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Spiral Ganglion Cell Loss is Unrelated to Segmental Cochlear Sensory System Degeneration in Humans

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Abstract

Objective—To demonstrate that contrary to what occurs in animals, neuron loss in the human spiral ganglion is not in proportion to organ of Corti hair or supporting cell loss.

Study Design—Histopathological review of archival temporal bone histological sections.

Setting—Nonprofit research facility

Methods—Four temporal bones, from an archival collection of 1,448 temporal bones, were found that had a total loss of hair and supporting cells limited to the basal segment of the cochlea and a hearing loss of 3 or more years (range 3–28 years). Cochlear reconstructions were carried out to demonstrate the populations of hair and supporting cells, peripheral processes (dendrites), spiral ganglion cells, and the amount of surviving stria vascularis in different cochlear segments.

Results—The total loss of hair and supporting cells of the organ of Corti in the base of the cochlea is not accompanied by a proportional loss of spiral ganglion cells in the modiolar base.

Conclusions—A long-term loss of hearing in frequencies above 2 kHz, and corresponding hair cell loss, does not result in a subsequent loss of spiral ganglion cells in humans, in contrast to what has been reported in animals. These findings suggest that the poor performance of cochlear implant patients after prolonged deafness is not due to ongoing degeneration of ganglion cells.

Keywords

human; spiral ganglion; hair cells; supporting cells

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A publication by Nadol, Young, and Glynn in 1989 stated that “multiple regression analysis demonstrated that the cause of hearing loss was the single most significant determinant of total spiral ganglion cell count”¹. In spite of this, there are still papers appearing in the literature that state that the poor performance of cochlear implant patients who are implanted many years after the onset of their hearing loss is due to the inevitable loss of spiral ganglion cells thought to occur after years of lack of stimulation by hair cells. These statements are based on animal studies showing that a loss of neurons begins shortly after hair cell loss.^{2–15} However, we recently reported that the loss of ganglion cells in individuals totally deaf for many years did not approach that seen in animals.¹⁶ The number of remaining ganglion cells was not related to duration of hearing loss or to remaining supporting cell population.

In order to determine if a discrete loss of hair and supporting cells of the organ of Corti is accompanied by a loss of neurons in the corresponding spiral ganglion, we compared cochlear

reconstructions of sensory elements to neuronal loss in the modiolus using the measurement methods pioneered by Guild and modified by Schuknecht.^{17, 18}

Materials and Methods

The database of 1,448 temporal bones in the laboratory was searched for cochleae with no hair cells in the base of the cochlea, i.e. 0 to 15 mm from the round window. The bones were from patients who had pledged their temporal bones to the institute so complete medical records were also available. Four were found that had no basal hair cells and had a hearing loss for high frequencies of at least three years duration (Fig 1A). The temporal bones had been removed intracranially by the block method and fixed in 10 percent buffered formalin for one month. They were decalcified with ethylenediaminetetraacetic acid (EDTA) until shown by X-ray to be calcium free; embedded in celloidin, and cut into 20 micron sections. Every tenth section was stained with hematoxylin and eosin and mounted on a glass slide; the other nine sections were stored for special evaluations. The mounted and numbered sections were used in the graphic two dimensional reconstructions described in this paper.

Cochlear reconstructions of hair and supporting cells and stria vascularis were performed using the technique first described by Guild and later modified by Schuknecht (Fig 1B).^{17,18} The dendrite population was determined by measuring the diameter of the neurite bundles in the osseous spiral lamina using a standard developed in our laboratory.¹⁹ The spiral ganglion counts were prepared using the Schuknecht method (Fig 1C). The amount of loss for each structure was plotted on a cytochleogram, the amount of loss being indicated by black filling (Fig. 1D).

The number of cases was too small for statistical analysis so the loss of structures is presented in the table.

RESULTS

The number of cases is too small for meaningful statistical analysis, but data are presented in table 1. We note first that complete loss of hair cells in the basal segments does not mean complete loss of ganglion cells in modiolar base. All four patients had a majority of ganglion cells remaining with the largest loss being 35% of normal and a mean loss of 25% for the four ears.

Case #354

This 84-year-old woman was first seen in the clinic at age 68 because of a bilateral hearing loss and tinnitus first noticed three months earlier after an airplane flight. Audiometric tests indicated a down-sloping loss averaging 50 dB in the speech frequencies in the right ear and 42 dB in the left, with 80% discrimination on the right and 92% on the left. There was no air-bone gap. Physical examination of the ears showed normal tympanic membranes. A hearing aid evaluation was performed and an appropriate recommendation made. There was a gradual deterioration in the hearing in the ensuing years, and three years before her death at age 84, thresholds were 70, 80, and 85 at 0.25 kHz, 0.5kHz, and 1kHz, with no response at 2kHz and above in the right ear and averaging 83 dB in the speech frequencies in the left ear. The SRT was not testable on the right due to the severity of the loss and was 80dB on the left with a discrimination score of 72%. Postmortem examination of the temporal bones showed a total loss of hair cells in the basal segments of the cochlea and slight loss of ganglion cells on the right side; i.e. 18,828. Normal for the patients age is 20,828 with a standard deviation of 5,345¹⁸. (Fig. 1D) There were similar but less severe findings on the left side.

Case #128

A 78-year-old woman was first seen at age 65 because of a hereditary progressive hearing loss of more than 10 years. Her mother and two other relatives had hearing losses. The patient's audiogram indicated an average sensorineural loss in the speech frequencies of 53 dB in the right ear and 45 dB in the left ear, with discrimination scores of 44% and 48%, respectively. There was a notch at 4kHz, but no history of noise or head trauma. SRT was 50 dB on the right side and 48dB on the left side. A hearing aid evaluation was performed and an appropriate recommendation made. At age 87, four years before her death, the patient could no longer hear 2 and 4 kHz in either ear, although the lower frequencies remained unchanged.

Histopathological examination revealed a total loss of sensory structures in the basal 15 mm of the cochleae but a loss of only 35 percent of ganglion cells in the corresponding basal segment of the spiral ganglia (Fig. 2). Total ganglion cell count was 15,822; normal for the patient's age is 22,871 with a standard deviation of 5,588.¹⁸

Case #546

A 65-year-old woman was first seen at age 34 because of a sudden hearing loss on the left side that occurred two years previously accompanied by severe vertigo. Audiometric tests indicated normal hearing on the right, but a severe sensorineural loss on the left. There were responses at 0.25 and 0.5 kHz but none at the higher frequencies. At 62 years, three years before her death, the levels in the left ear remained unchanged, but there had been a loss of some high frequencies in the right ear to a level of 75 dB at 8 kHz.

Histopathological examination of the left ear revealed a total loss of sensory and supporting cells of the organ of Corti in the basal 20 mm of the cochlea but a loss of only 15% of neurons that was evenly distributed throughout the spiral ganglion (Fig. 3). In the right ear, there was a loss of hair cells in the hook area. The ganglion cell count was 25,164 with an even distribution throughout. Normal ganglion cell population for the patient's age is 25,270 with a standard deviation of 6,785.¹⁸

Case #575

A 65-year-old woman first seen at age 26 because of a high frequency hearing loss for as long as she could remember. Re-examination at 54, 11 years prior to death revealed no hearing above 1 kHz and no discrimination in the right ear and a down-sloping sensorineural loss averaging 70 dB in the left ear with a discrimination score of 80%. Histological examination of the right ear showed a total loss of hair cells in the basal 20 mm of the cochlea and a spotty loss in the upper segments. There was a corresponding loss of supporting cells and peripheral processes and a rather severe loss of the stria vascularis. There was an overall loss of 25% of ganglion cells with only slightly more in the basal parts of the spiral ganglion (Fig. 4). Total ganglion cell count was 19,332; normal for the patient's age is 24,070 with a standard deviation of 6,186.¹⁸ There were similar less severe findings in the left ear.

Discussion

Two studies have shown an inverse relationship of the spiral ganglion population to performance of cochlear implants.^{20, 21} However, the minimum number of neurons necessary for a satisfactory response to electrical stimulation is unknown; two patients in our data base have less than 3,000 spiral ganglion cells (10%) but functioned at fair and excellent levels with word tests. There has been some concern that prolonged deafness might lead to a decrease in the neuronal population to a point where a cochlear implant would not be beneficial. This unease is based on the fact that individuals implanted after many years of total hearing loss do not do as well as those recently affected and that animal experimentation has shown a loss of

spiral ganglion cells proportional to the duration of hair cell loss. There has also been a concern that the introduction of even a short electrode in individuals with residual hearing might produce further hair cell damage and, thus, loss of neurons. The findings in this study indicate that these worries are unfounded because loss of hair cells does not result in ganglion cell loss in humans. Why the ganglion cells survive in humans, in contrast to animals, long after there is no auditory input is unknown. It is possible that because the life span of experimental animals is so much shorter than that of humans that the changes occur much faster in small animals; however if the time between hair cell loss and ganglion cell loss for animals is calculated, the interval is but a fraction of their life span whereas in humans it does not occur (Table 2). For instance, there is a pair of temporal bones in our laboratory, from an 89-year-old woman, deaf since birth, with cochlear saccular degeneration (the Scheibe deformity) that has 20,961 neurons in the right bone and 19,458 in the left, numbers well within the normal for the patient's age.¹⁶ Human spiral ganglion cells differ from animals in that 94% of human cells are unmyelinated in contrast to other mammals including monkeys.²² Rask-Andersen et al examined human spiral ganglia removed at surgery, using transmission and scanning microscopy, and suggested that the survival of the neurons might be due to the clustering propensity of the neurons, and the lack of myelin might allow for an intercommunication between neurons with neurites and other neurons and thus provide trophic support that accounts for their survival in humans.^{23, 24}

REFERENCES

1. Nadol RB, Young Y-S, Glynn RJ. Survival of spiral ganglion cells in profound sensorineural hearing loss: implications for cochlear implantation. *Ann Otol Rhinol Laryngol* 1989;98:411–415. [PubMed: 2729822]1989
2. Ernstson S. Vestibular physiology in a strain of the waltzing guinea pig. *Acta Otolaryngol* 1971;72:303–309. [PubMed: 5316984]
3. Spoendlin H. Degeneration behaviour of the cochlear nerve. *Arch Klin Exp Ohren Nasen Kehlkopfheilkd* 1971;200:275–291. [PubMed: 5159190]
4. Wicke W, Welleschik B, Firbas W, Sinzinger H. Streptomycin-induced damage of the spiral ganglion. *Acta Otolaryngol* May-June;1978 85:360–362. [PubMed: 665209]
5. Elverland HH, Mair IW. Hereditary deafness in the cat. An electron microscopic study of the spiral ganglion. *Acta Otolaryngol* Nov-Dec;1980 90:360–369. [PubMed: 7211330]
6. Webster M, Webster DB. Degeneration of cochlear neurons after amikacin intoxication in the rat. *Arch Otorhinolaryngol* Apr;1983 237:201–208. [PubMed: 6870653]
7. Bichler E, Spoendlin H, Rauchegger H. Degeneration of cochlear neurons after amikacin intoxication in the rat. *Arch Otorhinolaryngol* Apr;1983 237:210–218.
8. Staecker H, Kopke R, Malgrange B, Lefebvre P, Van de Water TR. NT-3 and/or BDNF therapy prevents loss of auditory neurons following loss of hair cells. *Neuroreport* Mar;1996 22:889–894. [PubMed: 8724667]
9. Miller JM, Chi DH, O'Keeffe LJ, Kruszka P, Raphael Y, Altschuler RA. Neurotrophins can enhance spiral ganglion cell survival after inner hair cell loss. *Int J Dev Neurosci* Jul;1997 15:631–643. [PubMed: 9263039]
10. Staecker H, Gabaizadeh R, Federoff H, Van De Water T. Brain-derived neurotrophic factor gene therapy prevents spiral ganglion degeneration after hair cell loss. *Otolaryngol Head Neck Surg* Jul; 1998 119:7–13. [PubMed: 9674508]
11. Takeno S, Wake M, Mount RJ, Harrison RV. Degeneration of spiral ganglion cells in the chinchilla after inner hair cell loss induced by carboplatin. *Audiol Neurotol* Sep-Oct;1998 3:281–290. [PubMed: 9705525]
12. Kimura N, Nishizaki K, Orita Y, Y M. 4-methylcatechol, a potent inducer of nerve growth factor synthesis, protects spiral ganglion neurons from aminoglycoside ototoxicity. *Acta Otolaryngol Suppl* 1999;540:12–15. [PubMed: 10445072]

13. Dodson HC, Mohuiddin A. Response of spiral ganglion neurones to cochlear hair cell destruction in the guinea pig. *J Neurocytol* Jul;2000 29:525–537. [PubMed: 11279367]
14. Lee JE, Nakagawa T, Kim TS, et al. Role of reactive radicals in degeneration of the auditory system of mice following cisplatin treatment. *Acta Otolaryngol* Dec;2004 124:1131–1135. [PubMed: 15768804]
15. Klein M, Koede U, Pfister HW, Kastenbauer S. Morphological correlates of acute and permanent hearing loss during experimental pneumococcal meningitis. *Brain Pathol* Apr;2002 13:123–132. [PubMed: 12744466]
16. Teufert KB, Linthicum FH Jr, Connell SS. The effect of organ of Corti loss on ganglion cell survival in humans. *Otol Neurotol* 2006;27:1146–1151. [PubMed: 16885783]
17. Guild SR. A graphic reconstruction method for the study of the organ of Corti. *Anat Rec* 1921;22:141–157.
18. Schuknecht, HF. Pathology of the Ear. Vol. 2nd ed.. Lea & Febiger; Philadelphia: 1993.
19. Chen MA, Webster P, Yang E, Linthicum FH Jr. Presbycusis neuritic degeneration within the osseous spiral lamina. *Otol Neurotol* Apr;2006 27:316–322. [PubMed: 16639268]
20. Nadol JB Jr, Shiao JY, Burgess BJ, et al. Histopathology of cochlear implants in humans. *Ann Otol Rhinol Laryngol* Sep;2001 110:883–891. [PubMed: 11558767]
21. Fayad JN, Linthicum FH Jr. Multichannel cochlear implants: relation of histopathology to performance. *Laryngoscope* Aug;2006 116:1310–1320. [PubMed: 16885730]
22. Ota CY, Kimura RS. Ultrastructural study of the human spiral ganglion. *Acta Otolaryngol* Jan-Feb; 1980 89:53–62. [PubMed: 7405577]
23. Rask-Andersen H, Tylstedt S, Kinnefors A, Schrott-Fischer A. Nerve fibre interaction with large ganglion cells in the human spiral ganglion. A TEM study. *Auris Nasus Larynx* 1997;24:1–11. [PubMed: 9148720]
24. Tylstedt S, Rask-Andersen H. A 3-D model of membrane specializations between human auditory spiral ganglion cells. *J Neurocytol* Jun;2001 30:465–473. [PubMed: 12037463]
25. Koenig W. A new frequency scale for acoustic measurements. *Bell Lab Record* 1949:299–301.

Fig. 1A. Horizontal cross section of the cochlea of case #354 demonstrating missing organ of Corti (a), missing neurites (dendrites) in osseous spiral lamina (b) but surviving spiral ganglion cells (c) in the basal part of the cochlea as well as neurites (d) and ganglion cells in the middle segment. (hematoxylin and eosin X 20)

Fig. 1B.
Cochlear reconstruction of case #354 showing of surviving hair cells (dots), surviving organ of Corti supporting cells without hair cells (mounds), and missing entire organ of Corti (M).

Fig. 1C.

Template for spiral ganglion reconstruction as described by Schuknecht¹⁸ The ganglion is divided into four segments. The number of neurons found on each part of the slide represented in the reconstruction is entered on the corresponding line of the reconstruction The total is added for each section and multiplied by 10, because every tenth section is counted and multiplied by 0.9 to account for cells that might be double counted because of repetition in two slides.

Fig. 1D.

Audio-cytocochleogram of case # 354 indicating, by black filling, loss of inner hair cells (IHC), outer hair cells (OHC), supporting cells, peripheral processes (neurites, dendrites), and stria vascularis. The audiogram is altered to make the frequency response coincide with the area of response within the cochlea.²⁵

Fig. 2.
Audio-cytocochleogram of case #128

Fig. 3.
Audio-cytocochleogram of case #546

Fig 4.
Audio-cytocochleogram of case #575

Table 1
Percent of segmental loss of ganglion cells and hair cells

Case #	segments	hair cells		ganglion cells	
		basal	apical	basal	apical
		1 & 2	3 & 4	1 & 2	3 & 4
354R		100	5	15	0
128L		100	10	35	0
546L		100	30	15	15
575R		100	30	30	25
Mean		100	20	25	10

Table 2

Human vs. Animal neuron survival after deafferentation

	life span	HC loss to GC loss	fraction of longevity
Chinchilla	15Yr.	3Mo.	1%
Cat	12Yr.	12Mo.	8%
Guinea pig	3Yr.	12Mo.	25%
Human	85Yr.	0	0

HC = hair cells GC = ganglion cells