Histologic Analysis of Folded Cochlear Implant Electrode Arrays

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Atraumatic placement of cochlear implant (CI) electrodes is a desired surgical technique as studies have shown that insertional trauma, over-insertion, and interscalar electrode translocation lead to poorer audiometric outcomes.1,2 Acute consequences of insertional trauma may reduce functional results from disruption of intracochlear structures with traumatic loss of spiral ganglion neurons (SGNs).1 Studies of human temporal bones (TBs) of patients having undergone CI additionally show that implantation frequently results in chronic changes, such as intracochlear fibrosis and ossification.3,4 These chronic post-implant sequelae may intensify in cases with acute traumatic electrode placement and are correlated with worse hearing outcomes.3,4

Recently developed electrodes with precurved conformations allow for perimodiolar placement within the scala tympani (ST) and may be placed atraumatically; however, they also present a greater potential for folding of the electrode array than with straight designs.3,5 Electrode folding may cause damage to intracochlear structures leading to both acute and chronic intracochlear changes. Herein, we examine the histologic findings of human CI cases where folding of the implant electrode array is observed.

Materials and Methods
TB specimens from patients having undergone CI during life were evaluated. Inclusion criteria were: 1) insertion of the electrode through an extended round window approach and 2) similar etiology, duration, and magnitude of hearing loss between ears. “Folded” specimens exhibited folding of the intracochlear electrode array and “control” specimens exhibited electrode placement entirely within the ST without evidence of electrode folding. ‘SGN count’ was quantified as the difference in normalized SGN (% age-matched controls) between the implanted ear of interest and contralateral ear within each patient.6 continued on page 2
Results

Four cases with folding of the electrode array within the basal turn and five controls with unilateral, normal electrode conformation were identified. All patients experienced progressive sensorineural hearing loss and the duration of hearing loss (3.8±1.7 vs. 9.6±5.3 yr), age at implantation (70±7 vs. 73±7 yr), and duration of implant use before death (8.3±4.3 vs. 10.3±2.2 yr) were comparable between the folded and control groups.

Throughout the ascending basal turn of the cochlea, folded cases qualitatively showed more osseous tissue compared to controls (Figure 1A). Quantitatively, there was greater neo-ossification within Segment I of folded cases versus controls (29.2±12.2 vs 6.6±4.9 percent, p<0.05), which corresponds to the region of array folding (Figure 2). Little to no osseous tissue formation was observed within the basal turn of 4 of 5 control cases and intracochlear structures remained identifiable and relatively normal in appearance within this group (Figure 1B). The length of proximal array folding varied between the four folded cases (range: 2.8–6.5 mm) and was strongly correlated with the degree of ossification (r=0.97, p<0.05). We quantified the amount of fibrosis within the cochlea similarly to osseous tissue and found no difference in fibrosis between folded cases and controls (Figure 3).

Overall, interaural SGN counts were decreased in folded cases (-14.1±13.4 percent), while controls showed no interaural SGN count differences (0.7±5.2 percent) (Figure 4). Within segments of Rosenthal's canal, folded cases showed the greatest difference in SGN counts in Segment I and II (-21.6±16.5 and -28.3±17.0 percent, respectively), which correspond to the locations of folding of the electrode array in each case. In contrast, SGN counts in Segments I and II were similar or slightly higher for all control cases (7.3±14.6 and 4.8±4.9 percent). Additionally, within the folded group, the specimen with the greatest length of array folding showed the greatest SGN count difference in Segment I and II (-44.7 percent, -52.3 percent).

Both ossification and lower SGN counts were more pronounced in folded cases than controls. SGN counts in Segments I, II, and overall were negatively correlated with the amount of ossification within these areas (r=-0.72, p<0.05; r=-0.71, p=0.05; r=-0.87, p<0.01, respectively).
Discussion

In this study, specimens with folding of the CI electrode showed significantly greater volumes of intracochlear osseous tissue than controls, which was most prominent in areas adjacent to sites of folding. In these same areas, folded cases showed lower SGN counts when compared to the contralateral ear, whereas controls showed stable interaural SGN populations. Interestingly, the degree of intracochlear fibrosis was similar between cases and controls. Additionally, our cases demonstrate a negative correlation between intracochlear ossification and local SGN counts.

Previous studies in human TBs have shown a positive association between gross intracochlear trauma and new intracochlear osseous tissue formation. We additionally demonstrate that folding of a CI electrode leads to local intracochlear osseous change that is dependent on the degree of electrode folding. While the effect of CI on SGN remains under debate, others have shown a local protective effect of CI on segments of the cochlea receiving stimulation. In line with these studies, we show that in the absence of electrode folding and with minimal intracochlear damage, stable populations of SGNs are observed. Therefore, loss of SGNs in our cases of electrode folding may result from acute trauma and chronic osseous deposition. Although unknown, this mechanism may be attributed to osseous occlusion of the inferior cochlear vein, which is proximal to the round window membrane and receives drainage from the SGN and ST through the posterior spiral vein.

Our findings show that folding of CI electrodes causes significant acute intracochlear damage. Insertional damage from misplaced electrodes may stimulate immediate ossification, but chronic placement of a folded array also may exert pressure on intracochlear structures leading to a progressive osteitic reaction. If the latter is true, then withdrawal and reinsertion of a CI electrode in the proper configuration could prevent further degeneration, which is particularly relevant for precurved devices. These findings highlight the need for proper, atraumatic initial insertion of CIs. Further analysis is necessary to determine if intracochlear degeneration may be prevented via immediate identification with intraoperative imaging and rapid correction of CI electrode placement.

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REFERENCES

Head injury is a major cause of worldwide morbidity and death. Although not commonly discussed in the trauma literature, head injury may also result in significant auditory dysfunction, such as hearing loss and tinnitus. Following a temporal bone (TB) fracture, hearing loss is commonly thought to be due to direct anatomic disruption of the middle ear or inner ear sensory neuroepithelium.

While hearing loss following TB fracture is well described, the epidemiology and pathophysiology of auditory dysfunction in the setting of head injury without TB fracture remains underinvestigated. In a recent review by Chen et al., the studies with the highest level of evidence reported hearing loss after head injury without associated TB fracture in 0.9 to 58 percent of the patients. When looking specifically at concussions in children, Thompson et al. suggested that the ability to understand speech in noise, particularly over extended periods of background noise, might be compromised even in the absence of hearing loss.

Over the past century, various terms such as “labyrinthine concussion” and “inner ear concussion” have been used to describe sensorineural hearing loss (SNHL) following head trauma without TB fracture. There are several proposed mechanisms for traumatic auditory injury in the literature: 1) pathologic inner ear fluid wave, 2) trauma to the cochleovestibular nerve, 3) direct injury to membranous labyrinth, 4) endolymphatic hydrops, and/or 5) injury to the central auditory pathway. A lack of data has made it difficult to determine the underlying mechanism by which head injury results in auditory pathology. Treatment options also remain largely nonexistent.

Taken together, while SNHL secondary to head injury without TB fracture is a recognized clinical phenomenon, the underlying pathophysiology remains unknown. We hypothesize that a unique set of changes occurs in the inner ear as a result of head injury that can be detected by otopathology techniques. Human otopathologic findings can provide insight into the pathophysiology of auditory dysfunction in head trauma without TB fracture.

**Table 1. Study inclusion and exclusion criteria**

<table>
<thead>
<tr>
<th>Inclusion criteria</th>
<th>Exclusion criteria</th>
</tr>
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<tbody>
<tr>
<td>1) Individuals with a history of head injury without TB fracture</td>
<td>1) History of noise exposure</td>
</tr>
<tr>
<td></td>
<td>2) Clinical, radiographic, or histologic TB fracture through the inner ear</td>
</tr>
<tr>
<td></td>
<td>3) Otologic surgery involving the middle and/or inner ear</td>
</tr>
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<td></td>
<td>4) Hearing loss prior to the head trauma or due to other otologic disorders (eg, chronic otitis media)</td>
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<td>5) Meniere’s syndrome or sudden sensorineural hearing loss prior to head injury</td>
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<td></td>
<td>6) Severe postmortem changes (eg, compression artifact or autolysis)</td>
</tr>
</tbody>
</table>

**Table 2. Clinical History**

<table>
<thead>
<tr>
<th>Case/Side</th>
<th>Age (yr.)/Sex</th>
<th>Type of trauma (Age, yr.)</th>
<th>HL at last audiogram (Age, yr.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/R</td>
<td>92/M</td>
<td>Concussions (NA, child)</td>
<td>Moderate (79)</td>
</tr>
<tr>
<td>1/L</td>
<td>92/M</td>
<td>Concussions (NA, child)</td>
<td>Profound (79)</td>
</tr>
<tr>
<td>2/L</td>
<td>71/F</td>
<td>Concussion (34)</td>
<td>Profound (71)</td>
</tr>
<tr>
<td>3/R</td>
<td>66/M</td>
<td>Fall (61)</td>
<td>Mild (63)</td>
</tr>
<tr>
<td>4/R</td>
<td>96/M</td>
<td>Fall (78)</td>
<td>Moderate (95)</td>
</tr>
<tr>
<td>5/L</td>
<td>72/M</td>
<td>MVA (57)</td>
<td>Moderate (69)</td>
</tr>
</tbody>
</table>

L: left; R: right; yr.: year; HL: hearing loss; NA: not applicable; M: male; F: female; MVA: motor vehicle accident.

studies may indicate potential future avenues of research for prevention and treatment algorithms in this clinical setting.

As a proof of concept study, the National Temporal Bone, Hearing and Balance Pathology Resource Registry was used to identify individuals with a history of head injury without TB fracture. Inclusion and exclusion criteria are summarized in Table 1. Inner ear anatomy of all TBs was evaluated by light microscopy, including condition of the stria vascularis, presence or absence of endolymphatic hydrops, and counts of spiral ganglion neurons (SGNs), which were compared to historical age-matched controls.  

Six TBs from five patients (4 men and 1 woman) met initial inclusion and exclusion criteria (Table 2). All subjects had an available post-head injury audiogram that demonstrated mild to profound SNHL. As a representative individual, Case 1 had a history of multiple concussions of unknown etiology during childhood. The patient subsequently experienced hearing loss that was bilateral and progressive, and experienced total loss of hearing by age 17. The patient died at age 92. Postmortem computed tomography of TBs were reviewed, and there was no evidence of TB fracture or other middle and inner ear pathology, such as enlarged vestibular aqueduct. When both TBs were

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analyzed, the left TB had presence of vestibulocochlear hydrops (Figure 1). The left TB demonstrated severe loss of inner and outer hair cells and pillar cells along the length of the cochlea, while the right TB showed moderate to severe loss at the basal turn of the cochlea and mild to moderate loss at the middle turn of the cochlea to the apex (Figure 2). Severe atrophy of the stria vascularis and spiral ligament were found throughout the cochlea in the left TB, while the right TB showed only mild degeneration of the stria vascularis in the basal and apical turns of the cochlea (Figure 3). Furthermore, both sides demonstrated decreased SGN populations (21 and 33 percent of historical age-matched controls, respectively) (Figure 4).

Additional review of four other patients with unilateral TBs available also demonstrated inner ear changes after head trauma. All four cases showed decreased total SGN populations with an average of 57 percent of historical age-matched controls (range, 21–79 percent of historical age-matched controls). In addition, there was loss of HC and mild to moderate degeneration of the stria vascularis. Cochlear endolymphatic hydrops was found in 50 percent (n=2) of cases.

The histopathologic changes in the present study are thought provoking and may partially explain auditory symptomatology that may develop following head trauma. Limited related human\textsuperscript{10,13,14} and animal studies\textsuperscript{4,15} have shown some similarity in the findings of our study. Lindsay and Zajtchuk\textsuperscript{13} reported a case in which both TBs demonstrated degeneration of organ of Corti, stria vascularis, and spiral ligament predominantly in the middle and apical turns of the cochlea as well as reduced SGN populations. Paparella et al.\textsuperscript{14} described a case that developed Meniere’s syndrome following a head trauma, in which otopathologic analysis showed vestibulocochlear hydrops, HC and SGN loss in the basal turn of the cochlea, and an eosinophilic precipitate in the endolymphatic duct. In a cat model of head trauma, Schuknecht and Davison\textsuperscript{15} found pathologic changes located within the basal turn of the cochlea, with damage of the outer hair cells. A feline model of head trauma developed by Wittmaack\textsuperscript{14} demonstrated severe degeneration of the membranous labyrinth and SGNs in the middle turn, with mild to moderate changes in the apical and basal turns of the cochlea.

There are limitations to otopathologic evaluation of the auditory periphery following head injury. The time of death is often years after the insult and additional unknown factors, including undocumented noise exposure, may contribute to the observed pathology. Although the study has distinct limitations, review of human TB may augment our understanding of auditory symptoms following head injury. Future prospective studies in animal models may elucidate whether or not these otopathologic findings are directly attributable to trauma.

REFERENCES


Portions of this manuscript have been accepted for publication in Otolaryngology–Head and Neck Surgery.
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