (e.g., stroke, Rasmussen encephalitis, hemimegalencephaly) and pre-existing hemiplegia may be good candidates for a hemispheric disconnection procedure to treat hemispheric epilepsy. The seizure outcome is excellent, particularly in children with an epileptic encephalopathy. Functional hemispherectomy or hemispherotomy is the procedure of choice in acquired atrophic lesions, and a more anatomic procedure with removal of cortex is the procedure of choice with dysplastic lesions, which result in highly epileptogenic hemispheric tissue mantles so that hemispherotomy procedures may not result in as good seizure control (Figure 1).

Cortical dysplasia: Abnormalities of corticogenesis are the most frequent cause of refractory focal epilepsy in children amenable to surgical treatment. The pathology is varied and may be exquisitely focal and difficult to appreciate on magnetic resonance imaging (MRI) or extensive affecting multiple lobes. The epilepsy syndromes are equally varied and include early onset infantile epileptic encephalopathies, including West syndrome with hypsarrythmia, Ohtahara syndrome with EEG in a burst suppression state, Lennox-Gastaut syndrome as a multifocal epileptic encephalopathy, and a well localized focal symptomatic epilepsy. A number of studies have shown that the seizure outcome depends on complete resection of the epileptogenic substrate. These cases may be complex to evaluate and may require invasive EEG evaluation with intracranial electrodes placed subdurally or intracerebrally.

Sturge-Weber syndrome: Children with Sturge-Weber syndrome (SWS), seizures, and strokelike episodes should be referred early for possible surgical intervention. In a subgroup of patients with early seizure onset that is refractory to therapy, surgery may halt this progressive vasculopathy.

Tuberous sclerosis complex (TSC): TSC is typically characterized by multiple cortical tubers of variable epileptogenicity. Children with single epileptogenic tuber complexes may be good surgical candidates with good long-term seizure control after tuberectomy. Recognition of these cases may be facilitated by a large size, the presence of calcifications of the tuber, and information from newer imaging modalities that might include alpha-methyl-L-tryptophan positron emission tomography (PET), diffusion tensor imaging in conjunction with EEG data, and magnetencephalography as well as other source localization techniques. Patients with TSC may be candidates for multistaged procedures (Figure 2).

Hypothalamic hamartoma: Gelastic epilepsy due to hypothalamic hamartoma is frequently therapy-resistant and carries a high risk for dementia and neuropsychiatric dysfunction. Ablation of the hamartoma, which is probably intrinsically epileptogenic without

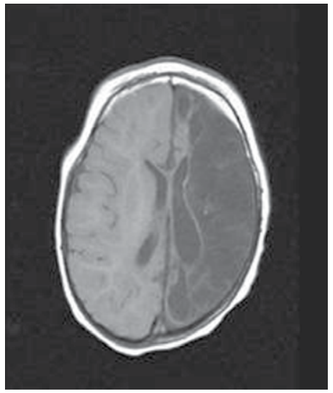

Figure 1: Left hemispheric multicystic encephalomalacia in a child with frequent medically refractory seizures that responded well to hemispherectomy. The presurgical evaluation with video-EEG monitoring from surface electrodes confirmed unilateral left-sided seizure onset. The patient, whose spastic hemiparesis did not worsen after surgery, became seizure free.

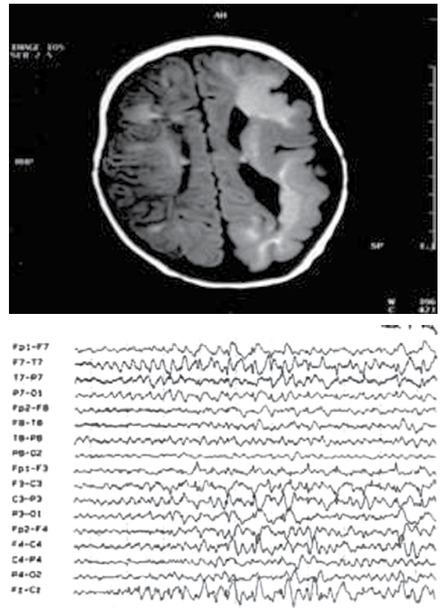

Figure 2: A 3-year-old with tuberous sclerosis had multiple tubers in both hemispheres and subependymal nodules. The hamartomatous left hemisphere was responsible for generating all seizures in this child, and a left hemispherectomy resulted in near complete seizure control. Prior to surgery, the child required frequent hospitalization and emergency care for prolonged seizures.

damage of the hypothalamus proper, is a challenge in these cases and poses a complex risk-benefit scenario. Stereotactic, endoscopic, and disconnective techniques have been applied as well as various other techniques such as radiosurgery and seed implantation. These patients need referral to a highly skilled and experienced center (Figure 3).

Temporal lobe epilepsy: Temporal lobe epilepsy is typically diagnosed in adulthood; however, a high proportion of adult patients have onset of mesial temporal lobe epilepsy due to hippocampal sclerosis in their early teens. Hippocampal sclerosis frequently follows a complicated febrile convulsion in early childhood with subsequent medically refractory seizures arising from the damaged mesial temporal structures. Seizure outcome is excellent after localized resection of the limbic structures with open but minimally invasive surgical resections.

In addition, a number of developmental tumors (e.g., ganglioglioma, dysembryoplastic neuroepithelial tumor) may cause early drug-resistant focal epilepsy that is amenable to surgical resection. As there is a high association with neuropsychiatric disorders, including autism spectrum and cognitive dysfunction, the epilepsy should be treated early with surgical options.

In school-age children and teens with lesions involving neocortical structures of the dominant lobe, a detailed invasive evaluation of the epileptogenic zone, lesional zone, and eloquent language, memory, motor, and sensory areas may need to be performed to minimize the risk of functional deficits and improve accuracy for surgical resection.

The Presurgical Evaluation

A presurgical evaluation should be considered as a multistep approach to assure that the individually available resources for presurgical evaluation and surgical therapy are efficiently utilized. The first diagnostic steps should include a characterization of the seizure semiology by history, parental documentation by home video, good quality surface interictal EEG, and structural imaging with MRI. Unifocal epilepsy due to a well demarcated lesion (tumor, malformation of cortical development, or other acquired vascular, ischemic, or inflammatory pathologies) carries the best seizure outcome prognosis. Referral to an experienced and well versed epilepsy center, where a standardized presurgical evaluation with surface interictal and ictal EEG, structural and functional imaging, language, memory and cognitive testing is performed, should be considered early in such cases.[2]

Even intractable epilepsies due to multicentric or extensive bilateral disease, such as tuberous sclerosis, SWS, or remote epilepsies due to strokes, may be surgically remedial with either cure or palliation.[8,9] Infants and children with epileptic encephalopathies due to well-defined epileptic lesions are excellent candidates for surgical treatment. The presurgical evaluation in these cases may require invasive video EEG monitoring with intracranial electrodes and functional interictal and ictal imaging with single photon emission computed tomography, PET, and functional MRI (fMRI) to localize the epileptogenic zone and delineate it from eloquent cortex that may not be sacrificed without resulting in permanent neurologic deficit.

Though congruence of diagnostic findings is the gold standard for presurgical selection, it has become apparent that generalized epileptiform discharges in the constellation of other localizing features (e.g., pathologic substrate, seizure semiology) may not be a contraindication to surgery. This suggestion may particularly apply to the static structural epileptic encephalopathies in infants and early childhood, which may be particularly challenging to demarcate from progressive metabolic disorders. These cases require the expertise of experienced and knowledgeable level IV pediatric epilepsy centers.[2]

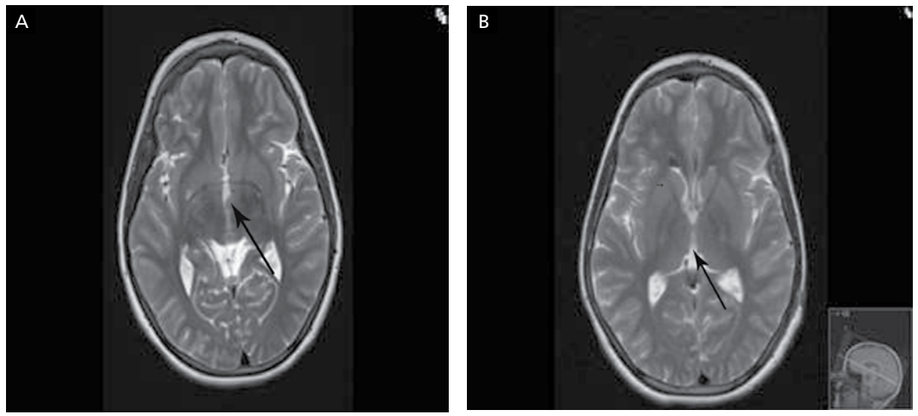

Figure 3: (A) Preoperative hypothalamic hamartoma visualized in the third ventricle. (B) Postoperative endoscopic removal resulted in significant seizure control of daily gelastic seizures and improved control of impulsive behavior disorder.

Outcomes

In children, as in adults, the primary aim of epilepsy surgery is freedom from seizures with minimal if any functional deterioration. However, the chances of seizure freedom will depend in part on the type of procedure, the degree of resection, and the type and extent of the pathology. After temporal lobectomy for hippocampal sclerosis, seizure outcome rates in children are similar to rates in adults and may be higher, approaching 75% to 85% in some series.[10] However, such rates may be lower in children with comorbidities, such as learning difficulty or pervasive developmental disorder.[11] However, these comorbidities should not lead to denying surgery to such children. With regard to extratemporal resection, the likelihood of seizure freedom will range between 40% and 70%, depending on the extent of resection possible of the epileptogenic and anatomic substrate causing the epilepsy.[10,11]

In children undergoing extensive procedures, such as hemi disconnections in the form of either anatomic hemispherectomy or variants of functional hemispherectomies, seizure outcome appears related to the underlying pathology. The lowest rates of seizure freedom for developmental malformations are reported for hemimegalencephaly, which may reflect the extreme epileptogenicity of this type of malformation, the technical challenge of disconnecting the highly abnormally configured hemisphere, and in some cases the risk of seizures originating from the normal appearing hemisphere. Though in some cases, there is the suggestion that seizure may also arise from the contralateral hemisphere, the completeness of disconnection will be highly relevant for seizure outcome, and anatomical hemispherectomy may lead to greater chance of seizure-free outcome. Anatomical hemispherectomy is the preferred procedure in a number of centers specialized in the surgical management of catastrophic epilepsy due to this malformation.

The point in time that the outcome is measured will be relevant in determining the degree of seizure freedom, particularly in children with cortical malformations. Series that monitor outcome up to 10 years following surgery have found that individuals undergoing resection for cortical malformations were less likely to be seizure free at 10 years compared to other pathologies.[11,12] It is more difficult to determine whether medication can be stopped. However, data suggest that reduction or withdrawal of anticonvulsant drugs cannot be guaranteed and may be achieved in 50% to 70% depending on the series.[11]

The risk of deficits following focal resection will depend on the area of brain to be removed and the likelihood that this area retains function despite causing seizures. With regard to hemi-disconnection procedures, children with pre-existing hemiplegia have little risk for additional motor deficits. In some patients, reorganization and persistent ipsilateral tracts may protect the child from loss of adequate motor function. Presurgical evaluation with motor fMRI, transcranial magnetic stimulation, and tractography will optimize risk assessment in these cases.

In infants and young children with catastrophic epilepsy, surgery in the dominant left hemisphere is possible; a number of case series show a strong potential for language acquisition due to interhemispheric shift of language in early onset severe epilepsy. In older children who have acquired normal language, the language dominance needs to be assessed with a Wada test and language fMRI studies. With left dominance, the risk of language deterioration or loss will be high in children undergoing left hemispherectomy for Rasmussen encephalitis. As there is a high risk for additional functional deficit in these cases, the gains to be achieved with regard to cognitive preservation by attaining seizure remission need to be weighed carefully against the likelihood of functional deficits, particularly with regard to language when the dominant hemisphere is affected. A hemianopia, if not already present, will be inevitable.

There is substantial data emerging on developmental, cognitive, and behavioral outcomes after epilepsy surgery in children. Early onset seizures are a high risk for poor developmental outcome. Similarly, early cessation of seizures is likely to lead to improved cognitive outcome. Early onset epilepsy under the age of 2 is associated with a lower IQ in the long term, presumably related to the early onset of seizures.[13]

Many studies show that IQ is maintained postoperatively and not impacted negatively as feared by parents or physicians unfamiliar with the outcomes of these patients. There is some evidence that development may stabilize or in some cases catch up to the norm rather than falling off as with static encephalopathies. The clinical variables predicting risk for loss and chance for gain are not well understood and need to be studied in greater detail in further long-term multicenter outcome studies.[6]

Behavior outcome is unpredictable and is often the most burdensome issue in children with ongoing seizures and global developmental impairment. However, there is encouraging evidence for improved attention and behavior following hemispherectomy for epileptic encephalopathies.[12] The rate of psychiatric symptoms in children requiring temporal lobe resection for epilepsy is very high,[14] and behavior problems are notable in children presenting for hemispherectomy.[11] The latter procedure was first reported for treatment of behavior disorders in children with epilepsy and congenital hemiplegia, but improvements in behavior cannot be guaranteed. In some children, a psychiatric disorder may evolve postoperatively. It is important to counsel parents about the variability of these outcomes and explain that dramatic improvements with regard to cognition or behavior may be realistic. Rehabilitative programs and support should be offered to children and families with significant preoperative comorbidities because of these issues.

Ingrid Tuxhorn, MD, reports no financial relationships with commercial interests relevant to the content of this article.

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A key component of the Division of Pediatric Epilepsy, the Epilepsy Center at UH Rainbow Babies & Children's Hospital provides comprehensive, integrated and state-of-the-art diagnosis and treatment – including surgery – to children with epilepsy across all age groups. The division is heavily involved in research that directly benefits patient care and translates into improving the lives of children with epilepsy and their families. Closely integrated with UH Rainbow Babies & Children's Hospital's Division of Pediatric Neurosurgery, the Epilepsy Center at UH Rainbow Babies & Children's Hospital has access to a vast number of specialists and surgeons, including renowned pediatric neurosurgeons Alan Cohen, MD, FACS, FAAP, Chief of Pediatric Neurological Surgery, and Shenandoah Robinson, MD, Surgical Director, Rainbow Spasticity and Epilepsy Programs. Its alignment with the Division of Pediatric Neurosurgery and access to the Pediatric Epilepsy Monitoring Unit and Pediatric Intensive Care Unit allows the center to offer the most advanced approaches to diagnosing, managing and treating epilepsy in infants and children.

The Neuropsychology of Sports-Related Concussion: Return-to-Play and the Management of Head Injury in Athletes

By
Christopher M. Bailey, PhD

Introduction

Concussion or mild traumatic brain injury (MTBI) is a particularly complex clinical phenomenon. Since the 1980s, the sports arena has provided a natural laboratory for examining the nature and consequences of concussion and, in the process, revealed a variety of circumstances and characteristics that are unique to the management of concussion in athletics.[1] This article will describe the pathophysiology of concussion, its epidemiology, risk factors for poor outcome, and the current methods for evaluation and clinical management of the injury.

What is Concussion?

The most recent consensus statement on concussion in sports defines concussion as "a complex pathophysiological process affecting the brain, induced by traumatic biomechanical forces."[2] Though most definitions reference concepts such as trauma-induced injury and altered mental status, a clear and widely accepted definition of mild head injury has been a topic of much controversy for decades. As a result, a variety of labels have been proposed to describe a concussion and symptoms associated with relatively mild head trauma, including minor head injury, mild traumatic brain injury, uncomplicated mild head injury, cerebral concussion, and simple or complex concussion.[1]

No matter how it is defined, concussion represents a public health problem. Approximately 1.5 million concussions per year lead to emergency department visits.[3] The true prevalence of the injury is unknown given that an estimated 30–50% of all concussions never receive medical attention.[4] MTBI represents 75% of all hospital visits associated with traumatic brain injury (TBI), with MTBI costing the nation approximately $17 billion per year in medical care, lost productivity, and litigation.[5] Concussion is particularly common in sports. The Centers for Disease Control and Prevention reported that 200,000 sports-related head injuries are treated in emergency departments annually within the United States and that sports-related concussion accounts for approximately 20% of all TBI per year.[6] Given the public health problem that concussion poses, a need for appropriate diagnosis and management is clear, particularly for athletic populations that participate in sports and may place themselves at greater risk for repeated head injury. This need is complicated by difficulties in identifying concussion through traditional imaging techniques, which is likely due to the mechanism of the injury that results in changes on a cellular and/or metabolic level.

The pathophysiologic mechanisms of concussion are generally thought to center around acceleration/deceleration forces that act on the brain and result in a complex metabolic cascade. Animal model research suggests that the force from concussive blows leads to stretching and shearing of neurons, irregular shifting of ions across cell membranes, and changes in cerebral blood flow, all of which leave neurons temporarily dysfunctional but not destroyed.[7]

The metabolic cascade following a concussion is thought to occur in three phases: an initial period of hyperglycolysis, followed by a metabolic depression, followed by a period of recovery. Neuroimaging with computerized tomography or magnetic resonance imaging (MRI) is often normal following sports concussion either because structural injury is absent or current techniques are not sensitive to the cellular and/or metabolic effects that occur in concussion. DiFiori and Giza describe promising neuroimaging techniques that may be sensitive to concussion (including diffusion tensor imaging, functional MRI, magnetic resonance spectroscopy, and positron emission tomography), though these techniques are impractical or not appropriately validated for current clinical use with concussion.[8]

Though concussion is a relatively mild injury by nature, it can be associated with complications and possibly enduring symptoms if not appropriately managed. Clinicians should be aware of a variety of risk factors that could predispose athletes to poorer outcomes. Athletes who have previously sustained a concussion are more than two times more likely to sustain a second concussion[9-11] and may be more likely to experience greater post-concussive symptoms.[12] Recent evidence suggests that high school and college athletes who sustain concussion may be at greatest vulnerability for repeated concussion within seven to 10 days following the injury, with evidence that approximately 80% of repeated concussion occurs during that period.[13] Multiple concussions over a career of professional athletics has been shown to lead to an increased likelihood of late life cognitive impairments/memory problems,[14] motor neuron disease,[15] and depression.[14] Women may be at greater risk for cognitive symptoms following concussion,[16] and children may require longer recovery periods than college athletes.[17-19] Studies also suggest that individuals with learning disorders may have greater cognitive difficulties following MTBI.[20] Rare but catastrophic outcomes related to cerebral edema have also been postulated as occurring from repeated concussion,[21] particularly if a second injury is sustained before symptom resolution from a first injury. Some authors postulate that the cases of so called Second Impact Syndrome may be the result of undiagnosed subdural hemorrhage,[22] though much remains to be understood about this phenomenon. Given these risk factors, current management guidelines are made according to the individual's presentation by tracking cognitive and physical symptoms post-injury while considering the above risk factors.[23]

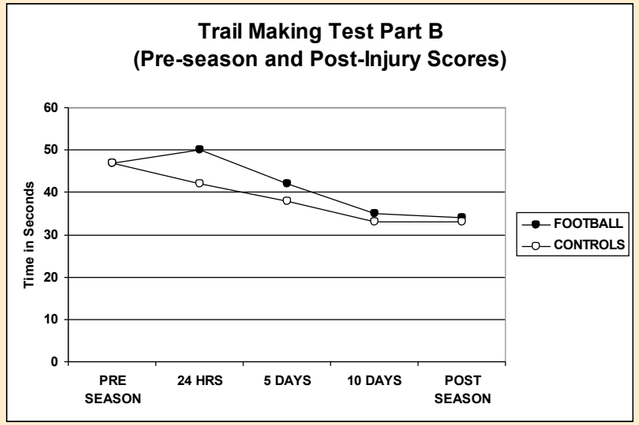
Evaluation of Sports Concussion and Neuropsychology

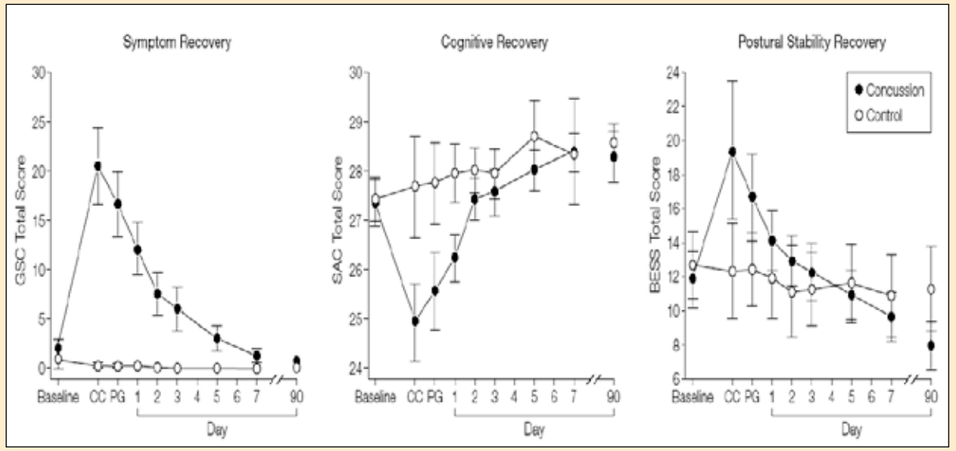
Since the seminal work of Barth, Alves, Ryan, and colleagues,[24] neuropsychological testing has been utilized as one of the primary methods for tracking and managing sports-related concussion. The comparative model developed by Barth and colleagues has become a generally accepted practice in the management of sports concussion and relies on pre-injury baseline neuropsychological testing of athletes,[24] which is later compared to serial post-injury testing. Well-documented literature supporting this practice has developed, which suggests that neuropsychological evaluation is sensitive to the residual cognitive effects of concussion in a variety of domains, including attention, working memory, verbal memory, visuospatial memory, verbal learning, information processing speed, reaction time, and executive functioning.[18,25-29] Belanger and Vanderploeg[30] conducted a meta-analysis of 21 studies involving 790 cases of sports-related concussion (high school, college, and professional athletes) and 2014 controls. Large effects (d = 1.00–1.43) were noted within seven days post-injury on measures of global functioning, neurocognitive status, memory acquisition, and delayed memory performance, with a moderate effect size for overall neuropsychological performance following sports-related concussion (d = .49).

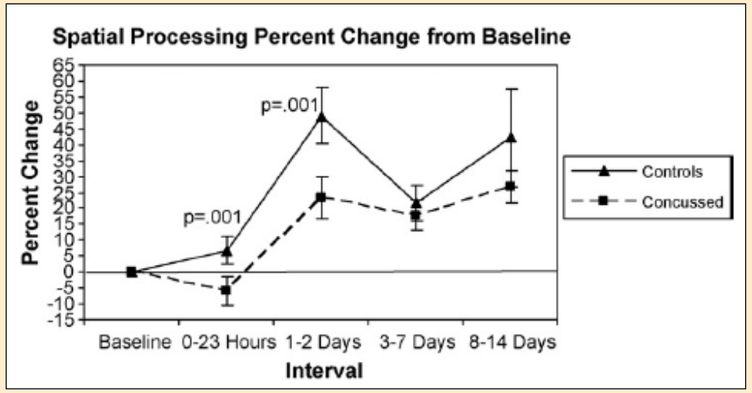
Neuropsychological management of concussion can occur in two phases: acute identification of concussion and later identification of return to baseline neurocognitive status. The acute assessment of concussion often occurs through the use of standardized measures of physical and cognitive symptoms that occur immediately following concussion (e.g., Sports Concussion Assessment Tool, 2nd Edition).[2] Once the athlete has been identified as concussed, a clinician should then focus on when the athlete is recovered and ready to return to play. Such evaluations generally do not occur on the sidelines and are best if a multidimensional team-approach is employed, with several professionals trained in sports concussion management tracking reported post-concussive symptoms (e.g., headache, nausea, sensitivity to light and noise), cognitive symptoms, and balance/postural stability. These methods also generally employ the comparative model described above in which athletes undergo a preseason baseline to establish reference points (pre-injury symptom endorsement, cognitive performance, and balance/postural stability testing). Following a concussion, athletes engage in serial evaluations to identify when he or she has returned to or exceeded baseline scores.

Most recently, several computerized neuropsychological test batteries have been marketed for use in the tracking and management of the cognitive repercussions of concussion. These include the Automated Neuropsychological Assessment Metric (ANAM),[25] CogSport,[31] Headminder Concussion Resolution Index (CRI),[26] and Immediate Post-concussive Assessment and Cognitive Testing (ImPACT).[28] Considerable overlap exists across these various batteries, each with relatively brief administration times (20–30 minutes), automatic development of alternate test forms to minimize practice effect, and a focus on the cognitive domains most susceptible to the effects of concussion (e.g., attention, reaction time, information processing speed, and memory). Though the computerized tests are easily administered, post-concussion interpretation of the data can be complicated, requiring incorporation of factors that can influence test accuracy such as procedural practice effects, test reliability, and effort. Interpretation by or consultation with a trained neuropsychologist is recognized as the best practice.

Athletes are generally expected to return to baseline levels within a relatively brief period of time. Barth and colleagues[24] demonstrated that football players typically returned to baseline performance in five to 10 days. This schedule is consistent with subsequent research that showed concussion symptoms, sideline cognitive screening performance, balance testing, and computerized neuropsychological testing all returned to baseline in three to seven days.[25,29] It is also consistent with meta-analytic data that show the vast majority of concussed athletes return to their previous level in seven to 10 days.[30] Some evidence finds that recovery may be somewhat prolonged in younger athletes,[28] though only by days. Examples of expected recovery curves are provided in Figures 1, 2, and 3.







Figures 1, 2, and 3: These data demonstrate a consistent pattern of expected recovery from sports-related concussion by three to seven days. This pattern has been noted since the seminal work of Barth and colleagues[24] and has been replicated in different samples using multiple methods: traditional cognitive testing, symptom report, balance testing, and computerized cognitive testing. Data were derived from Barth and colleagues,[24] McCrea and colleagues,[29] and Bleiberg and colleagues.[25]

Return-to-Play and Treatment Following Concussion

Possibly the best initial treatment for anyone who has sustained an MTBI is rest and education about the nature, symptoms, and high likelihood of recovery from the injury. In non-sports samples, authors have shown that early intervention with educational materials describing the expected symptoms and the natural recovery course of concussion has been associated with both a reduced mean symptom duration following concussion as well as reduced distress and reduced number of symptoms.[32,33] A similar approach with athletes is important, particularly for those individuals whose symptoms may endure longer than expected.

In addition to education, a stepwise increase in activity is the currently accepted method for return-to-play. This method differs from previously held guidelines for withholding athletes for varying periods based on concussion grade. The most recent consensus statement on concussion in sports lists six steps to return-to-play,[2] with presumed recovery from the concussion at that time. The statement suggests that an athlete should proceed from one step to the next if asymptomatic at the current level for approximately 24 hours, which would lead to approximately one week for full rehabilitation, if the athlete remains asymptomatic throughout. If any post-concussion symptoms occur while in the stepwise program, then the athlete should return to the previous asymptomatic level and attempt to progress again after a further 24-hour period of rest has passed. The return-to-play protocol is provided in Table 1.

In my own practice, once athletes have returned to the baseline level of symptom report, they undergo post-concussion computerized neuropsychological evaluation and begin the progressive increase in exertion outlined in Table 1. If computerized testing is also at baseline levels, the athletes are seen for a face-to-face neuropsychological exam, where traditional neuropsychological measures of attention, memory, and information processing speed are completed to confirm that the athletes' cognitive functioning does not reflect a need for further recovery from the injury. This follow-up examination also allows for assessment of and education about several variables that could prolong concussion recovery (e.g., a history of psychological distress, learning disorder, or previous head injury) and provides an opportunity to educate athletes and families about the injury and the impact that future injuries might have on continued participation in the athlete's sport.

Regarding the management of concussion, the National Athletic Trainers' Association (NATA) provides guidelines for when to disqualify athletes from participation in sports for differing durations.[34] The NATA suggests that any athlete who suffers any period of loss of consciousness or persistent concussion symptoms such as headache, dizziness, or amnesia (no matter how mild or transient) should be disqualified from play or practice for the remainder of the day. A recent meeting of the National Collegiate Athletic Association (NCAA) Concussion Committee has recommended more stringent guidelines that require immediate removal from the competition or practice upon diagnosis of concussion, even if symptoms disappear within minutes. Disqualifying an athlete for a season has generally been accepted as appropriate after the athlete's third concussion, though a variety of complications such as the severity of the injuries and duration between injuries can make this decision difficult. When to end an athlete's career in a given sport is a much more difficult question to answer and is often done on an individual basis and according to the number of previous concussions sustained, the apparent vulnerability of the athlete to concussion, and the duration of symptoms that the individual has experienced post-MTBI. The 2009 International Census Meeting recognized that one size does not fit all when it comes to concussion and that individual vulnerability must be taken into account when addressing this important issue.

Table 1: Return-to-Play Protocol

	Functional Exercise at Stage	Objective
1. No activity	Complete physical and cognitive rest	Recovery
2. Light aerobic exercise	Walking, swimming, or stationary cycling keeping intensity, 70% maximum predicted heart rate; no resistance training	Increase heart rate
3. Sport-specific exercise	Skating drills in ice hockey, running drills in soccer; no head impact activities	Add movement
4. Noncontact training drills	Progression to more complex training drills, e.g., passing drills in football and ice hockey; may start progressive resistance training	Exercise, coordination and cognitive load
5. Full contact practice	Following medical clearance, participate in normal training activities	Restore confidence and assess skills by coaching staff
6. Return to play	Normal game play	

Although pharmacotherapy is not considered a first-line treatment for concussion symptoms, it may be useful in the treatment of persistent symptoms. This statement is particularly true if an athlete experiences comorbid conditions that may be exacerbating the initial symptoms experienced post-concussion. Treatment for persistent headache, poor sleep, and symptoms of depression or anxiety can be particularly beneficial if an athlete has enduring symptoms. These treatments are typically best utilized after a comprehensive neuropsychological evaluation has been performed to better characterize the patient's enduring symptoms and likely exacerbating conditions. It is also important to recognize that an athlete should not be considered ready to return to play following a concussion if he or she is asymptomatic only because pharmacotherapy is masking the post-concussive symptoms that have yet to spontaneously resolve.

Conclusion

Sports concussion is one of the most common but challenging and complex clinical phenomena that sports medicine clinicians are asked to manage. Part of the complexity of this injury is associated with the fact that the basic and clinical science of the injury is still only partially understood. Cantu notes that there have been more publications on the topic of sports-related concussion since the year 2000 than all other publications on the topic prior to that date.[35] With the high level of recent public interest and this influx of research, great strides in the management of sports concussion and head injury in general have been made. No doubt, future research will assist clinicians in making more evidence-based diagnoses and treatment recommendations to minimize the risk of poor outcome in both athletic and non-athletic patients who sustain this injury.

Christopher Bailey, PhD, reports no financial relationships with commercial interests relevant to the content of this article.

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