Letters to the Editor

Neurosurgical Forum

Electrical activity in limb muscles after spinal cord stimulation is not specific for the corticospinal tract

TO THE EDITOR: We read with great interest the paper of Gandhi et al.2 (Gandhi R, Curtis CM, Cohen-Gadol AA: High-resolution direct microstimulation mapping of spinal cord motor pathways during resection of an intramedullary tumor. J Neurosurg Spine 22:205–210, February 2015). The authors try to demonstrate that electrical stimulation of the exposed spinal cord after tumor excision generates motor evoked potentials (MEPs) in upper- and lower-extremity muscles—presuming that this electrical stimulation exclusively activates fast-conducting axons of the corticospinal tract (CST) within the spinal cord. Unfortunately we are aware of a long history of similar but unsuccessful trials.

A method of translaminar stimulation of the spinal cord with recording of electrical activity from the peripheral nerves, so-called neurogenic MEPs,4 was introduced 2 decades ago. This method was subsequently disproved because strong evidence was found that the recorded activity is not generated by the CST.1,3 This was demonstrated by published data about 2 paraplegic patients with preserved “neurogenic MEPs.”1 Therefore, these recordings were never again called MEPs, and the method has been abandoned.

We now present evidence from a group of 13 patients with intramedullary spinal cord tumors (Seidel et al., unpublished data). In 7 of them, we recorded responses in muscles after stimulation of the dorsal column of the exposed spinal cord (Fig. 1A). On stimulation of the lateral column as judged by anatomical landmarks, responses in muscles were elicited as well (Fig. 1B). The elicited responses (in the muscles) after stimulation of the dorsal columns can be neurophysiologically explained by antidromic activation of the sensory fibers in the dorsal column that originated from spinal ganglion cells, which have collaterals to the alpha motor neurons.1 This is the so-called centrally activated H-reflex (Fig. 2).

Therefore we draw the conclusion that muscle responses to direct electrical stimulation of the exposed spinal cord are not specific for being transferred via the CST but can also be elicited by stimulation of the dorsal column alone. We conclude that the method of intraoperative stimulation of the exposed spinal cord cannot be recom-

FIG. 1. Stimulation of the dorsal and lateral column in a patient with a cervical intramedullary ependymoma at the C5–T1 level. The patient underwent a laminectomy via a dorsolateral approach, with recording of sensory and motor evoked potentials. Stimulation of the spinal cord was performed with a bipolar concentric probe applying a short train of 5 stimuli with a 0.5-msec pulse duration, an interstimulus interval of 4 msec, a 1.0-Hz repetition rate, and a stimulation intensity ranging from 0.5 to 2 mA. A: Intraoperative photograph showing the stimulation probe (Stim.probe) at the anatomical location of the dorsal column (left panel) and traces representing recordings from right tibialis anterior (TA) and right abductor hallucis (AH) muscles (right panel). B: Intraoperative photograph showing the stimulation probe laterally, representing the anatomical location of the lateral CST (left panel) and traces representing recordings from left TA and left AH muscles (right panel). Figure is available in color online only.
mended to anatomically identify the position of the CST within the spinal cord. This is especially important for the frequently distorted anatomy of the spinal cord in patients with intramedullary spinal cord tumors.

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References

Disclosures
The authors report no conflict of interest.

Response
We would like to thank Drs. Deletis, Kothbauer, Sala, and Seidel for their interest in our manuscript and for their elucidative comments regarding direct CST stimulation. In our manuscript, we described a case in which we used a Kartush concentric bipolar probe (Medtronic Xomed) to perform high-resolution microstimulation motor mapping of CSTs responsible for individual muscle groups during resection of a cervicomedullary junction cystic epidermoid. During stimulation mapping, we found that stimulation of a portion of the tumor margin led to the left lower-extremity electromyographic response. We limited tumor resection at that portion, and the patient suffered from a transient weakness in the left foot, further suggesting that the stimulation response was relevant. Due to the high morbidity associated with intramedullary tumor surgery, we hope that a proactive monitoring technique can potentially facilitate a more efficient and safer surgery. Dr. Deletis and colleagues have identified the unreliability of direct microstimulation of the spinal cord due to a suspected “centrally activated H-reflex.”

The authors discuss their experience in 13 cases of intramedullary spinal cord tumor. In 7 of those cases, they elicited motor responses by direct stimulation of the dorsal and lateral columns. We look forward to the authors’ final publication; the responses in the other 6 cases would be of value. One may hope for a detectable difference in response latency between direct stimulation of the CSTs and a collateral response after stimulation of the sensory tracts. Although the possibility of a centrally activated H-reflex would explain a false-positive stimulation, it does
not directly imply the clinical futility of spinal cord microstimulation.

In addition to our report, a few other authors have found positive results with direct stimulation.\textsuperscript{1,2} In our case, the findings of intraoperative stimulation mapping correlated with the postoperative findings. We fully recognize the possibility that intraoperative spinal cord stimulation may elicit motor reactions due to collateral responses. We await the authors’ final publication and believe that more work needs to be done in this arena to further improve the safety and efficacy of intramedullary surgery.

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References

Retro-odontoid mass


The authors have studied a relatively large series of patients with rheumatoid arthritis (RA) involving the craniovertebral junction. They have analyzed the possible causes of retro-odontoid pseudotumor in general and that caused by RA especially as it relates to atlantoaxial instability.\textsuperscript{1} It is unfortunate that the authors have not referred to our several articles pertaining to the subject of the pathogenesis of retro-odontoid pseudotumor, particularly as it relates to RA and to instability of the region.\textsuperscript{2,3,13,17,21,26,27}

The authors indicated that the transverse ligament is the primary component of retro-odontoid soft-tissue formation. They found that the retro-odontoid soft-tissue (ROST) thickness tends to be smaller when instability recognized by the atlantodental interval is large. They concluded that atlantoaxial subluxation may decrease the stress on the transverse ligament, which has an influence on the size of the retro-odontoid mass.

For the first time in the English literature, in 2004 we speculated that retro-odontoid pseudotumor formation is an indicator of atlantoaxial instability meriting the need for atlantoaxial fixation and that there is no need to directly remove the mass.\textsuperscript{22} The retro-odontoid pseudotumor is a result of buckling of the posterior longitudinal liga-

ment (or tectorial membrane) due to bilateral reduction of the atlantoaxial joint space, commonly identified in cases with degenerative involvement of the craniovertebral junction. We related the formation of retro-odontoid pseudotumor to osteophyte formation in the subaxial spine and ossification in the posterior longitudinal ligament (OPLL) in the cervical spine.\textsuperscript{12,13,27} Our current hypothesis regarding the pathogenesis of an osteophyte in degenerative spondylotic disease is that it is a secondary process to primary instability of the spine that is first manifested in the facet joints.\textsuperscript{3,4,9,10} Osteophyte formation is a consequence of a “periosteal reaction” related to buckling of the posterior longitudinal ligament and its detachment from the bone surface that is a result of vertical spinal instability or facetal telescoping.\textsuperscript{8} We indicated that the human long-term standing posture and misuse or disuse of muscles of the region are the primary incriminating causes of spinal instability.\textsuperscript{5,6} Accordingly, we suggested that facetal distraction and fixation or only fixation of the spinal segments may be the optimum form of treatment in degenerative spinal disease.\textsuperscript{2,10,11,15,18,19,23,25} We speculated that there may be no need for direct removal of the osteophyte.\textsuperscript{8} We reported our results of facetal fixation with or without facetal distraction and fixation for degenerative diseases involving the craniovertebral junction and the subaxial spine.\textsuperscript{10,11,23–25} Along similar lines, we have suggested that instability is the primary nodal point of the pathogenesis of OPLL meriting the need for stabilization of the spine and that there is no need to directly handle or resect OPLL.\textsuperscript{7,4,20}

In RA, the disease of the lateral mass is more pronounced, and the joint arthritis affecting the articular cartilage and facetal bone destruction can lead to lateral mass collapse resulting in mild to severe reduction in its height. These features result in buckling of the tectorial membrane in general and the posterior longitudinal ligament in particular. Consequently, the odontoid process migrates superiorly and can result in both atlantoaxial instability manifested by an abnormal increase in the atlantodental interval and basilar invagination. Both atlantoaxial instability and basilar invagination can be mild, as is seen in the cases shown by the authors, or they can be severe.

In cases with RA, in addition to the buckling of the tectorial membrane, there can frequently be arthritis or inflammation of multiple joints including in the retro-odontoid “joint.” The clinical parameters and radiological investigations demonstrating the presence of lateral mass effect and instability should be elaborately correlated with the size of the ROST prior to contemplating surgical stabilization. The authors showed that in cases with more significant atlantoaxial instability, there was relatively less marked presence of an ROST mass. Our understanding is that a retro-odontoid mass is a more chronic manifestation of atlantoaxial instability and may not be identified in acute forms of this instability. In general, surgical decisions must correlate clinical findings with the nature of the effects on the facets and joint, the degree of atlantoaxial instability, and the size of the retro-odontoid mass. Correct decisions regarding the need for surgical stabilization can lead to dramatic recovery from symptoms.

We recently reported an immediate postoperative reduction in the size of a retro-odontoid pseudotumor fol-
lowing atlantoaxial fixation.27 We also reported a case of the immediate postoperative disappearance of the ROST or “pannus” following surgery that involved facetal distraction and fixation. These cases give credence to our hypothesis.27

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Disclosures
The author reports no conflict of interest.

Response
We would like to thank Prof. Goel for his comments and thoughts regarding the pathogenesis of retro-odontoid pseudotumors in patients with and without RA. We appreciate this opportunity to clarify a few points of confusion. Please accept our apologies for not referring to his previous publications26–28 in our paper.

In his letter, Goel stated that retro-odontoid pseudotumors form as a result of buckling of the posterior longitudinal ligament (or torcularial membrane) due to bilateral reduction of the atlantoaxial joint space. He speculated that retro-odontoid pseudotumor formation is an indicator of atlantoaxial instability meriting the need for atlantoaxial fixation and that there is no need to directly remove the mass regardless of whether the patient has RA.6,8

We agree that atlantoaxial fixation is useful for symptomatic retro-odontoid pseudotumors and that there is no need to directly remove a retro-odontoid pseudotumor. As Goel suggested, several previous reports have indicated that retro-odontoid pseudotumors are related to instability of the atlantoaxial joint based on spontaneous mass reduction after spinal fusion.1,12,13 However, some reports have stated that retro-odontoid pseudotumors are not always associated with obvious atlantoaxial instability.2,3,10 Chikuda et al.5 reported that a retro-odontoid mass reduction occurred after posterior fusion even in the absence of radiographic atlantoaxial instability.

Our study revealed that the ROST thickness can decrease with atlantoaxial instability, but Goel pointed out that both atlantoaxial instability and basilar invagination may have been mild in our study population. Although no
cases of surgical treatment for retro-odontoid pseudotumors were included, many cases that represent the ROST thickness tend to be inversely correlated with the atlantoaxial interval (Figs. 1–3). In addition, there are few reports of retro-odontoid pseudotumors caused by RA, although atlantoaxial subluxation is commonly seen in patients with RA. These facts may imply that retro-odontoid pseudotumors are less closely associated with radiographic atlantoaxial instability. The present results are not consistent with our previous speculations; thus we hypothesized that excessive mechanical stress concentrated on the atlantoaxial complex rather than a sliding motion of the atlas causes retro-odontoid mass formation. This means that the ruptured transverse ligament no longer keeps the mechanical stress at the retro-odontoid space and that the ROST thickness decreases with atlantoaxial instability. This hypothesis can explain both the present results and the fact that surgical stabilization is effective for retro-odontoid mass lesions.

Notably, whether pseudotumors are pathologically similar to the ROST thickness remains unclear. However, our study is the largest to analyze the ROST thickness in patients with RA and the first to show that atlantoaxial subluxation may decrease stress on the ROST. We believe that the accumulation of this information may lead to the elucidation of the pathogenesis of and the development of new treatment methods for pseudotumors in patients with RA.

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Intradural extramedullary spinal tumor resection and quality of life

TO THE EDITOR: We read with great interest the paper by Viereck et al.1 (Viereck MJ, Ghoebrial GM, Beygi S, et al: Improved patient quality of life following intradural extramedullary spinal tumor resection. J Neurosurg Spine 25:640–645, November 2016). The authors report the efficacy of resection of intradural extramedullary tumors (IDEMTs) in terms of quality of life, analyzing outcomes by using the Oswestry Disability Index (ODI), visual analog scale (VAS), and the EuroQol-5D (EQ-5D) health survey in the pre- and postoperative period. We similarly reported2 a series of 107 patients affected by IDEMTs and evaluated the surgical results, assessing the graphic rating scale (GRS) score for pain, the presence of neurological deficits, and the EQ-5D for quality of life—and our work was cited in their article.

We congratulate them for their work, and we would like to point out some observations. Differently from our work, they evaluated the quality of life using the EQ-5D in the preoperative period, and then they compared it to the postoperative EQ-5D score. They demonstrated an overall improvement in all the aspects of EQ-5D. However, the authors do not clarify when the EQ-5D was used in the preoperative period. We think that it is important to know if it was used before or after the diagnosis of IDEMT was given to the patients. Factors like pain and discomfort and depression and anxiety can show a different score if the diagnosis of IDEMT was given days before or after the EQ-5D questionnaire was administered. In the same way, the authors do not specify if the ODI questionnaire was administered before or after the diagnosis of IDEMT was communicated to the patients. This questionnaire gives an evaluation of how sleeping, sex life, social life, and so on can be affected by pain. It is known that pain is usually worse when a diagnosis of tumor is given.

The EQ-5D also assesses several other factors such as mobility, self-care, usual activities, pain and discomfort, and anxiety and depression. Other circumstances (e.g., trauma, diseases) can compromise these factors and the patient may demonstrate a lower score independently from the presence of an IDEMT. Ideally it would be interesting to use the EQ-5D when the patient is still asymptomatic from the IDEMT, then reassess it when patients affected by IDEMT are symptomatic, and finally, after the operation to really know the outcome of the surgery for these tumors. We understand that this evaluation is impractical in real life.

In our series and in the study by Viereck et al. it emerges that patients affected by IDEMTs are highly symptomatic in the preoperative period. Viereck et al. reported some problems in mobility in 68.2% of the patients, 34.1% reported some problems with self-care, 63.6% reported some problems performing usual activities, 60.5% reported some problems with pain and discomfort, and 50% reported some problems with anxiety and depression. In our study we did not use EQ-5D in the preoperative period, but we evaluated the presence of neurological deficits, and a high incidence was demonstrated; 50.5% of the patients reported one or more neurological deficits. In terms of pain, our study analyzed GRS in the preoperative period and at 1 year after the operation, whereas their study used VAS in the preoperative period and at <1 month, at 1–3 months, 3–12 months, and at >12 months after the operation. Both the studies affirm that patients who undergo operation for IDEMTs usually still report slight pain at 1 year of follow-up.

Viereck et al. found that in the preoperative period the mean VAS score was 6.1, whereas at the 12-month follow-up it was 2.9. We similarly reported a mean preoperative GRS score of 6.05 and a mean postoperative GRS score of 3.65. We reported that pain is the main onset symptom of IDEMTs. It is usually well tolerated for months and can be confused with pain of another nature (arthritis, disc prolapse, osteoporosis), and the patient can be misdiagnosed. In our series the duration of the symptoms ranged from 2 to 91 months (average 15.7 months). At the 1-year follow-up, the proportion of patients who still report pain is 59.6%, and some asymptomatic patients reported a sporadic occurrence of pain in the postsurgical period.

Moreover, we evaluated how age, histological type of the tumor, and location (cervical, thoracic, lumbar, sacral) correlated with pain. Age had no effect on the rating of both presurgical and postsurgical pain (F [1.98] = 1.264; p = 0.44). The main effect of the histological type of tumor was not significant (F [1.98] = 0.956; p = 0.44). Pain (pre- and postsurgical) did not interact with histological type (F [1.98] = 0.454; p = 0.77). The ANOVA showed that the location of the tumor did not affect presurgical pain (F [1.106] = 0.120; p = 0.98).

We reported that postoperative pain is often defined qualitatively differently. It is described as a loss of sensitivity at the level of the surgical wound, or as a sensation of an open wound, with the tendency to become intense as the weather changes.

Nowadays we know that IDEMTs are painful lesions because their position within dura mater leads to a compression of the spinal cord or adjacent nerve root, but we do not know how much postoperative pain is linked to their previous intradural compression or to muscle dissection and laminectomy. In fact, our study demonstrated that pain is not determined by a surgical injury or a partial tumor removal. Only 3 patients of 107 cases had a new post-

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operative neurological deficit, whereas in 43 of 52 patients (83%) the preoperative neurological deficit completely recovered after surgery (11.5%), and a partial resection was executed only in 5 lumbar schwannomas and 2 filum terminale ependymomas: 7 of 107 cases (6.5%). Furthermore, no growth of the residual tumor has been shown in the follow-up period.

In our series most tumors were posterior or posterior-lateral (100 lesions, 93.5%) and only 7 meningiomas were anterior (6.5%). In all the cases a laminectomy or laminotomy was executed; no cases required instrumentation. Vieriek et al. reported that 7 patients (15.9%) underwent an instrumented fusion and 2 patients (4.5%) underwent anterior interbody instrumented fusion after removal of the tumor. Unfortunately they did not report whether patients who underwent instrumentation had a worse course in terms of pain. However, Vieriek et al. reported an accurate follow-up of postoperative pain, evaluating it at < 1 month, 1–3 months, 3–12 months, and > 12 months. From that outcome it emerges that postoperative pain is significantly lower than preoperative pain only at < 1 month, and then it remains almost stable in the following months.

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The authors report no conflict of interest.

Response
We read the insightful comments of the authors of this letter and thank them for their interest in our manuscript. In our study, the resection of 44 IDEMTs and outcome assessment performed using the ODI, VAS, and EQ-5D was reviewed, observing significant improvements in quality of life. The authors make several observations regarding the selection, timing, and measurement of functional outcomes measures, contrasted with their retrospective series on IDEMTs.3

The authors raise the concern that a known spinal tumor diagnosis and the time that may elapse prior to EQ-5D and ODI administration could potentially result in a significant bias. The rationale is that psychiatric influences have been described often in degenerative spinal conditions.2 Arguably, these influences are present to some extent in the population of patients with spinal tumor. New patients in our practice are given the EQ-5D prior to evaluation by a neurosurgeon. However, many patients are referred to our practice with a diagnosis of IDEMT, and this pattern of referral reflects a commonly encountered model in practice.

As the authors have said, the EQ-5D, along with most other outcomes tools, would ideally be obtained prior to the onset of pain. Although most large practices, including this one, follow patients with asymptomatic IDEMTs, a larger patient population would ideally be needed to perform a longitudinal study of patients with incidentally found IDEMTs, comparing them to a surgically managed subset. Moreover, in addition to Tarantino et al.’s series,3 the beneficial effect of resection has been demonstrated using numerous different outcomes measures in addition to EQ-5D, VAS, and ODI.2,5

Again, we would like to thank the authors both for their interest in this topic as well as for raising several important considerations for future study.

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