Chordomas are rare, pathologically benign tumors that arise from the notochord remnant. Although ~35% occur in the skull base, they represent only 0.1% of all skull base tumors. In addition to being rare, they are also challenging to treat due to their location, ventral to the brainstem, and their aggressive locally invasive nature. The natural history of chordomas entails a relatively poor survival of 0.9 years without treatment. The current therapeutic algorithm entails an aggressive surgical approach to attempt a radical resection, generally followed by focal radiation therapy.

Extended open skull base approaches to the clival region are traditionally the mainstay for achieving GTR in chordoma. Extended subfrontal transtemporal, anterior transfacial, and lateral transtemporal or far-lateral approaches have been described, as well as staged surgical approaches. These circuitous approaches to the ventral midline skull base often require extensive removal of bone and brain retraction, and they place critical neurovascular structures between the surgeon and the pathology. Nevertheless, complete resection is achieved in only 49.2–79% of cases. With the advent and incorporation of the rigid endoscope into neurosurgical practice and the active collaboration between endoscopic sinus surgeons and neurosurgeons, extended endonasal endoscopic approaches have become well-accepted, minimally invasive routes to the midline and paramedian skull base. The endoscopic endonasal approach to the clivus and anterior brainstem is the
most direct route to the epicenter of the clival chordoma and has been described in detail by several groups who have used cadaveric dissection and small surgical series.\textsuperscript{5,11,14,20,22–24,35,37,41} However, given the relative novelty of this approach, limited cases and clinical outcome data exist in the literature regarding patients with chordomas treated using an endoscopic endonasal transclival approach. The aim of this study was to present an additional series of patients to try and more clearly define the selection criteria for optimizing outcome with this approach.

Methods

Qualitative Literature Review

A PubMed search was performed to identify reports of patients with skull base chordomas treated using endoscopic endonasal resection. Cases were included if the publication provided data on tumor resection volume, recurrence, clinical outcome, and complications. Publications that used case examples to describe surgical/technical nuances without follow-up data were not included. Data were summarized with the following specific target outcome variables: rate of GTR, recurrence after GTR, use of adjuvant treatment, clinical outcome, progression-free status, CSF leakage rate, and perioperative complication rate.

Retrospective Case Series

We retrospectively reviewed a prospectively collected database of all patients undergoing fully endoscopic endonasal surgery between 2004 and 2008. From this database, we identified all patients whose final pathology revealed a chordoma. The senior neurosurgeon (T.H.S.) and otolaryngologist (V.K.A.) were the primary surgeons in each case. Demographics, lesion size and volume, pathology, operative time, ability to meet preoperative goals, complications, use of adjuvant treatment, and clinical outcome were analyzed. The incidence of CSF leakage was recorded. Extent of resection was determined using volumetric measurements of preoperative and postoperative Gd-enhanced MR images, and the findings were divided into $>$ 95\% and $<$ 95\% resection. Extent of resection was compared with the initial tumor volume using Kruskal-Wallis testing with a significant p value of 0.05. Institutional review board approval was obtained for this study.

Surgical Approach

A surgical team approach that included an otolaryngologist and neurosurgeon was used for all extended endoscopic skull base cases. A fully endoscopic transnasal transclival approach was used in all cases and was similar to that in previous reports.\textsuperscript{5,11,14,20,22–24,35,37,41} Some pertinent technical nuances used by our group included administration of 0.25 ml of 10\% fluorescein (AK-Fluor, AKORN) with 10 ml of CSF via lumbar puncture prior to the endoscopic approach to help visualize CSF leaks and to ensure there was no leak after reconstruction of the skull base. Neuronavigation with MR imaging and/or CT angiography was used in all cases. Vomer was harvested as a potential graft source for closure during the approach. The extent of clival dissection was dictated by the location of the tumor. The superior third of the clivus was exposed by drilling the back wall off the sphenoid sinus starting at the sella. It is important to remove the bone over the sella to be able to elevate the pituitary gland to reach tumor extending into the posterior clinoid processes. Neuronavigation and laser Doppler ultrasonography were used contiguously to localize vascular structures, most importantly the CA1s and basilar artery. If the tumors extend into the lower two-thirds of the clivus (below the sphenoid sinus), an inverted U-shaped incision was made in the basipharyngeal fascia and prevertebral musculature, which was flapped inferiorly to expose the anterior aspect of the clivus. Using the Eustachian tubes as the lateral limits of this exposure, the clivus was drilled back until flush with the dura. Dural opening, when necessary, was performed from medial to lateral in the shape of an I to avoid damaging the CN VI. For completely extradural tumors, small CSF leaks were closed by placing fat over the dura and held in place with DuraSeal (Confluent Surgical). Larger dural defects were sealed with fat to obliterate the dead space, followed by autologous fascia lata held in place with a countersunk rigid buttress (vomer bone or Porex, Porex Corp.). This technique has been called the “gasket seal” closure and is finally covered with DuraSeal.\textsuperscript{18} More recently we have begun using a vascularized nasoseptal flap directly over the gasket seal followed by a final layer of DuraSeal to hold everything in place and ensure a watertight closure.\textsuperscript{18} If a lumbar drain is placed, it is typically drained at $\sim$ 5 ml/hour for 1–2 days and then clamped and removed.

Results

Between 2004 and 2008, 7 patients underwent 10 endoscopic transclival chordoma resections (Table 1). Preoperative cranial neuropathies were present in 4 patients, the most common of which was abducens nerve palsy. Two patients were female, and the mean age was 52 ± 18 years. The mean operative time was 210 ± 108 minutes. Lumbar drainage was placed at the beginning of the operation in 1 patient. The tumors extended intradurally in 3 cases. The mean tumor volume was 34.9 ± 48.0 cm$^3$. One patient (Case 2) underwent 2 intentionally subtotal palliative debulking procedures for a multiply recurrent nasopharyngeal chordoma that caused recurrent nasal airway obstruction. For the other 6 patients in whom a GTR was attempted, $>$ 95\% resection was achieved in 7 of 8 operations (5 of 6 patients), and 80\% resection was achieved in the remaining case. The patient with a recurrent nasopharyngeal chordoma who underwent 2 palliative debulking procedures died of disease progression (Case 2). The initial tumor volumes among patients undergoing $>$ 95\% resection ranged from 4.1 to 15.9 cm$^3$ (median 6.0 cm$^3$), while volumes in the 2 patients undergoing $<$ 95\% resection were 80.6 and 124.3 cm$^3$ (median 102.5 cm$^3$); the difference between the 2 medians was statistically significant (p = 0.05). There were no intraoperative complications; 1 patient developed a pulmonary embolus postoperatively that was successfully treated medically. There were no postoperative CSF leaks.
Outcomes and further treatment are summarized in Table 2. Figure 1 compares representative postcontrast MR images from preoperative studies with the most recent postoperative study in each case. Figure 2 shows an intraoperative photograph of the approach in the patient in Case 7. The overall mean follow-up was 18.0 months. In 1 patient with brief clinical follow-up, the patient died of airway compromise at home due to disease progression after undergoing palliative debulking of a rapidly progressive nasopharyngeal tumor (Case 2). Cranial neuropathies improved in all patients except one with a fixed preoperative CN III palsy from a prior resection at another institution. One patient suffered 2 recurrences after radiographic GTR prior to receiving radiation therapy. The patient received PBRT and remains progression free. All but 2 surviving patients received adjuvant radiation. All surviving patients remain progression free.

**Literature Review**

A PubMed search of the literature yielded 8 case series of skull base chordomas resected through fully endoscopic endonasal approaches. Table 3 summarizes the operative results of the published case series.
series. A total of 66 detailed cases have been published to date. Rates of GTR ranged from 0 to 100% with a median rate of 62.5%. The rates of CSF leak ranged from 0 to 33.3%, with a median rate of 11.1%. Rates of major complications ranged from 0 to 100% with a median of 25%. These included new postoperative abducens nerve palsies, ICA injuries, stroke, hematoma, significant subarachnoid hemorrhage, and hydrocephalus requiring shunt treatment. Minor complications included nasal and eye dryness. Table 4 summarizes the follow-up and outcome results of the published case series. Although not all studies detailed the improvement, stability, or worsening of preoperative CN palsies, the series published by Dehdashti et al.11 (representing the largest series) demonstrated postoperative CN improvement in 9 patients (75%), with 1 patient reporting worsening deficits. The majority (46 of 66) of patients received adjuvant radiation therapy. Although not every study provided the same level of detailed reporting in follow-up, the majority of patients (63 of 66) were alive, and most had no evidence of disease or stable progression-free disease after a follow-up that ranged from 1 to 69 months overall; the median follow-up among published studies ranged from 9 to 36 months.

Discussion

Clival chordomas, which arise from the notochord, have their epicenter within the clivus, a midline structure. The bulk of the tumor often lies between the CAs, ventral to the brainstem. The most direct approach to the center of these tumors lies straight through the center of the face, through a corridor that is formed by the naturally aerated sinuses that can be accessed easily through natural orifices provided by the nostrils. Transbasal and far-lateral approaches are indirect, circuitous routes with which to access this central area and require extensive drilling, brain retraction, and manipulation of neurovascular structures to reach their intended target. Recent advances in rigid endoscope technology and instrumentation combined with real-time neuronavigation has facilitated a fruitful collaboration between neurosurgery and otolaryngology to develop the field of endoscopic skull base surgery. These extended endonasal approaches have been used to remove tumors in the midline and paracentral skull base including clival chordomas.5,23,24,32,36 Cadaveric studies have provided stepwise thorough descriptions of the approach and have provided detailed views of anatomical relationships of ventral skull base anatomy.
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viewed “head-on” through the nasal corridor. Cavallo et al.,3 most notably illustrated the extensive view of the ventral brainstem available through an endoscopic endonasal transclival approach. Such descriptions are vital as a first step in incorporating new surgical approaches to the CNS. Kassam et al.,24 published early case descriptions that demonstrated clear and successful utilization of these approaches to address clival pathologies. While cadaveric studies are helpful to document the approach, these case descriptions provide evidence of success in treating complex skull base pathologies. In this setting, several authors have published early case series detailing the use of the endoscopic transclival approach as the primary surgical procedure for resection of clival-region chordomas. We endeavored to review these series and to add our own data in an effort to demonstrate the early clinical experience with this approach.

Jho and Ha22 published the earliest reports and included detailed follow-up of 3 patients with chordomas that were resected via an endoscopic transclival approach. Although the authors achieved GTR in all 3 cases, 1 patient experienced a recurrence ~ 1 year after resection. The patient underwent SRS to the recurrence and remained progression free for 26 months.23 This early experience highlights the complexity of treatment paradigms needed in addressing clival chordomas. Although extent of resection is prognostically important, adjuvant radiotherapy can be used to control any small residual left attached to such structures.26 In our series, all but one surviving patient received PBRT. This is consistent with the limited published literature, as 33 (72%) of the 46 patients from other published series received radiotherapy. Thus, with postoperative radiotherapy as an available adjunctive tool, we have adopted a philosophy that seeks to maximize resection while minimizing risk to surrounding neurovascular structures. Toward this paradigm, endoscopic endonasal transclival resection is our preferred approach for midline tumors without significant extension lateral to the CAs.

The endoscopic endonasal transclival approach uses a minimal access corridor, but it can obtain maximal visualization to the clival region. At our institution, the approach represents a joint effort between otolaryngology and neurosurgery, taking advantage of the combined understanding of sinonasal and skull base anatomy. In addition, neuronavigation aids in localizing the lesion and surrounding vital structures, estimating depth through this long surgical corridor, and providing a verification tool for the surgeon’s understanding of anatomical relationships.7,25 Another important technology in this approach is the use of angled endoscopes. Thirty- and 45-degree endoscopes provide the ability to create a panorama of the exposed skull base, and extend the operative region without expanding the surgical corridor. By moving the lens and light source so close to the field, angled endoscopes extend the straight microscopic transsphenoidal view into a more extensive operative vista, which facilitates extended approaches to the skull base.

Postoperative CSF leak—the often-feared complication—was reported in 16.7% of cases in the published series, but there were no cases in our series. Clearly, the degree of intradural invasion of the tumor will have a major impact on the risk of this complication; however, even in our 3 cases with extensive intradural involvement, CSF leaks were successfully managed with multilayer closure. All of our patients remain progression free after resection and prescribed radiotherapy. Only 1 patient required further open skull base resection after the endoscopic approach, but radiation therapy was not used after the endoscopic resection to prevent further growth. These early results provide encouraging data for further use of the endoscopic endonasal approach to clival chordomas.

Previous studies have suggested that the endoscopic endonasal approach to resection of chordomas is equally successful at obtaining a radical resection as open approaches. Gross-total resection was achieved in 54.5% of published cases.11,14,20,22,23,35,38,41 However, in the one endoscopic publication citing average tumor volumes, Stippler et al.39 cited a mean tumor volume of 29.1 cm3, while the mean volume was slightly higher in our series (34.9 cm3); this is less than the average volume of transcranial series, which is on the order of 58 cm3.38 We graded our resection by using postoperative MR images. Greater than 95% resection was obtained in 88% of cases in which GTR was attempted (83% of patients). We found a significant relationship between size of tumor and degree of resection. Our results indicate that tumors with a diameter > 4.0 cm or a volume > 80 cm3 may be more difficult to remove completely through an endonasal approach. This may represent an important limitation of the endoscopic transnasal approach. However, it may represent a more global difficulty with achieving total or near-total resections in large clival chordomas. Although our series is small, it suggests a potential relationship between tumor size and potential for resection that requires further evaluation.

Fig. 2. Case 7. Endoscopic endonasal view of postresection cavity from the patient. CS = cavernous sinus. DURA = dura behind the clivus; PG = pituitary gland.
In viewing these results, it is important to qualitatively compare them with published results from open surgical series. Sekhar et al.33 described their experience in treating 64 patients with chordomas or chondrosarcomas of the skull base. Among the 42 patients with chordomas, the authors achieved GTR in 25 (59%) and subtotal resection (> 90% tumor resection) in 12 (28%). However, 9 patients (21%) with chordoma developed new abducens palsies, while 11 (26% of chordomas) developed CSF leaks.33 DeMonte et al.12 described 4 patients who underwent an open transmandibular, circumglossal, retropharyngeal approach for chordomas of the clivus and upper cervical spine. While the authors achieved > 95% resection in all patients (including 2 with GTR), the complications included 1 transient abducens palsy, 2 cases of lingual neuropathy, 1 case of soft-palate fistula, and 1 case of a hard palate defect requiring prosthetic repair.12 With follow-up ranging from 2 to 9 months, the authors noted 2 recurrences.12 Sen and Triana34 reported total resection in 18 (85.7%) of 21 patients using open skull base approaches; however, they reported 24 new postoperative complications including 3 CSF leaks and 2 minor strokes. In comparison, both the rates of new abducens palsies and CSF leaks in the endoscopic literature ranged from 0 to 33.3%. Al-Mefty et al.2 recently published a series of 43 patients with clival pathology resected via an open midline anterior clivectomy approach. Of the 38 with chordomas, GTR was achieved in 29 (76.3%). Among patients with chordoma, 6 (15.8%) developed CSF leaks (although 2 did so in a delayed fashion after radiotherapy). Among chordomas, there were 4 new postoperative abducens palsies in 3 patients (7.9%), although only 1 remained permanent. Finally, after surgery and radiotherapy, recurrence in this cohort was 15%.2 In their discussion, the authors made particular note of the important role of endoscopy in treating these tumors. This is especially relevant, as the open anterior clivectomy approach described provides a similar portal of access and visualization panorama as that provided by the endoscopic endonasal transclival approach.

Several studies have also evaluated the microscopic transsphenoidal approach to clival chordomas. In a report of 12 patients with clival chordomas treated with microsurgical transsphenoidal approaches by Maira et al.,27 total resection was achieved in 9 (75%). Couldwell et al.8 reported results of extended microsurgical transsphenoidal approaches in 105 patients, 18 of which were clival chordomas. Total resection was achieved in 12 (66.7%) of 18 chordomas. Among the chordomas, there were 3 ICA hemorrhages, 2 CN palsies, and 1 CSF leak.8 Fatemi et al.13 recently reported their microsurgical transsphenoidal results of clival chordoma resections in 14 patients; total resection was achieved in 43% and near-total resection was achieved in 43%, leaving 14% with subtotal resection. The authors noted in their report that the endoscope aided in tumor removal and assessment of resection.13 These reports of open skull base and microsurgical transsphenoidal approaches provide a frame of reference for understanding that the fully endoscopic endonasal approach can enable appropriate resection of a clival chordoma with acceptable complication rates in comparison with other approaches. In time we believe that the endonasal endoscopic approach will in fact produce fewer complications with equal or better rates of complete resection in carefully selected patients. Understanding appropriate patient selection will be a key principle in future evaluation of these approaches as part of the armamentarium of the skull base surgeon.

**TABLE 3: Operative results of the published case series**

<table>
<thead>
<tr>
<th>Authors &amp; Year</th>
<th>No. of Cases</th>
<th>GTR No. (%)</th>
<th>Recurrence After GTR</th>
<th>FU (mos)</th>
<th>CSF Leak No. (%)</th>
<th>Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jho &amp; Ha, 2004</td>
<td>3 (100)</td>
<td>1 (33.3)</td>
<td>26 20–28</td>
<td>1 (33.3)</td>
<td>4 PE, atrial fibrillation, stroke, abducens palsy</td>
<td></td>
</tr>
<tr>
<td>Solares et al., 2005</td>
<td>3 (66.7)</td>
<td>0 (0)</td>
<td>12 8–24</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Frank et al., 2006</td>
<td>9 (33.3)</td>
<td>0 (0)</td>
<td>15 10–69</td>
<td>1 (11.1)</td>
<td>1 ICA injury</td>
<td></td>
</tr>
<tr>
<td>Hwang &amp; Ho, 2007</td>
<td>3 (0)</td>
<td>NA</td>
<td>36 30–40</td>
<td>0</td>
<td>1 HCP requiring VPS</td>
<td></td>
</tr>
<tr>
<td>Dehdashti et al., 2008</td>
<td>12 (58.3)</td>
<td>0 (0)</td>
<td>16 4–26</td>
<td>4 (33.3)</td>
<td>3 postop hematoma, hemiparesis, HCP</td>
<td></td>
</tr>
<tr>
<td>Hong Jiang et al., 2008</td>
<td>9 (66.7)</td>
<td>0 (0)</td>
<td>17 6–30</td>
<td>0</td>
<td>14 nasal dryness (9) &amp; eye dryness (5)</td>
<td></td>
</tr>
<tr>
<td>Zhang et al., 2008</td>
<td>7 (66.7)</td>
<td>0 (0)</td>
<td>24 3–37</td>
<td>NR</td>
<td>1 subarachnoid hemorrhage</td>
<td></td>
</tr>
<tr>
<td>Stippler et al., 2009</td>
<td>20 (45)</td>
<td>2 (22.2)</td>
<td>9 1–54</td>
<td>5 (25)</td>
<td>5 brainstem hemorrhage, worsening CN palsy, intraop ICA rupture</td>
<td></td>
</tr>
<tr>
<td>total</td>
<td>66</td>
<td>33 (54.5)</td>
<td>11 (16.7)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* HCP = hydrocephalus; NA = not applicable; NR = not reported; VPS = ventriculoperitoneal shunt.
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Case Selection

Although the endoscopic endonasal transclival approach is the most direct method for reaching the epicenter of clival chordomas, it may not be suitable for all chordomas. Probably the most important limitation is the relationship between the CAs and the tumor. Although it is possible to reach lateral to the CAs through an endonasal approach, the risks of this maneuver may outweigh the benefits. The surgeon has 2 alternatives in this situation. One is to choose a lateral skull base approach using the corridor created by the lateral extent of the tumor. The other is to perform a combined or staged approach, removing the midline tumor endonasally and the lateral tumor transcranially. Likewise, tumors > 4 cm in diameter or 80 cm³ may have a higher rate of radical resection with a transcranial approach. Our data as well as that from Stippler et al. support this. In their review of 20 patients who underwent endoscopic endonasal resection of chordomas, the investigators obtained GTR in 9 patients (45%) and near-total resection in 4 patients (20%) for a total of 65%, with a CSF leak rate of 25%. While we obtained a > 95% resection in 71.4% of our total patients (87% of those in which GTR was the goal) with no CSF leaks, both studies share a commonality in the volumes of tumors resected. Although these data represent small numbers, they suggest that endoscopic endonasal resection may be most successful with smaller tumor volumes.

On the other hand, intradural extension is not a contraindication, although it does render the surgery more complex and requires harvesting of appropriate grafts for successful closure such as fat, fascia lata, and a vascularized nasoseptal flap.

Study Limitations

Given the preliminary nature of these data, there are several limitations to our study. The small number of patients limits the statistical power of any conclusions that one may draw from this report, although it is difficult to acquire relatively high case numbers as chordomas are very rare tumors. Second, the short follow-up provides only short-term outcomes; further follow-up will be necessary to determine the durability of disease control in patients treated with this type of resection compared with more traditional open skull base approaches.

Conclusions

Surgical management of clival chordomas is undergoing a paradigm shift as endoscopic endonasal approaches become more widely practiced. It is difficult to directly compare these approaches with open microsurgical approaches specifically for chordomas, as the rare epidemiology of the disease makes accumulation of significant case numbers difficult. However, in examining the lim-

### TABLE 4: Follow-up and outcome results of the published case series

<table>
<thead>
<tr>
<th>Authors &amp; Year</th>
<th>No. of Cases</th>
<th>Adjuvant Treatment</th>
<th>Neurological Outcome/Findings</th>
<th>Reported Radiographic Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jho &amp; Ha, 2004</td>
<td>3</td>
<td>no RT (1), GKS to site (1), GKS to recurrence (1)</td>
<td>CN VI palsy (1)</td>
<td>NR</td>
</tr>
<tr>
<td>Solares et al., 2005</td>
<td>3</td>
<td>no RT (1), IMRT to site (1), PBRT to residual (1)</td>
<td>NED (2), alive w/ disease (1)</td>
<td>PF (2), alive w/ active disease (1)</td>
</tr>
<tr>
<td>Frank et al., 2006</td>
<td>9</td>
<td>no RT (4), PBRT to site (2), PBRT to residual (2), CRT to residual (1)</td>
<td>CN VI palsy (2), anosmia (1)</td>
<td>recurrence 2 times (1)</td>
</tr>
<tr>
<td>Hwang &amp; Ho, 2007</td>
<td>3</td>
<td>SRT to residual (3)</td>
<td>CN VI palsy (1); improving hemiparesis/dysphasia (1); unchanged preop CN III/VI/VIII/IX palsies (1)</td>
<td>PF w/ stable remnants (3)</td>
</tr>
<tr>
<td>Dehdashti et al., 2008</td>
<td>12</td>
<td>preop RT (3), postop IMRT (9)</td>
<td>worsened CN IX/X palsy (1), new hemiparesis (1), improved CN palsies (9)</td>
<td>PF w/ stable remnants (12)</td>
</tr>
<tr>
<td>Hong Jiang et al., 2008</td>
<td>9</td>
<td>IMRT to site (6), IMRT to residual (1)</td>
<td>residual HA, epistaxis, &amp; visual changes (1), complete symptom resolution (8)</td>
<td>recurrence (1)</td>
</tr>
<tr>
<td>Zhang et al., 2008</td>
<td>7</td>
<td>not reported in detail</td>
<td>not detailed</td>
<td>alive w/ disease (1), no active disease (6)</td>
</tr>
<tr>
<td>Stippler et al., 2009</td>
<td>20</td>
<td>postop RT (8), preop RT (SRT or PBRT, 5)</td>
<td>new quadriparesis (1); died of disease progression (1)</td>
<td>recurrence (2); progression of residual (5)</td>
</tr>
<tr>
<td>total</td>
<td>66</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* CRT = conformal RT; GKS = Gamma Knife surgery; IMRT = intensity-modulated RT; NED = no evidence of disease; PF = progression free; SRT = stereotactic RT.
oted published data and adding our own experience, it is clear that the early short-term results of endoscopic endonasal transcricoid resection, combined with radiotherapy, provide encouraging data for high rates of tumor control and progression-free survival with limited morbidity for selected cases of moderate-sized predominantly midline tumors.

Disclaimer

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

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Accepted July 28, 2009.
Please include this information when citing this paper: published online August 21, 2009; DOI: 10.3171/2009.7.JNS081504.
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