Aneurysm rupture

To the Editor: We read with interest the article by Tsuang and colleagues (Tsuang FY, Su IC, Chen JY, et al: Hyperacute cerebral aneurysm rupture during CT angiography. Clinical article. J Neurosurg 116:1244–1250, June 2012), in which they described 21 subarachnoid hemorrhage (SAH) patients with active contrast extravasation from a ruptured aneurysm during initial cerebral CT angiography (CTA). They divided these patients with “reruptured” aneurysms into two subgroups: those with a good initial neurological status who showed rapid neurological deterioration, and those with a poor neurological status. The former may still have a favorable outcome if they undergo timely and successful decompressive surgery and appropriate aneurysm obliteration; there is no effective treatment for the latter.

We recently surveyed a series of patients with SAH who underwent CT perfusion (CTP) with 18-phase dynamic-enhancement, confirmed the presence of extravasated contrast medium in the source image, and reported that active bleeding from an aneurysm was observed with increasing enhancement in 25.5% (13 of 51 cases). All CTP results in patients with extravasation were obtained within 2 hours of its onset. Moreover, the incidence of active bleeding in patients scanned within 2 hours was 42.3% (11 of 26 cases).

We believe that bleeding from a ruptured aneurysm is arrested immediately when the intracranial pressure is increased to the level of the systolic blood pressure. We could observe rerupture from an aneurysm by the extravasation of contrast material from the aneurysm on intracerebral angiography in patients with marked changes in vital and neurological signs. We have encountered many patients with extravasation of contrast material during CTA and CTP without marked neurological deterioration, which may reflect the inclusion of patients with continuous bleeding, as seen with other systematic injuries. It is time to recognize that extravasation from an aneurysm on CTA and CTP does not always mean rerupture and that bleeding from an aneurysm is not arrested immediately.

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Disclosure

The authors report no conflict of interest.

References


Response: In their article, Suzuki and colleagues stated that active bleeding was observed with increasing enhancement in 25.5% of patients (13 of 51). All patients with extravasation had Claassen Grade 3 or 4 and World Federation of Neurosurgical Societies (WFNS) Grade III, IV, or V. The other group without extravasation included patients in all grades. In our series of patients with acute extravasation on CTA, those who presented with a good neurological status initially, mainly those with WFNS Grade I or II, had the chance for a favorable outcome if timely and successful decompressive surgery and appropriate aneurysm obliteration were done. Those who showed a poor neurological status at presentation died no matter what kind of treatment they received.

In our article, the group with favorable outcomes that had presented with a good neurological status experienced rebleeding from the aneurysm during CTA, and thus further neurological deterioration was reasonable. Patients who had an initial poor neurological status showed extravasation during CTA, indicating that primary active bleeding of the aneurysms had not been stopped yet or that those aneurysms bled again, but this could not be clarified. Their neurological status remained poor throughout the clinical course.

The time from ictus to the CT suite also matters. If that period is relatively long and if neurological status deteriorates abruptly during the examination, rebleeding is more likely. There must be another small group of patients whose primary bleeding was not stopped and whose bleeding was so minimal that we could detect the primary bleeding on CTA with intra-examination neurological deterioration.

If the extent of extravasation is great and the time from ictus to CTA examination is long, then rebleeding is more likely; if the time from ictus to examination is short, then extravasation might indicate either primary bleeding or rebleeding. At that time, the best indicator for differentiation is whether the clinical neurological status deteriorates. Our article emphasized that timely intervention might offer better outcomes for any patients with acute extravasation, except those who present with a poor neurological status initially.

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Reference


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Intracranial pressure monitoring and traumatic brain injury


Severe traumatic brain injury (TBI) often leads to a high mortality rate. Therefore, intensive monitoring of intracranial pressure (ICP) or imaging studies is crucial to save the patient’s life. Farahvar et al.1 used a massive, prospectively enrolled database to identify the effect of ICP monitoring on the 2-week mortality of patients with severe TBI. They found that several parameters, including age, initial Glasgow Coma Scale score, low blood pressure, and CT findings, were correlated with the 2-week mortality. Moreover, patients of all ages who underwent ICP monitoring had decreased mortality at 2 weeks (p = 0.02) compared with those who did not have ICP monitoring.

Since this is not a randomized controlled trial, it would be unavoidable not to have some potential interfering factors, such as family decision on whether or not to resuscitate the patient, comorbidities, associated major trauma, and the extent of primary underlying brain injury,2 that contribute to mortality.

Despite these minor limitations, the authors’ study has called on neurosurgeons to pay more attention to performing ICP monitoring to improve the outcome in patients with severe TBI. Further large-scale randomized controlled trials for consideration of ICP monitoring in patients with severe TBI are warranted to reduce the mortality rate.

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Disclosure

The authors report no conflict of interest.

References


Response: We thank Peng and colleagues for the letter on our paper. Our study was a prospective severe TBI study, but patients were not randomized. The neurosurgeons in the respective trauma centers made a decision to monitor ICP or not. In order to address known parameters that independently affect 2-week mortality, we adjusted for Glasgow Coma Scale score, hypotension, age, pupil examination findings, and CT parameters. After this adjustment, patients treated without ICP monitoring had a significantly higher mortality than those treated with ICP monitoring. Patients who had a do not resuscitate order or lacked brainstem reflexes were not included in the analysis.

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The lucid interval and the role of Benjamin Bell

To The Editor: Ganz2 is to be congratulated on his detailed description of our evolving understanding of the lucid interval following skull trauma in which he kindly acknowledges my careful reading over of the text (Ganz JC: The lucid interval associated with epidural bleeding: evolving understanding. Historical vignette. J Neurosurg 118:739–745, April 2013). However, this was not as careful as it should have been, as I must take issue with the statement that in Benjamin Bell’s A System of Surgery “there is absolutely no mention of a symptom-free lucid interval between injury and deterioration.” Nor is it true to say that “There is nothing in his A System of Surgery to show he understood the time element separating concussion and compression.”

Bell describes the lucid interval on more than one occasion in chapter 4 of his A System of Surgery,3 expressing the concept on page 171 in section 5, when he writes “In every case, indeed, of injuries done to the head, in which the symptoms do not commence till several days after the accident, as it is clear that the cause of the disorder has not originally affected the brain or its membranes, for if it did so its effects would be immediate, it is probable that it operates almost solely by forming some effusion externally between the pericranium and the skull.”

Bell appreciated the dangers of posttraumatic cerebral compression, for when describing on page 117 “cases of extravasation,” he goes on to say, “A patient, in such circumstances, we suppose to be in great hazard, from the brain being compressed in one part or another: unless this compression be removed by an operation, he must in all probability die.”

Bell describes on page 115 circumstances when the trepan is indicated “without any appearance either of fracture or depression” and states that “The sole object of the operation of the trepan is to remove compression from the brain.” As other surgeons like Pott would only trepan in the presence of a fracture, I would argue that Bell did indeed appreciate the mechanics and time scales of posttraumatic compression and the need for its relief by operation.

Bell’s A System of Surgery was popular and influen-
tial in Europe and America, and he deserves more credit for his contribution.

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Disclosure

The author reports no conflict of interest.

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fute, 1801
739–745, 2013

Response: I was very happy when Professor Macintyre agreed to discuss, analyze, and read this paper. He is a distinguished retired general surgeon (Vice President of the Royal College of Surgeons of Edinburgh and also Queen’s surgeon). He is also still the history editor of the Journal of the Royal College of Physicians of Edinburgh.

In this journal he published a most informative paper on Benjamin Bell (1749–1806), which was the reason we came into contact, since the paper mentions that one of Bell’s teachers was a Dumfries surgeon whom I was and am investigating. The title of the paper is “Scientific surgeon of the Enlightenment or ‘plagiarist in everything’: a reappraisal of Benjamin Bell (1749–1806).”

Nonetheless, I fear I must disagree with Professor Macintyre’s comments. Let us take each of the issues in turn.

First are the comments about page 117 in Bell’s A System of Surgery.1 There is no discussion that Bell understood the dangers of extravasated fluids pressing on the brain. In consequence he proposed the most aggressive policy of trepanation of any 18th-century author. However, this has nothing to do with a lucid interval, which is an issue of timing, not danger. The same argument applies to the statement on page 114.

The statement in my paper that reads “There is nothing in his A System of Surgery to show he understood the time element separating concussion and compression” would have been clearer if the words “due to epidural bleeding” had been added. Even so, the suggestion that he did have such an understanding is based on the following statement from page 171 of the 1785 edition of his book:

“In every case, indeed, of injuries done to the head, in which the symptoms do not commence till several days after the accident, as it is clear that the cause of the disorder has not originally affected the brain or its membranes, for if it did so its effects would be immediate, it is probable that it operates almost solely by forming some effusion externally between the pericranium and the skull.”

There are two difficulties with Professor Macintyre’s interpretation of this passage. Firstly, it is not usual for epidural collections to accumulate on the outer surface of the skull between the pericranium and the bone. Secondly this passage comes from a section on infection, where the presenting delayed symptoms were headache and a tender swelling over the injury, which is not a characteristic presentation of epidural bleeding. What is described in this section of the book is a pattern of delayed infection, no longer seen today but first described by Pott. An important detail is that the delay is always several days. The delays before deterioration following epidural bleeding with few exceptions last for some hours to a day or two, very rarely several days. The lucid interval due to extravasation as we understand it was first properly described by Abernethy, as mentioned in my paper, and was made more detailed by Hutchinson and subsequently Jacobson. As outlined in the paper, all the earlier so-called lucid intervals refer to the above-mentioned pattern of delayed infection.

Thus, while naturally appreciating Professor Macintyre’s interest in this paper I have no alternative but to respectfully disagree with his arguments and conclusions. Benjamin Bell’s A System of Surgery was in its own day criticized as plagiarism by John Bell (1763–1820), also in Edinburgh, a surgeon and the brother of the famous Sir Charles Bell (1774–1842). (The two Bell families were not related.) It was criticized by Sylvester O’Halloran (1728–1807), who wrote, A much later author seems to have bestowed no small pains and labour, to illustrate this very interesting subject [head injuries]; nor does he forget to pay himself some compliments on his success; “but, however diffident I am” (says he) “in first dissenting from an established doctrine, IF MY OWN EXPERIENCE IS FOUND TO JUSTIFY THIS DISSENT, the more respectable the authority, by which the contrary opinion is supported, the more I think necessary to investigate the merits of it.” But, alas! on a close and critical examination of this performance it will appear, that observations and experience, almost every where militate against his assertions and opinions—for they are nothing more.

In conclusion, it would be incorrect for me to comment on any aspect of Benjamin Bell’s work except neurosurgery, because such writings are outside my area of competence. Within the field of neurosurgery, the only new feature is his wish to perform far too many trepanations. The reasons for doing so are more informed by enthusiasm than argument. The reason to find a given procedure indicated must rest on the demonstration that the risks of the procedure are less than the risks of avoiding it. Bell does not present this argument lucidly, not least because the only risk of surgery he describes is failure to relieve pressure. More serious, this voluminous text was not supported by case studies, the use of which was, at his time, the norm. This absence also significantly reduces the originality of his writing, so that as far as neurosurgery is concerned, one is left with an impression of plagiarism as claimed by John Bell, rather than originality.

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4. Macintyre IMC: Scientific surgeon of the Enlightenment or...
Atypical meningiomas


The role of radiotherapy for atypical meningioma is still debated and urgently needs further clarification. Mair et al.5 conducted the largest retrospective study to date to investigate the potential role of radiotherapy for atypical meningioma. Their study showed that postoperative radiotherapy revealed a significant advantage only in patients who had undergone gross-total tumor resection. They concluded that radiotherapy is not adequate after first-time removal of those lesions in which a gross-total resection (Simpson Grade I or II) has been completed. They also suggested that any residual tumor shown on postoperative imaging should receive adjuvant radiosurgery instead of conventional radiotherapy. Moreover, postoperative radiotherapy after a first-time resection was recommended for residual tumor that is too large for radiosurgery and for which a subsequent surgery is not intended.

Radiotherapy has been applied in clinical tumor control for several decades. Once the tumors are radiosensitive, then they are presumed to be well controlled. Mair et al.5 proposed that atypical meningioma did not respond to conventional radiotherapy well when resection did not achieve Simpson Grade I or II, suggesting that a remnant of atypical meningioma would have some radioresistant parts. A recent update of molecular cell biology in tumor stem-like cells1–3,5 provided a better understanding of radioresistance. Hueng et al.2 first isolated and characterized the meningioma stem-like cells from WHO Grade I benign meningiomas and WHO Grade II atypical meningioma. Meningioma stem-like cells exhibited radioresistance, surviving after radiation delivery doses of 5, 10, or 15 Gy in a sphere-form culture system. The theory of meningioma stem-like cells2,6 or meningeal progenitor cells2 was further proved by Rath et al.3,5 Kalamarides et al.,3 and Hu et al.7 Currently, meningioma stem-like cells have been well characterized from either human meningiomas3,7 or murine meningioma.3

Molecular profiles of atypical meningiomas are one of the potential breakthrough points in future study. Laurendeau et al.8 characterized the molecular pathway in the Hedgehog signaling pathway from WHO Grade I, II, and III human meningiomas, providing novel molecular therapeutic targets in the future. Further multicenter large-scale prospective studies of molecular target–based adjuvant therapy for atypical meningiomas are warranted to reduce the recurrence.

REFERENCE


RESPONSE: No response was received from the authors of the original article.
authors about the importance of identifying factors that predict seizure outcome in epilepsy surgery. However, we think that more attention should be paid to the histological pattern facing the following issues.

Besides the clinical, neurophysiological, and imaging factors, the underlying histological type and subtype of MTS affecting the hippocampus and dentate gyrus have emerged as having an increasing role in seizure outcome in the last years. Seizure prognosis in patients undergoing epilepsy surgery for MTS has been hypothesized to depend on either the subtype of hippocampal sclerosis or the status of the dentate gyrus, namely the absence or presence of granule cell pathology (GCP). Indeed, the histopathological classification system for MTS recognizes 2 main groups, MTS Type 1a and 1b (grouped into MTS Type 1 in the latest hippocampal sclerosis classification), and 2 atypical variants, MTS Type 2 and Type 3, with a worse seizure outcome. Furthermore, in a classification system for GCP was elaborated, distinguishing 3 different histological patterns: 1) no GCP, normal granule cell layer; 2) GCP Type 1, substantial granule cell loss; and 3) GCP Type 2, architectural abnormalities in the granule cell layer, mainly granule cell dispersion.

In our retrospective study about seizure outcomes in drug-resistant mesial temporal lobe epilepsy, in which we analyzed an MTS group as a whole, seizure outcome was optimal, with Engel Class I outcomes in 82% of cases (although Engel Class IA outcomes occurred in only 50%), whereas Engel Class II outcomes occurred in the remaining 18%. The various outcome classes were scattered among the different MTS subtypes. Regarding the 14 patients with the best outcome, Engel Class IA was attained in 11 (61%) of 18 patients with MTS Type 1a (with or without GCP), in 2 (40%) of 5 patients with MTS Type 1b, and in 1 (20%) of 5 patients with MTS Type 2. Our findings suggested good results after surgery in patients with MTS Types 1a and 1b (MTS Type 1 in the latest hippocampal sclerosis classification), with up to 80% of patients having Engel Class I outcomes.

Considering the presence of GCP, we observed that 2 (20%) of 10 patients without GCP were in Engel Class IA, while 12 (66.7%) of 18 patients with GCP attained complete seizure freedom. These findings indicated better postsurgical results in patients with GCP than in those without GCP. The demonstration that a decreased potential to generate neurospheres from the subgranular zone is related to MTS and to alterations of dentate gyrus granule cells, especially in MTS Type 1b and GCP Type 1, suggests the existence of a relationship between dentate gyrus pathology and postsurgical seizure outcome and neuropsychological outcome. Indeed, these histological findings may have relevant prognostic implications in seizure and neuropsychological outcomes in patients affected by hippocampal sclerosis as compared with patients with other epileptogenic lesions (such as focal cortical dysplasia [FCD], glioneuronal tumors, or vascular lesions).

In our opinion, with the adoption of the more recent neuropathological classification systems, some subgroups of pathological abnormalities conditioning outcomes have emerged and have to be considered among the factors predictive of seizure outcome. We suggest that the recognition of the different subgroups of pathological conditions associated with different seizure outcomes should stimulate the investigation of the specific epileptogenic mechanisms, relating outcome mainly to the pathological substrate. This approach is also in agreement with the recent suggestions of the International League Against Epilepsy (ILAE) Commission on Classifications and Terminology to put more emphasis on the underlying pathological substrate in the assessment of postsurgical seizure outcome and in future epilepsy classifications.

**Disclosure**

The authors report no conflict of interest.

**References**

Neurosurgical forum


RESPONSE: We thank the authors for their insightful comments. Their work and remarks certainly coincide with the direction in which the field is heading. In truth, we did a preliminary analysis of pathological findings in our series, but sufficient detail was not available for subclassification in the clinical reports. We plan to conduct a blinded review of the pathology findings using the current classification systems to correlate such findings with seizure control.

There are 2 major shortcomings of postoperative pathological analyses, however. First, there is currently no way to know the pathology classification before surgery. Therefore, this information cannot be used to guide therapy or prognosticate. To fully realize the benefits of correlative studies between subclassification of MTS pathology and outcomes, viable presurgical biomarkers are necessary. Such biomarkers would allow for a priori prognostication on outcomes, thus providing better presurgical counseling to patients and families.

The second limitation of postoperative pathological analysis is that we do not know what is left behind after resection. As Daniel Kahneman notes in Thinking, Fast and Slow, “what you see is all there is.” What may be more critical to failures in epilepsy surgery is not what is seen, but what is left unseen or left behind. Thus, the pathological correlate for a poor surgical outcome may relate to the pathology available for analysis, the unsectioned margins, or even distant regions.

The purpose of our study was to analyze our own methods of patient selection for single- or multistage epilepsy surgery for MTS to determine if our criteria were sound. We believe such results may help surgeons determine who is best suited for single-stage surgery. We congratulate the advancement made in pathological analysis to help us further understand this disease and welcome new advancements to make the treatment of MTS more successful and safe.

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Deep brain stimulation for obesity

To The Editor: With great interest we have studied the article by Whiting et al.10 (Whiting DM, Tomycz ND, Bailes J, et al: Lateral hypothalamic area deep brain stimulation for refractory obesity: a pilot study with preliminary data on safety, body weight, and energy metabolism. Clinical article. J Neurosurg 119:56–63, July 2013). This article is critical, primarily because it is a well-designed pilot study that explores a new application for deep brain stimulation (DBS) coupled with results that may give evidence of an ability to modulate metabolic rate.4,10 These results further support the existence of a hidden metabolic circuit buried in our brain. Herein, we raise some concerns regarding certain aspects of the theoretical framework design of such a study. Our concerns are mainly because, even though the aim of this study was safety, we still do not see the robust results as seen in DBS for Parkinson’s disease (the main aspiration of this kind of study). Furthermore, there is still no strong explanation for why we did not observe results as impressive as those originally seen in animal models.2,9

Our comments on this paper are an attempt to highlight and address some aspects that, as we believe, should be considered when a larger study is conducted for the sake of efficacy. These concerns are summarized in the following points:

1) The stimulation strategies and parameters. The intimate relationship between circadian system and feed homeostasis makes the neurocircuit of feeding a complicated one, and it becomes even more so in humans when we add the effect of higher centers in eating habits.2 On one hand, this makes finding the optimal target for DBS a challenging mission. On the other hand, using stimulation parameters that are basically driven from the stimulation parameters utilized in movement disorders (with the ignorance of the circadian component) is a questionable strategy in achieving the wanted efficacy.

2) Patient selection. One criterion of patient selection in this study is based on nonresponse to bariatric surgery. We believe it is important to know more details about this selection criterion in terms of why this type of surgery failed in the patients and the pattern of failure. Recently published data show that the patient’s genetic profile may play an important role in the success of bariatric surgery.5,8 This factor (the genetic profile) should be considered and addressed when exploring DBS for obesity. It may play a role in the results of DBS as it does in bariatric surgery. In this group of patients the cause of obesity may not simply be high food intake, which makes the ultimate goal of treatment to remedy this cause irrelevant. In fact, it has been shown that several genetic defects could lead to refractory obesity.2 Pairing the complicated organization of appetite control with genetic factors raises the possibility that refractory obesity (in patients in whom bariatric surgery has failed) may be associated with different types of corrupted neurocircuits. The possibility of different types of corrupted neurocircuits may imply that we may have to utilize different targets (on a case by case basis, which
raises a question about the reasonability of investigating a novel application for DBS in this group of patients) rather than utilizing 1 target for all cases.

3) What really is the physiological function of the lateral hypothalamus? Even though targeting the lateral hypothalamus is based on animal studies that have shown high-frequency stimulation or lesioning leading to weight loss, this somehow counteracts with other reports about the physiological function of this part of the hypothalamus. To clarify this point, the orexinergic neurons of the lateral thalamus have a main role in wakefulness and arousal.1 It is considered that they affect feeding through modulating arousal levels.2,3 It was found that under food restriction, the activity of orexinergic neurons increases in anticipation of food. That being said, we can speculate that modulating these neurons by high-frequency stimulation should lead to less anticipation of food, less arousal, and a lower metabolic rate, or more specifically, as seen in orexinergic neuron–ablated mice, to narcolepsy in a study conducted by Chemelli et al.3 or to narcolepsy, hypophagia, and late-onset obesity in a study done by Hara et al.5 Interestingly, the last effect contradicts what is shown by inhibiting the lateral hypothalamus by DBS (high-frequency stimulation) or by lesioning in rats.5,9 However, orexinergic neuron–ablated mice seem more reliably to mimic the effect of inhibiting the lateral hypothalamus than does trying to inhibit this small area of the brain in the small animals surgically. This makes the article by Hara et al. worth reading and thinking about to explain why the effect of high-frequency stimulation does match the effect of genetic ablation for neurons specifically located in the lateral hypothalamus. This is important to determine that we really understand the physiology of this area of the hypothalamus and that we really have a strong theoretical basis.

Finally, we would like to congratulate Whiting and colleagues on their pioneering work. Since the impact of such studies is profound, especially on other future applications for DBS, it should be reviewed and discussed from several angles and perspectives to guarantee optimal progress.

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Disclosure
The authors report no conflict of interest.

References

RESPONSE: We appreciate the thoughtful analysis Drs. Salma and Al-Otaibi have provided on our article. Our comments to their concerns with the paper are summarized below. First, we reiterate that the primary focus was one of safety given that this is the first reported series of humans implanted with chronic lateral hypothalamic DBS. The fact that the FDA regards DBS as a significant risk device puts significant constraints on clinical studies of new DBS targets and indications.3 Our efforts to secondarily look at efficacy are clearly limited by the sample size and primary outcome design of the study. The small sample size (n = 3) in this pilot study is a lamentable but unavoidable reality of such government oversight into certain medical device research. Nevertheless, we hope that by demonstrating safety (with more than 2 years of follow-up) this study has surmounted the first hurdle in considering lateral hypothalamic DBS as a treatment for refractory cases of obesity.

Our choice of standard movement disorder DBS parameters as starting points for programming lateral hypothalamic DBS in our patients was also based on the well-established long-term safety of these parameters for DBS in patients with movement disorders. We agree with Dr. Salma and Dr. Al-Otaibi that future studies of DBS for refractory obesity may benefit from a more complex patient selection process in which patients in whom bariatric surgery has failed are preoperatively characterized by baseline resting metabolic studies and genetic studies. However, despite the fact that dozens of obesity-related genes have been identified, a genotype with high penetrance and high risk for obesity has not been uncovered.3 Moreover, the growing pandemic of obesity in the developed world is not likely attributable to genetic changes or mutations but more likely to environmental factors.

Finally, we defend our choice of the lateral hypothalamus as the best investigational target of DBS in obesity. Drs. Salma and Al-Otaibi correctly point out that the physiology of the lateral hypothalamus remains
largely unknown and many of the neurons in the lateral hypothalamus have been primarily shown to be involved with arousal. Interestingly, with certain DBS contacts and stimulation parameters we did observe rapid changes in arousal in our patients undergoing lateral hypothalamic DBS. Similar to the dichotomy between the rational drug designers who want to fashion specific drugs based on shapes of known receptors and the combinatorial chemists who aim to find treatments regardless of mechanism by rapidly screening through massive libraries of compounds, it remains to be seen if future new target DBS surgery is encouraged more from new knowledge regarding the physiology of the brain or more from a continued curiosity about whether electrical stimulation can mimic or augment the historical consequences of brain ablation. Clearly, the lateral hypothalamus has been shown under conditions of both lesioning and stimulation in animals and humans to affect body weight, appetite, and metabolism. Similar to what movement disorder DBS and microelectrode recording has done for basal ganglia physiology, DBS may prove to be a powerful tool for expanding our knowledge of hypothalamic physiology and neural circuits. In fact, less invasive, ablative neurosurgery such as single-session radiosurgery may someday be reconsidered for obesity once DBS has been used as a mapping tool for brain function and physiology. We feel that the brain-obesity link is strong enough to encourage continued study of DBS in this disease and hope our safety data provide the green light for a larger efficacy-focused study.

**References**


**Morbidity in vestibular schwannoma surgery**

**To The Editor:** We are interested in the article by Sughrue et al.² (Sughrue ME, Yang I, Aranda D, et al: Beyond audiofacial morbidity after vestibular schwannoma surgery. Clinical article. J Neurosurg 114:367–374, February 2011).

Vestibular schwannomas (VSs) are located in the cerebellopontine angle, close to cerebrovascular structures, cranial nerves, the brainstem, and the cerebellum. Traditional surgical treatment of these lesions carries high risks for morbidity and some risks for mortality, even for well-trained neurosurgeons. The complications of cerebrospinal fluid leakage, vascular injury, neurological deficits, and postoperative infection have been reported.² Recent advances in stereotactic radiosurgery (SRS) have greatly reduced the risks of morbidity and mortality associated with the management of VSs. Lee et al.¹ reported no radiosurgery-related instances of morbidity or mortality associated with Gamma Knife stereotactic radiosurgery (GKS). However, an adverse radiation effect was found, with perifocal edema, tumor enlargement, and cyst enlargement identified at a median of 26 months (range 3 months–6 years) after GKS.

Using PubMed, Sughrue et al.² summarized the results of microsurgery from various institutions. In this study, the authors reviewed 100 articles providing information on 32,870 patients; their analysis showed an overall mortality rate of 0.2% (95% confidence interval [CI] 0.1%–0.3%). Twenty-two percent of patients (95% CI 21%–23%) suffered from at least 1 microsurgery-related complication other than those affecting cranial nerve VII or VIII. Cerebrospinal fluid leakage was a complication in 8.5% of patients (95% CI 6.9%–10.0%). This complication rate was significantly increased when the translabyrinthine approach was used but was unaffected by the size of the tumor. Vascular complications, such as ischemic injury or hemorrhage, were found in 1% of patients (95% CI 0.75%–1.2%). Neurological complications developed in 8.6% of cases (95% CI 7.9%–9.3%) and were less likely to occur with resection of smaller tumors (p < 0.0001) and use of the translabyrinthine approach (p < 0.0001). Infections happened in 3.8% of cases (95% CI 3.4%–4.3%), and 78% of these were meningitis. These results were significantly higher than those associated with SRS.

The contribution made by Sughrue et al.² in pointing out instances of morbidity beyond audiofacial complications after VS surgery alerts neurosurgeons to take great precautions during decision making before choosing a treatment modality. Contemporary advances in SRS have resulted in a reduction of morbidity in the treatment of VSs. Therefore, comparisons of complications related to SRS and microsurgery should be carefully considered during the decision-making process.

There is one minor concern that we have about this retrospective study. Patient demographic data should be stratified based on patient age, sex, and underlying comorbidities when performing a univariate and/or multivariate analysis of these morbidity, because advanced age carries higher risks of morbidity than younger age. Despite these limitations, the study by Sughrue et al.² provides significantly potent evidence for neurosurgeons to use in advising patients on the published risks of complications other than injury to audiofacial nerves following microneurosurgery for VS. Further large scale, prospective studies are mandatory to better address the potential risks of surgery for VS.

**Kuan-Nien Chou, M.D.**
**Bing-Huang Tsai, M.D.**
Some issues in the management of VSs.5,6,8 Sughrue et al.5 proposed comments to improve the quality of studying the natural history of vestibular schwannoma surgery Clinical article. J Neurosurg 114: 367–374, 2011

RESPONSE: No response was received from the authors of the original article.

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Vestibular schwannoma growth and hearing loss


A patient’s hearing course is one of the most worrisome issues in the management of VSs.5,6,8 Sughrue et al.5 performed their study to evaluate radiological images, patient profiles, and audiograms in patients with VSs. They showed that faster rates of tumor growth (> 2.5 mm/year) are positively correlated with hearing loss. Importantly, the pearl of this study is a follow-up period longer than 10 years. The authors found a simple conclusion that all patients lost their hearing acuity after a decade, regardless of the initial tumor size, the patient’s age at diagnosis, and the presence of neurofibromatosis Type 2. This conclusion provides neurosurgeons with the information needed to advise patients to take necessary steps during follow-up to VS treatment.

Some minor limitations exist in the study of hearing loss. First, what factors contribute to a faster rate of tumor growth? Personalized medicine is a rising issue of concern. More aggressive analyses of noninvasive magnetic resonance spectrography studies or minimally invasive means of obtaining cerebrospinal fluid prior to surgical intervention would provide some potential clues in future studies. Moreover, genome-wide analyses of VSs would lead to a more in-depth view of tumor biology in this disease. Furthermore, an analysis of the molecular profiles in VSs would yield more information about the functional roles of key proteins regulating tumor growth, such as osteopontin,2,7 and Nodal in brain tumors.1,3

In the modern genomics era, knowledge of more messages in the tumor biology of VS could lead to novel breakthroughs in hearing preservation. Despite these minor limitations, the studies by Sughrue and colleagues have provided many valuable references for clinicians in the management of VS. Additional prospective studies in clinical practice are necessary to prevent patients from losing their hearing.

RESPONSE: No response was received from the authors of the original article.

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Medial temporal epilepsy

TO THE EDITOR: We have read with great interest the

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The authors’ study is an effort to compare seizure and memory outcomes after 2 surgical techniques generally used for the surgical treatment of pharmacoresistant mesial temporal lobe epilepsy (MTLE)—that is, selective amygdalohippocampectomy and anterior temporal lobectomy. First and foremost, the authors should be congratulated for their effort to perform an exhaustive meta-analysis of the pertinent literature concerning this still-debated issue. We obviously agree with the authors about the importance of identifying the surgical approach for achieving the best seizure and neuropsychological outcomes. However, we consider it useful to highlight a limitation of this study represented by the lack of the histological data.

Indeed, an increasing role for underlying pathological disorders has emerged in recent years\textsuperscript{2–8,10,12–16} therefore, to better understand seizure and neuropsychological outcomes in temporal lobe epilepsy surgery, more attention should be paid to the histological diagnosis. Seizure prognosis of patients undergoing temporal lobe epilepsy surgery appears strictly related to the type of lesion.\textsuperscript{2–4,7,8,10,12–16} Even neuropsychological dysfunction may be related to the histological pattern of dentate gyrus granular cell pathology (GCP) and preserved neurogenetic ability.\textsuperscript{7,13} In our retrospective study about seizure outcome in drug-resistant MTLE\textsuperscript{10} treated with a tailored anterior temporal lobectomy along with amygdalohippocampectomy, patients with MTLE and an epilepsy-associated low-grade tumor, mesial temporal sclerosis (MTS), or MTS associated with focal cortical dysplasia (FCD) showed the best postsurgical seizure outcome (Engel Class I\textsuperscript{9} in >80% of cases), whereas only 63% of patients with isolated FCD achieved the same type of outcome.

Our results support the thesis that the pathological substrate represents a significant predictor of seizure recurrence, with rates of Engel Class I outcomes ranging from 59% for patients with isolated FCD to 82%, 83%, and 84%, respectively, for those with isolated MTS, epilepsy-associated low-grade tumor, and FCD associated with MTS. According to the recent literature,\textsuperscript{2–4,6,12–16} our findings suggest that different pathological subtypes are associated with different postsurgery seizure outcomes. The analysis of seizure outcome in histopathological subtypes of FCD showed different prognoses in the different pathological subgroups, with worse outcomes for patients with isolated FCD Type I.\textsuperscript{10}

Analyzing the pathological group of MTS, we have to consider that the histopathological classification system for MTS recognizes 2 main groups—MTS Type Ia and Ib (grouped in hippocampal sclerosis [HS] Type I in the latest HS classification\textsuperscript{1})—and 2 atypical variants—MTS Type 2 and MTS Type 3 with a worse seizure outcome. Furthermore, in 2009 a classification system for GCP was reported,\textsuperscript{3} distinguishing among 3 different histological patterns: 1) no GCP (normal granule cell layer); 2) GCP Type 1 (substantial granule cell loss); and 3) GCP Type 2 (architectural abnormalities in the granule cell layer, mainly granule cell dispersion).\textsuperscript{3} Our findings suggested good results after surgery in patients with HS Type 1, with up to 80% of patients having Engel Class I outcomes.

Considering the presence of GCP, we observed that 2 (20%) of 10 patients without GCP were in Engel Class IA, while 12 (66.7%) of 18 patients with GCP achieved complete seizure freedom. These findings indicate better postsurgical results in patients with GCP compared with those without GCP. The decreased potential to generate neuromolecules from the subgranular zone appears related to MTS and to alterations of dentate gyrus granule cells, especially in MTS Type Ib and GCP Type 1, suggesting the existence of a relationship between dentate gyrus pathology and postsurgical seizure outcome\textsuperscript{10,14} and neuropsychological outcome.\textsuperscript{7}

Indeed, these histological findings may have relevant prognostic implications in seizure and neuropsychological outcomes for patients with HS compared to patients with other epileptogenic temporal lobe lesions (such as FCD, glioneuronal tumors, or vascular lesions). In our opinion, with the adoption of the more recent pathological classification systems,\textsuperscript{2–6,12–16} some subgroups of histological abnormalities influencing outcomes have emerged and should be considered among factors predictive of seizure outcome such as the type of surgical approach and the extent of resection.

This approach is also in agreement with the recent suggestions of the International League Against Epilepsy (ILAE) Commission on Classifications and Terminology—that is, to put more emphasis on the underlying pathological substrate in the assessment of postsurgical seizure outcome and in future epilepsy classifications.

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Disclosure
The authors report no conflict of interest.

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RESPONSE: We thank Dr. Giulioni and colleagues for their constructive comments on our study. We also agree with them that pathological substrate is essential to predict seizure outcome after temporal lobe epilepsy (TLE) surgery. However, since pathological results were absent in some studies reported in the literature2,8,9 or an FCD diagnosis could not be made in one old study,6 it was difficult to extract adequate pathological data from the studies included in our meta-analysis.

In TLE patients, most isolated FCD lesions are located in the neocortex, and thus they are rarely found in specimens from patients undergoing selective amygdalohippocampectomy (SelAH). This means that isolated FCD is more likely to be diagnosed in an anterior temporal lobectomy (ATL) group than in a SelAH group. The study by Giulioni et al suggested that isolated FCD was a poor predictor of seizure outcome in TLE patients.5 Our meta-analysis indicated that although it was less frequently performed in patients with isolated FCD, patients undergoing SelAH showed statistically lower odds of being seizure free than those undergoing ATL. Based on the aforementioned findings, the conclusion could be made that the 2 different surgical procedures may produce different seizure outcomes.

In addition to the pathological substrate, other factors such as major depressive disorder,4 extratemporal cortical hypometabolism,1 and epilepsy duration1 were also considered as postoperative seizure outcome predictors in TLE. Randomized grouping is essential to alleviate outcome biases induced by the aforementioned factors. As we recommended in our article, well-designed randomized trials with a sufficient sample size are needed to compare SelAH and ATL in terms of seizure outcome, IQ scores, memory, language ability, visual deficits, and other complications or adverse effects.

References

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Role of subconcussion and repetitive TBI

To The Editor: Recent publication of an article by Bailes et al.1 (Bailes JE, Petraglia AL, Omalu BI, et al: Role of subconcussion in repetitive mild traumatic brain injury. A review. J Neurosurg 119:1235–1245, November 2013) caught our eye, as we were dismayed by how they inaccurately represented parts of an article by Smith et al.10 published last year in Neurosurgery, even though we are supportive of the proof-of-concept offered.

The clinical evidence supports the concept of a subconcussion, as well, and that evidence is a cornerstone of Bailes and colleagues’ idea: The concept of increased neck mass and strength that may diffuse the forces imparted to the head and brain inside the skull (“slosh”) seems far-fetched.

We are not convinced that it is possible to extrapolate the research of Smith et al.10 to subconcussed individuals practicing neck-strengthening exercises, all the more so as this idea was not supported by the work of Mihalik et al.7

Smith et al. conducted research on rats, and the brain injury they caused in their experiments was of a greater magnitude than that seen in the human subjects with subconcussion as reported by Bailes et al. This flaw could be highlighted even more by the argument that the model suggested by Bailes et al. was introduced by Marmarou et al.6 to induce diffuse axonal injury (DAI) in rats. DAI is on the most severe end of the traumatic axonal injury spectrum. The mildest end of the spectrum includes reversible axonal injury. A range of injuries that lies in the middle of the spectrum, and for which we do not know the clinical correlates, falls short of DAI in severity. On the other hand, sometimes clues in a patient’s history strongly indicate that DAI was present despite a lack of evidence of hematoma or severe brain swelling on imaging studies.

By systematically studying the brains of individuals who suffered a recent documented mild head injury but died of an unrelated cause, some authors have identified scattered, hemispherically distributed traumatic axonal damage after mild head injury in patients without any noteworthy neurological or psychological symptoms.

Be that as it may, the literature suggests that extreme forces are necessary for axons to rupture soon after impact. Precisely for this reason, primary axotomy is unlike- forces are necessary for axons to rupture soon after im - pact. Precisely for this reason, primary axotomy is unlike- forces are necessary for axons to rupture soon after im - pact. Precisely for this reason, primary axotomy is unlike-


Response: We appreciate the comments of Drs. Sosa and Stemberga concerning our article and will address their concerns over neck strengthening and the phenomenon of brain slosh. We agree that there is no scientific proof or controlled studies that demonstrate that neck strengthening is an effective strategy for reduction of brain injury or the effects of subconcusive impacts. There are several aspects, including static muscle contraction, player anticipation, gender differences, and the ability of an athlete to control sudden neck movements, that indeed make this an uncertain strategy for concussion mitigation. Nonetheless, some disciplines, such as in aerospace, have encouraged pilots to perform strengthening exercises for the neck to help control sudden head movements.

We are familiar with the concepts of intracranial slosh, as the original work was performed in our laborato- ry. Since mild traumatic brain injury results from cranial impacts, a theory of brain slosh contends that the forces imparted to the outside of the skull cannot be interpreted without understanding how slosh dynamics translate inside the skull. In this regard, we believe that there are 2 arguments to support neck strengthening. The first is that through better tethering of the cranium, through the con- traction of stronger cervical musculature on both sides, the imparted forces may be converted from rotational

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1. Bailes JE, Petraglia AL, Omalu BI, Nauman E, Talavage T;
to less injurious linear vectors. Also, tensing, toning, or thickening the neck musculature could aid in the mere act of shortening the arc or rotational distance through which the head undergoes acceleration-deceleration. If the cranium is translated along the path of a straight line, the distance traveled is relatively less than that along an arc.

The second argument involves the potential for neck musculature strengthening to potentiate the actions of the omohyoid muscles as they impede internal jugular venous outflow. The omohyoid is an elongated, thin muscle that is directed obliquely in the anterolateral region of the neck, extending from the superior edge of the scapula to the hyoid bone. It is composed of 2 fleshy portions, the anterior and posterior bellies, separated by an intermediate tendon. One might question why teleologically there are 2 bellies, with a tendon situated directly atop the internal jugular vein (IJV). This little-understood muscle was once thought to be just an evolutionary vestige and to serve no actual purpose. However, we have postulated that the true function of this muscle may be to gently and efficiently potentiate the impedance of outflow by contracting against the IJVs, thus reducing slosh within the cranium. In doing so, the compliance of the intracranial space would thus be minimized and, like the inflating of “bubble wrap,” the brain will be better “packaged” from the inside. In the Smith et al. study, significant impact forces were imparted, and it was found that there was a marked reduction in the signature axonal injury with IJV compression.4

The contraction of the omohyoids has been shown by echographic study to cause IJV compression.2 Thus, neck strengthening and training could make the omohyoids more efficient in restricting the outflow of the IJV. The omohyoid muscle leads to a direct localized and short compression of IJV, and this in spite of possible diffuse compression by the sternocleidomastoid muscle. The latter can compress all the vascular elements of the neck it overlies, whatever the position of the head. The ability of an athlete to realize the sudden need for neck muscle contraction and the timing of such a maneuver is another matter. The above notwithstanding, the concept of neck strengthening to mitigate the forces transmitted to the human brain has not been proven and thus remains a simple suggestion for athletic training that should cause no harm, and may, in certain instances, eventually be shown to have some benefit.

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