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Factors affecting auditory performance of postlinguistically deaf adults using cochlear implants: an update with 2251 patients*.

* The authors are listed in alphabetical order, except for the first and last authors.

Peter Blamey^{1,2}, Françoise Artieres^{3,4}, Deniz Başkent^{5,6}, Francois Bergeron⁷, Andy Beynon⁸, Elaine Burke⁹, Norbert Dillier¹⁰, Richard Dowell², Bernard Fraysse¹¹, Stéphane Gallégo¹², Paul J Govaerts¹³, Kevin Green¹⁴, Alexander M Huber¹⁰, Andrea Kleine-Punte¹⁵, Bert Maat⁵, Mathieu Marx¹¹, Deborah Mawman¹⁴, Isabelle Mosnier¹⁶, Alec Fitzgerald O' Connor⁹, Stephen O'Leary², Alexandra Rousset², Karen Schauwers¹³, Henryk Skarzynski¹⁷, Piotr H Skarzynski^{17,18}, Olivier Sterkers¹⁶, Assia Terranti¹⁹, Eric Truy¹², Paul Van de Heyning¹⁵, Frédéric Venail⁴, Christophe Vincent¹⁹, Diane S Lazard^{1,16}.

1. Bionics Institute, Melbourne, Australia
2. Department of Otolaryngology, The University of Melbourne Cochlear Implant Clinic, The Royal Victorian Eye and Ear Hospital, Melbourne, Australia
3. Institut Saint Pierre Service d'Audiophonologie et ORL, Palavas les flots, France
4. CHU Gui de Chauliac, Service d'ORL et Chirurgie Cervico-Faciale, Montpellier, France
5. Department of Otorhinolaryngology / Head and Neck Surgery, Cochlear Implant Center Northern Netherlands, University Medical Center Groningen, University of Groningen, The Netherlands
6. Graduate School of Medical Sciences, Research School of Behavioural and Cognitive Neurosciences, University of Groningen, The Netherlands
7. Faculté de médecine, Université Laval, Québec, Canada
8. Otorhinolaryngology, Radboud University Nijmegen Medical Center, The Netherlands
9. St Thomas' Hospital, Auditory Implants Department, London, United Kingdom
10. Department of Otorhinolaryngology, University Hospital of Zurich, Zurich, Switzerland
11. Hôpital Universitaire Purpan, Service d'ORL et Chirurgie Cervico-Faciale, Toulouse, France
12. Hospices Civils de Lyon, Hôpital Edouard Herriot, Département d'ORL, de Chirurgie Cervico-Maxillo-Faciale et d'Audiophonologie, Lyon, France
13. The Eargroup, Antwerp, Belgium
14. University of Manchester, Central Manchester University Hospitals NHS Foundation Trust, Manchester, United Kingdom
15. Univ Dept Otorhinolaryngology and Head and Neck Surgery, Antwerp University Hospital, University of Antwerp, Belgium
16. AP-HP, Hôpital Beaujon, Service d'ORL et Chirurgie Cervico-Faciale, Clichy, France
17. Institute of Physiology and Pathology of Hearing, Warsaw, Poland
18. Institute of Sensory Organs, Kajetany, Poland
19. Service d'otologie et d'otoneurologie, hôpital R.-Salengro, CHRU de Lille, Lille, France.

Short title: Predictors of CI outcome in postlingual deafness

Corresponding author:

Diane Lazard, dianelazard@yahoo.fr

Bionics Institute, 384-388 Albert Street, East Melbourne, VIC 3002, Australia

P +61 3 9667 7500; F +61 3 9667 7518

Abstract

Objective: To update a 15-year-old study of 800 post-linguistically deaf adult patients showing how duration of severe to profound hearing loss, age at cochlear implantation (CI), age at onset of severe to profound hearing loss, etiology and CI experience affected CI outcome.

Study design: Retrospective multi-centre study

Methods: Data from 2251 adult patients implanted since 2003 in 15 international centres were collected and speech scores in quiet were converted to percentile ranks to remove differences between centres.

Results: The negative effect of long duration of severe to profound hearing loss was less important in the new data than in 1996; the effects of age at CI and age at onset of severe to profound hearing loss were delayed until older ages; etiology had a smaller effect; and the effect of CI experience was greater with a steeper learning curve. Patients with longer durations of severe to profound hearing loss were less likely to improve with CI experience than patients with shorter duration of severe to profound hearing loss.

Conclusions: The factors that were relevant in 1996 were still relevant in 2011, although their relative importance had changed. Relaxed patient selection criteria, improved clinical management of hearing loss, modifications of surgical practice, and improved devices may explain the differences.

Key words: cochlear implant; percentile rank; hearing loss; plasticity; general linear model; predictors; learning curve; multicentre.

Introduction

The outcome measures for adult recipients of cochlear implants vary over a wide range, and it is of scientific and clinical relevance to understand the factors underlying this variability. In 1996, a retrospective analysis of speech recognition in quiet for 808 postlinguistically deafened adults using cochlear implants (CIs) described clinical predictors that accounted for 21% of the variance in CI performance [Blamey et al., 1996]. This is still the largest study that has been published, although there are numerous other papers that have considered smaller datasets and generally concentrated on a few factors [Cullen et al., 2004; Durisin et al., 2010; Finley et al., 2008; Green et al., 2007; Mack et al., 2006; Matterson et al., 2007; Rubinstein et al., 1999; Yukawa et al., 2004].

The factor accounting for the largest proportion of the variance in the 1996 study was duration of deafness, defined as the time between the onset of profound hearing loss (pure-tone hearing threshold average PTA \geq 90 dB HL) and the date of implantation. Longer duration of deafness negatively influenced the outcomes. Two factors, linked to the duration of deafness, age at onset of deafness and age at implantation, were also negatively correlated with the outcomes. Within the etiologies, bacterial labyrinthitis resulted in poorer outcomes than the average for all etiologies and Meniere's disease resulted in better than average outcomes. The duration of implant experience played a positive role yielding increasing performance up to three years postoperatively.

The typical patient journey was described in a three-stage model of auditory performance over time, taking into account the factors above (Figure 1). The first stage corresponded to the period of normal hearing in a postlinguistically deaf population with auditory performance of 100% (on a speech perception task, for example). Stage 2 began at the onset of profound hearing loss with a drop in auditory performance, which was assumed to be abrupt. A variable effect of etiology on the potential CI outcome was incorporated into the model. The following

evolution encompassed gradual changes of the peripheral and central auditory system, whose effect depended on the duration of auditory deprivation. The third stage corresponded to the period starting from implantation, showing a learning curve that may have reflected several factors such as devices, speech processing strategies, surgical trauma and surgical placement of the electrode array, existence and type of rehabilitation, cerebral reorganization, etc,

Even though this model and the factors considered by Blamey et al. in 1996 [Blamey et al., 1996] are still relevant, the model may be improved and better understood in the light of new findings. Indeed, the development of improved neurofunctional investigations has led, for example, to better understanding of auditory cortex maturation in prelinguistic deafness [Finney et al., 2001; Lee et al., 2001] and of cognitive factors that may influence CI outcome in postlinguistic deafness [Lazard et al., 2011; Lazard et al., 2010b; Lee et al., 2007; Strelnikov et al., 2010]. These new findings in postlinguistic deafness research may improve the description of auditory performance proposed in the model.

Moreover, many factors have changed substantially since 1996 and may influence outcomes in different ways. In the intervening 15 years, CI eligibility requirements have become less restrictive. In 1996, the majority of the patients being implanted were bilaterally profoundly deaf, i.e. the Pure Tone Average threshold at 500, 1000, and 2000 Hz (PTA) was greater than 90 dB HL and their pre-operative open-set sentence recognition score with best-fitted hearing aids and without lipreading was less than 30% [NIH Consensus conference, 1995]. Indications were later extended to sentence recognition scores with best-fitted hearing aids less than 60%, following the findings that patients with residual hearing could also benefit from a CI [Cullen et al., 2004; Dooley et al., 1993; Kiefer et al., 1998; Lenarz, 1998; Rubinstein et al., 1999]. These days, bimodal listening, i.e. combining the use of a CI on one side and the use of a hearing aid on the other ear [Armstrong et al., 1997] or on the same ear [Hodges et al., 1997], is widely recommended for CI recipients with residual hearing [Ching

et al., 2004; Firszt et al., 2008; Gifford et al., 2010]. Access to information has changed dramatically with the advent of the internet, providing greater awareness of rehabilitation opportunities. The proportion of candidates for a CI with long durations of profound deafness should be smaller, because patients are being operated on earlier in the time course of their deafness. Thus, compared to the 1996 study, the proportion of speech scores in the high range, preoperatively and postoperatively, is likely to be greater nowadays, and the effect of duration of severe to profound deafness may be less strong in the CI population in light of greater residual hearing and improved hearing aid technology prior to cochlear implantation [Blamey, 2005; Johnson et al., 2010; McDermott, 2011].

Nowadays, meningitis (bacterial labyrinthitis) and temporal bone fracture are considered “surgical emergencies”. The surgery is preferably performed within the month following the disease in order to insert the electrode-array before the occurrence of cochlear ossification that would compromise a full insertion [Durisin et al., 2010]. The outcome for patients presenting with these two etiologies is likely to have improved comparatively to 1996, due to improved screening, less ossification, and deeper insertion.

It is also likely that the proportion of patients older than 70 and even 80 years old at the time of their CI operation is greater in 2011. The improvements in anesthesiology [Coelho et al., 2009], the standardization and reduction of the time required for the surgical procedure [Loh et al., 2008; Mack et al., 2006] may have simplified the whole procedure, extending the indications to more fragile patients.

The surgical procedure has been improved due to better knowledge of the histological modifications and trauma it may induce [Handzel et al., 2006; Somdas et al., 2007], and better knowledge of the importance of electrode-array placement within the scala tympani versus the scala vestibuli [Finley et al., 2008; Skinner et al., 2002], leading to the concept of

“soft surgery” [Frayssse et al., 2006; Friedland and Runge-Samuelson, 2009]. These modifications in medical practice should result in fewer extremely poor performers and in better retention of residual hearing in the implanted ear [Frayssse et al., 2006].

Finally, devices have improved in the last 15 years. In the 1996 article, the coding strategies used by the patients were F0F2, F0F1F2 and MPEAK. These strategies are not used anymore and have been replaced by Continuous Interleaved Sampling (CIS), and spectral-maxima (ACE or N-of-M) strategies [Loizou, 2006]. Other sound processing has been added, such as ADRO® (Adaptive Dynamic Range Optimization) that selects the most information-rich part of the signal and restores it to the optimal part of the listener’s dynamic range [Blamey, 2005]. Other modifications in stimulation rates [Di Lella et al., 2010] or settings [James et al., 2003] have been implemented by each manufacturer, bringing improvements in outcomes [Firszt et al., 2009; Lazard et al., 2010a]. Such modifications, by easing central deciphering of CI stimulation of the auditory nerve, should result in better speech understanding in the whole of the CI population, with a shift of the distribution toward higher speech perception scores.

The aim of the present study was to explore the effects listed above in a larger group of more recent CI recipients using the same methods, model, and statistical analysis as in the 1996 article.

Methods

This project was approved by the Royal Victorian Eye and Ear Hospital Human Research Ethics Committee (Project 10/977H, Multicentre Study Of Cochlear Implant Performance In Adults). Fifteen centres from Australia, Europe, and North America participated, the co-authors generously providing access to the records from their clinics.

Retrospective data from 2251 patients were collected. Selection criteria, similar to the 1996 study, were:

- Adult at the time of implantation. The youngest patient included was 17 years old when implanted.
- Onset of severe to profound hearing loss after the age of 15, for equivalent speech and language acquisition across subjects. The definition for severe to profound hearing loss was as in [Lazard et al., 2011; Lazard et al., 2010b]. It referred to the time from when the patient could no longer use hearing alone to communicate (*i.e.* without lipreading), even with the best-fitted hearing aids, and/or understand TV, and/or stopped using the telephone. This definition implicitly included consideration of PTA, but not explicitly, because of the discordance between PTA and speech recognition abilities sometimes observed in clinical practice. This discordance is particularly obvious for patients with auditory neuropathy spectrum disorder (ANSO) [Deltenre et al., 1997; Rance et al., 1999]. When the onset of deafness was different for the two ears, the shorter duration was chosen, *i.e.* the time when all useful auditory input to the central auditory system ceased. The dates of onset for each ear were estimated by practitioners within each clinic.
- Four brands of CIs were included (Advanced Bionics, Cochlear, Med-el, and Neurelec). Their proportions in the sample were 21%, 50%, 17%, and 7%, respectively (plus 5% missing data for this variable).
- Date of implantation after 2002 for all recipients to ensure technical improvements comparable across brands.

Two postoperative speech intelligibility scores in quiet for each recipient were requested from the clinics: one score collected early after activation of the CI (T1) and one score collected later (T2). The choice of the date of the tests was free and varied between and within centres.

However, within each centre, all the subjects were tested with the same test material. In total, 3787 speech perception test scores in quiet were received (1934 for T1 and 1853 for T2).

Statistical analyses

As in the 1996 study, the fundamental assumptions behind the analysis were that the patient groups from each centre were independent but similar samples from the same population, and that the different auditory performance measures and languages used in each clinic would not affect the rank ordering of patient scores from lowest to highest. Figure 2 shows four examples of pre-operative and post-operative score distributions for different auditory performance measures used by some clinics. To combine different speech test scores in quiet (phonemes, monosyllabic words, disyllabic words, sentences) in different languages and different levels of presentation (from 55 to 75 dB SPL), a percentile rank for each patient within each centre, was calculated from the speech test scores. In order to include the effect of CI experience (i.e. the effect of time postoperatively) the scores at T1 and T2 were both included in the rankings. Using ranking removes differences in clinic practice without removing the relative differences between patients within each clinic. Indeed, for each clinic, the distribution varied uniformly from 0 to 100. The best performers from each centre had a percentile rank close to 100, and the poorest performers from each group had a percentile rank close to 0. The ranked data of the centres were combined for the global analysis. For further details on ranking, please refer to [Blamey et al., 1996].

Similarly to the 1996 analysis, the same independent factors were chosen and partitioned into ranges (although note that the definitions of the onsets of severe to profound hearing loss were slightly different). The means of the ranges were compared using a four-factor unbalanced analysis of variance using the General Linear Model (GLM; Minitab version 12). The first factor was *duration of severe to profound hearing loss* defined as the time in years

between the onset of severe to profound hearing loss and the date of implantation. The ranges for duration of severe to profound hearing loss were 0-4, 5-9, 10-14, 15-19, 20-24, 25-34, 35-44 and over 45 years. The second factor, *age at onset of severe to profound hearing loss* was split into the ranges 15-29, 30-39, 40-49, 50-59, 60-69, 70-79, and 80 or over years. The classification for age at onset was slightly different from the 1996 classification in which the two first ranges were 0-9, and 10-19 and stopped at 70 or over years. *Duration of implant experience* was defined as the time elapsed between the date of first activation and the dates of testing (T1 and T2). It was divided into the same ranges as the 1996 analysis, i.e. 0-5, 6-11, 12-23, 24-35, 36-47, and over 47 months. Classes of *etiologies* were slightly different from the previous analysis. “Autoimmune” and “viral labyrinthitis” etiologies were regrouped into “labyrinthitis” because the differences in etiopathology of these two diseases are not perfectly understood and these sub-groups displayed similar performance in the 1996 dataset. To avoid confusion, “bacterial labyrinthitis” was renamed “meningitis”. The “traumatic” etiology was split into 3 new groups: “temporal bone fracture”, “acoustic trauma” and “pressure trauma”, as the consequences for nerve survival and ossification are not necessarily the same for all trauma [Kujawa and Liberman, 2009; Serin et al., 2010]. As “congenital syphilis” was not reported in the new dataset, this etiology was omitted. Four new categories were added to the list of etiologies in the 1996 study: “auditory neuropathy spectrum disorder (ANSO)” (diagnosed on clinical and electrophysiological features), “chronic otitis media”, “acoustic neuroma” (regrouping isolated cases or those included in a neurofibromatosis), and “miscellaneous”. “Miscellaneous” included non-genetic congenital etiologies, cerebral ischemia, drepanocytosis, cephalic trauma without temporal bone fracture, etc. The final factor, *age at implantation*, was partitioned as follows: 17-29, 30-39, 40-49, 50-59, 60-69, 70-79, and 80 or over years. The oldest group (80 or over years) was added, compared to the 1996 analysis, because of broadened inclusion criteria in the past 10 years. Because *age at*

implantation is equal to the sum of age at onset of severe to profound hearing loss and duration of severe to profound hearing loss, at most two of these three variables should be included in a single statistical analysis to avoid violating the requirement for independent factors. For this reason, two GLM analyses were performed excluding one or the other age factor. The results are detailed in the result section.

The dependent variable used for the GLM analyses was the percentile ranked score. In total, 1856 patients had complete data for the independent variables listed above and at least one ranked score at T1 and/or T2. Technically, a repeated measures analysis should be used for these data since there were ranked scores for both T1 and T2 for most subjects. Our statistics software was unable to analyse an unbalanced repeated measures design for 1856 subjects, and so the design was simplified by selecting only one ranked score for each subject. When there were ranked scores for both T1 and T2, one was chosen randomly. Five different randomizations were performed for each analysis and the range of statistical results are reported in Table 1.

Data from the 1996 analysis were not available for specific statistical comparisons, such as modifications of clinical characteristics (amount of residual hearing in the two samples, HA use, etc).

Results

The mean age at implantation per centre ranged from 48 to 65 years, and the mean duration of severe to profound hearing loss per centre ranged from 2 to 13 years.

The ANOVA statistics for two analyses are shown in Table 1. Table 1a includes age at CI as a factor and Table 1b includes age at onset of severe to profound hearing loss as a factor.

Similarly to the 1996 analysis, all tested factors had a significant main effect (Table 1).

Nevertheless, the relative influence of each factor was different from the 1996 study. In 1996,

duration of severe to profound hearing loss accounted for more of the variance than the other factors. Then came age at onset of severe to profound hearing loss or age at implantation, etiology, and finally duration of CI experience. In 2011, duration of CI experience had the largest effect (F ranged from 12.03 to 20.67, from the 5 different randomizations), followed by age at onset of severe to profound hearing loss or age at implantation, duration of severe to profound hearing loss, and etiology. The four factors accounted for an average of 9.5% of the variance using age at CI as a factor and 10.5% of the variance using age at onset of severe to profound hearing loss as a factor. These percentages were calculated as (Total sum of squares – Error sum of squares) / Total sum of squares.

For convenience, the description of the results for each factor follows in the order used in 1996, and the graphs compare the older and newer data directly. Wherever possible, the complete dataset of 3787 ranked scores were used in the graphs, and the numbers on the graphs refer to the number of data points, not the number of subjects.

Duration of severe to profound hearing loss

Figure 3a shows the averaged percentile rank as a function of duration of severe to profound hearing loss for results from the 1996 and 2011 analyses. A negative influence of duration of severe to profound hearing loss was observed in both studies, but it was less important in 2011 than in 1996, with a 19% difference between the two extreme ranges in 2011 vs. 48% in 1996, mainly due to the dramatic drop for durations more than 45 years observed in 1996 but not observed in 2011. Mean percentile ranks of this sub-group (durations more than 45 years) were not significantly different from the 35-44 year sub-group, in 2011.

Averaged percentile ranks for the 2011 dataset were subsequently graphed separately for times of testing T1 and T2 (Figure 3b). On average, the range of time of testing for T1 was 0.3-0.6 years, and the range of time of testing for T2 was 1.2-2 years. The groups with the

smallest durations of severe to profound hearing loss were tested at 0.5 (T1) and 2 (T2) years, on average, and the groups with the longest durations of severe to profound hearing loss were tested at 0.5 (T1) and 1.3 (T2) years, on average. The graphic representation shows that the amount of gain in performance between T1 and T2 is smaller in case of longer durations of severe to profound hearing loss: + 17.8% for the group with the shortest durations of severe to profound hearing loss and + 9.4% for the group with the longest durations of severe to profound hearing loss. The smaller gain in performance may have been partially due to the shorter period of CI experience in the recipients with long durations of severe to profound hearing loss. The improvement was significantly greater than zero for patients presenting with durations of severe to profound hearing loss less than 30 years, while it was not for patients with longer durations. The error bars extending ± 2 standard errors are approximately equivalent to the 95% confidence interval for each mean value shown on the graph. The confidence intervals for patients presenting with long durations of severe to profound hearing loss were wider due to the smaller numbers of data points contributing to the mean values.

Age at implantation

Age at implantation had a negative influence on the outcomes for ages over 60 years in 1996, and for ages over 70 years in 2011 (Figure 4). The shapes of the performance versus age at implantation curves were similar in the two studies but the effect of age was delayed by about ten years in the more recent study. Age at implantation accounted for about 2.86 % of the variance in the 2011 data. A greater number of older patients (70 + years) were being implanted in 2011 than in the 1996 study. They represented 8% in 1996 versus 28% in 2011 (21% for the range 70-79 and 7% for the range 80+).

Age at onset of severe to profound hearing loss

Increasing age at onset of severe to profound hearing loss from 15 to 79 years yielded 21% decrease in performance in 1996 and 11% in 2011 (Figure 5), the group 60-69 years performing significantly better in 2011 than in 1996. A significant drop in outcome was observed in 1996 for the range 60-69 years. In 2011, this drop was significant from 70 years onwards. The average age for the range 70-79 years of the 2011 analysis was the same as the range 70 and over years of the 1996 analysis, while a new category (80 + years) was added in 2011. The effect of age at onset appears to be delayed by about ten years in the 2011 dataset compared by the 1996 dataset. Age at onset of severe to profound hearing loss accounted for about 3.30 % of the variance in the 2011 data.

Etiology

Figure 6 shows mean residual percentile rank for each etiology. The “unknown etiology” group was by far the largest, including about 50% of the patients in 1996 and 2011. The ANSD sub-group performed significantly below the average of all etiologies ($p = 0.03$), while genetic and Meniere’s disease groups performed above the average ($p = 0.001$ and $p = 0.04$, respectively). The Meniere’s disease group also performed significantly better than average in 1996. Meningitis patients performed close to average in 2011, while they performed lower than average in 1996. The three sub-groups for cochlear ossification, labyrinthitis, meningitis, and temporal bone fracture, performed similarly to each other in 2011.

Duration of implant experience

Performance increased as a function of duration of implant experience up to 3.5 years after implantation (Figure 7). The amount of improvement was about 10% in 1996 and 20% in 2011, with a steeper slope within the first year of experience. CI experience was the most significant factor in the analyses with the largest F values in 2011 ($12.03 < F(5,1823) < 20.67$ in the 5 different randomizations, $p < 0.001$), and one of the least significant factors in 1996

($F(5,1033) = 3.66, p = 0.003$). The slight decrease in performance observed after 5 years of CI use in 2011 was not statistically significant.

Discussion

The present study aimed to update and compare the results of a previous published study [Blamey et al., 1996] about predictors of auditory performance of post-linguistically deaf adults receiving a CI. Similarly to the 1996 study, percentile ranking of speech scores was used in order to combine data from different centers. However, as in 1996, the assumption that the patient groups from each centre were similar samples from the same population may not be applicable for all the factors. For example, the mean age at implantation and the mean duration of severe to profound hearing loss per centre were different, indicating that there may have been significant differences in the populations treated by each centre. In this case, the use of ranking may have reduced the natural variation between the samples and therefore reduced the relative effects of some factors, including the effect of age at implantation and duration of severe to profound hearing loss. Constraints imposed by the multicentre nature of these studies make it impossible to check this possible bias, but the effects of the factors are more likely to be underestimated than overestimated in the study, by the use of percentile ranking.

A second caveat arises from the use of separate percentile ranks in 1996 and 2011. This means that equal ranks in 1996 and 2011 do not imply equal speech perception scores and we cannot detect changes in the absolute levels of performance that may have occurred between 1996 and 2011. Therefore, because the raw data from 1996 are no longer available, our discussion is constrained to cover only changes in the relative importance of different factors between 1996 and 2011. We may speculate as to whether these changes in relative

importance are due to changes in absolute performance arising from improvements of devices or surgical and medical practices, but direct evidence for such improvements can only come from direct comparison of raw scores for patients implanted at different times, with different devices, and with different surgical techniques (e.g. [Dowell, 2012; Rubinstein et al., 1999]).

Although the factors affecting auditory performance of CI recipients in the earlier study also had statistically significant effects in 2011, the detailed patterns observed in the data were different between the two studies. Before commencing the discussion, we will firstly consider the basic physiological processes that affect auditory performance and may have given rise to the observed positive and negative effects of the factors in the analyses, and then we will speculate on the possible reasons for the changes in patterns observed between 1996 and 2011.

Table 2 of Blamey et al. [Blamey et al., 1996] listed the physiological processes affecting auditory performance as: bone growth, malformation, decalcification, disease, trauma and toxicity associated with etiology; natural degeneration of peripheral and central neurons (in their numbers and functions) associated with age; accelerated degeneration of peripheral and central neurons associated with severe to profound hearing loss; plasticity, learning, and protective effects associated with cochlear implant experience and with electrical stimulation of the cochlea. All of these physiological processes are still thought to be relevant, although it is becoming clearer that plasticity changes and degeneration of central auditory processing play a much more important role than peripheral factors such as the number of surviving spiral ganglion cells [Moore and Shannon, 2009]. Theoretically, the number and distribution of spiral ganglion cells ought to have a significant effect on basic auditory perception measures [Cohen, 2009]. In 1996, there was no strong evidence that the number of spiral ganglion cells affected cochlear implant outcomes, and so far as the authors are aware, no strong evidence has emerged since 1996 [Blamey, 1997; Khan et al., 2005; Nadol and

Eddington, 2006]. In contrast, there is strong emerging evidence that central factors such as plasticity and central auditory processing are highly significant [Champoux et al., 2009; Doucet et al., 2006; Giraud and Lee, 2007; Lee et al., 2007; Moore and Shannon, 2009; Rouger et al., 2007; Strelnikov et al., 2010].

The basic effects of the physiological processes are unlikely to have changed between 1996 and 2011. Therefore, the different patterns in the data must be due to differences in the patients in the two studies, improvements in surgical and clinical practice, and/or differences in the cochlear implant devices. We speculate that these factors are all needed to explain the data. Patient differences are likely to have arisen because of relaxation of CI patient selection criteria [Cullen et al., 2004; Dooley et al., 1993; Kiefer et al., 1998; Lenarz, 1998; Rubinstein et al., 1999], and because of improvements in the management of hearing loss during stage 2 of the model, such as improvements in hearing aid technology [Blamey, 2005; Johnson et al., 2010; McDermott, 2011]. Evidence for differences between the patients in the two studies can be seen in Figure 3a where the median duration of severe to profound hearing loss was about 8 years in the 1996 dataset and 4 years in the 2011 dataset. In Figure 5 the median age at onset of severe to profound hearing loss was about 39 years in 1996 and 52 years in 2011. Thus selection criteria in 2011 resulted in shorter periods of severe to profound hearing loss with later onset in life than in 1996. The changes in hearing loss management are likely to have resulted in a slowing of the degenerative effects of severe to profound hearing loss (presumably at a central level), and the changes in selection criteria are likely to have resulted in a higher average level of auditory processing and less reorganized cognitive function in patients immediately prior to cochlear implantation. These changes could thus account for the reduced effect of duration of severe to profound hearing loss in the 2011 data compared to the 1996 data. Figure 3b shows that patients with longer durations of severe to profound hearing loss tended to improve less between T1 and T2. This may represent increased reorganization

of the brain [Lazard et al., 2011; Lazard et al., 2010b] and a slowing down of the CI learning curve as a consequence. However, we cannot exclude that the smaller gain in performance may have been partially due to the shorter period of CI experience at T2 in the recipients with long durations of severe to profound hearing loss. It should also be noted that the smaller numbers of evaluations for recipients with longer severe to profound hearing loss duration reduces the statistical significance of the difference between T1 and T2.

A change in clinical practice is likely to account for difference in the close to average performance of Meningitic patients in 2011. The significant negative effect of Meningitis, which was labeled as Bacterial Labyrinthitis in 1996, was based on a sample of 135 patients, many of whom may have had ossification of the cochlea as a consequence of the disease. The 90 patients in the 2011 study are likely to have been implanted very soon after the disease, before ossification took place, and are therefore more likely to have had a better outcome than the 1996 patients [Durisin et al., 2010]. The emergence of ANSD as a new negative etiology in 2011 occurred because these patients were not identified clinically in 1996 [Deltenre et al., 1997; Rance et al., 1999]. Other differences in the etiology pattern of results are probably due to the larger number of patients and thus greater power in the analysis in 2011.

The effect of age at onset of severe to profound hearing loss reflects the natural processes that occur prior to onset of hearing loss, and is thus presumably less affected by changes in clinical practice. In both datasets, the effect of age at onset begins at around age 60, but the magnitude of the effect was larger in 1996 than in 2011. On one hand, we may speculate that the amount of natural peripheral and central degradation might have been reduced in 2011 by more frequent use of hearing aids in the period preceding severe to profound hearing loss, encouraged by improved sound quality and speech understanding [Blamey, 2005; Johnson et al., 2010; McDermott, 2011]. Alternatively, the greater information content and processing improvements in the CI devices used by the 2011 group may have imposed less cognitive and

auditory processing load than the earlier devices and therefore the effects of natural cognitive degradation were reduced for the 2011 group. A similar argument may explain the ten-year delay in the effect of age at implantation. If these speculations are correct, it appears that the average reduction in the cognitive and auditory processing load for the newer devices is equivalent to the average amount of cognitive and auditory processing degradation that occurs naturally in ten years after the age of 60 years.

The most striking difference between the 1996 and 2011 studies is the greater and faster improvement in postoperative auditory performance observed in 2011. This change is most likely due to improvements in sound processing and in the implant devices themselves, as well as the greater average capacity of the population of implant patients to take advantage of the new auditory information provided by the devices. For example, Dowell [Dowell, 2012] indicates an improvement in open-set sentence scores from less than 40% for sound processors used in the 1990's to more than 80% for modern sound processors. The corresponding improvements for CNC words were from 40% to 70%. The improvements in surgical management (soft surgery [Frayssse et al., 2006; Friedland and Runge-Samuelson, 2009]) may have also contributed by preserving the anatomical structures. The slight decrease in performance after 5 years of CI experience represents patients who had been operated on before 2005. They may not have benefited from the most recent improvements in coding strategies [Zeng, 2011] and in surgical techniques [Friedland and Runge-Samuelson, 2009].

The difference in total variance explained in the two studies (21% in [Blamey et al., 1996] and 10% in the present study) may be explained by the smaller influence of some of the factors, as detailed earlier, and the possibly greater random variance in the 2011 study, due to the inclusion of more centres. A large proportion of the residual variance may be due to inherent test/retest variability in the materials used, which typically have a relatively small number of items per list, however there are obviously many potential factors that have not

been included in the model used in this study. The influence of new factors, such as hearing aid use, residual hearing, influence of duration of moderate hearing loss, will be studied in a separate study (Lazard et al, in preparation).

Conclusions

Five of the main factors influencing individual differences in auditory performance of cochlear implant recipients in 1996 still had significant effects in 2011, although the detailed pattern of results and the relative importance of the factors had changed. Cochlear implant experience became the most significant factor and the relative effects of duration of deafness and age reduced. The changes between 1996 and 2011 are likely due to relaxed patient selection criteria, improved clinical management of hearing loss, modifications of surgical practice, and improved devices. Durations of severe to profound hearing loss of more than 40 years negatively influenced performance, but this effect then stabilized, possibly because of fixed central reorganizations. Patients implanted after 75 years of age performed poorly compared to younger recipients, but it is well known that older patients still receive significant improvement in life quality and maintain independence once implanted. The use of hearing aid before the period of severe to profound hearing loss may dampen the cognitive changes that appear with age, and should be encouraged. The influence of new factors, such as hearing aid use, residual hearing, influence of duration of moderate hearing loss, will be included in a new model of auditory performance and central evolution over time (Lazard et al, in preparation).

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Figure captions:

Figure 1. The three-stage model of auditory performance over time shows the factors used in the analyses. Reproduced from Blamey et al. (1996) with permission.

Figure 2. Each centre used a different speech perception test and presentation level as the measure of auditory performance. Example distributions of pre-operative and post-operative scores from individual centers are shown for (a) phoneme scores in CNC words presented at 65 dB SPL; (b) monosyllabic words at 70 db SPL; (c) disyllabic words presented at 60 dB SPL; and (d) sentences presented at 70 dB SPL.

Figure 3a. Duration of severe to profound hearing loss had a significant effect on percentile rank in the 1996 study (dashed lines and crosses) and in the current study (solid lines and squares). Error bars indicate +/- two standard errors of the mean for each duration range. The numbers next to each symbol indicate the number of scores contributing to the mean for that duration range.

Figure 3b. The improvement in performance (percentile rank) over time became smaller with longer duration of severe to profound hearing loss. Error bars indicate +/- two standard errors of the mean for each duration range. The numbers next to each symbol indicate the number of data points contributing to the mean for that duration range.

Figure 4. Age at implantation had a significant effect on the residual percentile rank after accounting for the effect of duration of severe to profound hearing loss for people over the age of 60 years in 1996 (dashed lines and crosses). There was a significant effect of age at implantation for people over age 70 years in the current study (solid lines and squares).

Residual percentile rank represents the amount of performance explained after allowing for the influence of the other factors. Error bars indicate +/- two standard errors of the mean for each age range. The numbers next to each symbol indicate the number of scores contributing

to the mean for that age range.

Figure 5. Age at onset of severe to profound hearing loss had a significant effect on the residual percentile rank after accounting for the effect of duration of severe to profound hearing loss for people over the age of 60 years in 1996 (dashed lines and crosses). There was a significant effect of age at onset of severe to profound hearing loss in the current study (solid lines and squares). Residual percentile rank represents the amount of performance explained after allowing for the influence of the other factors. Error bars indicate +/- two standard errors of the mean for each age range. The numbers next to each symbol indicate the number of scores contributing to the mean for that age range.

Figure 6. Etiology had a significant effect on the residual percentile rank in the current study. Error bars indicate +/- two standard errors of the mean for each etiology. Residual percentile rank represents the amount of performance explained after allowing for the influence of the other factors. The numbers next to each symbol indicate the number of patients in that etiology. Results for pressure trauma are not presented because there were only two cases in this group.

Figure 7. Cochlear implant experience (date of testing minus date of first activation) had a significant effect on the residual percentile rank after accounting for the effects of other factors in 1996 (dashed lines and crosses) and in the current study (solid lines and squares). Residual percentile rank represents the amount of performance explained after allowing for the influence of the other factors. Error bars indicate +/- two standard errors of the mean for each CI experience range. The numbers next to each symbol indicate the number of scores contributing to the mean at that CI experience range.