Otology & Neurotology
35:1446–1450 © 2014, Otology & Neurotology, Inc.

Within-Subject Comparison of Word Recognition and Spiral Ganglion Cell Count in Bilateral Cochlear Implant Recipients

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Objectives: Although published reports have not demonstrated a positive correlation between the number of residual spiral ganglion cells (SGCs) and word recognition scores in patients with unilateral multichannel cochlear implants, this study was designed to retest this hypothesis in patients with bilateral multichannel cochlear implants.
Materials and Methods: From a pool of 133 temporal bones, all subjects with bilateral multichannel cochlear implants who were deafened bilaterally by the same etiology were studied. A total of 12 temporal bones from 6 subjects were identified and processed after death for histology. The SGCs were counted using standard techniques. The differences between left and right SGC counts as well as the differences in word recognition scores were calculated for each subject. Correlation analysis was performed between the differences of SGC counts and the differences of word recognition scores.
Results: Differences in SGC counts were highly correlated with the differences in word recognition scores ($R = 0.934$, $p = 0.006$).
Conclusion: This study suggests higher residual SGCs predicted better performance after implantation in a given patient. The results also support attempts to identify factors which may promote survival of SGCs. **Key Words:** Cochlear implantation—Correlation, Performance—Spiral ganglion cell—Word recognition.
Otol Neurotol **35:**1446–1450, 2014.

Spiral ganglion cells (SGC) are the first order neurons that transmit the electrical stimuli generated by cochlear implants to the central nervous system. Thus, it seems reasonable to assume that in subjects with profound hearing impairment, more residual SGCs would result in better word recognition and performance after cochlear implantation. This assumption has been the basis of many studies, which focused on identifying factors that tend to promote the number of SGCs or at least reduce the deleterious effect of insulting factors on the survival of spiral ganglion cells. Seyyedi et al. (1) and Leake et al. (2) reported that chronic bipolar stimulation through cochlear implants has a protective effect on the survival of SGCs. Likewise, It has been reported that some neurotrophins such as brain-derived neurotrophic factor (BDNF), neurotrophin 3 (NT-3) and cometin promote the survival of SGCs in subjects with profound hearing loss (3–5). However, the findings in some human temporal bone studies (6–8) raised a question about the validity of this assumption.

Khan et al. (7), in a postmortem temporal bone study of 15 human subjects with unilateral cochlear implants did not find a significant correlation between the number of residual SGCs in implanted ears and word recognition scores (WRS) after cochlear implantation. Xu et al. (6) reached similar conclusions in a human temporal bone study of 4 subjects. Fayad et al. (8), in histologic examination of 14 implanted temporal bones, reported a statistically significant negative correlation between total SGC count and word recognition scores ($R = -0.632$, $p \leq 0.047$). These conflicting results suggested a need to revisit the question.

The critical factor in any comparison is the context in which the comparison takes place and certainly, comparison between highly matched subjects results in a stronger and more reliable outcome. In all previous human temporal bone studies, SGC counts and word recognition scores were compared across the implanted ears of different subjects, although other variables such as etiology of deafness, central processing, cognitive ability, and age were not controlled across the patients.

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This work was supported by grant R01-DC000152 from the National Institute of Deafness and Other Communication Disorders.
The authors disclose no conflicts of interest.

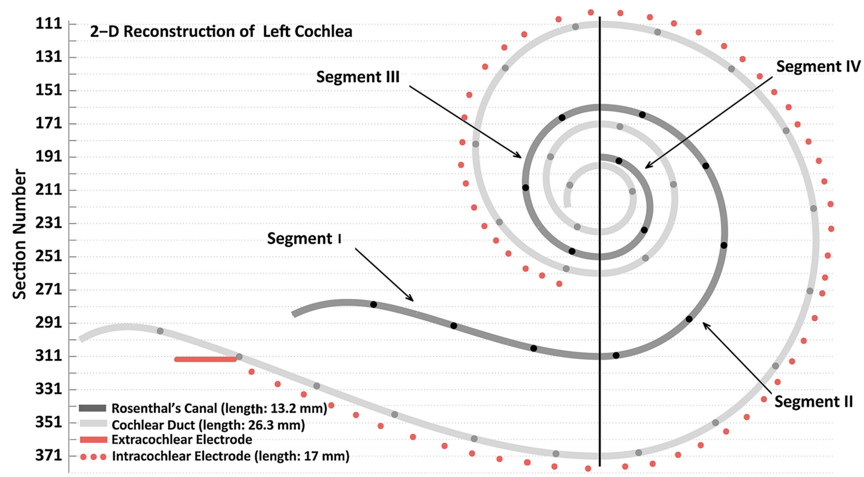

FIG. 1. Two-dimensional reconstruction of left cochlear duct, Rosenthal's canal and path of electrode array of Case 5. The *vertical line* divides Rosenthal's canal to 4 segments. The black circles on Rosenthal's canal and on the cochlear duct are 1 mm apart.

Nadol et al. (9) reported that patients with deafness due to different etiologies had different ranges of residual spiral ganglion cells. They also demonstrated that even in patients within each diagnostic subgroup, there was great variability in the SGC counts. Likewise, in unilateral cochlear implant recipients (6–8), great variability in spiral ganglion cell count was observed in cases with similar word recognition scores.

On the other hand, Seyyedi et al. (10), in an attempt to find a desirable control in temporal bone studies evaluating the impact on SGC survival of a medical intervention, reported that one ear of the patient serves as a desirable control for the other ear. In the study of 42 temporal bones of 21 patients with profound hearing loss, the results demonstrated that the number of surviving spiral ganglion cells was similar between the ears of each patient when both ears of each patient were deafened by the same etiology and both ears had the same level of hearing loss.

Thus, based on the findings of Seyyedi et al. (10) and Nadol et al. (9) and using one ear as the control for the other ear in each patient, we designed this study to evaluate whether differences in word recognition score can be predicted by the differences in SGC count.

SUBJECTS AND METHODS

All 133 implanted temporal bones from the collections of Massachusetts Eye and Ear Infirmary, House Research Institute and University of Minnesota constitute the statistical population of our study. All subjects who met the following criteria were included in the study: 1) bilateral implantation using multichannel cochlear implants; 2) postoperative documented word recognition scores were available for both ears; 3) both ears had been deafened by the same etiology. A total of 12 temporal bones from 6 subjects were identified.

The temporal bones were removed after death, fixed in Heidenhain Susa solution or 10% buffered formalin, and decalcified in ethylene diamine tetra acetic acid (EDTA) and embedded in celloidin (11). The temporal bones were sectioned at a thickness of 20 μm in the horizontal plane, and every tenth section was stained with hematoxylin and eosin and mounted on a glass slide. Rosenthal's canal and the cochlear duct were

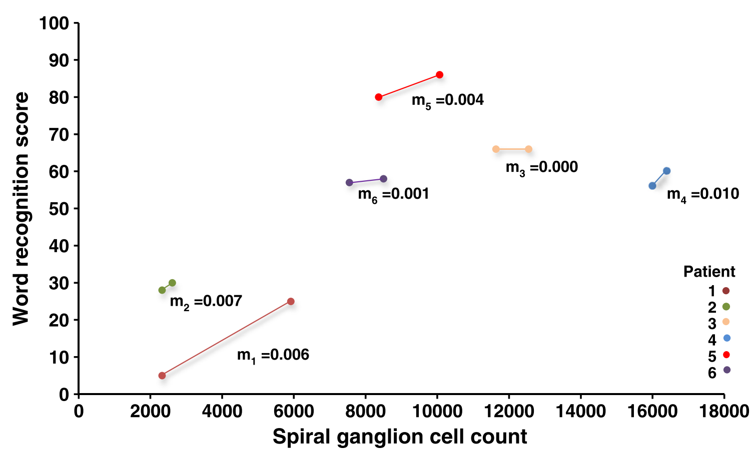

FIG. 2. Word recognition scores plotted as a function of spiral ganglion cell counts. The data points for both ears of each patient were connected by a line. The slope (m) of each line is shown.

TABLE 1. *Demographic data in the 6 patients studied*

Patient	Age	Sex	Age at deafness AS	Age at deafness AD	Deafness etiology
1	66	M	21	21	Bilateral Mondini malformation
2	76	F	34	34	Bilaterally unknown
3	74	F	12	12	Bilateral otosclerosis
4	71	F	58	58	Bilaterally unknown
5	88	M	26	70	Bilateral Ménière's disease
6	83	M	70	70	Bilateral Ménière's disease

AS indicates left; AD, right.

reconstructed in 2 dimensions (Fig. 1) by a method described by Schuknecht (12) and Otte et al. (13), and the length of Rosenthal's canal, cochlear duct and the depth of insertion of the electrode were calculated.

Using the method described by Konigsmark (14) and Nadol (15), all SGCs with visible nuclei were counted on every tenth section by an observer blinded to the performance of patients after implantation. SGC counts for the 4 cochlear segments, identified in Figure 1, were computed by adding all counts across slides from the same segment. Each segmental count was multiplied by 10 to account for unmounted sections and again multiplied by a correction factor of 0.68 (14,15) to account for doubly counted SGCs. The total spiral ganglion cell count was calculated as the sum of the 4 segmental counts (9,15).

To measure the strength of association between the values of word recognition score and SGC count, depth of electrode insertion, duration of implant use, and age at implantation between the ears of each patient, differences were calculated by the subtraction of values of the right ear from the left ear for each variable separately, and then, the differences were compared using Pearson's correlation analysis. For instance, Case 1 had 5916 residual SGCs with 25% WRS on the left and 2326 SGCs with 5% WRS on the right. The differences for SGC and WRS were computed by subtracting the values of right ear from left ear for each variable ($\Delta SGC_{L\text{-}R} = 5916 - 2326 = 3590$; $\Delta WRS_{L\text{-}R} = 25 - 5 = 20$). Similarly, the differences were computed for WRS and SGC in the other 5 cases, and finally, using correlation analysis, the association between the differences of WRS and SGC was evaluated.

To measure the rate of change in word recognition score as a result of a change in spiral ganglion cell count, for each patient, the slope of the line connecting the data points of left and right ears (Fig. 2) was determined, and then, the average of slopes was calculated and tested as to whether it was significantly greater than 0. The slope for each patient was calculated by dividing the difference in WRS between left and right ears by the difference in SGC (slope = m = $\Delta WRS_{L\text{-}R} / \Delta SGC_{L\text{-}R}$). The average of 6 slopes was computed, and 1-sample *t* test (one-tailed) was used to evaluate whether the calculated average was statistically greater than 0. A positive slope suggested that an increase in spiral ganglion cell count was correlated with a higher word recognition score.

RESULTS

From 133 temporal bones, 12 temporal bones from 6 patients who were implanted bilaterally during their life with multi-channel electrodes met the criteria for inclusion. As shown in Table 1, there were 3 male and 3 female subjects with an average age of 76 years. The etiology of deafness and the age at deafness (except in Case 5) were the same across the ears of each patient. In all subjects, both ears were deafened postlingually, and PTA test results bilaterally showed profound hearing impairment before implantation. In 3 of 6 patients, both ears were implanted at the same time with the same type of electrode using a similar mode of stimulation and strategy (Table 2). In three others, there was an interval between the implantation of both sides that varied between 2 and 11 years.

Tables 3 and 4 illustrate the total spiral ganglion cell counts, word recognition scores, the depths of electrode insertion in the cochlea, duration of cochlear implant use, age at implantation, and the differences across the ears of each patient (left-right). The evaluation of performance after cochlear implantation was reported using CNC scores in all cases except Case 5 in which only the HINT scores were available. All word recognition scores used in the equations were the last available measurements, which were measured bilaterally for each patient at the same time. As can be seen in Table 3 and Figure 2, in the comparison across all 12 ears, the 4 ears with the largest number of residual SGCs did not have the highest word recognition scores. It can be seen also in Figure 2 that despite having similar word recognition scores, Cases 3, 4, and 6 had great variability in SGC count.

Interaural comparison demonstrated (Fig. 2) that patients with small differences in word recognition scores between both ears had small differences in surviving spiral ganglion cell counts and patients with larger differences had larger differences in spiral ganglion cell counts. Even more importantly, comparison between the

TABLE 2. *Cochlear implant and strategies used in the 6 patients*

Patient	Left ear CI device	Left ear Stimulation mode	Left ear Strategy	Right ear CI device	Right ear Stimulation mode	Right ear Strategy
1	Nucleus 22	BP	SPEAK	Nucleus 24 C	MP	ACE
2	Nucleus 24 M	MP	SPEAK	Nucleus 22	BP	SPEAK
3	Hi Focus	MP	Hi Res 90k	Hi Focus	MP	Hi Res 90k
4	Nucleus 24 M	MP	SPEAK	Nucleus 24 M	MP	SPEAK
5	Nucleus 22	BP	SPEAK	Nucleus Advance	MP	ACE
6	Nucleus 24 M	MP	SPEAK	Nucleus 24 M	MP	SPEAK

AS indicates left; AD, right; BP, bipolar; MP, monopolar; CI, cochlear implant.

TABLE 3. *Spiral ganglion cell counts, word recognition scores, depth of insertion, and other variables of the left and right ears of 6 patients*

	Right ear					Left ear				
Patient	WRS	SGC count	DI	Duration of IM use	Age at IM	WRS	SGC count	DI	Duration of IM use	Age at IM
1	5	2326	6	1	65	25	5916	11	18	48
2	28	2326	17.8	4	70	30	2611	17.3	2	74
3	66	11635	18.3	8	66	66	12546	19.6	8	66
4	56	16000	19	11	60	60	16401	19.8	11	60
5	86	10064	10.6	6	82	80	8364	17	11	71
6	57	7548	19	12	71	58	8500	16.4	12	71

WRS indicates word recognition score; SGC, spiral ganglion cell; IM, implantation; DI, Depth of electrode insertion (mm).

ears of each patient showed that all the ears with higher score in word recognition had a higher spiral ganglion cell count (except Case 5).

Pearson's correlation analysis was used to determine how the differences in SGC count, depth of electrode insertion, duration of cochlear implant use, and age at implantation were associated with the difference in word recognition score. The results of correlation analysis (Table 5) showed that there was a significant positive correlation between the differences of word recognition scores and SGC counts between the ears of each patient ($R = 0.934$, $p = 0.006$). There was no correlation between the differences of word recognition scores and the depth of electrode insertion (Table 5). Likewise, there was no significant correlation between the differences in duration of cochlear implant use, age at implantation, and word recognition scores between the ears of each patient.

As shown in Figure 2, all had positive slopes except Case 3 in which the slope was 0. The average of slopes was 0.005, and the t test showed that it was significantly greater than 0 (t_5= 2.950 and $p_{\text{(one–tailed)}} = 0.016$). The slope of 0.005 implies that an increase of 1000 spiral ganglion cells was correlated with an increase of 5% in word recognition score.

DISCUSSION

The outcome of cochlear implantation is evaluated by postoperative speech perception and word recognition scores. A wide spectrum of variables may affect post-implantation speech perception (16–18). These factors can be classified into 2 major groups: 1, device-related factors such as electrode design, configuration, and processing strategy; and 2,- patient's variables such as duration of deafness, duration of cochlear implant use, depth of insertion, age, age at implantation, etiology of deafness, and auditory neuroplasticity.

Otte et al. reported a positive correlation between the number of SGCs and word recognition score in a study of 82 unimplanted human temporal bones (13). In implanted animals, a correlation between psychophysical parameters and residual spiral ganglion cell counts was reported (19,20). However, 2 histopathologic human temporal bone studies (6,7) reported no correlation between word recognition score and spiral ganglion cell count in implanted ears, and surprisingly, Fayad and Linthicum (8) reported a significant negative correlation between the number of residual SGCs and the performance after cochlear implantation.

In all previous human studies of implanted ears (6–8), the SGC count and word recognition score of 1 patient were compared with the same variables in other patients where other possible factors affecting word recognition were not controlled. If we treat our data in a similar fashion as done in previous studies (6–8) (one ear from each patient), correlation analysis between word recognition scores and associated spiral ganglion cell counts yield similar results that is no significant correlation ($R = 0.599$, $p = 0.2$, n = 6).

Nadol et al. (9) showed widely variable SGC count in patients with profound deafness with different etiologies of deafness and a similar PTA and in patients with a similar etiology of deafness and similar levels of hearing loss. Likewise, in the previous human studies (6–8), there were many cases with similar speech discrimination scores, which had wide variability in spiral ganglion cell

TABLE 4. *The differences between the left and right ear values of spiral ganglion cell counts, word recognition scores, depth of insertion, and other variables in the 6 patients*

Patient	AS-AD WRS	AS-AD SGC count	AS-AD DI	AS-AD duration of IM use	AS-AD age at IM
1	20	3590	5	17	−17
2	2	285	−0.5	−2	4
3	0	911	1.3	0	0
4	4	401	0.8	0	0
5	−6	−1700	6.4	5	−11
6	1	952	3.5	0	0

AS indicates left; AD, right; WRS, word recognition score; SGC, spiral ganglion cell; IM, implantation; DI, Depth of electrode insertion (mm).

TABLE 5. *Bivariate correlation analysis of selected clinical variables in the 6 patients*

	AS-AD WRS	Sig. (2-tailed)	n
AS-AD WRS	1	—	6
AS-AD SGC count	0.934[a]	0.006	6
AS-AD DI	0.167	0.751	6
AS-AD duration of IM use	0.760	0.079	6
AS-AD age at IM	−0.512	0.300	6

AS indicates left; AD, right; WRS, word recognition score; SGC, spiral ganglion cell; DI, depth of electrode insertion; IM, implantation.
[a]Correlation is significant at the 0.05 level (2-tailed).

counts. This suggests that there are other factors that may alter the correlation of spiral ganglion cell counts with word recognition scores, and comparison across the ears of different patients is not valid unless the effect of all other confounding factors are controlled across the ears.

On the other hand, a previous report (10) demonstrated that spiral ganglion cell counts in patients with symmetrical bilateral profound deafness were statistically not different in both ears of a given subject, if both sides were deafened by the same etiology. These findings suggested that a study of the correlation between the number of residual spiral ganglion cells and word recognition scores in cases with bilateral cochlear implants using one ear as the control for the other ear, where many variables such as etiology of deafness, age, and cognitive ability had been controlled was warranted. This matching technique in the methodology resulted in a very strong correlation between differences in word recognition score and differences in spiral ganglion cell count (R = 0.934, p = 0.006, n = 6), which confirms the assumption that a larger number of surviving spiral ganglion cells result in better performance after cochlear implantation in a given patient. This implies that in bilaterally implanted patients deafened bilaterally by the same etiology, patients have minimally different word recognition scores when they have roughly equal spiral ganglion cell counts in both ears and when there is a meaningful difference in word recognition score across the ears, the ear with greater residual spiral ganglion cell count tends to have a better performance. In this study, the findings of Otte et al. (13) in unimplanted ears were confirmed in ears with cochlear implantation. In the other bivariate correlation analyses, duration of cochlear implant use, depth of insertion, and age at implantation did not show a significant correlation with word recognition score. The effect of these factors was variable in previous reports (17,18,21,22).

CONCLUSION

The results of this study suggest that the number of surviving spiral ganglion cells is positively correlated with word recognition scores after implantation in a given patient. This finding supports efforts to protect SGCs against deleterious factors such as implantation trauma.

Acknowledgments: The authors thank Dr. Hang Lee from Harvard Catalyst Group for his statistical consultation.

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