Outcomes of Cochlear Implantation in an Auditory Deprived Ear

Isabelle Boisvert
B.Sc, MPA

Audiology Section, Department Linguistics
Faculty of Human Sciences
Macquarie University, Sydney, Australia

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Abstract

This thesis challenges the assumption that poor functional outcomes are likely to be obtained when a cochlear implant is placed in an ear with long-term auditory deprivation. While previous research has shown that poor outcomes tend to be associated with long-term deafness and poor residual hearing in both ears, outcomes have not been examined in cases where implantation is performed in the sound-deprived ear of individuals with long-term asymmetric hearing; that is, individuals still receiving benefits from a hearing aid in the other ear. As suggested in functional imaging studies, it is possible that input from one ear could maintain synaptic activity within the auditory pathways and cortex, and contribute to outcomes obtained with the implant placed in the long-term sound-deprived ear.

The research described in this thesis is based on five retrospective cohort studies (n=10 to 151) using different methodologies. It examines speech recognition scores obtained after cochlear implantation in adults with a long-term (≥15 yrs) monaural sound deprivation (bilateral hearing loss aided monaurally). In order to increase the sample size and applicability of the findings, analysis is based on data collected in five implantation centres, located in Australia, Canada, and Sweden.

The results of the studies demonstrate that adults with an acquired hearing loss and monaural sound deprivation can obtain similar outcomes with the implant placed either in the sound-deprived or aided ear. These results occur regardless of the duration of sound deprivation in the implanted ear. However, for adults with a prelingual hearing loss, poorer outcomes typically occur when implanting the sound-deprived ear compared with the aided ear. The duration of bilateral significant hearing loss appears to be the most reliable predictor of implantation outcomes in a sound-deprived ear. Furthermore, the results of the studies suggest that the duration of sound deprivation in the implanted ear should not be considered as a relevant variable for clinical decision-making, with regards to speech recognition score outcomes.

It is anticipated that these results will influence clinical guidelines and offer new insight into auditory plasticity and contributors to outcomes of cochlear implantation.
The research questions addressed in this thesis stem directly from clinical dilemmas I faced during my work as a cochlear implant audiologist. At that time, I followed the literature closely, hoping to find answers that would support my clinical decision-making. It took some years however, before I realised that during this quest, I had actually developed the basis for my PhD.

It is often said that doing a PhD is a lonely process. This has not been true for me, and I want to thank all those who have given me support. I often felt as if I was running a marathon, and all along the way, I had friends, family, supervisors, and colleagues cheering and giving me what I needed to reach the finish line.

My first thanks go to my husband Erik, who took an honest interest in discussing my ideas and hypotheses, giving me unlimited emotional and academic support during this incredible journey that brought us around the world.

I am of course extremely grateful for all the help, guidance and advice I received from my principal supervisor, Associate Professor Catherine McMahon. Thanks Catherine for offering me the opportunity to undertake this degree, thanks for all the trust you put in me, and thanks for constantly helping me to progress as a researcher. Every meeting we had carried me forward.

I also want to express my sincere appreciation and thank my Adjunct Supervisors: Professor Björn Lyxell and Professor Richard Dowell.

Björn, thanks for engaging in this research project with me and with such enthusiasm. I am very grateful to have benefited from your experience and knowledge, and particularly for your guidance in the world of *Cognition*. Thanks for introducing me to the HEAD graduate school and for welcoming me in your department when I was in Sweden.

Richard, I truly appreciate the time you gave me. Thanks for all your support and advice; both have clearly helped with improving my thesis. Thanks also for helping me to keep a focus on the transferability of the research findings to the clinical setting.
Many thanks go to all the clinicians, researchers and managers in Canada, Sweden and Australia who warmly welcomed me into their clinics, gave me access to their data, and took time to discuss this research. In particular, thanks to Geneviève, Catherine C., Catherine G., Louise, François, Elina, Henrik, Eva K., Eva A., Erik, Alexandra, Michelle, Colleen, Monica, Kirsty, Sharan, Carol and Rachel. This type of research project would not be possible to conduct without clinical collaboration.

Thanks to all of you who via Macquarie University, the HEARing CRC (Australia) or the Linnaeus Centre HEAD (Sweden), have taken time to help me with this work. I was very lucky to be part of these research groups, which has given me a strong sense of belonging to a wide research community. In particular, thanks to Associate Professor Robert Cowan and to Associate Professor Elina Mäki-Torkko. Your support and advice facilitated greatly my progression through the PhD. Thanks also to all of you, within those groups, who improved my social life.

Moreover, I am grateful to have had the help of expert academics who read and commented on parts of this thesis; heartfelt thanks go to Professor David Ryugo and Professor Stig Arlinger.

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Statement from Author

I state that this work has been submitted exclusively to Macquarie University (Sydney, Australia) for the consideration of a PhD degree.

The empirical content of this thesis is based on data collected at: Institut de Réadaptation en Déficience Physique de Québec, Canada (part of the Québec expertise centre for cochlear implantation), Sydney Cochlear Implant Centre, Australia (part of Sydney University), Melbourne Cochlear Implant Clinic, Australia (at the Royal Victorian Eye and Ear Hospital), Linköping cochlear implant program, Sweden (at Linköping University Hospital) and Karolinska cochlear implant program, Sweden (at Karolinska University Hospital).

Signed authorisation to collect data has been obtained from each centre.

Ethical review, guidance and approval have been obtained from:

- Macquarie University Ethics Review Committee (Human Research). No. HE01MAY2009-D06475.
- New South Wales Department of Health, Human Research Ethics Committee No. X10-0158 & HREC/10/RPAH/290 (RPAH zone).
- Royal Victorian Eye and Ear Hospital, Human Research and Ethics Committee. No. 10/940H.

I certify that I developed the original idea and taken leadership to conduct all part of this research work, including writing the content of this thesis. My three supervisors (A/Prof Catherine McMahon, Prof Richard C. Dowell, and Prof Björn Lyxell) have assisted in improving the research protocol, analyses, and interpretation of the data, as well as the quality of the written presentations. Co-authors (Supervisors, A/Prof Elina Mäki-Torkko, and Ms Geneviève Tremblay) and reviewers of the papers (A/Prof Robert Cowan, Members of HEAD graduate school, Dr Erik Lundmark, and anonymous reviewers from the publications’ journals) have helped in improving the manuscripts. I also conducted the majority of the data collection, with the support of clinicians in each centre (in particular: A/Prof Elina Mäki-Torkko, Ms Geneviève Tremblay, Ms Catherine Champagne, Ms Eva Agelfors, Mr Erik Pihl, Dr Eva Karltoft, Ms Colleen Piarros, Ms Monica Bray, and Ms Alexandra Rousset). Statistical support has been obtained from Prof Peter Petocz and Dr Örjan Dahlström when required.

Copyright clearance has been obtained from Wolters Kluwer Health to include the published manuscripts in the thesis.

________________________________________
Isabelle Boisvert
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<tr>
<td>CI</td>
<td>Cochlear implant</td>
</tr>
<tr>
<td>CNC</td>
<td>Consonant-Nucleus-Consonant</td>
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<tr>
<td>CUNY</td>
<td>City University of New York</td>
</tr>
<tr>
<td>CVC</td>
<td>Consonant-Vowel-Consonant</td>
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<td>HL</td>
<td>Hearing loss</td>
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<tr>
<td>PTA</td>
<td>Pure-tone threshold average</td>
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<tr>
<td>SPB</td>
<td>Swedish Phonemically-Balanced</td>
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<tr>
<td>SRS</td>
<td>Speech recognition score</td>
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<tr>
<td>SSD</td>
<td>Single-sided deafness</td>
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<tr>
<td>TAM</td>
<td>Test Auditif Multimedia</td>
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Chapter 1  Introduction

1.1 Preamble

Excerpt from Volta (1800):

\[ I\ introduced, \ well\ before, \ in\ both\ ears,\ two\ types\ of\ probes\ or\ metallic\ rods,\ with\ rounded\ endings;\ and\ I\ made\ them\ communicate\ immediately\ to\ the\ extremities\ of\ the\ apparatus\ (i.e.\ a\ battery).\ At\ the\ moment\ that\ the\ circle\ was\ this\ way\ completed,\ I\ received\ a\ shock\ in\ the\ head;\ and,\ some\ moments\ later\ (without\ interrupting\ the\ communications,)\ I\ began\ to\ feel\ a\ sound,\ or\ more\ of\ a\ noise,\ in\ my\ ears,\ that\ I\ would\ not\ be\ able\ to\ describe;\ it\ was\ a\ type\ of\ cracking\ shocks,\ or\ sparkling,\ as\ if\ batter\ or\ tough\ material\ was\ boiling.\ This\ noise\ continued\ without\ pausing,\ and\ without\ increasing,\ all\ the\ time\ that\ the\ circle\ was\ complete.\ The\ unpleasant\ sensation,\ and\ that\ I\ feared\ to\ be\ dangerous,\ of\ the\ shock\ in\ the\ brain,\ lead\ me\ to\ not\ repeat\ often\ this\ experiment\ (author’s\ translation). \]

The above statement would represent the first attempt to electrically stimulate hearing. With the research development that occurred in the 1950s, and more particularly in the 1970s, cochlear implants (CIs) can now offer astonishing outcomes, even permitting some recipients to easily follow a conversation on a mobile telephone. Nowadays, hundreds of thousands of severely hearing-impaired individuals have received a CI to access hearing for communication. Although the majority of CI recipients obtain great benefits from the intervention, the outcomes are highly variable and relatively difficult to predict. This thesis aims to examine the outcomes of cochlear implantation in the case of bilateral hearing loss, where only one ear is aided and the other has had essentially no hearing for many years (i.e. the sound-deprived ear). In this particular scenario, a clinically-focussed research question emerges: \textit{In which ear should a CI be placed?}

Some clinicians and researchers may quickly assume an answer to this question, and judge further research on the subject irrelevant. However, the best practice to follow in this situation is not well defined, and clinical practice is therefore inconsistent. Furthermore, the rationales used for decision-making are weakly grounded in scientific evidence. Accordingly, some clinicians will recommend implanting the aided ear (i.e. the only hearing ear), assuming that implantation in a long-term sound-deprived ear will provide only limited outcomes. Whereas others will prefer implanting the sound-deprived ear to minimise any risk of further damage and save
the only useful ear, but will also counsel patients on possible poor outcomes because of the long duration of sound deprivation. The assumption is that long-term sound deprivation leads to poor cochlear implantation outcomes, but what evidence exists to support this perception?

The detrimental effects of amplifying only one ear with a hearing aid in the case of bilateral sensorineural hearing loss have been documented. Additionally, long-term deafness has been linked to anatomical and physiological changes in the auditory pathways and to poor outcomes of cochlear implantation. It therefore seems reasonable to assume that the outcomes of cochlear implantation in a long-term sound-deprived ear will be poor. However, this assumption appears to be derived from studies investigating mainly bilateral symmetric hearing loss, where the severity and duration of the hearing loss may be similar in each ear.

Where a difference between the ears exists, it is possible that the hearing in the better ear influences cochlear implantation outcomes. That is, hearing in only one ear could: (i) preserve the memory of what sound sounds like (phonological representations), facilitating brain adaptation to the sound delivered by the CI; (ii) limit the anatomical or physiological degradation that typically occurs with deafness; and (iii) enable bimodal hearing (hearing aid in one ear and CI in the other).

Examining outcomes of cochlear implantation in a long-term sound-deprived ear can appear to have a very specific and limited clinical application. However, knowledge gained from the present work has applications extending to all types of hearing asymmetries in auditory rehabilitation, including unilateral hearing aid use, unilateral cochlear implantation, bimodal hearing, bilateral cochlear implantation, and implantation in single-sided deafness (normal hearing in one ear). Therefore, knowledge gained from this work should also give a new perspective on the factors influencing cochlear implantation outcomes, even in cases of symmetric hearing.

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1 In this thesis, the concept of bimodal hearing refers to an electric device in one ear (CI) and an acoustic device in the other (hearing aid). It is however acknowledged that this concept could, in another context, refer to the use electric and acoustic stimulation in the same ear (i.e. hybrid devices).
Because different practices are found in implantation clinics around the world, in regard to selection criteria and follow-up after implantation, five implantation centres located in three countries have contributed to the development of this work. The objectives of this choice were to increase sample size, increase the reliability, validity and applicability of the findings, and offer multiple occasions for insightful clinical discussions.

The thesis by publication format was selected to allow for a stepwise approach, where the ideas, questions and methods initially used could be continuously verified and improved through the evaluation process of peer-reviewed journals. This approach also prompted discussions and made the current subject matter accessible to the clinical and research community. Accordingly, five manuscripts are included, three of which were published at the time the thesis was written.

1.2 Conceptual review

This section reviews the current state of knowledge within which this thesis has evolved and where the research questions and methodology are framed (sections 1.3 and 1.4).

1.2.1 The multiple meanings of deafness

Deafness: lacking or deficient in the sense of hearing.

Cochlear implantation is a common treatment for deafness. Duration of deafness is often cited as the main predictor of cochlear implantation outcomes (Blamey et al. 1996; Rubinstein et al. 1999; Van Dijk et al. 1999; Green et al. 2007). However the term deafness is not precisely defined and its meaning can vary widely. A thorough examination of the outcomes of cochlear implantation therefore should consider the use of the term deafness. Deafness is used broadly and may represent different magnitudes of hearing loss (HL). This broad usage varies from having no residual hearing at all, to not hearing when not using hearing aids, or even having any level

2 Definitions used are taken from the Merriam-Webster online dictionary (2011), unless specified otherwise.
of HL. Although different scales have been developed to standardise the classification of different degrees of HL, based on the three frequency pure-tone thresholds average (PTA) (as discussed in Schlauch and Nelson 2009, p.39), or on the four frequency PTA (WHO 2012), a universal standard has not been adopted. Therefore, the definition of mild, moderate, moderately-severe, severe and profound HL, and deafness, depends on the scale a hearing services professional chooses as a reference and is thus variable across countries. In addition, the term deafness is not used by the general public in the same sense that hearing service professionals use deafness, and could actually represent any of the clinically defined degrees of HL.

Clinically, it appears to be generally accepted that a PTA of 90dBHL or more, which is defined as a profound HL, represents the boundary between hearing and deafness (Schlauch and Nelson 2009). However, deafness can also be represented by a moderate to profound HL (Van Dijkhuizen et al. 2011), or a severe or severe to profound HL (Yang et al. 2011; Caposecco et al. 2012). The problem with defining deafness as an average PTA boundary is that it does not consider the complex interactions between the multiple structures of the auditory system that can be impaired. For example, a conductive or mixed HL will not have the same impact on real-world hearing abilities compared with a sensorineural loss (Hood and Poole 1971). A sloping loss, where low-frequencies are typically significantly better than high-frequencies, will be more difficult to effectively amplify with a hearing aid than a flat HL (Sullivan et al. 1992; Ching et al. 1998). Moreover, with any degree of HL, the individuals will decide to wear one, two, or no hearing aids, thus affecting their hearing abilities in everyday life. As a consequence, much variability exists in the types and impacts of auditory impairment that could result from the same degree of HL (Flynn et al. 1998). Importantly, PTAs are not informative of the quality of the auditory input that reaches the cortex and of how this information is being processed by the individual. Therefore, many researchers have chosen to measure deafness with regard to more functional hearing abilities, for example by evaluating whether or not individuals are able to have a conversation on the telephone (Rubinstein et al. 1999; Green et al. 2007; Matterson et al. 2007).

In the cochlear implantation literature, when studying duration of deafness as a possible predictor of outcomes, a broad, non-standardised and sometimes vague
definition of the term deafness is also found. This is highlighted in Table 1.1. While some authors prefer using hearing levels and others prefer using hearing abilities, it is interesting to note that many do not specify in which ear the measurement is taken. It is probable that the measure was taken in the ear to be implanted or that it was assumed that the measure would be the same for both ears.

### Table 1.1. Different and sometimes vague measurement methods are used to represent deafness in cochlear implantation literature.

<table>
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<td>(Van Dijk et al. 1999; Dunn et al. 2008)</td>
<td>“Duration of deafness” (no indication regarding measurement method).</td>
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<tr>
<td>(Dowell et al. 2004)</td>
<td>“Duration of severe or profound HL”.</td>
</tr>
<tr>
<td>(Blamey et al. 1996)</td>
<td>“Average pure-tone hearing threshold of 90dB or more at 500, 1000 and 2000Hz”.</td>
</tr>
<tr>
<td>(Roditi et al. 2009)</td>
<td>“Duration of severe-to-profound HL determined by a review of available medical records or by patient report”.</td>
</tr>
<tr>
<td>(Gomaa et al. 2003)</td>
<td>“Duration of severe to profound HL, […] was determined either subjectively from the patient’s history, or by reviewing serial audiograms if available”.</td>
</tr>
<tr>
<td>(Bodmer et al. 2007)</td>
<td>“Duration of deafness in the more recent setting has […] become an impossible factor to evaluate”.</td>
</tr>
<tr>
<td>(Rubinstein et al. 1999)</td>
<td>“Each patient was asked when he or she stopped being able to use the telephone”.</td>
</tr>
<tr>
<td>(Green et al. 2007)</td>
<td>“Patients were asked how long they had been experiencing severe hearing problems. For the majority […] this was determined as the time at which they were no longer able to have an easy interactive telephone conversation”.</td>
</tr>
<tr>
<td>(Matterson et al. 2007)</td>
<td>“Deafness was defined as severe/profound when the patient could no longer use a telephone on the affected ear even when using a hearing aid at the time, or when they had stopped wearing an aid because it was not providing benefit”.</td>
</tr>
<tr>
<td>(UK Cochlear Implant Study Group 2004)</td>
<td>“Subjects used a touch screen to draw a graph, […] illustrating the evolution of their HL in that ear, […] the number of years that had elapsed since the graph dropped below a value of 20 was calculated. This number was taken as a measure of the duration of profound deafness.”</td>
</tr>
<tr>
<td>(Lazard et al. 2010)</td>
<td>“The time elapsed since the post-lingually deaf subjects could no longer communicate by hearing, even with the best-fitted hearing aids.”</td>
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Although deafness may appear to be an easily understandable and measurable concept, no consistent standards are being used for its definition, which may reflect the intrinsic complexity of the term. It is also possible that the difference in measurement methods that are used, as shown in Table 1.1, contributes to the variability found in research results and complicates meta-analyses.
In the empirical part of this thesis, an effort is made to limit the use of the unspecified term *deafness*. Instead, the hearing impairment is defined for the individual ears, using the severity of the HL according to the PTA and hearing abilities (i.e. speech recognition score and ability to use the telephone). The use of hearing aids is also considered. Nevertheless, when referring to general concepts and reviewing literature, *deafness* will be used to refer to at least a severe-to-profound HL for each ear individually.

1.2.2 Auditory changes related to profound hearing loss

*Plasticity:* the capacity for continuous alteration of the neural pathways and synapses of the living brain and nervous system in response to experience or injury.  
*Anatomy:* a branch of morphology that deals with the structure of organisms.  
*Physiology:* the organic processes and phenomena of an organism or any of its parts or of a particular bodily process.

Congenital and long-term profound HL have been shown to lead to anatomical and functional changes at all levels of the auditory pathways (Shepherd et al. 2006). Such changes have been put forward when discussing the reasons that individuals with long-term deafness, whether congenital or acquired, obtain limited outcomes from cochlear implantation (Shepherd and Hardie 2001). By extension, it has been assumed that cochlear implantation in a long-term deafened ear would yield only limited outcomes (Ramsden et al. 2005a; Connell and Balkany 2006), regardless of the hearing function in the non-implanted ear. This assumption might have been sufficient when cochlear implantation was performed only in individuals with a bilateral profound HL, but nowadays, individuals with greater levels of residual hearing, in particular in the non-implanted ear, are receiving a cochlear implant (CI). Research suggests that bilateral HL does not have the same impact on the auditory system as unilateral HL (Hardie and Shepherd 1999). Therefore, it seems reasonable to hypothesise that implantation in unilateral HL may lead to different outcomes than those expected with bilateral HL. A review of the current state of knowledge regarding anatomical and physiological changes occurring with bilateral and with unilateral HL gives support to this hypothesis. This review is presented in the following section.
Changes related to bilateral deafness

In the cochlea, the loss of inner hair cells causes a decrease in the availability of neurotrophic factors, which has in turn been correlated with a reduction in the number of surviving spiral ganglion cells (Green et al. 2008). This receptor cell loss initiates a rapid loss of unmyelinated peripheral dendrites within the organ of Corti (Terayama et al. 1977), followed by the degeneration of the myelinated neurons within the spiral lamina (Leake and Hradek 1988). Because the spiral ganglion is a mandatory conduit to the brain for auditory information (Nayagam et al. 2011), its eventual decrease in density has often been identified as the probable cause of poor outcomes of implantation in long-term deafened individuals (Shepherd et al. 2008; Atkinson et al. 2011). However, human data have shown no clear relationship between the number of surviving spiral ganglion cells and implantation outcomes (Blamey 1997; Khan et al. 2005). As discussed in Wilson and Dorman’s review of cochlear implantation (2008), a small number of surviving ganglion cells appears sufficient for the function of the current CIs.

In the cochlear nuclei, bilateral deafness causes a shrinkage of nuclear volume and a concomitant increase in neural density, which may be associated with the loss of axon terminals, dendrites and glial cells, or to cell shrinkage (Hardie and Shepherd 1999). In congenitally deaf cats, a decrease in the anatomical complexity of the synaptic endings (endbulb of Held) in the cochlear nucleus can be observed, compared with normal hearing cats (Ryugo et al. 1997), with greater changes related to poorer hearing (Ryugo et al. 1998). In the inferior colliculus, neuronal shrinkage has been observed in neonatal bilateral deafness (Nishiyama et al. 2000). Structural cortical imaging in humans suggests that HL causes a decrease in the volume of grey matter, mainly observed in regions distal from the auditory cortex (Shibata 2007; Husain et al. 2011). Changes in white-matter connectivity can also be observed in adults with congenital deafness and with deafness acquired in early childhood (Li et al. 2012).

Physiologically, animal studies have shown that long-term bilateral deafness causes degeneration in temporal resolution (Snyder et al. 1995; Shepherd and Javel 1997) and increased thresholds within the auditory nerve fibers (Shepherd and Javel 1997; Javel and Shepherd 2000). Modifications of the tonotopic representation of
frequencies in the auditory cortex also occurs in relation with the specific hearing damage (Harrison et al. 1991). In humans, functional studies suggest that long durations of bilateral HL decreases the cortical metabolic activity (Ito et al. 1993; Lee et al. 2003; Green et al. 2005) and can modify the cortical activation patterns involved in speech processing (Giraud and Lee 2007; Lee et al. 2007). The consequence of these results may be degraded phonological abilities (Lyxell et al. 1998; Lyxell et al. 2003; Lazard et al. 2010), suggesting a necessity to involve additional cognitive resources for speech processing (Pisoni 2000; Akeroyd 2008; Lazard et al. 2010) and perhaps initiating cross-modal plasticity, where visual stimuli can be represented in the auditory cortex (Lee et al. 2001).

Deafness also causes greater anatomical and functional changes in the auditory pathways when it occurs during the time of rapid brain development (congenital, neonatal and prelingual deafness), commonly referred to as the critical period, where the damage sustained to the auditory pathway is far greater to that caused by acquired deafness (Shepherd et al. 2006).

Changes related to unilateral deafness

The aim of this section is to compare the neurophysiological impacts of bilateral deafness to those of unilateral deafness. However, it is important to note that different study designs have typically been used to examine these two types of deafness. In particular, a large majority of studies examining the impact of unilateral deafness have used cochlear ablation in animal models. This deafening method is known to cause considerably greater change/damage in the auditory pathways than other methods of deafening typically used in studies of bilateral deafness (i.e., genetic, ototoxic drugs, noise trauma, and cochlear lesion). Therefore the use of cochlear ablation to induce unilateral deafness restricts the ability to compare between bilateral and unilateral deafness easily. Nevertheless, studies using such models are presented in the following paragraphs to supplement the limited number of available studies that have used other types of deafening.

As for bilateral deafness, anatomical changes observed with unilateral deafness are more extensive when deafness occurs before the critical period as compared with later in life (Trune 1982; Moore 1990; Mostafapour et al. 2000). With unilateral
deafness, shrinkage of the cochlear nucleus occurs on the side of the deafened ear (Moore and Kowalchuk 1988), particularly in the ventral cochlear nucleus (Moore and Kowalchuk 1988), where an important increase in the expression of GAP-43 (Illing et al. 2005), which signals synaptic remodelling, is also observed.

It is suggested that the majority of the central auditory neurons receive input from both ears, starting at the level of the superior olivary complex (Irvine 1986; Moore 1991). Unilateral deafening at an early age has been shown to modify the complex interaction patterns in the excitatory and inhibitory neuronal networks in the brainstem (Moore 1991; Vale et al. 2004). While a decrease in the volume of neurone’s soma in the midbrain is reported with unilateral deafness in young and mature animals (Powell and Cowan 1962; Pasic et al. 1994), the synaptic density in the inferior colliculus seems to be maintained (Shepherd and Hardie 2001). An increased density of the axon terminals and neurons between the cochlear nucleus and the inferior colliculus on the side contralateral to the deafened ear accompanies these changes (Moore and Kitzes 1985; Moore 1994). An increase in the number of sites where activity in the inferior colliculus contralateral to the deafened ear can be recorded has also been observed (McAlpine et al. 1997). These results suggest that a synaptic remodelling is occurring, which may be related to an increase in ipsilateral excitatory activity from the hearing ear and/or to a decrease in the contralateral inhibitory activity from the deafened ear (Moore 1991).

Physiologically, immediately after unilateral cochlear ablation in young animals there is a cessation of spontaneous action potentials measured in the ventral cochlear nucleus (Koerber et al. 1966). This observation is consistent with a decrease in neuronal activity in the cochlear nucleus of young and adult animals (Moore 1990; Rubel et al. 1990). A rapid increase in activity in the inferior colliculus contralateral to the deafened ear has also been measured when stimulating the hearing ear (Popelár et al. 1994; McAlpine et al. 1997). Despite this increase in activation measured on the ipsilateral side to the hearing ear, contralateral activation appears to remain the strongest (McAlpine et al. 1997). Adult animals with neonatal unilateral deafness maintain normal temporal resolution (measured in the midbrain with single-unit recordings and current pulses ranging from 5 to 200pps (Shepherd et al. 1999)). With electrophysiology and imagery studies in humans with unilateral hearing loss, a
decrease in the ipsilateral/contralateral differences in cortical activity has also been shown (Scheffler et al. 1998; Ponton et al. 2001; Langers et al. 2005).

Changes in the cortical frequency representations have also been observed in animal models of unilateral HL, on the side contralateral to the lesion (Robertson and Irvine 1989). However, a study examining frequency-place function in patients with unilateral deafness using a cochlear implant suggested that frequency representation is better preserved when one ear has normal hearing compared with bilateral HL (Vermeire et al. 2008). Imaging studies have shown multiple differences in functional activation and connectivity patterns in the auditory cortex of children with unilateral deafness compared with normal hearing peers (Propst et al. 2010; Tibbetts et al. 2011). However, these imaging studies cannot be easily performed with individuals having bilateral deafness because of the task requiring listening to stimuli at a comparable audibility level and the complications related to hearing aid/cochlear implant usage during fMRI. It is also assumed that limited cross-modal plasticity and degradation of phonological representation occurs with unilateral deafness.

**Summary of differences between the auditory changes occurring with bilateral and unilateral deafness**

It is clear that plasticity affecting the anatomy and physiology of the auditory pathways occurs following both bilateral and unilateral deafness. However the effects of bilateral deafness are different to those of unilateral deafness. The main differences being that for unilateral deafness, an increase in activity is observed on the side ipsilateral to the hearing ear (Popelár et al. 1994; McAlpine et al. 1997; Scheffler et al. 1998; Ponton et al. 2001), whereas temporal (Shepherd et al. 1999) and spectral (Vermeire et al. 2008) processing appear to be better maintained. It is possible that this increase in neuronal activity and the better preserved temporal and spectral processing occurring in unilateral deafness facilitate speech processing with a CI placed in a long-term deafened ear.
1.2.3 Effect of monaural sound deprivation and restoration via a hearing aid

Silman et al. (1984) were the first to present data suggesting that speech discrimination abilities deteriorate in the unaided ear, in cases of bilateral sensorineural HL aided unilaterally. Several studies have replicated these results (Gelfand et al. 1987; Hattori 1993; Silman et al. 1993; Silverman et al. 2006), while others did not find such effects (Jauhiainen 2001) or related the effect to differences in presentation levels where the non-aided ear had better performance at low levels (Gatehouse 1989). Nevertheless, the question that arose was whether the changes in speech discrimination abilities were reversible with the introduction of bilateral hearing aids, a phenomenon referred to as acclimatisation (Arlinger et al. 1996). Studies showed that these changes were sometimes, but not always, reversible (Silverman and Silman 1990; Silman et al. 1992; Boothroyd 1993; Silverman and Emmer 1993; Gelfand 1995). These findings provided strong support for promoting the use of bilateral hearing aids for all individuals with bilateral HL (Arlinger et al. 1996; Arlinger 2003). This knowledge also supported the idea that poor outcomes may be obtained when implanting a long-term sound-deprived ear. However, as discussed in Tyler and Summerfield (1996), for individuals with a significant hearing loss, hearing with a hearing aid is different from hearing with a CI because the possibilities for improvement are greater with the latter treatment option. Consequently, it is possible that the detrimental effect of auditory deprivation on speech recognition abilities, which is not always reversible when reintroducing a hearing aid, could be reversible with cochlear implantation given that the implanted ear is likely to become the stronger of the two ears.

1.2.4 Cochlear implantation as a treatment for hearing loss

\textit{Cochlear implant:} an electronic prosthetic device that enables individuals with sensorineural HL to recognize some sounds and consists of an external microphone and speech processor and one or more electrodes implanted in the cochlea.

In the past 40 years, more than 200 000 people around the world have received a cochlear implant (CI) to partly restore their hearing (Shannon 2012). The first models only transmitted very rudimentary auditory information, which was mainly useful to facilitate speech recognition with sufficient access to lipreading (Chouard and
MacLeod 1976; Clark and Tong 1982). More recently, improvements in technology have allowed for increased performance, where some individuals can easily follow a conversation on a mobile telephone or in background noise, without the support of lipreading. Despite the technological improvements allowing for high performance, outcomes of cochlear implantation are still highly variable and limitations remain, in particular when listening to speech in background noise (Fu et al. 1998; Nelson et al. 2003) or music (Limb and Rubinstein 2012). In this section, a brief and general review of current CI technology is presented, followed by a discussion of various implantation options (unilateral CI, bilateral CIs, bimodal hearing, and implantation for single-sided deafness).

**CI Technology**

At the time of writing this thesis, there are three companies that manufacture cochlear implants approved by the United States Food and Drug Administration (FDA). These are Cochlear Ltd (Sydney, NSW, Australia), Advanced Bionics (Valencia, CA, United States) and MED-EL (Innsbruck, Austria). Although the devices differ in respect to the number and design of electrodes, and the speech information coding they use, they seem to offer relatively similar speech recognition outcomes (Zeng 2004; Bergeron 2012). Over the years, speech coding strategies have evolved to offer improved performance, particularly for recognition of speech in background noise (Lenarz et al. 2011).

The role of the CI is to extract meaningful acoustic auditory information, electrically code this information and deliver it via the electrodes in a way that can be interpreted by the central nervous system. To accomplish this, bandpass filtering is applied to the signal to extract the relevant independent frequency bands (or channels) that will be delivered via the electrodes (Rubinstein 2004; Wilson and Dorman 2008). Because the spread of current from the electrodes in the cochlea to the auditory neurons is relatively large and not well understood, a very limited number of frequency channels can be efficiently used (Henry and Turner 2003; Wilson and Dorman 2008). Additionally, because profound HL causes a greatly reduced dynamic range (the difference between the softest sound an individual can hear and the loudest they can tolerate), and because of the way the auditory nerve responds to electric stimuli,
compression must be applied to the signal for it to be audible and comfortable, which
is similar to the compression used in hearing aids (Popper et al. 2004; Blamey 2005).
This necessary electronic processing of the auditory signal implies that the sound
delivered by the CI is not as rich and complex as the sound that would be processed
by a normal auditory system. CI technology is particularly limited in the delivery of
complex and quickly changing acoustic information. Nevertheless, cochlear
implantation can now offer outstanding performances to deafened individuals, which
demonstrates that the human auditory system is able to process and recognise
degraded speech (Shannon 2012). As discussed in section 1.2.2, long-term unilateral
deafness can cause anatomical and physiological degeneration in the auditory
pathways. However, these changes might not affect the outcomes obtained with the
current CI systems.

**Implantation options: unilateral CI, bilateral CIs, bimodal hearing, and
implantation for single-sided deafness**

Historically, cochlear implantation has been performed unilaterally and for profound
bilateral deafness. This was largely to minimise the costs and the risk of destroying
usable hearing (Litovsky et al. 2006). It was also argued that it was sensible to *save*
one ear for future possible development of knowledge and technology, for example:
hair cell regeneration (Kawamoto et al. 2003; Zeitler et al. 2008). Over the years,
many studies have shown or reviewed the benefits of listening with two ears (Day et
al. 1988; Feuerstein 1992; Dillon 2001; Hawley et al. 2004; Firszt et al. 2008; Ching
et al. 2009; Dorman et al. 2011), and consequently, bilateral cochlear implantation
has become more common (Gantz et al. 2002; Litovsky et al. 2004; Offeciers et al.
2005; Van Hoesel 2012), particularly in children to optimise the development of
binaural auditory skills (Kühn-Inacker et al. 2004; Papsin and Gordon 2008; Lovett
et al. 2010; Dowell et al. 2011). In many clinics, patients with deafblindness who
rely on hearing for localisation, are also a priority for bilateral implantation (Niparko
et al. 2009; Bergeron 2010). In adults, bilateral cochlear implantation is more often
performed sequentially rather than simultaneously. This is typically done to assess
the benefits with the first implant before proceeding with the second (Zeitler et al.
2008), and partly because funding bodies often only pay for one implant at a time. In
the case of sequential bilateral implantation, the choice of ear to implant first remains
problematic and questions are raised regarding the potentially detrimental effects of a long duration between implantation of the first and second ear (Ramsden et al. 2005a; Sharma et al. 2007; Zeitler et al. 2008; Gordon et al. 2011a).

Additionally, the development of technology and better knowledge of implantation outcomes has allowed patients with more residual hearing to become candidates for implantation (Osberger et al. 2002; Dowell et al. 2004; Tremblay et al. 2008). This permitted many patients to maintain hearing via their hearing aid in the non-implanted ear, in conjunction with the use of a CI (bimodal hearing) (Ching et al. 2004; Hamzavi et al. 2004; Ching 2005; Ching et al. 2006). It has been shown that benefits of bimodal hearing are superior to those of unilateral CI (Ching et al. 2004) and can be at least comparable to those of bilateral CIs (Ching et al. 2009; Sucher and McDermott 2009; Cullington and Zeng 2011; Sammeth et al. 2011). For long-time users of a single hearing aid, choosing the more appropriate ear for cochlear implantation is still debated: is it better to implant the more recently stimulated ear or to save this ear for possible bimodal hearing?

In addition to individuals using unilateral CI, bilateral CIs, or bimodal hearing, a new group of patients are considered for cochlear implantation; individuals with single-sided deafness (SSD), having normal hearing in one ear. At the moment of writing this thesis, recommendations to perform implantation in SSD are mainly when an incapacitating tinnitus accompanies the deafness, and within a defined research project considering only short duration of deafness (Van De Heyning et al. 2008; Vermeire and de Heyning 2009; Arndt et al. 2011). However, because of the great outcomes this group of patients appear to obtain from cochlear implantation (Arndt et al. 2011), candidates without tinnitus have also been considered for implantation (Jacob et al. 2011). The results of this thesis should be informative regarding the relevance of considering participants with long duration of single-sided deafness for cochlear implantation. As presented recently, some individuals with long duration (up to 40 yrs) of single-sided deafness would have obtained high outcomes with a cochlear implant (Tavora-Vieira et al. 2012).
1.2.5 Auditory plasticity following cochlear implantation and auditory training

Plasticity: the capacity for continuous alteration of the neural pathways and synapses of the living brain and nervous system in response to experience or injury.
Learning: modification of a behavioural tendency by experience.
Training: teaching so as to make fit, qualified, or proficient.

Multiple studies over the last 20 years have shown that the mature sensory systems retain some plasticity, which in particular allows adults to learn new skills (as discussed in Ryugo and Limb 2009; Irvine 2010). As presented in section 1.2.2, plasticity occurs in the auditory pathways following hearing loss, particularly in childhood, but also when the hearing loss is acquired in adult age. Another question relating to auditory plasticity is whether cochlear implantation leads to further plasticity which may limit or reverse the changes caused by long-term profound hearing loss.

Improvement of speech recognition immediately after the initial switch-on of the CI in adults is not necessarily a demonstration of plasticity. This improvement may simply reflect the reconnection of a stable neuronal network to a clearer, more audible sound. The improvement of performances associated with longer experience with the CI is, on the other hand, a manifestation of plasticity (Ryugo and Limb 2009). Enhanced plasticity and performance may be further associated with auditory training (Moore and Shannon 2009; Ryugo and Limb 2009; Irvine 2010).

Animal studies can provide insight into the auditory plasticity that follows cochlear implantation. In young animals, early chronic stimulation with a cochlear implant is associated with preservation or partial recovery of neurophysiological features in the afferent auditory pathways known to otherwise degrade with deafness (Kral et al. 2002; Leake and Rebscher 2004; Vollmer et al. 2005; O'Neil et al. 2011). With congenital deafness, later electrical stimulation would result in less recovery as compared with early stimulation (Kral et al. 2002; O'Neil et al. 2011). In mature animals deafened later in life, chronic electrical stimulation also leads to some recovery in the afferent auditory pathways (Moore et al. 2002; Kral et al. 2006). The results of these animal studies demonstrate that plasticity does occur following cochlear implantation, although to a lesser extent with congenital deafness when implantation occurs at older ages.
In humans, the improvement in speech recognition performance observed over time after cochlear implantation may represent an improved specificity in the auditory processing relating to the afferent pathways (bottom-up). Alternatively, it can also represent an increased efficiency in processing highly degraded signals delivered by the CI, via the use of cognitive resources involved in language processing. This is commonly referred to as top-down processing, but it could also be a later aspect of bottom-up processing (Davis et al. 2011). In this latter situation, for example, speech recognition could be improved by an increased ability to infer, from contextual cues (whether linguistic, visual, or situational), the auditory information that is not clearly heard. It can be assumed that a contribution of both bottom-up and top-down learning/plasticity is involved in the improvement of speech recognition score (SRS) observed over time following cochlear implantation (Davis and Johnsrude 2007; Kral and Eggermont 2007).

Functional imaging studies conducted in human adults after cochlear implantation support the contribution of both bottom-up and top-down processing to improved speech recognition performances. Specifically, these studies suggest the occurrence of cortical changes in both auditory and non-auditory areas, the latter likely being related to modifications in the cognitive processing of speech information (Giraud et al. 2000; Giraud et al. 2001a; Giraud and Truy 2002; Halliday et al. 2011; Lazard et al. 2011). For example, there may be different processing networks involved in speech sound recognition (Lazard et al. 2010), involvement of visual regions associated with speech-reading (Giraud et al. 2001a; Giraud and Truy 2002), increased attention (Amitay and Moore 2006), effort (Davis and Johnsrude 2003; Limb et al. 2010) or demand on working memory to successfully recognise speech (Müller and Knight 2006). There is some data that suggests that these changes are related to a longer experience with the CI (Giraud et al. 2001b) and not only an adaptation to a long-duration of deafness, supporting that plasticity occurs after implantation.

Specific auditory training, which aims at improving detection, identification and interpretation of common sounds such as speech, may also further the learning/plasticity after cochlear implantation (Fu et al. 2005; Ryugo and Limb 2009; Irvine 2010; Oba et al. 2011). In animal research, specific auditory training with the
use of meaningful stimuli where, for example, an intra-cochlear electrical stimulus can be associated with food (positive conditioning) or a slight electrical shock (negative conditioning), increases the neurophysiological changes related to the stimulus delivered with a CI, when compared to a simple exposure to meaningless stimuli (Beitel et al. 2011; Vollmer and Beitel 2011). Auditory training in humans has also been shown to cause changes in neural activity (Tremblay and Kraus 2002; Tremblay et al. 2010) and to further improve performance after cochlear implantation (Fu and Galvin 2008b; Oba et al. 2011). In clinics, auditory training after cochlear implantation is usually carried out for children, to facilitate development of speech, language and learning in school. On the other hand, auditory training for adults is conducted inconsistently. This is mainly because the causes and drives of the improvements are unclear (Clinard et al. 2008), but also because limited reimbursement is made available from funding organisations to cover the costs of auditory training (Gates and Miyamoto 2003). Moreover, limited scientific evidence exists to justify the cost/benefit of auditory training for adults as compared with simply relying on the daily listening experience with the CI.

Limited research also exists to guide the listening condition in which training should be performed. For example, it has been suggested that, because of the effect of cross-modal plasticity, visual input may impede the auditory performance with a CI in adults with long duration deafness (Champoux et al. 2009). However, an opposing view has also been suggested, where auditory-visual training could improve performance with a CI (Kawase et al. 2009). In the same way, it is also possible that the auditory input transmitted via the hearing aid, in the case of bimodal hearing, limits the performance obtained when listening with the cochlear implant alone. This appears logical as plasticity may have occurred in the auditory pathways of adult long-time users of a single hearing aid, and this plasticity could potentially complicate the use of binaural hearing, or of hearing via the cochlear implant alone. For optimal auditory performance, some suggest training should be done in bimodal condition when both a CI and a hearing aid are used (Sammeth et al. 2011), while others suggest training should be done with the CI alone (Offeciers et al. 2005; Pedley et al. 2005) or alternating both listening conditions depending on the listening needs (Incerti et al. 2011). Empirical support for the relevance and modalities of training in adults is unfortunately lacking (Stacey et al. 2010).
As discussed, plasticity in the auditory and cognitive-linguistic pathways occurs following cochlear implantation. This plasticity is involved in the improvement in performance observed over time and with auditory training following implantation. However, it is not known whether different modalities or intensities of auditory training could enhance this plasticity and lead to greater performance with the CI, particularly in cases of long-term unilateral sound deprivation when the CI is placed in the sound-deprived ear. This question is raised on multiple occasions throughout this thesis, but could not be specifically addressed within the research design.

1.2.6 Prognosis and cochlear implant candidacies

_Prognosis:_ the prospect of recovery as anticipated from the usual course of disease or peculiarities of the case.

The evaluation of candidacy for cochlear implantation follows two main aims (Niparko et al. 2009): i) to evaluate whether the candidates meet predefined criteria to proceed to implantation, and ii) to establish a prognosis of implantation. Candidacy criteria vary between countries and clinics because they may be defined within specific clinical guidelines or by the funding bodies. During the evaluation of candidacy, both the clinical team and the prospective implant candidates seek to obtain sufficient information to make a judgement on the likely performance after implantation. For the candidates, this information will help them decide if the emotional and (sometimes) financial investments are worth proceeding with implantation, when comparing the benefits obtained with their current hearing aids. For the clinical team, accepting to proceed with implantation is generally based on the high likelihood of improvement in speech recognition over those given by optimally fitted hearing aids. This prognosis will also be useful in counselling the patient about realistic expectations and will help establish rehabilitation objectives. Making a prognosis of probable outcomes of implantation is consequently a central aspect of candidacy evaluation. Unfortunately, the outcomes of cochlear implantation are highly variable and difficult to predict (Blamey et al. 1996; Dunham and Limb 2007). Much effort in research is therefore devoted to finding the most reliable predictors of implantation outcomes. The research questions addressed in this thesis (section 1.4) aim to further knowledge regarding the outcomes of cochlear implantation.
Typical predictors of cochlear implantation outcomes

*Predictor:* Indication that foretells future events on the basis of observation, experience, or scientific reason.

a) **Duration of deafness** is the most cited variable identified as a predictor of implantation outcomes (Dorman et al. 1989; Shea et al. 1990; Kileny et al. 1991; Blamey et al. 1992; Gantz et al. 1993; Battmer et al. 1995; Shipp and Nedzelski 1995; Summerfield and Marshall 1995; Blamey et al. 1996; Van Dijk et al. 1999; Dowell et al. 2002a; Friedland et al. 2003; Gomaa et al. 2003; Dowell et al. 2004; Green et al. 2007; Roditi et al. 2009). This occurs despite the vague meaning of *deafness* and the multiple methods used to measure it, as discussed in section 1.2.1. *Duration of deafness* aims to represent the length of time the auditory pathways and cortex have received limited or no auditory input. Although duration of deafness is the most frequently identified contributor to outcomes of implantation, not all studies found this relationship to be significant (Francis et al. 2005; Matterson et al. 2007).

b) **Residual hearing** is also often cited as a significant predictor of implantation outcomes (Summerfield and Marshall 1995; Van Dijk et al. 1999; Gomaa et al. 2003; Dowell et al. 2004; Bodmer et al. 2007; Roditi et al. 2009). This variable roughly represents the hearing that remains in spite of the hearing loss, and therefore indicates which magnitude of useful input the auditory pathways are still receiving just before implantation. Similarly, as with examining *duration of deafness*, the methods used to evaluate *residual hearing* are often imprecise. Residual hearing is usually measured using the **pre-operative SRS** (Rubinstein et al. 1999; Gomaa et al. 2003; Bodmer et al. 2007; Roditi et al. 2009), with or without hearing aids. At other times, it is a measure of the **severity of the hearing loss** (Francis et al. 2004b; Francis et al. 2005; Green et al. 2007). In that latter case, it is assumed that if more hair cells remain, the auditory pathways should be better preserved. Some authors have used both the SRS and the severity of deafness when discussing residual hearing (Van Dijk et al. 1999; Roditi et al. 2009). Note, however, that the changes in hearing abilities over time are not considered when measuring *residual hearing*.

c) **Choice of ear** is a common decision that must be taken in CI clinics (Pedley et al. 2005; Perreau et al. 2007). It is also a core variable that is examined in this thesis. When the choice of ear does not involve a medical condition (for example, middle-
ear effusion, eighth nerve anomaly, cochlear malformation, asymmetric balance function), the decision is typically based on audiological aspects to identify the better and worse ear. In particular, duration of deafness and residual hearing are usually measured in each individual ear, and prognoses are made in accordance with the respective values obtained for each ear. Often, the values presented in CI studies refer only to the values measured in the implanted ear (before implantation). Accordingly, the choice of ear will often be based on the poorer or better ear before implantation, with regards to duration of deafness and/or residual hearing in the implanted ear (UK Cochlear Implant Study Group 2004; Niparko et al. 2009). Only a small number of studies actually consider the potential impact of contralateral hearing on CI outcomes when discussing choice of ear (Friedland et al. 2003; Francis et al. 2004b; Francis et al. 2005; Matterson et al. 2007; Roditi et al. 2009). The majority of these studies consider the hearing in the better ear a representation of the input received by the central auditory pathways and find it to be the most significant contributor to outcomes of implantation. They conclude that the choice of ear is not a significant predictor of outcomes (Friedland et al. 2003; Francis et al. 2004b; Francis et al. 2005; Matterson et al. 2007). Conversely, Roditi et al. (2009) considers the longer duration of any HL and of a severe-to-profound HL in either ear (which typically relates to the poorer ear), but not the shorter duration, which would have represented the input received via the better ear (Roditi et al. 2009). Also of relevance to choice of ear is the potential for using bimodal hearing, combining a CI and a contralateral hearing aid (Perreau et al. 2007).

d) The presence of prelingual deafness has also been associated with poorer SRS after cochlear implantation in older children and adults, when compared with the SRS of those who acquired deafness later in life (Manrique et al. 1999; Dowell et al. 2002b; Waltzman et al. 2002; Dowell et al. 2004; Teoh et al. 2004; Bodmer et al. 2007; Santarelli et al. 2008; Caposecco et al. 2012). As discussed in section 1.2.2, congenital deafness leads to extensive neural degeneration in the auditory pathways, particularly if the hearing loss remains uncorrected (late implantation). A prelingual deafness also influences the development of oral language skills, which is discussed further in 1.2.6j. As a group, children deprived of hearing early in life are a highly heterogeneous population exhibiting multiple linguistic and general cognitive impacts related to the hearing loss (Pisoni et al. 2008). Consequently, their outcomes
after cochlear implantation are highly variable and difficult to predict (Pisoni et al. 2008; Wass 2009).

e) **Age at time of implantation** is another frequently cited variable affecting implantation outcomes (Millar et al. 1986; Dorman et al. 1989; Blamey et al. 1992; Gantz et al. 1993; Blamey et al. 1996; Dowell et al. 2004; Francis et al. 2005; Roditi et al. 2009). In children with a prelingual hearing loss, this refers to the critical period for cochlear implantation, where early implantation may facilitate increased outcomes with a CI (however, the actual presence of a cut-off age for implantation is debated, Harrison et al. 2005). When referring to outcomes of cochlear implantation in adults, age relates to elderly CI recipients. However, age at time of implantation is often related to duration of deafness (Budenz et al. 2011). When controlling for such confounders, some studies have found that age may remain significantly related to outcomes of implantation, but to a lesser extent (Van Dijk et al. 1999). Other studies though have found that age is not significantly associated with CI outcomes (Dorman et al. 1989; Shea et al. 1990; Bodmer et al. 2007; Matterson et al. 2007). It is also important to note that elderly cochlear implant recipients may need more time to learn using the sound delivered with the CI (Yeagle et al. 2010). Intertwined with this, any magnitude of normal cognitive decline that occurs in older age may complicate the listening tasks, where for example memory, information processing and speed are affected (Pichora-Fuller et al. 2006) (this is discussed further in 1.2.6j).

f) **Use of hearing aid** is a variable often discussed in clinics (Connell and Balkany 2006; Perreau et al. 2007) and sometimes in research (Bodmer et al. 2007; Roditi et al. 2009; Caposecco et al. 2012) in regards to outcomes of implantation. However, this is a complicated variable to evaluate on its own because hearing aid use is undoubtedly related to the progression of the hearing loss. For example, if a profound hearing loss occurs suddenly, evaluating the effects of whether a hearing aid is used, or for how long it has been used or not used, becomes irrelevant. On the other hand, the absence of hearing aid use in the case of a long-duration severe hearing loss, referred to as the duration of monaural sound deprivation, may be relevant to assess. It is often assumed that implantation in a long-term sound-deprived ear leads to poorer outcomes of implantation (see section 1.2.3). This is supported by studies raising concerns for poorer outcomes when implanting a long-term sound-deprived
ear, whether with unilateral (Chen et al. 2001 [examined the impact of 2-15 yrs with unilateral deprivation]; Balkany et al. 2002; Connell and Balkany 2006 [suggested to place CI in the better ear when more than 10 yrs of disuse]) or sequential bilateral cochlear implantation (Offeciers et al. 2005 [recommended that the time between surgeries should not exceed 12 yrs]; Ramsden et al. 2005a [excluded deafness durations longer than 15 years in either ear from their study]). Duration of monaural sound deprivation may also be confounded with duration of deafness and use of residual hearing. The impact of the duration of monaural sound deprivation on implantation outcomes is thoroughly examined within this thesis.

g) Aetiology of hearing loss has been proposed to affect outcomes of implantation (Waltzman and Roland 2006), although the association demonstrated between outcomes and aetiologies is often weak (Tyler et al. 1988; Van Dijk et al. 1999; Pyman et al. 2000). Hearing loss aetiology for CI candidates is often unknown or is a combination of multiple aetiologies, which complicates possible analyses. Moreover, prelingual vs. acquired and progressive vs. stable HL is often inappropriately considered as aetiologies (for examples: Gantz et al. 1994; Moon et al. 2012). Nevertheless, some specific aetiologies are known to affect outcomes. For example, meningitis, which causes bone growth to occur in the cochlea shortly after the infection, can complicate the insertion of the electrode array (Philippon et al. 2009). This can affect the current spread from the electrodes to the auditory neurons or causes the eventual deactivation of electrodes (Cosetti et al. 2011). Meningitis can also have impacts beyond the cochlea which can affect auditory and language processing and lead to decreased SRS with the CI (Francis et al. 2004a). However, when implantation is conducted shortly after the infection, similar outcomes can be obtained compared with other aetiologies (Francis et al. 2004a), probably in relation to a very short duration of deafness, although it is reported that the impact of meningitis may continue following implantation (Cosetti et al. 2011). Similar to meningitis, otosclerosis may complicate the surgical insertion of electrodes (Karino et al. 2004), broaden the current spread in the cochlea and increase the risk of facial stimulation which ultimately impacts CI programming (Matterson et al. 2007; Sainz et al. 2009). However, because of the conductive component of the hearing loss that typically accompanies otosclerosis, aided hearing is often better than in other aetiologies, which may allow better preservation of the auditory pathways,
potentially leading to higher SRS with the CI (Blamey et al. 1992; Quaranta et al. 2005). Neonatal infections such as rubella and cytomegalovirus, which are the two most frequently reported neonatal infections that lead to deafness in cochlear implant candidates, can also impact the central auditory pathways, resulting in potentially poorer outcomes with the CI (Clark 2003). Moreover, the most common form of non-syndromic genetic hearing loss, mutation of gene GJB-2 (Connexin 26) may impact the development of the auditory pathways differently than other aetiologies, potentially leading to poorer outcomes of implantation (Lalwani et al. 2009; Gordon et al. 2011b).

h) Surgical considerations can affect outcomes of implantation, particularly with cochlear malformations or ossification, which, as described when discussing aetiologies, will complicate or prevent complete insertion of the electrode array. It has been suggested that the optimal placement of the electrodes results in increased outcomes following implantation (Aschendorff et al. 2007; Finley et al. 2008). Accordingly, an atraumatic insertion in the scala tympani would be beneficial (Briggs et al. 2005; Roland et al. 2006; Meshik et al. 2010). However, other studies found no relationship between SRS and positioning the electrodes exclusively in the scala tympani (Wanna et al. 2011) or the number of electrodes implanted (Green et al. 2007).

i) Psychological considerations for cochlear implantation are rarely examined within research papers. Nevertheless, they will usually be considered during candidacy evaluation. The goal here is to ensure the CI candidate and their significant others have realistic expectations regarding the hearing abilities they can obtain with the implant (English 2010; Newberry 2011), and that the prospective CI recipient will be able to use and care for the CI (Dunham and Limb 2007). Abandonment of the CI after implantation occurs, and this appears to be related to limited benefits experienced with the CI (Summerfield and Marshall 2000; Ray et al. 2006), which may sometimes be more related to expectations than actual hearing abilities. Infrequent use of the CI will also limit the abilities that can be gained, because there is less opportunity for adaptation to the sound of the CI (Pedley et al. 2005) and also compromises the stability of the CI programming (MAP) in relation
to increased impedances that are observed in periods of non-use (Newbold et al. 2004; Van Wermeskerken et al. 2006).

j) Cognition in relation to oral language processing has recently gained interest when discussing outcomes of cochlear implantation. Cognition in this context is the mental resources and processes that are used when listening to speech, particularly in complex listening conditions, in order to actually recognise and understand what is said, and not just perceive a series of meaningless sounds (Pisoni 2000; Rönnberg 2003; Pichora-Fuller 2007). This has been recently labelled cognitive hearing (Arlinger et al. 2009). Examining cognition is of particular interest when measuring speech recognition scores (SRS), because the score obtained is actually a representation of combined auditory and cognitive abilities (George et al. 2007; Obleser et al. 2007; Pichora-Fuller 2008). Cognition in this context includes the phonological representation of speech sounds (Lyxell et al. 1998; Andersson 2002; Lyxell et al. 2003) and the semantic representations of words that are stored in the long-term memory (Shtyrov and Pulvermüller 2002; Rönnberg et al. 2008), the speed required to access these representations (Lyxell et al. 2003; Larsby et al. 2008; MacGregor et al. 2012), the working-memory that is necessary to make sense of longer utterances (Lyxell et al. 2003; Cowan 2005; Rönnberg et al. 2008; Rudner et al. 2011), knowledge of and ability to use contextual information to make sense of degraded speech (inference-making) (Boothroyd and Nittrouer 1988; Wingfield 1996; Flynn and Dowell 1999; Grant and Seitz 2000; George et al. 2007; Pichora-Fuller 2008), and the attention required to understand degraded speech (Singh et al. 2008; Zion Golumbic et al. 2012). In particular, Lyxell et al. (1998) and Andersson (2002) demonstrated that the quality of phonological representations, measured with rhyming judgement of words presented visually, deteriorates with long-term deafness. Such phonological deterioration may complicate the recognition of speech sounds delivered by the CI. Lunner (2003) showed that working memory ability, assessed with a reading span paradigm (Daneman and Carpenter 1980), is related to speech recognition scores, particularly in background noise. This implies that individuals with more efficient working memory could obtain better SRS with their CI, particularly in background noise. It is also apparent that poor CI performers access the meaning of spoken language by using different cognitive resources
compared with individuals with normal hearing or good CI performers (Giraud et al. 2000; Giraud and Truy 2002; Lazard et al. 2010).

A variable related to cognition that has been shown to be linked to cochlear implantation outcomes in recent years is **quality of speech**, particularly when discussing outcomes of implantation in adults with prelingual hearing loss (Kaplan et al. 2003; Klop et al. 2007; Van Dijkhuizen et al. 2011). Quality of speech is believed to be a proxy for the quality of auditory input that was accessible in early life (Van Dijkhuizen et al. 2011), but it might also be a proxy for how language is cognitively processed. In particular, speech quality has been shown to deteriorate in adults with an acquired profound hearing loss (Leder and Spitzer 1990; Gilbertson et al. 1996). Additionally, it is possible that adults with high speech quality have better-preserved phonological representations and/or inference-making abilities (Lyxell et al. 1996; Lyxell et al. 1998). Therefore, individuals who have developed and maintained high speech quality, even with neonatal or long-term deafness, have access, presumably, to better representation of speech sounds in their long-term memory, which may explain higher outcomes obtained with the CI.

Similar to the variable **quality of speech**, **auditory verbal training in childhood** (Kaplan et al. 2003; Bodmer et al. 2007) and **exclusive use of oral/aural communication** (Dowell et al. 2002a; Waltzman et al. 2002; Geers et al. 2003) have been related to greater outcomes of implantation. It appears probable that this type of training in childhood reinforces the cognitive resources involved in speech processing. **Pre-implantation lip-reading abilities** (Cohen et al. 1993; Summerfield and Marshall 1995), which have been related to CI outcomes, may also relate to the cognitive processing of speech (Lyxell et al. 2003).
Table 1.2. Typical predictors of cochlear implantation outcomes and their probable substrate(s).

<table>
<thead>
<tr>
<th></th>
<th>Integrity of auditory pathways</th>
<th>Integrity of cognitive-linguistic resources</th>
<th>Potential for neural plasticity and learning with a CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>a) Duration of deafness</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>b) Residual hearing</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>c) Better vs. worse ear</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>d) Presence of a prelingual deafness</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>e) Age at time of implantation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>f) Use of hearing aid</td>
<td>X-related to b)</td>
<td>X-related to b)</td>
<td>X-related to usage</td>
</tr>
<tr>
<td>g) Aetiology of hearing loss</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>i) Psychological considerations</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>j) Cognition / language processing</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
</tbody>
</table>

In summary, multiple variables have been related, with varying degree, to outcomes of cochlear implantation. Except for surgical complications, the variables can all be associated with the integrity of the auditory pathways, the integrity of cognitive resources involved in speech processing, and/or the potential for neural plasticity and learning after implantation (Table 1.2). More research is needed to gain a better understanding of the relative contribution of the different predictors in order to increase understanding and precision in the prognosis of cochlear implantation. This thesis particularly examines duration of deafness, residual hearing, choice of ear for implantation, and hearing aid use, in relation to outcomes of cochlear implantation.

### 1.2.7 Decision-making in the absence of scientific evidence

**Decision-making:** the ability to make judgments and choose between two or more alternatives (Mosby's Medical Dictionary 2009).

Decisions that are made within cochlear implantation clinics are influenced by factors beyond knowledge specifically relating to outcomes of implantation. For example, the socio-political context of the implantation centre, as well as the specific clinical experience and personal factors of the professional and/or clinical team will influence decisions made. These influences are faced in multiple health sectors and are difficult to avoid despite the desire to follow universal guidelines of best practice (Polacek et al. 2007; Cartwright and Munro 2010; Kristensen et al. 2012). On the other hand, some suggest that best practice necessarily involves being aware of and
considering these influences in the decision process (Lavis et al. 2010; Oxman et al. 2010b). This is particularly true in situations where scientific evidence is lacking (Oxman et al. 2010a). For example, little is known regarding whether long-term sound deprivation affects outcomes of cochlear implantation. However, the presence or absence of such influences certainly impact the decision of which ear should be implanted. In fact, such knowledge even influences whether implantation should be conducted at all in adults with long-term monaural sound deprivation having considerable residual hearing in the aided ear. Influences of sound deprivation on implantation outcomes may also impact the decision of performing simultaneous or sequential cochlear implantation and in the latter situation, when the second implantation should be performed. Because limited scientific evidence exists surrounding this variable, other socio-political and experiential factors may be supporting decision-making in implantation clinics. Some of those factors, which relate to clinics who collaborated in this research work, are presented in the following paragraph. They are also likely to be relevant to the decision-making process in other clinics around the world.

**Socio-political influences**

The source(s) of funding of the country’s health system will impact the amount of funding allocated to CI programs, as well as the distribution of these funds to different resources or activities within the programs. Typically, in welfare states, a fixed quantity of CIs will be publically funded every year. Because waiting lists exist before receiving a CI, priorities must be defined regarding who will benefit from these implants. For example³, in Sweden and in the province of Quebec (Canada), cochlear implantation is fully publically funded, and private insurance cannot be used to cover the costs related to implantation. Accordingly, each adult CI candidate is normally offered only one CI, with limited exceptions being made when bilateral hearing is identified as an essential benefit (e.g. deafblindness, work-life involving listening in noise). In comparison, cochlear implantation in New South Wales and

³ Examples listed here refer to personal communications with managers and/or clinicians in each CI clinic.
Victoria in Australia can be funded publically and/or privately. At Sydney Cochlear Implant Centre, public funds only cover the cost of one CI per adult CI candidate. Candidates who have access to private health insurance have the possibility of obtaining two CIs. On the other hand, at the Melbourne Cochlear Implant Clinic, two CIs can be offered either via public or private funding.

The possibility to offer/receive a second CI affects the weight of the decision regarding which ear is the more appropriate to implant. That is, when an eventual implantation in the contralateral ear is possible, the impression of risks associated with implanting a long-term sound-deprived ear diminishes. Consequently, clinics having easy access to funds for sequential bilateral cochlear implantation may be more likely to recommend implantation in the worse ear, despite a long-term sound deprivation. Conversely, clinics who can offer only or mostly unilateral implantation will be more likely to avoid implanting a long-term sound-deprived ear. Patients of these clinics usually agree with these tendencies, although some will choose to go against the recommendation of the professionals, preferring, for different reasons, to implant the opposite ear.

**Influences from clinical experiences**

Although decision-making guidelines may exist in implantation clinics, professionals cannot easily or completely dissociate themselves from their own past experiences. As discussed in Cowlrick et al. (2011), who studied the pharmacological industry, there are considerable differences in the individual intuitive judgement of health professionals, in regard to evaluating benefits and risks of making one decision over another, particularly in the event of incomplete data. Moreover, with cochlear implantation, the occurrence of unexpectedly poor outcomes often results in a search for possible explanations (i.e. a sensemaking process, Weick 1995). This is highlighted in the clinical records where justifications for the poor outcomes can be found, for example: meningitis, infrequent user, long-term deafness, and in particular: has not heard in that ear for many years. When high outcomes are obtained, the presence of antecedents for potentially poor outcomes is often omitted from the records.
Additionally, the human mind registers more strongly negative than positive experiences (Rozin and Royzman 2001). Thus, following unexpectedly poor outcomes, CI professionals may experience guilt and/or regret about potentially having guided the patient towards a non-optimal decision. The feeling of regret after a decision enhances the impact of a negative experience (Chua et al. 2009). Therefore, even if the clinical experience of a professional would involve an equal number of high and poor outcomes after implantation in a long-term sound-deprived ear, relying on clinical experiences would likely involve a bias towards the poor outcomes. This would presumably lead to higher perceived risks with implantation in a long-term sound-deprived ear. In comparison, when unexpectedly poor outcomes are obtained following implantation in the aided ear, causes other than the sound deprivation would be suggested to explain the poor outcomes. Nevertheless, in both cases, it is unknown if similar outcomes could have been obtained with either ear.

As stated previously, scientific support is lacking when considering the more appropriate ear to implant in the case of long-term monaural sound deprivation. Despite this lack of evidence, decisions on which ear is to be implanted must be made and will involve socio-political aspects and personal influences. Ideally, increased knowledge regarding the outcomes of implantation in a long-term sound-deprived ear will decrease the reliance on a highly variable professional judgement and will support evidenced-based policy-making of clinical guidelines and program funding.
1.3 Objective of the thesis

The main objective of this thesis is to gain a better understanding of the relative contribution of factors that may affect outcomes of cochlear implantation in adults with a severe hearing loss bilaterally, but using unilateral hearing aid (i.e. monaural sound deprivation). Because it is becoming more common for CI candidates to have a hearing asymmetry prior to implantation, this knowledge could ultimately reduce the clinical uncertainty that exists when predicting outcomes of implantation in relation to the choice of ear, leading to more effective clinical decision-making for this population.

1.4 Research questions and justifications

i. Is the duration of sound deprivation (severe unaided hearing loss) in the implanted ear a relevant variable to consider as part of candidacy evaluation for cochlear implantation?

Relevance: In most cochlear implantation clinics, when a patient presents using a single hearing aid despite a bilateral severe hearing loss, it is common practice to consider the duration for which one ear has had no auditory stimulation (Balkany et al. 2002; Connell and Balkany 2006). This information appears useful when choosing the ear to implant, because it is often assumed that poorer results will be obtained if an ear that has not heard for many years is implanted, in comparison to an aided ear. Moreover, the same assumption is used in regard to single-sided deafness, where a cochlear implant would be recommended mainly if the deafened ear has been sound-deprived for a short duration ($\leq 10$ years) (Arndt et al. 2011). However, this assumption has not been tested.

ii. What influence does the hearing in the non-implanted ear have on cochlear implantation outcomes?

Relevance: There are three ways in which the non-implanted ear may influence outcomes of implantation in a sound-deprived ear: 1) hearing in the better ear may contribute to maintaining the synaptic activity in the auditory pathways and
cortex, which may facilitate better outcomes when implanting a sound-deprived ear (Friedland et al. 2003); 2) implanting the sound-deprived ear may promote the use of bimodal hearing (use of the CI in conjunction with the hearing aid). Bimodal hearing with the CI in the sound-deprived ear may offer increased auditory benefits compared to the use of unilateral CI (Firszt et al. 2008); and 3) maintaining hearing in the better ear with a hearing aid may limit the development of optimal hearing abilities with a CI, particularly when speech recognition tests are conducted with the CI alone (Offeciers et al. 2005). As auditory experience after implantation is via both a cochlear implant and a hearing aid, it is reasonable to assume that testing in the non-habitual CI alone condition will show poorer outcomes than for individuals using the CI alone for their daily listening. This question has received very limited attention in the literature.

iii. Which factors significantly contribute to outcomes of cochlear implantation in adults with a monaural sound deprivation?

**Relevance:** Estimating the probable outcome that an individual can reach with a CI is a major component of counselling before and after implantation. This prognosis supports decision-making about whether to proceed with implantation, and the choice of ear in which a first cochlear implant should be placed. After implantation, this prognosis may be used to set patient and professional expectations and rehabilitation objectives. It appears then worthwhile to identify the factors that contribute to the outcomes of implantation in the case of monaural sound deprivation, amongst the usual possible predictors of implantation outcomes and those relating specifically to monaural sound deprivation. This is particularly important because implantation is now being considered in asymmetric hearing loss and single-sided deafness.
Chapter 2  Methodology

2.1 General methodology

Five manuscripts form this thesis; to date, three have been published and two are to be submitted. All five manuscripts describe retrospective cohort studies based on data collected in five cochlear implantation centres: the Québec Cochlear Implant Program at Institut de Réadaptation en Déficience Physique de Québec (Canada), the Sydney Cochlear Implant Centre (Australia), the Melbourne Cochlear Implant Clinic at the Royal Victorian Eye and Ear Hospital (Australia), the Cochlear Implant Program at Linköping University Hospital (Sweden) and the Cochlear Implant Program at Karolinska University Hospital (Sweden). The three first manuscripts present country-specific data while the fourth and fifth manuscripts merge the data collected in the three countries.

Participants with a bilateral hearing loss were considered eligible to be included in the studies if they were using only 1 hearing aid before implantation and had a severe and unaided hearing loss in the other ear (monaural sound deprivation) for a minimum of 15 years before implantation. The CI device was implanted between 2000 and 2009 (i.e. recent devices). Speech Recognition Score (SRS) had to be available in the clinical files\textsuperscript{4}, measured at least three months after the initial switch-on, with recorded material using the main language of the Centre and the participants’ first language. The reason for this is that outcomes of speech recognition tests have been related to linguistic proficiency (Vale et al. 2004). Participants were excluded from eligibility if they were less than 18 years old at time of implantation (to minimise the contribution of developmental aspects to the variability in outcomes), or if there was evidence of surgical complication, device failure or cognitive limitations (all of which could affect outcomes of implantation).

\textsuperscript{4} The most common reasons for not obtaining SRS in the files were that clients did not attend their regular follow-ups or that they received services in a distant location that did not have the facilities to conduct speech recognition tests with recorded material.
The following three variables, which are described in detail further in this section, were used for the core of the analyses described in the five manuscripts:

- **Main outcome measure:** speech recognition score (SRS).
- **Independent variables:** duration of monaural sound deprivation; duration of bilateral significant hearing loss.

In each manuscript, the duration of bilateral significant hearing loss is analysed in parallel to the duration of monaural sound deprivation. This is because the former variable mainly relates to the total hearing experience the auditory pathways and brain have had before implantation, while the latter is related to the hearing experience the ear that received the CI has had before implantation.

**Main outcomes measure: Speech Recognition Score (SRS)**

SRS measured in quiet was used as the main outcome measure in the five manuscripts of this thesis. SRS is the typical measure used within implantation centres to evaluate outcomes of cochlear implantation in adults. It is commonly obtained by presenting recorded words or sentences in auditory mode only (without lipreading), in free field via one or two loud speakers located 1 metre in front of the participant or at 45° azimuth, at a level between 60 and 65dB SPL. The participant is asked to repeat what they hear and their response is marked as a percentage of correctly recognised phonemes or words. Different speech material was used to measure SRS in the centres where data were collected (as noted in Table 2.1 – from manuscript 4).

<table>
<thead>
<tr>
<th>Country</th>
<th>Speech material</th>
<th>Standardised Test</th>
<th>Language</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quebec</td>
<td>Sentences</td>
<td>Test Auditif</td>
<td>Canadian-French</td>
</tr>
<tr>
<td>Sweden</td>
<td>Monosyllabic words (word score)</td>
<td>Multimedia (TAM)</td>
<td>Swedish</td>
</tr>
<tr>
<td>Australia</td>
<td>Sentences and monosyllabic words (word and phonemic score)</td>
<td>Swedish Phonemically-Balanced words (SPB)</td>
<td>Australian English</td>
</tr>
</tbody>
</table>

**Table 2.1. Speech recognition test material used in the implantation centres.**
Where data from different countries were merged for analysis, SRSs were transformed into z-scores, using the mean and standard deviation of the respective population (see manuscript 4 for more details).

**Rationalisation and challenges related to the use of SRS as the main outcome measure**

SRS measured in quiet is the typical outcome measure that can be consistently found in clinical files when conducting retrospective cohort studies. Testing with background noise is becoming more common, in particular with CI recipients obtaining good outcomes from their implant. However, this practice is not yet standardised. It is generally agreed that speech recognition testing in quiet cannot represent the range of hearing abilities and limitations an individual faces with a cochlear implant. Other measures of outcomes can be additionally used, for example: satisfaction questionnaires, hearing in spatially separated background noise, electrophysiological testing or evaluation of temporal and spatial processing. However, because time is a scarce resource for the clinicians and for the patients, testing time is generally restricted to SRS in quiet when the follow-up is not part of a predefined research project. Consequently, SRS measured in quiet is the main outcome measure used in this thesis, which has limited the extent of the research questions (described in section 1.4).

In order to address the main aim of this thesis with more complex outcome measures, a prospective study including multiple behavioural and electrophysiological outcome testing was attempted. Unfortunately, the strict but necessary inclusion criteria regarding the duration of monaural sound deprivation of at least 15 years was a major obstacle in recruiting a sufficient number of participants.

For the purpose of this thesis, it was decided to examine the benefits of implantation using the speech recognition performance with the CI alone, and in the daily listening condition (CI alone or bimodal). This method acknowledges the possibility that although poorer outcomes with the CI alone could be obtained by implanting the sound-deprived compared with the aided ear, the functional outcome measured in the daily listening condition may be similar. Benefits of implantation could also have been measured as an improvement in speech recognition scores compared to a
baseline condition, but this would have created a bias towards the sound-deprived ear, which typically has poorer performance before implantation.

The reliability of the SRS data collected may have been affected by using a retrospective research design, where the test conditions could not be controlled or verified. However, the five CI centres involved in this research have extensive experience with cochlear implantation and follow similar and standardised testing protocol after implantation. In other words, they have established routines for measuring SRS, which increases the reliability of the data used in this thesis. Nevertheless, it is assumed that there was some testing variability between clinicians, which could have led to increased variability in the research results. As presented in the empirical chapters of the thesis (chapters 3 to 7), a similar pattern of results was found across countries, which indicates that this testing variability did not significantly affect the results.

**Duration of monaural sound deprivation**

Duration of monaural sound deprivation is used in the five manuscripts because it is the main variable that is challenged in this thesis as a contributor to outcomes of cochlear implantation (see section 1.4). The term *sound deprivation* is sometimes used broadly and may represent any level of hearing loss, aided or unaided. In this thesis, the duration of monaural sound deprivation represents the length of time an ear has had no relevant auditory input under normal listening conditions. It is defined as an *at least severe* (pure-tone threshold average measured at 500Hz, 1000Hz and 2000Hz $\geq 70$dBHL) and *unaided* hearing loss in one ear. This does not imply that all sound-deprived ears had a complete absence of hearing, because low frequency sounds with loud levels may occasionally have been heard. However, it is assumed that this stimulation, if it was present, would have been infrequent and insufficient for daily speech processing.

It is often clinically anticipated that poor outcomes will be obtained when implanting an ear that has been sound-deprived for many years (see section 1.2.6f). Additionally, some studies have raised concerns regarding the outcomes of implantation in an ear deprived of auditory stimulation for periods longer than 10 years (Balkany et al. 2002; Connell and Balkany 2006) or 15 years (Chen et al.
A minimum duration of 15 years of sound deprivation was used in response to these studies, while ensuring that there was a considerable difference in stimulation between the ears and a sufficient number of participants could be recruited.

**Duration of bilateral significant hearing loss**

The concept of duration of bilateral significant hearing loss was developed to represent the length of time the auditory pathways and cortex have received very degraded auditory input, prior to cochlear implantation. Although this exact concept has not been used prior to this thesis, it refers to what Friedland et al. (2003) named the *overall auditory experience*. For the purposes of the current study, it was deemed necessary to develop a practical measure of this concept in the context of studying more precisely the duration of deafness in the cases of hearing asymmetries. The duration of bilateral significant hearing loss measures hearing abilities over time, regardless of the ear, integrating *duration of deafness* (1.2.6a) and *use of residual hearing* (1.2.6b), the two most cited predictors of implantation outcomes. The duration of bilateral significant hearing loss is the time for which two of the following factors are met in both ears: i) the hearing loss is severe (pure-tone threshold average $\geq 70$dBHL), ii) the use of the telephone is not possible, and/or iii) the SRSs are $\leq 30\%$ for sentences or $\leq 10\%$ for words. The alternative approach would have been to measure the three factors independently, which, as discussed in section 1.2.1, would have potentially led to increased measurement variability, affecting the validity of the results.

**2.2 Statistical approach**

Multiple statistical methods are used in each of the five manuscripts to verify whether the results obtained are related to the choice of test, or whether they can be reproduced with an alternative approach. Overall, similar patterns of results were obtained irrespective of the type of test used, which increases the reliability of the results.

Further methodological decisions are specific to each study and relate to the specific research questions, the availability of the data or to learning gained from the previous
studies. Thus, the next section presents the details of the analyses that were used in each manuscript.

**Specific methodology used in each manuscript**

**Manuscript 1**

**Relative importance of monaural sound deprivation and bilateral significant hearing loss in predicting cochlear implantation outcomes.**

Objective: To compare the relationships between SRS and the duration of i) auditory deprivation in the implanted ear, ii) bilateral significant hearing loss, and iii) auditory stimulation before bilateral significant hearing loss.

Study design: CI outcomes were examined in 16 adults with monaural sound deprivation all implanted in the sound-deprived ear.

Setting: Québec Cochlear Implant Program, Canada.

Statistical analyses: Correlation analyses were conducted in this study as a preliminary examination of the relationship between variables. Non-parametric tests were preferred because the distribution of the data was not normal; however, similar results were obtained with parametric testing. The small sample size limited the possible analyses.

Outcome measure(s): The best SRS obtained with Canadian-French sentences, within the first year following implantation, was used.

**Manuscript 2**

**Long-term monaural auditory deprivation and bilateral cochlear implants**

Objective: To compare the unilateral outcomes of bilateral sequential cochlear implantation in adults with long-term monaural sound deprivation.

Study design: Unilateral CI outcomes were examined in 10 adults with monaural sound deprivation implanted bilaterally. For all participants, the first CI was received in the sound-deprived ear.
Setting: Sydney Cochlear Implant Centre and Melbourne Cochlear Implant Clinic (Royal Victorian Eye and Ear Hospital), Australia.

Statistical analyses: Paired t-tests were undertaken to compare outcomes between the first and the second implanted ear. Correlation and multiple regression analyses were also undertaken between the SRS obtained after implantation and multiple variables that could possibly contribute to outcomes. While it was acknowledged that multiple regression analyses in small samples may lead to statistical errors and mislead interpretation of results, these were included to complement the paired comparisons, which were the main analyses.

Outcome measure(s): Outcomes were the averaged SRS obtained 1 year after implantation on CUNY sentences and CNC word recognition (entire word and phoneme scores) and preferences reported by participants for the implant in one ear as compared with the other.

Manuscript 3

Choice of ear for cochlear implantation in adults with monaural sound deprivation and unilateral hearing aid

Objectives: To identify whether cochlear implantation outcomes are influenced by the choice of ear in adults with monaural sound deprivation.

Study design: Matched cohort study. SRS were examined in 30 adults with monaural sound deprivation. 15 received the CI in the sound-deprived ear and 15 in the aided ear. Matches between participants were based on duration of monaural sound deprivation, duration of bilateral hearing loss, age, and aetiology where possible, while blinding the outcomes obtained with the CI.

Setting: Linköping University Hospital and Karolinska University Hospital, Sweden.
Statistical analyses: Paired comparisons of SRS obtained with the implant alone and in the usual listening condition (CI alone or bimodal) were conducted, between individuals implanted in the sound-deprived and those implanted in the aided ear. Once again, the small sample size limited the possibilities for further and more elaborated statistical testing, which is the reason that supported the use of matched cohorts. As discussed in the manuscript, the authors acknowledge the risk of committing type 1 errors when conducting multiple comparisons, where a significant difference found between groups could actually have happened by chance. However, the authors intuitively hypothesised that there would be a difference between the groups, which goes in the direction of a potential type 1 error. Therefore, if a type 1 error has occurred, this implies that the groups may be even less different than what was found.

Outcome measure(s): SRS measured with Swedish monosyllabic words. All participants were tested at least 1 year post-CI and the best SRS obtained during the post-operative evaluation period was used.

Manuscript 4
Cochlear implantation in a long-term monaural sound-deprived ear in adults with postlingual hearing loss
Objectives: To examine: i) the differences in outcomes of implantation in a sound-deprived or an aided ear, and ii) the relative contribution of possible factors to implantation outcomes, in adults with postlingual hearing loss and unilateral sound deprivation.

Study design: CI outcomes were examined in 99 adults with acquired hearing loss and monaural sound deprivation whether they received the CI in the aided (n=29) or in the sound-deprived ear (n=70).
Setting: All five cochlear implant centres involved in this research work.

Statistical analyses: To allow for collation of the data, SRS were standardised via a z-score transformation using the mean and standard deviation of the population where data was collected. This increased sample size also increased the possibility for, and reliability of, further statistical testing. Analyses of variance were used to compare SRS obtained after implantation of an aided or a sound-deprived ear, whether the CI is used alone or in bimodal condition. Multiple regression analyses via general linear modeling were used to identify predictors of outcomes of implantation in the case of long-term unilateral sound deprivation. A longitudinal comparison was conducted with the Australian data collected 3 to 6 months and 1 year after implantation to verify the effect of longer experience with the implant.

Outcome measure(s): SRS measured 3 to 6 months after implantation, with the speech material used in the respective centres.

Manuscript 5
Adults with prelingual hearing loss and monaural sound deprivation

Objectives: To examine: i) the differences in outcomes of implantation in a sound-deprived or an aided ear, and ii) the relative contribution of possible factors on implantation outcomes in adults having a prelingual hearing loss in the implanted ear.

Study design: CI outcomes were examined in 48 adults with a prelingual hearing loss in the CI ear whether they received the CI in the aided (n=20) or in the sound-deprived ear (n=28).

Setting: All five cochlear implant centres involved in this research work.

Statistical analyses: The standardised and collated data was used in these analyses, as described in manuscript 4. T-tests were used to compare
SRS obtained after implantation of an aided or a sound-deprived ear. Multiple regression analyses via general linear modeling were used to identify predictors of outcomes of implantation in the case of long-term unilateral sound deprivation and prelingual hearing loss.

Outcome measure(s): SRS measured 3 to 6 months after implantation, with the speech material used in the respective centres.

In summary, manuscript 1 examines the relative contribution of duration of bilateral significant hearing loss compared with duration of unilateral sound deprivation in adults implanted in the sound-deprived ear; manuscript 2 examines outcomes of bilateral cochlear implantation in adults with a unilateral sound deprivation; manuscript 3 compares outcomes of implantation in the sound-deprived ear with outcomes obtained in a matched group implanted in the aided ear; manuscript 4 expands on manuscript 3 by using a larger sample size, including only adults with postlingual hearing loss, but not matching participants implanted in either ear; and manuscript 5 compares outcomes of adults with a prelingual hearing loss implanted in either ear.

The following chapters (3 to 7) contain manuscripts 1 to 5. The format of the published papers (manuscripts 1 to 3) has been partly adapted to the format of the thesis for increased consistency (e.g. the references have been included in the thesis’ reference list, but the language and number formatting of the journals were maintained). In addition minor amendments were performed to increase the quality of the published papers (e.g. grammatical corrections, presentation of more detailed values). Further analyses of the data follow manuscripts 3, 4 and 5 (Chapters 5, 6, and 7). These analyses were not included in the manuscripts because of the word limits of the journals, poor statistical power of the analyses that could not justify publication, or to improve readability by limiting the information presented in the manuscripts. Nevertheless, the analyses were judged to be informative to the conclusions of this thesis and the discussion of further research.
Chapter 3

Relative importance of monaural sound deprivation and bilateral significant hearing loss in predicting cochlear implantation outcomes

Isabelle Boisvert¹²³, Catherine M. McMahon¹², Geneviève Tremblay⁴, and Björn Lyxell³⁵.

¹Centre for Language Sciences, Macquarie University, Sydney, New South Wales, Australia; ²HEARing Cooperative Research Centre, Victoria, Australia; ³Linnaeus Centre HEAD, The Swedish Institute for Disability Research, Linköping, Sweden; ⁴Institut de Rédadaptation en Déficience Physique de Québec, Québec, Canada; and ⁵Linköpings Universitet, Linköping, Sweden.

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ABSTRACT

Objectives: Making evidence-based recommendations to prospective unilateral cochlear implant recipients on the potential benefits of implanting one or the other ear is challenging for cochlear implant teams. This particularly occurs in cases where a hearing aid has only been used in one ear for many years (referred to here as the “hearing ear”), and the contralateral ear has, in essence, been sound-deprived. In such cases, research to date is inconclusive, and little anecdotal evidence exists to inform the debate and support best clinical practice.

Design: Retrospective data on speech recognition outcomes of 16 adult participants who received a cochlear implant in an ear deprived of sound for a minimum of 15 yr were analyzed. All subjects were implanted through the Quebec Cochlear Implant Program and were provided with personalized intensive rehabilitation services. Data obtained from clinical records included demographic data and speech recognition scores measured after implantation with the sentences of a multimedia auditory test battery in the auditory-only condition. Speech recognition outcomes were compared with the duration of auditory deprivation in the implanted ear, bilateral significant hearing loss, and auditory stimulation before bilateral significant hearing loss.

Results: Using nonparametric correlation analyses, a strong negative correlation was demonstrated between speech recognition scores and the duration of bilateral significant hearing loss and with the duration of auditory stimulation before bilateral significant hearing loss. No significant correlation with the duration of auditory deprivation or with the duration of prior auditory stimulation in the implanted ear was found.

Conclusions: These findings suggest that functional outcomes of cochlear implantation for unilateral sound deprivation may be more strongly influenced by central processes than peripheral effects stemming from the deprivation per se. This indicates the relevance of considering the client’s history of binaural hearing rather than the hearing in each ear individually when discussing possible outcomes with a cochlear implant.
Chapter 3

Relative importance of monaural sound deprivation and bilateral significant hearing loss in predicting cochlear implantation outcomes

Isabelle Boisvert¹,²,³, Catherine M. McMahon¹,², Geneviève Tremblay⁴, and Björn Lyxell³,⁵.

¹Centre for Language Sciences, Macquarie University, Sydney, New South Wales, Australia; ²HEARing Cooperative Research Centre, Victoria, Australia; ³Linnaeus Centre HEAD, The Swedish Institute for Disability Research, Linköping, Sweden; ⁴Institut de Réadaptation en Déficience Physique de Québec, Québec, Canada; and ⁵Linköpings Universitet, Linköping, Sweden.

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Chapter 4

Long-term monaural auditory deprivation and bilateral cochlear implants

Isabelle Boisvert\textsuperscript{a,b,e}, Catherine M. McMahon\textsuperscript{a,b} and Richard C. Dowell\textsuperscript{b,c,d}

\textsuperscript{a}Centre for Language Sciences, Macquarie University, Sydney, New South Wales, \textsuperscript{b}HEARing Cooperative Research Centre, \textsuperscript{c}Department of Audiology and Speech Pathology, The University of Melbourne, \textsuperscript{d}Audiology, Royal Victorian Eye and Ear Hospital, Melbourne, Victoria, Australia and \textsuperscript{e}Linnaeus Centre HEAD, The Swedish Institute for Disability Research, Linköping, Sweden

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ABSTRACT
Long-term binaural auditory deprivation is associated with poorer speech recognition outcomes after cochlear implantation, even for postlingual hearing loss. It is, however, unknown to what extent the outcomes of implantation are related to the peripheral changes occurring monaurally or to changes at a higher level in the auditory system related to binaural deafness. This retrospective study aimed to unravel peripheral and central contributions to cochlear implantation outcomes by comparing outcomes obtained in individual ears for adults with long-term monaural auditory deprivation (i.e. unilateral use of hearing aid) who received bilateral cochlear implants. Results showed that similar outcomes can be obtained with the implant placed in the auditory-deprived or in the aided ear. This suggests that the peripheral changes related to monaural auditory deprivation have little effect on outcomes of cochlear implantation.

INTRODUCTION
Auditory deprivation results in physiological changes observable at all major relays of the auditory pathways (see O'Neil et al. 2011 for a review). In individuals with cochlear implants (CIs), it has been suggested that long duration deafness before implantation is related to decreased speech recognition scores (SRS) (Shepherd and Hardie 2001). It is, however, unknown whether the peripheral physiological changes related to long-term monaural auditory deprivation are sufficient to cause a decrease in functional outcomes of implantation.

Animal studies of auditory deprivation demonstrate that a loss of cochlear hair cells impedes the release of neurotrophic factors, needed to maintain the integrity of peripheral auditory neurons (Terayama et al. 1977). Degeneration of these neurons can eventually cause variable reductions in numbers of spiral ganglion neurons and a concomitant decrease in neural activity (Webster and Webster 1981; Nayagam et al.
Long-term monaural auditory deprivation and bilateral cochlear implants

Isabelle Boisvert\textsuperscript{a,b,c}, Catherine M. McMahon\textsuperscript{a,b} and Richard C. Dowell\textsuperscript{b,c,d}

\textsuperscript{a}Centre for Language Sciences, Macquarie University, Sydney, New South Wales, \textsuperscript{b}HEARing Cooperative Research Centre, \textsuperscript{c}Department of Audiology and Speech Pathology, The University of Melbourne, \textsuperscript{d}Audiology, Royal Victorian Eye and Ear Hospital, Melbourne, Victoria, Australia and \textsuperscript{c}Linnaeus Centre HEAD, The Swedish Institute for Disability Research, Linköping, Sweden

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ABSTRACT

Objectives: To identify whether speech recognition outcomes are influenced by the choice of ear for cochlear implantation in adults with bilateral hearing loss who use a hearing aid in 1 ear but have long-term auditory deprivation in the other.

Study Design: Retrospective matched cohort study. Speech recognition results were examined in 30 adults with monaural sound deprivation. Fifteen received the implant in the sound-deprived ear and 15 in the aided ear.

Setting: Tertiary referral centers with active cochlear implant programs.

Patients: Adults with bilateral hearing loss and a minimum of 15 years of monaural sound deprivation who received a cochlear implant after meeting the traditional implantation criteria of the referral centers.

Intervention: Cochlear implantation with devices approved by the U.S. Food and Drug Administration.

Main Outcome Measure(s): Paired comparisons of postoperative monosyllabic word recognition scores obtained with the implant alone and in the usual listening condition (CI alone or bimodal).

Results: With the cochlear implant alone, individuals who received the implant in a sound-deprived ear obtained poorer scores than individuals who received the implant in the aided ear. There was no significant difference, however, in speech recognition results for the 2 groups when tested in their usual listening condition. In particular, poorer speech recognition scores were obtained with the cochlear implant alone by individuals using bimodal hearing.

Conclusion: Similar clinical outcomes of cochlear implantation can be achieved by adults with a long-term monaural sound deprivation when comparing the usual listening condition, irrespective of whether the implant is in the sound-deprived or in the aided ear.
Chapter 5
Choice of ear for cochlear implantation in adults with monaural sound deprivation and unilateral hearing aid

**Isabelle Boisvert, Björn Lyxell, Elina Mäki-Torkko, Catherine M. McMahon, and Richard C. Dowell.**

*Centre for Language Sciences, Macquarie University, Sydney, Australia; †HEARing Cooperative Research Centre, Melbourne, Australia; ‡Linnaeus Centre HEAD, The Swedish Institute for Disability Research, Sweden; §Department of Behavioural Sciences and Learning, Linköping University, Sweden; ‖Department of Clinical and Experimental Medicine, Division of Technical Audiology, Linkoping University, Sweden; ‡Department of ENT-Head Neck Surgery UHL, County Council of Östergötland, Sweden; #Department of Audiology and Speech Pathology, The University of Melbourne, Australia; and **Audiology, Royal Victorian Eye and Ear Hospital, Melbourne, Australia.

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5.1 Manuscript 3 – Further analyses of the data

The following analysis was not included in manuscript 3 because of a word limit request from the journal where it has been accepted for publication.

Analysis of the relationship between SRS and duration of monaural sound deprivation and between SRS and duration of bilateral significant hearing loss

To support the selection of the pairing variables, correlation analyses were performed between the duration of sound deprivation and the SRS of individuals implanted in the sound-deprived ear, and between the duration of bilateral significant hearing loss and the SRS of all participants. The duration of sound deprivation, expressed as a number of years and as a percentage of lifetime, was significantly correlated with the SRS measured with the use of the implant alone (n=15, respectively: $r_s=-0.64$, $p=0.01$ and $r_s=-0.53$, $p=0.02$). However, the duration of sound deprivation was not significantly correlated with their SRS obtained in the usual aided condition (n=13, respectively: $r_s=-0.29$, $p=0.17$ and $r_s=-0.31$, $p=0.15$). On the other hand, the duration of bilateral significant hearing loss, expressed in years and as a percentage of lifetime, was not significantly correlated with the SRS measured with the CI alone (n=30, respectively: $r_s=-0.19$, $p=0.16$ and $r_s=-0.20$, $p=0.15$), but was significantly correlated with the SRS measured in the usual aided condition (n=28, respectively: $r_s=-0.55$, $p<0.00$ and $r_s=-0.55$, $p<0.00$). When the analysis was performed only with participants using the CI alone, duration of bilateral significant hearing loss measured in years and in percentage of lifetime was significantly correlated with the SRS obtained with the CI (n=21, respectively: $r_s=-0.49$, $p=0.01$ and $r_s=-0.50$, $p=0.01$). This analysis suggests that for this population, SRS measured with the implant alone are related to the duration of monaural sound deprivation in the implanted ear, whereas SRS measured in the usual aided condition are related to the duration of bilateral significant hearing loss.

From these results, it seems reasonable to consider the duration of bilateral significant hearing loss when discussing CI outcomes. That is, for the individuals implanted in the sound-deprived ear, a significant correlation was found between the duration of monaural sound deprivation and SRS measured with the CI alone.
However, when including all participants, a significant relationship was found between the duration of bilateral significant hearing loss and SRS measured in the usual aided condition. When excluding participants using bimodal hearing, the duration of bilateral significant hearing loss was significantly related to the SRS. Because of the relationship found between duration of bilateral significant hearing loss and SRS for individuals using the CI alone daily, it can be hypothesized that with specific auditory training with the CI alone, the SRS of individuals preferring the use of bimodal hearing, measured with the CI alone, could increase. This could also occur in individuals who eventually stop the use of their hearing aid because of a progressing hearing loss in the non-implanted ear. However, further research in that direction is needed to verify these hypotheses.
Chapter 6

Cochlear implantation in adults with postlingual hearing loss and monaural sound deprivation

Isabelle Boisvert, Catherine M. McMahon, Richard C. Dowell, and Björn Lyxell.

To be submitted

ABSTRACT

Objectives: To examine: 1) the differences in outcomes of implantation in a sound-deprived or an aided ear, and 2) the relative contribution of possible factors on implantation outcomes, in adults with postlingual hearing loss and unilateral sound deprivation.

Study Design: Retrospective cohort study. Cochlear implantation outcomes were examined in 99 adults with postlingual hearing loss and monaural sound deprivation who received the implant in the aided (n=29) or in the sound-deprived ear (n=70). And for the latter groups, whether they used the implant alone or bimodal hearing for daily listening.

Setting: Tertiary referral centres with active cochlear implant programs, located in three countries.

Patients: Adults with bilateral hearing loss and a minimum of 15 years of monaural sound deprivation who received a cochlear implant after meeting the traditional implantation criteria of the implantation centres.

Intervention: Cochlear implantation with devices approved by the U.S. Food and Drug Administration.

Main Outcome Measure(s): Speech recognition scores obtained 3 to 6 months after implantation were compared between groups with an analysis of variance. Potential predictors of speech recognition scores were examined with regression analyses via general linear modelling.

Results: Similar speech recognition scores were obtained between groups, whether the implant was placed in the aided or the sound-deprived ear. Duration of bilateral significant hearing loss and age explained the majority of the variance in speech recognition scores.

Conclusion: Similar functional outcomes can be obtained in adults with long-term monaural sound deprivation and postlingual hearing loss, whether the implant is placed in the aided or the sound-deprived ear. The duration of monaural sound deprivation in the implanted ear does not significantly contribute to outcomes of cochlear implantation in this population.
INTRODUCTION

Long duration deafness (Blamey et al. 1996; Rubinstein et al. 1999; Van Dijk et al. 1999; Green et al. 2007) and poor residual hearing (Rubinstein et al. 1999; Van Dijk et al. 1999; Gomaa et al. 2003) are amongst the most reported predictors of limited outcomes of cochlear implantation in adults, in cases of unremarkable surgery and normal cognitive abilities. These predictors are generally well accepted in the event of bilateral long-term deafness and poor bilateral residual hearing. However, it is still unclear whether this relationship should apply with unilateral or asymmetric deafness. The neurophysiological changes occurring in the auditory pathways following bilateral deafness are different to those following unilateral deafness (Shepherd and Hardie 2001; Firszt et al. 2006). In particular, with normal hearing, a sound presented to one ear is processed by both the ipsilateral and the contralateral auditory pathways, with the majority of the excitatory neural activity being observed in the pathway contralateral to the stimulated ear. In animal models of unilateral deafness, an increase in excitatory neuronal activity appears to occur ipsilaterally to the hearing ear when stimulating that ear, at multiple levels of the auditory pathway, diminishing the difference between ipsilateral and contralateral activity (Popelár et al. 1994; McAlpine et al. 1997). This ipsilateral enhancement of activity is also demonstrated in electrophysiological and functional imaging studies in humans (Scheffler et al. 1998; Ponton et al. 2001). Further, it is assumed that humans with unilateral deafness should show intact phonological representations in the long-term memory, potentially maintained via auditory input through the better ear, which presumably facilitates speech processing after cochlear implantation (Andersson 2002; Lazard et al. 2010). It is therefore possible that outcomes of implantation in a long-term unilaterally deafened ear are different to those obtained with long-term bilateral deafness. If that is the case, the choice of ear may not be a significant predictor of outcomes. This paper investigates differences in outcomes following implantation of the better or the poorer ear in individuals having a long-term unilateral sound deprivation (bilateral hearing loss, but hearing aid used in only one ear).

A growing body of clinical research suggests that the choice of ear does not significantly influence cochlear implantation outcomes. Chen et al. (2001) showed that patients with bilateral hearing loss who have been using only one hearing aid for...
periods of 2 to 15 years can obtain similar outcomes with the cochlear implant (CI) placed in the non-aided ear compared with patients implanted in their aided ear. Friedland et al. (2003) demonstrated that the Iowa University Formula for predicting outcomes of implantation (Rubinstein et al. 1999), derived from patients implanted in their better ear, was applicable to patients implanted in their poorer ear. Additionally, Francis and colleagues (2004b; 2005), showed that implantation in a profoundly deaf ear when the other ear was severely deaf, resulted in similar outcomes to implantation in individuals with bilateral severe hearing loss, and better outcomes to individuals with bilateral profound hearing loss. Matterson et al. (2007) analysed outcomes of individuals with hearing asymmetries caused by otosclerosis where the ears differed in duration of deafness. They concluded that in the long term, patients were not disadvantaged by the implantation of the longer deafened ear. Taken together, these studies suggest that for hearing asymmetries measured with audiometric thresholds, hearing abilities or hearing aid use, the outcomes of implantation are not worse when implanting the poorer ear as compared to the better ear. Despite these results, clinicians are often hesitant to implant a long-term deafened ear when there is a choice (Chen et al. 2001; Connell and Balkany 2006).

To further test the influence of hearing asymmetries on implantation outcomes, Boisvert et al. (2011; 2012a; 2012b) examined CI outcomes in individuals with larger magnitude and longer duration of hearing asymmetries. That is, although the hearing loss was bilateral at the time of implantation, one ear had essentially no hearing for at least 15 years (unaided severe hearing loss). In a preliminary study conducted in Canada, speech recognition outcomes after implantation in the sound-deprived ear were found to be strongly related to the hearing in the better and non-implanted ear (Boisvert et al. 2011). In a matched cohort study conducted in Sweden, no significant difference in speech recognition outcomes was found whether the implant was placed in the sound-deprived or in the aided ear, when comparing the daily listening condition (i.e. where some participants used bimodal hearing: the CI in one ear in conjunction with a hearing aid in the other ear) (Boisvert et al. 2012a). Finally, in individuals with long-term unilateral sound deprivation implanted bilaterally, it was found that the ear that would yield the better speech recognition outcomes and that would be identified as the preferred ear after implantation could not be predicted (Boisvert et al. 2012b). With different groups of participants and
using different methodologies, these papers support the hypothesis that the choice of ear has limited influence on cochlear implantation outcomes when there are no obvious differences in pathology from one side to the other.

To strengthen the argument, this multicentre study conducted in Australia and Sweden aimed to verify these results in a larger population of adults with postlingual hearing loss by investigating: (1) the differences in outcomes of implantation in a sound-deprived or an aided ear, and (2) the relative contribution of predictors of implantation outcomes in adults with unilateral sound deprivation.

METHODS
Data collection
Retrospective data from five cochlear implantation centres was systematically gathered for analyses. The centres were: 1) Sydney CI Centre (Australia), 2) Melbourne CI Clinic, within the Royal Victorian Eye and Ear Hospital (Australia), 3) The CI Program of Östergötland, within Linköping University Hospital (Sweden), 4) Karolinska University Hospital CI Programme (Sweden), and 5) the Québec Rehabilitation Centre for Physical Disabilities and Hotel-Dieu Hospital, both part of the Québec Expertise Centre for Cochlear Implantation (Canada).

Participants
The 99 individuals included in this study had a bilateral postlingual hearing loss and a long-term (≥ 15 yr) monaural sound deprivation before implantation, and received a CI as an adult (≥ 18 yr old), between 2000 and 2009. All had outcome measures obtained 3 to 6 months after implantation with recorded speech test material using their first language. Participant files were excluded from this study if there was evidence of surgical complication, device failure, or cognitive limitations. 70 participants received the CI in their sound-deprived ear and 29 received the CI in the other ear (demographics of the groups are presented in Table 6.1). 67 files were sourced from the Australian Centres, 21 from the Swedish Centres (from the dataset presented in (Boisvert et al. 2012a)) and 11 from the Canadian Centre (from the dataset presented in (Boisvert et al. 2011)). Cochlear implanted devices were approved by the USA Food and Drug Administration (Advanced Bionics, Cochlear, and MED-EL).
Table 6.1. Mean age and hearing characteristics of participants.

<table>
<thead>
<tr>
<th></th>
<th>CI in sound-deprived ear</th>
<th>CI in aided ear</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>67yr (31-88)</td>
<td>65yr (34-90)</td>
</tr>
<tr>
<td>SRS with HA</td>
<td>40% (0-98)</td>
<td>7% (0-42)</td>
</tr>
<tr>
<td>PTA in CI ear</td>
<td>114dB (85-130)</td>
<td>107dB (80-125)</td>
</tr>
<tr>
<td>PTA in non-CI ear</td>
<td>96dB (53-122)</td>
<td>113dB (88-125)</td>
</tr>
<tr>
<td>Duration monaural sound deprivation</td>
<td>28yr (15-64)</td>
<td>33yr (15-66)</td>
</tr>
<tr>
<td>Duration bilateral significant HL</td>
<td>4yr (0-26)</td>
<td>6yr (0-35)</td>
</tr>
<tr>
<td>Australian/Swedish CI centre</td>
<td>81% / 19%</td>
<td>65% / 34%</td>
</tr>
<tr>
<td>Cochlear / MED-EL</td>
<td>91% / 9%</td>
<td>86% / 14%</td>
</tr>
<tr>
<td>SRS with CI</td>
<td>58% (3-98)</td>
<td>62% (0-98)</td>
</tr>
</tbody>
</table>

**Monaural sound deprivation**

The duration of monaural sound deprivation is measured from the time when the pure-tone average (PTA) obtained at 500, 1000 and 2000Hz was ≥ 70dB in one ear and no hearing aid had been used in that ear for the same number of years.

**Bilateral significant hearing loss**

The duration of bilateral significant hearing loss is defined as the time that at least two of the following criteria are met for both ears: a) the hearing loss is at least severe i.e. average of hearing thresholds calculated at frequencies 500Hz, 1000Hz and 2000Hz ≥ 70dB HL, b) telephone use is not possible, and c) the speech recognition score with recorded material is below 10% for words or 30% for sentences.

The duration of bilateral significant hearing loss is used to represent the integration of duration of deafness and use of residual hearing. The concept of bilateral significant hearing loss was developed to measure more precisely the binaural hearing history of the auditory pathways and cortex, and refers to what Friedland et al. (2003) refers to as overall auditory experience.

**Speech Recognition Score (SRS)**

SRS had to be available in the clinical files, measured between 3 and 6 months after the initial switch-on, with standardized recorded material using the main language of the Centre and the participants’ first language. All available scores were from tests conducted in the auditory mode only, at a level between 60 and 65dB SPL, in quiet,
via 1 or 2 loudspeakers at a distance of 1m. Table 6.2 summarises the test material used at each centre.

Three speech recognition measures were available for the Australian participants (recognition of sentences, words and phonemes). To obtain the optimal representation of their speech recognition abilities, the SRS used in this study was an average of these three measures. This use of the average as an overall measure of speech perception outcome was supported by a principal component analysis that indicated that one factor (with approximately equal weightings for the three measures) accounted for a large majority of variance in the scores. Extrapolation based on linear regression ($R^2=.99$ [2,381], $p<.001$) was used to fill in missing data points for 13 individuals in the Australian dataset. That is, when data on a specific test was missing for a participant, their averaged score was estimated from their available data, in comparison to grouped data of participants having a score available on all 3 tests.

Table 6.2. Speech recognition test material used in each centre.

<table>
<thead>
<tr>
<th>Country</th>
<th>Quebec</th>
<th>Sweden</th>
<th>Australia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Speech material</td>
<td>Sentences</td>
<td>Monosyllabic words (word score)</td>
<td>Sentences and monosyllabic words (word and phonemic score)</td>
</tr>
<tr>
<td>Standardised Test</td>
<td>Test Auditif Multimedia (TAM)</td>
<td>Swedish Phonemically-Balanced words (SPB)</td>
<td>City University of New York (CUNY sentences) Consonant-Vowel-Consonant (Melbourne: CVC words, Sydney: CNC words)</td>
</tr>
<tr>
<td>Language</td>
<td>Canadian-French</td>
<td>Swedish</td>
<td>Australian English</td>
</tr>
</tbody>
</table>

**Statistical analyses**

To allow the merging of data obtained with different speech recognition test material, SRS were converted to z-scores, where the scores represent a standardized distance from the mean. For the Swedish and Australian data, z-scores were obtained using the mean and standard variation of scores obtained by individuals in this study (including both prelingual and acquired hearing losses), for each country. Because all participants from the Canadian group were implanted in the sound-deprived ear, their z-scores were obtained using the mean and standard variation of the adult population.
implanted at that centre during approximately the same period (François Bergeron, personal communication, 2012). In doing so, each SRS was expressed as a distance from the mean of its group. Once the z-scores of all participants were merged, the data was reconverted on a 0-100 scale (using mean=55 and standard deviation=25). This transformation to a scale that is typically used to discuss SRS aimed at facilitating the analyses, interpretation and applicability of the results.

Analyses of variance were used to compare SRS obtained after implantation of an aided or a sound-deprived ear, whether the CI was used alone or in bimodal condition (use of a hearing aid in conjunction with a CI on the other ear). This follows Boisvert et al. (2012a), who suggested that the use of a hearing aid may affect the outcomes measured with the CI alone. Multiple regression analyses via general linear modelling of SRS in relation to multiple factors and covariates were used to identify predictors of outcomes of implantation in the case of long-term unilateral sound deprivation. These factors were: whether the implant was placed in the sound-deprived or the aided ear, if a hearing aid was used in the ear contralateral to the CI, and the ear of the CI (right or left). The covariates were: age, the duration, in years and percent of lifetime, of sound deprivation in the implanted ear, and the duration, in years and percent of lifetime, of bilateral significant hearing loss.

This study was approved by the regional ethical committee at Linköping University and Karolinska University Hospital, the Human Research Ethics Committees of Sydney South West Area Health Service, the Royal Victorian Eye and Ear Hospital, and Macquarie University. It was conducted in accordance with the National Health and Medical Research Council of Australia Guidelines, under the terms of the World Medical Association Declaration of Helsinki.

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6 To confirm that the different methods that were used to convert data to Z-scores did not affect the conclusions, the analyses were also conducted excluding the Canadian data. Similar patterns of results were found and it therefore appears sensible to present all data using the z-score conversions described in the methodology.
RESULTS

The results are presented as follows: (1) Differences in SRS between groups over time; (2) Comparison of outcomes obtained between groups; and (3) predictors of implantation outcomes.

Within and between groups SRS differences over time

In the Australian data, 68 participants had SRS available 3-6 months as well as 1-2 years after switch-on. A repeated measures analysis of variance was conducted with this data to compare improvement of SRS over time between individuals implanted in the sound-deprived ear and those implanted in the aided ear. Results indicate that there was a significant improvement over time for both groups ($F_{[1,66]}=7.73$, $p=.001$), but no significant difference between the groups ($F_{[1,66]}=0.94$, $p=.76$), Fig. 6.1.

![Fig. 6.1. Speech Recognition Scores (SRS) obtained over time in individuals implanted in the sound-deprived or the aided ear (mean and SE are shown).](image)

The following analyses were conducted using the SRS measured 3 to 6 months after switch-on because a greater number of participants had available data measured during that period, compared with later.

Comparison of outcomes between groups

SRS were compared for individuals who received the CI in: (1) the aided ear; (2) the sound-deprived ear using the CI alone daily (not using a contralateral hearing aid); and (3) the sound-deprived ear using bimodal hearing daily. Analyses of variance showed no significant difference between groups when SRS were measured with the CI alone ($F_{[2,103]}=1.27$, $p=.29$), as well as in the daily listening condition ($F_{[2,94]}=.283$, $p=.75$). Group descriptions are presented in Table 6.3.
Table 6.3. Mean Speech Recognition Scores (SRS) and standard deviation obtained after implantation in individuals with a monaural sound deprivation.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n (ref fig. 4)</th>
<th>Mean SRS±SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>1) CI in aided ear</td>
<td>29 (a, e)</td>
<td>62.35% ±24.20</td>
</tr>
<tr>
<td>(CI alone = daily condition)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2) CI in sound-deprived ear using CI alone</td>
<td>19 (b, f)</td>
<td>60.98% ±19.11</td>
</tr>
<tr>
<td>daily (CI alone = daily condition)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3) CI in sound-deprived ear using bimodal</td>
<td>Tested CI alone: 51 (c, g)</td>
<td>55.33% ±22.92</td>
</tr>
<tr>
<td>hearing daily</td>
<td>Tested bimodal: 42 (d, h)</td>
<td>65.02% ±16.92</td>
</tr>
</tbody>
</table>

Fig. 6.2. Speech Recognition Scores (SRS) obtained by individuals implanted in the aided or the sound-deprived ear, whether tested with the CI alone or in the daily listening condition, in relation with the duration of bilateral significant hearing loss (I) and the duration of sound deprivation in the implanted ear (II). Regression lines are shown for significant correlations.

Fig. 6.2 presents individual data for each group, plotted as a function of duration of significant bilateral hearing loss (I), and as a function of duration of sound deprivation in the implant ear (II).
Predictors of implantation outcomes

Analyses were conducted to identify the most relevant variables that could potentially contribute to the prediction of implantation outcomes for individuals with a monaural sound deprivation. For the purpose of these analyses, all SRS were measured with the CI alone despite many participants using bimodal hearing daily. A correlation matrix (see Table A.1 in the appendix) was first generated with the following variables: [1] age, [2] duration of sound deprivation in the implanted ear (in years and [3] in % of lifetime), [4] duration of bilateral significant hearing loss (in years and [5] in % of lifetime), [6] use of a contralateral hearing aid, and [7] CI ear (right or left). Regression analyses via full factorial general linear modelling were then conducted for all participants. Each of the factors and covariates used in the correlation matrix were tested (with the exception of the durations of hearing loss measured in percent of lifetime). In addition we tested whether placing the implant in the aided or the sound-deprived ear contributed to SRS.

The prediction model was statistically significant ($F_{10,88} = 2.97, p < .01$) and accounted for approximately 25% of the variance in SRS. Modelling was continued by removing 1 by 1 the variables contributing the least to SRS. However, no other model increased the variance explained with the first model. Duration of bilateral significant hearing loss and age were the two variables identified as significantly affecting SRS. More specifically, the model estimated that SRS decreased by 1% unit for every additional year of bilateral significant hearing loss ($t_{92}=-3.40, p = .001$) and by 0.4% unit for every additional year of age ($t_{92}=-2.67, p = .01$). Interactions between variables were not identified as significant predictors of SRS.

Table 6.4 presents the F-statistics and significance values of the variables tested. A similar pattern of results was obtained when including only participant implanted in the sound-deprived ear.
Table 6.4. Variables tested as predictors of Speech Recognition Scores (SRS) with general linear modelling for individuals implanted in the sound-deprived ear and individuals implanted in either ear, when tested with the CI alone.

<table>
<thead>
<tr>
<th>Predicting variables</th>
<th>F (p)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of bilat sign. HL</td>
<td>11.54 (.001)</td>
</tr>
<tr>
<td>Age</td>
<td>7.08 (.01)</td>
</tr>
<tr>
<td>Duration of sound-dep. in CI ear</td>
<td>1.90 (.17)</td>
</tr>
<tr>
<td>Side of CI (right or left ear)</td>
<td>0.83 (.37)</td>
</tr>
<tr>
<td>Bimodal hearing</td>
<td>0.06 (.81)</td>
</tr>
<tr>
<td>CI in sound-deprived or aided ear</td>
<td>0.04 (.83)</td>
</tr>
</tbody>
</table>

R² = .25

DISCUSSION

When an individual has had essentially no hearing in one ear for many years and wishes to evaluate the potential benefits of cochlear implantation, it appears necessary to have reliable knowledge about the benefits of implanting one ear over the other. This multicentre study compared outcomes of cochlear implantation in a large sample of adults with postlingual hearing loss and long-term unilateral sound deprivation, examining the relative contribution of predictors of SRS in this population.

The results showed that highly variable outcomes are obtained by individuals with a long-term unilateral sound deprivation who have been implanted in the sound-deprived or in the aided ear. For both groups, similar improvement in SRS was measured over time. More than 2/3 of the individuals implanted in the sound-deprived ear maintained the use of their hearing aid in the non-implanted ear, allowing for bimodal hearing. None of the individuals implanted in their aided ear began using a hearing aid in the other ear after implantation. When SRS were measured with the CI alone or in the daily listening condition (bimodal or CI alone), similar SRS were obtained by all participants. Using a larger population sample and a different methodology, these results strongly support previous findings that similar SRS in quiet can be obtained after implantation of an aided or a long-term sound-deprived ear (Matterson et al. 2007; Boisvert et al. 2012a). Therefore, these results also support that in adults with post-lingual hearing loss and long-term monaural
sound deprivation, the choice of ear for implantation has limited prognostic value in regards to SRS obtained with the CI (Francis et al. 2005; Friedland 2006).

Amongst multiple possible predictors of implantation outcomes for individuals with a unilateral sound deprivation, duration of bilateral significant hearing loss was identified as the variable having the greatest effect on SRS. This replicates and strengthens the finding presented in Boisvert et al. (2011). The other significant contributor to SRS identified in this study was age at implantation. Age has previously, although inconsistently, been reported as a contributor to outcomes of implantation in adults (Blamey et al. 1992; Van Dijk et al. 1999; Francis et al. 2005). This is often related to the general cognitive decline associated with aging (Pichora-Fuller 2006), in addition to the effect of age on the central processing of speech and a decreased potential for neurophysiological plasticity in the auditory pathways following implantation (Yeagle et al. 2010).

Duration of sound deprivation in the implanted ear was not identified as a significant contributor to SRS. While this variable was significantly correlated to SRS when examined independently, its co-variation with other variables, such as duration of bilateral significant hearing loss and age, suggests its independent contribution to SRS is minimal. In addition, outcomes were not significantly affected by whether the sound-deprived ear or the aided ear was implanted. These findings are noteworthy because they have implications for clinical decision-making for patients with a long duration of deafness in one ear. While poor outcomes of implantation may intuitively appear more likely when implanting a sound-deprived ear, the duration of the monaural sound deprivation should not be taken into account when discussing prognosis. It is clear from this study that good outcomes can be obtained in ears that have been sound-deprived for more than 40 years and poor outcomes can be obtained in ears with much shorter sound deprivation.

Importantly, the decision to implant a sound-deprived ear should be influenced by the likelihood that a patient would maintain hearing aid use in the contralateral ear after implantation. There are potential advantages for speech perception, music perception and localization from the use of bimodal hearing after cochlear implantation (Ching et al. 2004; Firszt et al. 2008; Ching et al. 2009; Sucher and McDermott 2009). These benefits have not been measured in this study because it
was based on retrospective data, but should be included in further studies. In particular, it is possible that greater benefits may be obtained by implanting the sound-deprived ear because of the greater probability to use bimodal hearing. On the other hand, it remains unknown whether performances on more complex tasks (e.g. speech in noise, low presentation levels or sentences with low predictability) would be affected by a long-term sound deprivation. Questions are also raised regarding the reasons why individuals using bimodal hearing obtain poorer results when tested with the CI alone (Boisvert et al. 2012a). It would be interesting to examine whether performances with the CI alone could be improved through controlled auditory exposure using the CI alone, or specific auditory training.

In conclusion, adults with postlingual hearing loss and long-term monaural sound deprivation can obtain similar functional outcomes with the CI placed in either ear. While duration of bilateral significant hearing loss was identified as the strongest predictor of implantation outcomes, duration of sound deprivation did not contribute to explain additional variability. These results are expected to influence clinical practice, as it appears inappropriate to consider the duration of sound deprivation in one ear when discussing outcomes of cochlear implantation in adults with postlingual hearing loss.

ACKNOWLEDGMENTS
This study was supported by Macquarie University Research Excellence Scheme, the HEARing CRC established and supported under the Australian Government’s Cooperative Research Centres program, and the HEAD Graduate School in Sweden. We are grateful to all staff of Sydney CI Centre, Melbourne CI Clinic, Karolinska Hospital CI Centre, Linköping Hospital CI Centre, and Québec Expertise Centre for Cochlear Implantation, who facilitated this study.
6.1 Manuscript 4 – Further analyses of the data

Speech recognition in background noise
To increase sample size in regard to the available data, analyses in manuscript 4 uses speech recognition scores (SRS) obtained in quiet. Results show that similar SRS can be obtained in adults with acquired hearing loss and unilateral sound deprivation, with the implant placed in either ear. However, speech tests conducted in quiet are relatively simple and questions remain whether the impact of a long-term sound deprivation could be greater when listening in background noise.

Data available in this sample can help address this question. Amongst the adult participants in this study, 41 had SRS measured with sentences in background noise (+10 signal to noise ratio) 3 to 6 months after implantation. It can be assumed that these participants were amongst the best cochlear implant (CI) performers. In this group, 21 received the CI in the aided ear and 20 received the CI in the sound-deprived ear. When tested in quiet, similar results are obtained by both groups with the CI alone (t=.24, p=.81, d=.08, Table 6.5). When tested in noise, SRS obtained by participants implanted in the sound-deprived ear appear poorer than SRS obtained by participants implanted in the aided ear, but the difference is non-significant (t=1.02, p=.32, d=.32). When tested in noise in the daily listening condition, SRS obtained by participants implanted in the sound-deprived ear increase to resemble those obtained by participants implanted in the sound-deprived ear (t=.07, p=.95, d=.02).

<table>
<thead>
<tr>
<th>Table 6.5. Speech recognition scores obtained in quiet and in noise</th>
</tr>
</thead>
<tbody>
<tr>
<td>CI in aided ear</td>
</tr>
<tr>
<td>Mean (SD)</td>
</tr>
<tr>
<td>Sentences in quiet, CI alone 76.81 (31.75)</td>
</tr>
<tr>
<td>Sentences in noise, CI alone 47.38 (34.20)</td>
</tr>
<tr>
<td>daily listening condition 47.29 (34.22)</td>
</tr>
</tbody>
</table>
Postlingual hearing loss and long-term binaural sound deprivation

Comparing implantation outcomes of individuals with a long-term monaural sound deprivation to those of individuals with a long-term binaural sound deprivation would strengthen the argument that hearing in one ear contributes to the outcomes of cochlear implantation in the other ear. However, individuals having a long-term binaural sound deprivation (severe unaided hearing loss in both ears) are rare and questions may be asked regarding characteristics leading them to use no hearing aid, which complicates group analyses. In the data collected within this research work, 14 individuals, all from the Australian dataset, had a long-term binaural sound deprivation. Nine had a postlingual hearing loss in the implanted ear. Six of them had SRS measured 3 to 6 months after implantation, and eight had SRS measured 1 to 2 years after implantation. Age, duration of monaural or binaural sound deprivation and duration of bilateral significant hearing loss are detailed in table 6.6. Not surprisingly, individuals with a long duration of binaural sound deprivation also have a long duration of bilateral significant hearing loss, which is expected to be related to poorer outcomes with the CI.

Table 6.6. Age and duration of hearing loss for participants with long-term monaural and binaural sound deprivation.

<table>
<thead>
<tr>
<th></th>
<th>Monaural sound deprivation</th>
<th>Binaural sound deprivation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CI in aided ear mean (SD)</td>
<td>CI in sound-deprived ear mean (SD)</td>
</tr>
<tr>
<td>n</td>
<td>38</td>
<td>77</td>
</tr>
<tr>
<td>Age</td>
<td>63.48 (15.39)</td>
<td>67.53 (12.94)</td>
</tr>
<tr>
<td>Duration of sound deprivation</td>
<td>37.10 (15.27)</td>
<td>28.69 (11.71)</td>
</tr>
<tr>
<td>Duration of bilat. Sign. hearing loss</td>
<td>5.62 (7.33)</td>
<td>4.35 (7.12)</td>
</tr>
</tbody>
</table>

Analyses of variance followed by a post-hoc Tuckey analysis suggested poorer outcomes were obtained with individuals having bilateral sound deprivation when tested 3 to 6 months after implantation (3-6 months - $f_{[2,77]}=4.49$, $p=.01$). Their outcomes were non-significantly poorer when tests were conducted later ($f_{[2,77]}=2.76$, $p=.07$). Figure 6.3. illustrates the outcomes obtained by each group.
Fig. 6.3. Speech recognition score obtained after implantation in individuals with unilateral and bilateral long-term sound deprivation. The horizontal lines represent the median.

The interpretation of these results is limited because of the small and heterogeneous sample having a binaural sound deprivation. Nevertheless, as suggested, it appears that poorer outcomes may be obtained when both ears had a long-term sound deprivation, compared to a monaural sound deprivation.
Chapter 7

Cochlear implantation in adults with prelingual hearing loss and monaural sound deprivation

Isabelle Boisvert, Catherine M. McMahon, Björn Lyxell, and Richard C. Dowell.

To be submitted

ABSTRACT

Objectives: To examine: 1) the differences in outcomes of implantation in a sound-deprived or an aided ear, and 2) the relative contribution of possible factors to implantation outcomes, in adults with prelingual hearing loss and monaural sound deprivation

Study Design: Retrospective cohort study. Cochlear implantation outcomes are examined in 46 adults with a prelingual hearing loss in the implanted ear whether they received the implant in an aided (n=19) or a sound-deprived ear (n=28).

Setting: Tertiary referral centres with active cochlear implant programs, located in three countries.

Patients: Adults with bilateral hearing loss and a minimum of 15 years of monaural sound deprivation who received a cochlear implant after meeting the traditional implantation criteria of the implantation centres.

Intervention: Cochlear implantation with devices approved by the U.S. Food and Drug Administration.

Main Outcome Measure(s): Speech recognition scores obtained 3 to 6 months after implantation were compared between groups with a t-test. Potential predictors of speech recognition scores were examined with multiple regression analyses via general linear modelling.

Results: In adults with prelingual hearing loss and monaural sound deprivation, poorer outcomes were obtained with the implantation of the sound-deprived compared with the aided ear. However, the duration of the sound deprivation was not significantly related to outcomes. Duration of bilateral significant hearing loss explained the majority of the variance in implantation outcomes.

Conclusion: It appears appropriate to consider sound deprivation in the individual ears when choosing the ear for cochlear implantation in adults with prelingual hearing loss. Nevertheless, outcomes are better predicted with the duration of bilateral significant hearing loss than the duration of sound deprivation in the implanted ear.

INTRODUCTION

Chapter 6 focused on adults with postlingual hearing loss and long-term unilateral sound deprivation. In that chapter, it was demonstrated that similar speech recognition scores (SRS) can be obtained with the cochlear implant (CI) whether it is
placed in the sound-deprived or aided ear. The current chapter focuses on adults with a prelingual hearing loss in the implanted ear.

Outcomes of cochlear implantation in adults with a bilateral prelingual hearing loss are variable and, on average, considerably poorer in comparison to outcomes in adults with a postlingual hearing loss (Manrique et al. 1999; Waltzman et al. 2002; Teoh et al. 2004; Santarelli et al. 2008; Caposecco et al. 2012). In this population, implantation at a young age (within the critical period for optimal neural plasticity) offers better outcomes compared to implantation at older ages (Kral and Sharma 2012). Prelingually deaf adults have developed using a degraded auditory input, which would have caused a degeneration and reorganisation in the auditory pathways (O'Neil et al. 2011). This neural reorganisation is thought to affect the linguistic and general cognitive development of these individuals in highly heterogeneous ways that are complicated to evaluate (Pisoni et al. 2008).

In particular, the degraded auditory input caused by early childhood deafness (whether unilateral or bilateral) leads to significant neurophysiological changes in the auditory pathways and cortex (Ryugo et al. 1997; Kral and O'Donoghue 2010; O'Neil et al. 2011). When bilateral, this diminished auditory input negatively affects the development of oral language skills (Svirsky et al. 2004b; Bergeson et al. 2005; Sarant et al. 2009). Since the integrity of the auditory pathways (Leake et al. 2008), the cognitive abilities related to language processing (Andersson 2002; Lazard et al. 2010; Van Dijkhuizen et al. 2011) and the age in relation to critical periods for auditory plasticity after implantation (Kral and Sharma 2012) have been related to outcomes of cochlear implantation, it appears logical that prelingually deafened individuals who received a CI at adult age would obtain more limited outcomes.

In prelingually deafened adults and older children (>8yr) without associated disability, the following variables have been related to implantation outcomes:

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1 The concept of prelingual hearing loss literally refers to any hearing loss diagnosed before the development of speech and language, usually 2-3 years old. However, clinically and in the literature, prelingual hearing loss often refers to a significant bilateral hearing loss diagnosed before the development of speech and language, therefore affecting speech development. In this paper, it should be noted that the prelingual component of the hearing loss may have any severity and be unilateral.
duration of profound hearing loss (Dowell et al. 2002b; Teoh et al. 2004), stable versus progressive hearing loss (Caposecco et al. 2012), greater speech recognition scores before implantation (Dowell et al. 2002b), age at implantation (Schramm et al. 2002; Teoh et al. 2004) good oral language skills or auditory-verbal therapy in childhood (Dowell et al. 2002b; Kaplan et al. 2003; Caposecco et al. 2012), and duration without an aid in the implanted ear (Caposecco et al. 2012). These studies examined outcomes of implantation in older children and adults having a bilateral severe to profound prelingual hearing loss. In comparison, the present thesis focuses on adults having a bilaterally severe hearing loss, and using a hearing aid unilaterally. The previous chapter of this thesis included exclusively participants with postlingual hearing loss who used a unilateral hearing aid prior to implantation. It demonstrated that similar outcomes of implantation can be obtained with the implant placed in the sound-deprived or in the aided ear, and that the hearing in the non-implanted ear contributes to outcomes of cochlear implantation. The aim of this manuscript is to examine the outcomes of implantation in adults with prelingual hearing loss who have been using a unilateral hearing aid prior to implantation. This is of particular interest following Caposecco et al’s study (2012), where a long duration without a hearing aid in the implanted ear was related to poorer outcomes of implantation in adults with prelingual hearing loss.

METHOD
The methodology used in this chapter is the same as described in Chapter 6, but with participants having a prelingual hearing loss in the implanted ear.

Data collection
Retrospective data from five cochlear implantation centres was systematically gathered for analyses. The centres were: 1) Sydney CI Centre (Australia), 2) Melbourne CI Clinic, within the Royal Victorian Eye and Ear Hospital (Australia), 3) The CI Program of Östergötland, within Linköping University Hospital (Sweden), 4) Karolinska University Hospital CI Programme (Sweden), and 5) the Québec Rehabilitation Centre for Physical Disabilities and Hotel-Dieu Hospital, both part of the Québec Expertise Centre for Cochlear Implantation (Canada).
Participants
Outcomes of cochlear implantation were examined in 47 adults having a long-term unilateral sound deprivation (severe and unaided hearing loss) and any severity of prelingual (≤3 yrs old) hearing loss in the implanted ear. All participants used oral communication as their main mode of communication. Amongst the 28 participants who received the CI in the sound-deprived ear, 15 had a bilaterally severe hearing loss before the age of 3, of which 9 had never used a hearing aid in the implanted ear. Following implantation, 20 maintained the use of their hearing aid in the contralateral ear in conjunction with their CI (bimodal hearing). In comparison, none of the participants implanted in the aided ear used bimodal hearing after implantation. All participants who received the CI in the aided ear had a prelingual hearing loss bilaterally, while five of the participants implanted in the sound-deprived ear had a prelingual hearing loss in the implanted ear only. Information about age, hearing thresholds, SRS before and after implantation, duration of sound deprivation, and duration of bilateral significant hearing loss are presented in Table 7.1, for each group.

<table>
<thead>
<tr>
<th>Characteristics of participants</th>
<th>CI in sound-deprived ear</th>
<th>CI in aided ear</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>28 (23 prelingual bilat)</td>
<td>19 (all prelingual bilat)</td>
</tr>
<tr>
<td>Age</td>
<td>42.79 ±15.62</td>
<td>44.63 ±14.98</td>
</tr>
<tr>
<td>PTA (CI ear)</td>
<td>111.73±11.25</td>
<td>110.37 ±10.31</td>
</tr>
<tr>
<td>PTA (contra ear)</td>
<td>100.50±11.59</td>
<td>112.11±9.90</td>
</tr>
<tr>
<td>SRS before CI (better ear)</td>
<td>22.57±27.41</td>
<td>9.68±15.02</td>
</tr>
<tr>
<td>SRS after CI (CI alone)</td>
<td>26.95±22.24</td>
<td>58.54±20.42</td>
</tr>
<tr>
<td>SRS after CI (daily listening condition)</td>
<td>38.23±25.56</td>
<td>All use CI alone</td>
</tr>
<tr>
<td>Duration monaural sound dep (CI ear)</td>
<td>32.32±13.78</td>
<td>No sound dep in CI ear</td>
</tr>
<tr>
<td>Duration bilat. sign. HL</td>
<td>16.54±17.73</td>
<td>11.21±17.13</td>
</tr>
</tbody>
</table>

Table 7.1. Age, hearing loss characteristics and outcomes of implantation in either the sound-deprived or the aided ear in adults with a prelingual hearing loss. PTA: Pure-tone threshold average; SRS: Speech recognition scores CI: Cochlear implant; HL: Hearing loss.
Monaural sound deprivation

The duration of monaural sound deprivation is measured from the time when the pure-tone average (PTA) obtained at 500, 1000 and 2000Hz was $\geq 70$dB in one ear and no hearing aid had been used in that ear for the same number of years.

Bilateral significant hearing loss

The duration of bilateral significant hearing loss is defined as the time that at least two of the following criteria are met for both ears: a) the hearing loss is at least severe i.e. average of hearing thresholds calculated at frequencies 500Hz, 1000Hz and 2000Hz $\geq 70$dB HL, b) telephone use is not possible, and c) the speech recognition score with recorded material is below 10% for words or 30% for sentences.

Speech Recognition Score (SRS)

SRS had to be available in the clinical files, measured between 3 and 6 months after the initial switch-on, with standardized recorded material using the participants’ first language. All available test results were from tests conducted in the auditory mode only, at a level between 60 and 65dB SPL, in quiet, via 1 or 2 loudspeakers at a distance of 1m.

Statistical analyses

A t-test was used to compare SRS obtained after implantation of the aided or the sound-deprived ear, whether the CI was used alone or in bimodal condition. Multiple regression analyses via general linear modelling of SRS in relation to possible predictive factors and covariates were used to identify predictors of outcomes of implantation. The factors were: whether the implant was placed in the sound-deprived or the aided ear, whether a hearing aid was used in the ear contralateral to the CI, and the ear of CI, and the covariates were: age, the duration, in years and percent of lifetime of sound deprivation in the implanted ear, and the duration, in years and percent of lifetime of bilateral significant hearing loss.

This study was approved by the regional ethical committee at Linköping University and Karolinska University Hospital, the Human Research Ethics Committees of Sydney South West Area Health Service, the Royal Victorian Eye and Ear Hospital,
and Macquarie University. It was conducted in accordance with the National Health and Medical Research Council of Australia Guidelines, under the terms of the World Medical Association Declaration of Helsinki.

RESULTS
A t-test was conducted to compare differences in outcomes of implantation between groups (Fig. 7.1). For adults with a prelingual hearing loss implanted in the aided ear, higher SRS were obtained when tested with the CI alone (t=4.94, p<.001) and in the daily listening condition (t=2.84, p=.01), as compared to adults implanted in the sound-deprived ear.

![Fig. 7.1. Speech recognition scores obtained by individuals with a prelingual hearing loss (HL) in the implanted ear (★ = non-severe prelingual HL, O = severe prelingual HL, ◆ = prelingual sound deprivation [severe unaided HL]).](image)

A correlation matrix (see Table A.2 in the appendix) facilitated the identification of the most relevant variables to include in a model examining predictors of SRS in adults with prelingual hearing loss and long-term unilateral sound deprivation.

Regression analyses via general linear modelling were then conducted with the following factors and covariates: 1) use of bimodal hearing, 2) age, 3) duration of sound deprivation in the CI ear, and 4) duration of bilateral significant hearing loss (Table 7.2). The duration of bilateral significant hearing loss was the only significant contributor to SRS after implantation in a sound-deprived ear for individuals with a prelingual hearing loss (model; $R^2=.54$, $F_{[4,23]}=6.84$, p=.001). It was estimated that
SRS decreased of 0.4% unit for every additional year of bilateral significant hearing loss.

Five participants in this study had a unilateral prelingual hearing loss (normal hearing in the non-implanted ear when toddlers). However, the heterogeneity in the history of hearing loss in these five participants restricts the possibility to draw any conclusions.

**DISCUSSION**
Adults with a bilateral prelingual deafness commonly have poorer implantation outcomes in comparison to adults with a postlingual deafness (Manrique et al. 1999; Waltzman et al. 2002; Teoh et al. 2004; Santarelli et al. 2008; Caposecco et al. 2012). This is in agreement with animal studies showing significant structural and physiological changes occurring with early childhood deafness (Moore 1991; Mostafapour et al. 2000; O'Neil et al. 2011). In the present study, in the group of participants having prelingual hearing loss and unilateral sound deprivation, those who received the CI in the sound-deprived ear obtained poorer outcomes compared to those who received the CI in the aided ear. This can be compared to results obtained by Caposecco et al. (2012) where duration without a hearing aid was identified as a significant predictor of outcomes. However, in the present study, the duration without a hearing aid was not identified as a significant contributor to outcomes. SRS were highly related to the duration of bilateral significant hearing loss, which is predominantly based on the hearing in the non-implanted ear. In addition, age and use of bimodal hearing were not found to be significant contributors to outcomes. Comparing these results with those obtained in adults with postlingual hearing loss suggests that the impact of a sound deprivation is greater in the event where the auditory system has been affected by a prelingual hearing loss.

<table>
<thead>
<tr>
<th>Predicting variables</th>
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<tr>
<td>Duration bilat. sign. hearing loss</td>
<td>20.65 (&lt;.001)</td>
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<tr>
<td>Bimodal hearing</td>
<td>2.72 (.11)</td>
</tr>
<tr>
<td>Duration sound deprivation - CI ear</td>
<td>2.55 (.12)</td>
</tr>
<tr>
<td>Age</td>
<td>.00 (.96)</td>
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</tbody>
</table>

Table 7.2. Variable tested as predictors of Speech Recognition Scores (SRS) with general linear modelling for individuals with prelingual hearing loss who received the CI in the sound-deprived ear ($R^2=.54$).
In this study, having any degree of prelingual hearing loss affected the outcomes of implantation. It appears logical that any level of bilateral early childhood hearing loss will affect the integrity of the auditory pathways (Eggermont and Komiya 2000), which may lead to poorer outcomes with the CI, although greater severity of prelingual hearing loss would be expected to have a greater impact (Ryugo et al. 1998; Tibussek et al. 2002).

In this group of participants, the majority had a bilateral prelingual hearing loss, but only one ear was aided with a hearing aid prior to implantation. Amongst the five participants who had a postlingual hearing loss in the non-implanted ear, three had a short duration of bilateral hearing loss (≤ 5 years). According to the hypothesis that a short duration of bilateral significant hearing loss would yield greater outcomes with a CI placed in either ear, these participants would be expected to have higher SRS with the CI than participants with a bilateral prelingual hearing loss. The premise is that undamaged hearing prelingually in one ear would promote a normal development of language (Lieu 2004) and would also possibly limit degradation in the bilateral auditory pathways (Shepherd et al. 1999). Accordingly, two of these participants obtained SRS in the higher end of the outcomes obtained by their group, but one obtained poor SRS. The heterogeneity observed in this small sub-group limits the possibility to draw a sensible conclusion about the outcomes of implantation in a prelingually sound-deprived ear in the case of unilateral deafness. To properly study the contribution of the non-implanted ear on CI outcomes in a unilaterally and prelingually deafened ear, the ideal model would be an adult with a prelingual sound deprivation in one ear and a recent sudden hearing loss in the better ear, and receiving the CI in the prelingually sound-deprived ear. Alternatively, implantation in a prelingually single-sided deafened ear (normal hearing in one ear) would surely be informative.

The greater impact of early childhood sensory impairment compared with impairment acquired later in life has also been demonstrated in the visual system (Banks et al. 1975; Lewis and Maurer 2005). Monocular deprivation in young age causes neural reorganisation that is not observed in adults and that is also different from binocular deprivation (Wong-Riley 1979; Fagiolini et al. 1994; Takamura et al. 2007). The present study provides further evidence to the argument that early
childhood auditory experience is necessary for optimal development of hearing (Kral et al. 2006; Kral and Sharma 2012). However, while unilateral hearing loss appears to have less detrimental impact on the auditory pathways compared with bilateral hearing loss, the opposite appears to occur with vision. Lewis & Maurer (2005) reports that the adverse effects observed in the primary visual cortex after monocular deprivation are much more severe than those observed after bilateral deprivation. This is presumably because balanced visual acuity is necessary for the optimal development of vision in both eyes (Lewis and Maurer 2005). Consequently, it is often recommended to patch the stronger eye for different periods to rehabilitate the weaker eye, when a visual asymmetry exists (Kim and Bonhoeffer 1994; Faulkner et al. 2006). This idea appears tempting to apply in the case of auditory asymmetry, where input from one ear could impede the optimal functioning of the other. For example, Offeciers et al. (2005) indicates: In cases with good HA (hearing aid) performance, the results obtained with the CI may be delayed. In these patients it is recommended to stop using the HA for a few weeks.

In the present study, the possible impact of using bimodal hearing daily on outcomes measured with the CI alone, obtains very weak support, with statistical tests being slightly above or below significance levels depending on the analyses conducted. This might be because of the limited impact bimodal hearing has on outcomes measured with the CI alone or alternatively, that these impacts are prominent only in certain individuals that this study could not identify. However, in the visual system, bilateral input is integrated only at the level of cortex (Trobe 2001), as compared to the multiple integration levels in the auditory pathways for auditory input. This could lead to a more noticeable impact of forced experience in visual as compared to auditory rehabilitation. More research in this direction is necessary before modifying clinical guidelines.

In conclusion, in adults with prelingual hearing loss, poorer SRS were obtained when implanting a sound-deprived ear as compared to an aided ear. However, the duration of the sound deprivation was not related to outcomes. In accordance with our previous studies, duration of bilateral significant hearing loss appears to be the most reliable predictor of outcomes of implantation in a sound-deprived ear, even with adults having a prelingual hearing loss. Careful application of this conclusion is
recommended; predicting poorer outcomes does not imply that the sound-deprived ear should not be implanted. Clinicians and patients may still choose to preserve the aided ear.

ACKNOWLEDGMENTS
This study was supported by Macquarie University Research Excellence Scheme, the HEARing CRC established and supported under the Australian Government’s Cooperative Research Centres program, and the HEAD Graduate School in Sweden. We are grateful to all staff of Sydney CI Centre, Melbourne CI Clinic, Karolinska Hospital CI Centre, Linköping Hospital CI Centre, and Québec CI Programme, who facilitated this study.
7.1 Manuscript 5 – Further analyses of the data

Empirical support for analysing independently outcomes of implantation in adults with prelingual hearing loss

An analysis of the data collected in the five collaborating cochlear implantation centres was conducted with all participants having a unilateral sound deprivation, whether they had prelingual or postlingual hearing loss. The methodology used was the same as described in Chapter 6, but including all participants. In this group of 151 adults, 98 received the CI in their sound-deprived ear and 53 received the CI in the aided ear. All participants with a prelingual hearing loss in this study used oral communication as their main mode of communication.

RESULTS

Correlation and regression analyses were conducted with participants implanted in the sound-deprived ear, to identify the variables that were mostly related to speech recognition scores (SRS). The following variables, all related to the hearing loss history, were examined: 1) the presence of any severity of prelingual hearing loss in the implanted ear, 2) the presence of any severity of prelingual hearing loss in both ears, 3) the presence of a prelingually severe hearing loss in the implanted ear, 4) the presence of a prelingually severe hearing loss in both ears, 5) the duration, in years, of sound deprivation in the implanted ear, 6) the duration, in percent of lifetime, of sound deprivation in the implanted ear, 7) the duration, in years, of bilateral significant hearing loss, and 8) the duration, in percent of lifetime, of bilateral significant hearing loss. All variables examined were significantly related to SRS (see Table A.3 in the appendix), which is consistent with the fact that these variables are measuring similar representations of prelingual deafness and duration of deafness, variables related to SRS. Amongst variables relating to the prelingual nature of the loss, the presence of any level of prelingual hearing loss in the implanted ear showed the strongest correlation with SRS ($r=-.53$, $p<.001$). A stepwise regression suggested the three other variables were not additionally contributing to the variance of SRS.
Amongst the four variables relating to the duration of the hearing loss, a stepwise regression suggested that the duration, in percent of lifetime, of bilateral significant hearing loss, accounted for 35% of the variance ($p<0.001$) increasing to 41% ($p<0.002$) when also considering the duration, in percent of lifetime, of sound deprivation in the CI ear. The same pattern of results was obtained when conducting the analyses with all the participants. Accordingly, the presence of any severity of prelingual hearing loss in the implanted ear, duration of bilateral significant hearing loss (percent of lifetime) and duration of sound deprivation in the CI ear (percent of lifetime), were the most significant variables representing the history of the hearing loss related to SRS. Therefore, they were kept as independent variables in the following analyses.

Full factorial general linear modelling of SRS was then conducted including all participants. The predicting variables tested were: 1) the presence of any severity of prelingual hearing loss in the implanted ear, 2) the duration, in percent of lifetime, of sound deprivation in the implanted ear, 3) the duration, in percent of lifetime, of bilateral significant hearing loss, 4) whether the implant was placed in the sound-deprived or the aided ear, 5) whether a hearing aid was used in the ear contralateral to the CI, 6) age at time of implantation, and 7) side of CI (left or right ear). Table 7.4 presents the F-statistics and significance values of the variables tested. This model explained approximately 43% of the variance in SRS ($F_{16,134}=7.31$, $p<.001$). Interactions between variables were not identified as significantly contributing to SRS. Duration of bilateral significant hearing loss was identified as having the most significant effect on SRS ($b=-0.37$, $t_{(143)}=-5.00$, $p<.001$), followed by age ($b=-0.42$, $t_{(143)}=-3.32$, $p=.001$) and by the presence of any severity of prelingual hearing loss in the implanted ear ($b=-0.20.35$, $t_{(143)}=-1.02$, $p<=.01$). The effect of duration of sound deprivation in the implanted ear on SRS was smaller and at the border of significance. Whether the implant was placed in the sound-deprived or aided ear, or in the right or left ear, did not significantly contribute to SRS. The same pattern of results was obtained when including only participants implanted in the sound-deprived ear, with the exception that using a hearing aid in the contralateral ear had a statistically significant effect on SRS obtained with the CI alone ($p=0.04$). This is relevant, because none of the participants implanted in the aided ear used bimodal hearing after implantation. The same pattern of results was also obtained when using the durations of hearing losses measured in years instead of in percent of lifetime.
This empirical evidence supports that the prelingual nature of the hearing loss contributes to implantation outcomes in adults with unilateral sound deprivation. The contribution of duration of bilateral significant hearing loss and duration of sound deprivation is not sufficient to explain variance in SRS, without considering the contribution of having a prelingual hearing loss. When examining SRS in this population, having any degree of prelingual hearing loss in the implanted ear was more related to outcomes than having a hearing loss in both ears, or having a severe hearing loss in the CI ear or in both ears. For this reason, subgroup analyses were conducted including exclusively participants having any severity of prelingual hearing loss in the implanted ear.

<table>
<thead>
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</tr>
<tr>
<td>Age</td>
<td>11.02 (=.001)</td>
</tr>
<tr>
<td>Prelingual HL - CI ear</td>
<td>7.96 (.01)</td>
</tr>
<tr>
<td>Duration sound deprivation - CI ear</td>
<td>3.90 (.05)</td>
</tr>
<tr>
<td>Bimodal hearing</td>
<td>3.31 (.07)</td>
</tr>
<tr>
<td>Side of CI (right or left ear)</td>
<td>1.03 (.31)</td>
</tr>
<tr>
<td>CI in sound-deprived or aided ear</td>
<td>.33 (.57)</td>
</tr>
</tbody>
</table>

Table 7.4. Variables tested as predictors of Speech Recognition Scores (SRS) with general linear modelling for individuals with unilateral sound deprivation implanted in either ear (R²=.43). HL: Hearing loss; CI: Cochlear implant.
Chapter 8  General results, discussion and conclusion

8.1 General results

This thesis examined speech recognition outcomes following cochlear implantation in adults with long-term monaural sound deprivation. Data from 151 cochlear implant recipients were collected and analysed within five manuscripts. Together, these manuscripts provide strong insight into the following three research and clinical questions: i) is the duration of sound deprivation (severe unaided hearing loss) in the implanted ear a relevant variable to consider as part of candidacy evaluation for cochlear implantation? ii) what influences does the hearing in the non-implanted ear have on cochlear implantation outcomes? and iii) which factors significantly contribute to outcomes of cochlear implantation in adults with a monaural sound deprivation?

i) Is the duration of sound deprivation (severe unaided hearing loss) in the implanted ear a relevant variable to consider as part of candidacy evaluation for cochlear implantation?

Duration of severe unaided hearing loss (sound deprivation) is a variable commonly assessed in implantation clinics. It is assumed that the longer the sound deprivation, the poorer the outcomes. Results included in this thesis demonstrate this assumption is not correct. That is, duration of sound deprivation is not a significant contributor to cochlear implantation outcomes assessed using speech recognition scores (SRS). No significant correlation was found between duration of sound deprivation and outcomes of implantation in either postlingually or prelingually deafened adults who received a CI in the sound-deprived ear (respectively manuscript 1 and 5), or bilateral CIs (manuscript 2). Specifically, variable outcomes are obtained with shorter or longer durations of sound deprivation. Where duration of sound deprivation is examined independently in data including all participants, it is found to be related to cochlear implantation outcomes (see manuscript 4 and the first analysis of manuscript 5). However, when considering covariates, such as duration of bilateral sound deprivation and age, the contribution of the duration of sound deprivation becomes non-
significant. This result suggests that the common assumption of poorer outcomes being associated with longer duration of sound deprivation may be due to the relationship between duration of sound deprivation and age/duration of bilateral significant hearing loss.

In particular, adults with a long-term sound deprivation are often older and/or have a long-term bilateral significant hearing loss, in which case, implanting the better ear may also lead to poor outcomes. In the further analyses that follow manuscript 3, it is suggested that the duration of sound deprivation is related to SRS obtained with the CI alone, but not to SRS measured in the daily listening condition. Nevertheless, the relationship between the duration of sound deprivation and SRS becomes non-significant when examining outcomes exclusively in adults using the CI alone daily. This suggests that if the duration of sound deprivation affects implantation outcomes, the relationship is relatively weak.

Moreover, in individuals with long-term monaural sound deprivation who received bilateral cochlear implants (manuscript 2), the ear that would offer the greater SRS and would be subjectively preferred, with regards to hearing benefits and sound quality, could not be predicted. This counter-intuitive result supports that the duration of sound deprivation has a restricted prognostic value.

For individuals with a prelingual hearing loss, poorer outcomes were obtained with the CI placed in the sound-deprived ear (manuscript 5). However, the duration for which the ear had been sound-deprived prior to implantation was not significantly related to outcomes. This result may lead to confusing interpretation, where adults with prelingual hearing loss have a longer duration of deafness, but it is important to distinguish between the duration of the deprivation and the prelingual nature of the hearing loss.

In addition, the time of measurement of SRS did not appear to affect the results differently between individuals implanted in the sound-deprived or the aided ear. That is, the increase in performance over time was similar for both groups (manuscript 4). However, in these groups, the first outcome measures were obtained 3 to 6 months after the switch-on of the devices. It is therefore possible
that different rates of improvement could have been obtained with SRS measured in the first months following switch-on.

In summary, the \textit{duration} of sound deprivation in the to-be-implanted ear appears to be a non-significant factor to assess during candidacy evaluation, in regard to predicting functional outcomes of implantation.

\textbf{ii) What influences does the hearing in the non-implanted ear have on cochlear implantation outcomes?}

Better hearing in the non-implanted ear was found to be related to higher outcomes of implantation in the sound-deprived ear. This was assessed with the duration of bilateral significant hearing loss; i.e. for how long was hearing in both ears significantly degraded. This variable, which integrates the typical implantation predictors: \textit{duration of deafness} and \textit{use of residual hearing}, was found to be strongly related to SRS (manuscripts 1, 2, 4 and 5). When including participants implanted in either ear, duration of bilateral significant hearing loss was related to SRS measured in the daily listening condition, and to SRS measured with the CI alone when excluding participants using bimodal hearing (manuscript 3).

Amongst all participants with long-term unilateral sound deprivation implanted in the aided ear, none began using a hearing aid in the non-implanted ear following implantation. Conversely, more than half of individuals implanted in the sound-deprived ear maintained the use of their hearing aid in the non-implanted ear following implantation (bimodal hearing). Overall, an increase in SRS was observed when tested with bimodal hearing as compared with the CI alone (as demonstrated in manuscripts 3, 4, and 5). This suggests that for individuals with long-term unilateral sound deprivation, there is an increased possibility to regain bilateral hearing by implanting the sound-deprived ear. The probable benefits of bilateral hearing in the bimodal condition over unilateral hearing with the CI alone have not been examined within this thesis. However, SRS measured in bimodal condition for individuals implanted in the sound-deprived ear were at least comparable to SRS obtained after implantation of the aided ear (manuscripts 3
and 4). Therefore, the use of a hearing aid in the ear contralateral to the CI shows a positive influence on functional outcomes of implantation.

At multiple occasions during this research, questions have been raised regarding a potential negative influence a contralateral hearing aid may have on cochlear implantation outcomes obtained with the CI alone. That is, could the daily use of bimodal hearing limit the outcomes measured when the hearing aid is not used? This question is examined in manuscript 3 where it is shown that there is a difference in the outcomes when speech recognition tests are conducted with the CI alone, depending on whether the individual uses bimodal hearing or the CI alone for daily listening. In particular, those who use bimodal hearing obtain lower outcomes when their CI is tested alone than those using only the CI for daily listening. The same pattern of results is observed in manuscripts 4. In particular, for individuals still receiving considerable benefits from their hearing aids (0 year of bilateral significant hearing loss), highly variable outcomes are obtained when tested with the CI alone (manuscripts 3 and 4). This variability is not observed with individuals using the CI alone daily, where the majority of individuals with short duration of bilateral significant hearing loss obtain high outcomes after implantation (manuscripts 3 and 4). However, analyses could not clearly demonstrate the negative impact of bimodal hearing on implantation outcomes measured with the CI alone.

These results indicate that the hearing in the non-implanted ear, which is rarely considered when making a prognosis of implantation, influences the outcomes of cochlear implantation in different ways. Most importantly, shorter duration of significant hearing loss in the non-implanted ear is associated with increased SRS after implantation.

iii) Which factors significantly contribute to outcomes of cochlear implantation in adults with a monaural sound deprivation?

The ultimate question to examine with adults having a long-term unilateral hearing loss is whether the choice of ear for implantation affects the outcomes obtained with the CI, in relation to other influential factors. It is suggested that in adults with monaural sound deprivation, outcomes are related to a much greater
extent to the hearing in the non-implanted ear than to the hearing in the implanted ear (manuscripts 1 and 2). In particular, unpredictable outcomes were obtained in adults with unilateral sound deprivation implanted in both ears, suggesting that the choice of ear is not a significant predictor of outcomes, at least when the first CI is placed in the sound-deprived ear (manuscript 2). A stronger relationship was also demonstrated between SRS and the duration of bilateral significant hearing loss as compared with the pure-tone threshold average, the duration of a severe hearing loss in the implanted ear, age (manuscripts 2, 4, and 5), and time between implantation of the first and second ear (manuscript 2). By matching participants implanted in the sound-deprived or the aided ear based on hearing loss history, the outcomes measured with the CI alone were poorer when the sound-deprived ear was implanted, but similar when outcomes were measured in the daily listening condition (manuscript 3).

Manuscripts 1, 2, and 3 are country specific (respectively Canada, Australia and Sweden), which reduced the variability of the data that was collated and analysed, but consequently limited the complexity of the analyses that could be conducted because of the small sample sizes. Once it was identified that a similar pattern of results were obtained with the data of each country, data were merged to permit more extensive analyses (manuscripts 4 and 5). Results show that adults with unilateral sound deprivation can obtain similar outcomes with the CI placed in the aided or the sound-deprived ear, when the hearing loss in the CI ear is postlingual (manuscript 4). Therefore, the choice of ear does not matter in regard to SRS obtained with the CI in this population. On the other hand, the choice of ear does matter in adults with a prelingual hearing loss, where poorer outcomes were obtained with the CI placed in the sound-deprived ear as compared with the aided ear (manuscript 5). For individuals implanted in the sound-deprived ear whether the hearing loss was post- or prelingual, duration of bilateral significant hearing loss was the variable most related to SRS after implantation (manuscripts 4 and 5). Age was found to be significantly related to outcomes of implantation in manuscript 4 only. Duration of sound deprivation (manuscripts 3 and 4) and use of bimodal hearing (manuscripts 3 and 4) appear to have only a weak predictive power, if any, on implantation outcomes. The other variables tested: severity of hearing loss, duration of hearing loss in CI ear, residual hearing prior to
implantation and side of ear for implantation were not found to be significant predictors to implantation outcomes.

Altogether, results suggest that in adults with long-term unilateral sound deprivation, prognoses of implantation should consider the duration of bilateral significant hearing loss (manuscripts 1, 2, 3, 4, and 5) and possibly age (manuscript 4) over other possible predictors. Choice of ear in regard to SRS obtained after implantation should be considered only for adults with a prelingual hearing loss, where poorer results may be obtained when implanting the sound-deprived ear. However, the duration of the sound deprivation should not contribute to outcomes.

8.2 General discussion

Better outcomes of implantation related to the hearing in the better ear

The importance of the contribution of hearing in the non-implanted ear to cochlear implantation outcomes was consistently replicated in the five studies supporting this thesis. That is, higher outcomes could be obtained with the implant placed in a long-term sound-deprived ear, when the other ear had a non-significant or a short duration of significant hearing loss. This conclusion had already been hypothesised: “access to auditory speech information through the non-implanted ear may be effective in maintaining a high potential performance with a cochlear implant” (Blamey et al. 1997, p. 274). Further, it was supported by the work of Friedland et al. (2003) and Francis et al. (2004b, 2005), which suggested that the overall auditory experience, determined by the hearing in the better ear, is more predictive of outcomes of implantation compared to ear-specific measures. However, the conclusion appeared to be accepted with small hearing asymmetries or short duration of unilateral sound deprivation. This thesis represents the first time this hypothesis has been tested in a large group of adults with long-term (≥15 years) sound deprivation, where one ear was specifically unaided.

The relationship between better outcomes of implantation and hearing in the non-implanted ear implies that the structural and functional changes occurring in the spiral ganglion, the auditory nerve and the cochlear nucleus following deafness have
minimal consequences on speech recognition performance after cochlear implantation (at least with the current devices). It is possible that the anatomical and physiological changes occurring with hearing asymmetry, where an increase in activity is typically observed in the pathways contralateral to the deafened ear (McAlpine et al. 1997; Ponton et al. 2001), facilitate the efficient use of a cochlear implant placed in the sound-deprived ear. There is also a possibility that hearing in one ear affects structures on the contralateral side, assumed to have exclusively monaural influences. For example, as described in Moore (1991), connections between the cochlear nuclei on the two sides exist, although they are not dominant. Moreover, O’Neil et al. (2010) recently observed changes in the cochlear nucleus of both ears following implantation in only one ear.

Better hearing in one ear is also assumed to preserve speech quality and cognitive abilities involved in aural language processing. Accordingly, phonological and lexical representations as well as access to these representations may be better preserved, and promote better outcomes with the CI placed in a long-term deafened ear. The contribution of cognition to outcomes of implantation is gaining interest and acknowledgment amongst clinicians and researchers (Lyxell et al. 1998; Pisoni 2000; Andersson 2002; Wass 2009) although the concept of cognition is still broadly used. Moreover, knowledge regarding the impact of the individuals’ cognitive skills on speech recognition is relatively limited.

Better hearing in one ear may also limit cross-modal recruitment of vision in the auditory cortex, afferent input from each ear activates the auditory cortex bilaterally (Lambertz et al. 2005). Less cross-modal recruitment would suggest better preservation of the auditory areas for processing the sound delivered by the CI (Giraud and Lee 2007).

**Similar outcomes obtained with CI in either ear with postlingual hearing loss, but not with prelingual**

With adults having a postlingual hearing loss and a long-term monaural sound deprivation, implanting the aided or the sound-deprived ear may lead to similar outcomes of implantation when tested with the CI alone. This extends the work of Chen et al. (2001) who found similar outcomes in adults with short-term (≤15 years)
unilateral sound deprivation implanted in either ear. It also extends the work of Matterson et al. (2007) who found no significant disadvantage in the long-term with implanting the shorter or the longer deafened ear in adults with otosclerosis. This does not imply that all adults with a long-term monaural sound deprivation obtain high outcomes with their implant placed in either ear. On the other hand, outcomes are highly variable, but similar in both groups. It is interesting to question the impact of the hearing asymmetry (or the aetiology that caused the asymmetry) on outcomes of implantation in the better ear. Could higher or less variable outcomes be obtained in adults with symmetrical hearing receiving a unilateral implant? This would need to be verified with data gathered in the centres involved in this study. However, figures comparing speech recognition outcomes in relation with duration of deafness in studies including all adults CI recipients are comparable to the results presented in this study (see Tyler and Summerfield 1996; Rubinstein et al. 1999; Green et al. 2007).

In the current study, poorer outcomes were obtained in adults with prelingual hearing loss when implanting the sound-deprived ear, with the CI alone and in the daily listening condition. This is comparable to results obtained by Firszt et al. (2012), where poorer benefits were obtained by adults with pre/perilingual hearing loss with asymmetric hearing implanted in their poorer ear. It is also comparable to Caposecco et al. (2012), where duration without a hearing aid in adults with prelingual hearing loss was related to poorer outcomes of implantation. However, in the present study, having a long-term (≥15 years) sound deprivation in the implanted ear per se was related to outcomes, but the duration of sound deprivation was not identified as a significant contributor.

Consequently, for adults with a postlingual hearing loss, it appears sensible to recommend implantation in the sound-deprived ear, regardless of the duration of sound deprivation. Doing so, it increases the possibility of accessing bilateral hearing by maintaining the hearing aid in the non-implanted ear. Moreover, it prevents sacrificing the only hearing ear (destroying residual hearing during insertion of the electrodes), which is the option assumed to be preferred by cochlear implant candidates.
For adults with a prelingual hearing loss and long-term unilateral sound deprivation, knowledge about probable poorer outcomes when implanting a long-term sound-deprived ear is expected to facilitate decision-making about whether to implant or not, and which ear would be the more appropriate for implantation. However, adults with a prelingual hearing loss who have been using only one ear for hearing over the majority of their life may be the least prepared to accept the possible risks of implantation in that ear. In particular, the potential risk of destroying all remaining hearing and of obtaining poorer outcomes with the CI than what was obtained with the hearing aid might influence their decision towards preferring implantation in the sound-deprived ear. It is possible that in this situation, greater auditory training may be necessary to optimise the outcomes with the CI.

The different impacts observed when implanting a sound-deprived ear in adults with postlingual hearing loss and those with prelingual hearing loss probably reflects the greater extent of the neurophysiological consequences observed in animal models of early childhood deafness. For example, the morphological changes observed in the endbulb of Held of congenitally deaf cats have not yet been observed in cats for which deafness was acquired later in life (D. Ryugo, personal communication). Auditory experience in young age is essential for normal development of synaptic activity in the auditory pathways. If this development was not optimal because of a hearing impairment, the consequences of a long-term sound deprivation occurring in childhood or later in life appear to be greater. These results support that different processes occur with early childhood deafness and with long duration of sound deprivation. In animal models, fewer studies have examined the impact of long-term acquired deafness compared with early childhood deafness.

Possible impact of different rehabilitation models following cochlear implantation

The question pertaining to whether increased auditory training would increase performances, either in the daily listening condition, but in particular in the CI alone condition, was considered during this research work. While different models of rehabilitation were not analysed within this thesis, certain related observations can be noted:
i) amongst the different CI centres where data was collected, it is at the centre where recipients received the greatest amount of auditory training with the CI alone, that duration of bilateral significant hearing loss explained the greatest amount of variability in SRS (manuscript 1);

ii) individuals using bimodal hearing daily obtained poorer SRS when tested with their CI alone; and,

iii) in the clinical records, SRS with the CI alone were anecdotally appearing to increase after the abandonment of the hearing aid in the contralateral ear.

These are only observations, but it is known that passive (exposure via daily use) and active (auditory training) experience can affect neural activity and performances (Ryugo and Limb 2009; Irvine 2010). It is also possible that for adults with long-term monaural sound deprivation implanted in the sound-deprived ear, a specific training program may facilitate the attainment of optimal outcomes. This is particularly true if the use of bimodal hearing is considered (more details about this is found in the discussion section of manuscript 3). However, the costs/benefits of training over daily exposure are related to a number of interindividual differences, including expectations, personality, and motivation (Edgerton 1985). Moreover, the most efficient modalities for training, as well as the substrates underlying the increase in performances are unclear. The data presented within this thesis cannot justify changes in rehabilitation models following implantation. However, it may promote ideas and encourage the development of further research in that direction.

8.3 Further considerations

The population of adults using a cochlear implant is relatively small and their hearing history and abilities are characterised by a high degree of heterogeneity. To address the research questions of this thesis, a large sample of participants meeting strict inclusion criteria was required. This forced the use of a retrospective research design, which limited the extent of the study questions and control over the testing paradigms. In particular, the main outcome measure that was retrospectively available was SRS in quiet, which does not represent the extent of hearing abilities provided with a cochlear implant and does not allow one to separate the auditory and cognitive abilities that are involved in speech recognition. Additionally, participants
were recruited from five implantation centres located in three countries, which challenged the data collection and its interpretation. Inevitably, the data collected was dependent on the clinical practice of each implantation centre. Despite differences in speech material used for testing, candidacy criteria, and rehabilitation programs that were offered to patients after implantation, a similar pattern of results was observed across countries. This implies that the conclusions reached are more than likely to be replicable and valid in other implantation centres.

8.4 Limitations and future research

This thesis examined the effect of a long-term monaural sound deprivation on SRS measured after cochlear implantation in either ear. Much insight can be derived from the results obtained with this retrospective study, but many questions remain unanswered. This is partly due to limitations inherent in using a retrospective study, including the constraint of using standard clinical outcome measures of speech recognition in quiet rather than being able to use more complex stimuli and varied outcome measures. In particular, the methodology used did not permit the examination of monaural or binaural auditory processing of complex stimuli, differentiation between auditory and cognitive processing, or the identification of the relative contribution of different brain areas involved in speech processing with a cochlear implant. There is also a paucity of animal models in the area of asymmetric hearing. Further research is needed to more effectively identify the impacts of long-term monaural sound deprivation, which might require different outcome measures, imaging technologies and models of deafness. Additionally, a greater understanding of the potential benefits of different listening modalities and auditory training in enhancing outcomes is an important research direction in translating this knowledge into clinical practice.

Gaining a better understanding of the relative contribution of auditory (bottom-up) and cognitive processing (higher feed-forward or top-down processing) on the SRS measured after cochlear implantation is necessary to identify whether, or to which extent, a long-term sound deprivation affects auditory processing with a CI. To examine this, more specific measures of auditory processing are needed, examining temporal (e.g. temporal modulation, gap detection) and spectral processing (e.g.
spectral ripple), with simple and complex stimuli (e.g. by manipulating the auditory scene with competing sounds). In conjunction with this, more specific measures of cognitive processing are also needed, measured with visually presented speech material so it is not affected by the auditory processing (e.g. reading span, rhyming judgment). Electrophysiological or imaging measurements (e.g. PET) of the spread of neural activity during simple and complex speech listening tasks would also provide further information about which cortical regions are recruited in individuals with hearing asymmetries implanted in the poorer ear. Knowledge about the relative contribution of auditory and cognitive processing on SRS could guide decisions about device programming and rehabilitation programs, enhancing outcomes for cochlear implant recipients. For example, the CI map could be adjusted to improve/facilitate auditory processing in conjunction with decreased demands on cognitive resources. This knowledge could also support the development of individually adapted training programs that would optimise the functional outcomes of implantation.

Animal models of deafness are useful to gain insight into specific anatomical and physiological changes in the auditory pathways following deafness. However, deafness can have a myriad of characteristics that will affect the auditory system differently (e.g. severity, duration, neonatal or acquired as a young or older adult, amplified with a hearing aid or not, symmetrical or not). Accordingly, there appear to be a limited number of studies using animal models to understand the impact of a long-term monaural deafness acquired in adulthood. It is also unclear whether the changes known to be associated with deafness are related to the degeneration of the hair cells per se or to the absence of (or decrease in) auditory stimulation (that could be reversed with amplification via hearing aids). The various causes of deafness found in animal models may also influence the auditory pathways in specific ways (e.g. cochlear ablation, hereditary, chemically or noise induced). Because hearing loss in humans is rarely complete and is often acquired, progressive, and amplified to various degrees, studies using animal models must consider this variability in order to translate this knowledge into clinical applications. Studies involving cochlear implantation in animals are also limited by the inherent differences in cognitive abilities between the two species, which probably differently affects the way plasticity occurs in the auditory pathways and cortex of animals and humans.
While many previous studies have focused on the impacts of sound deprivation on the monaural perception of speech, fewer have identified the consequences on bilateral or binaural processing. Additionally, the role of auditory training is assumed to be important in maximising the use of a degraded auditory signal, although this is typically not systematically evaluated. The results of this thesis demonstrate that similar SRS can be measured after implantation of an aided or a long-term sound-deprived ear, in particular in the daily listening condition (CI alone or bimodal). However, the potential benefits of using bimodal hearing (which is promoted by implanting the sound-deprived ear) may surpass the benefits obtained with the CI alone in the aided ear. For example, recognition of speech in noise, sound localisation, music appreciation and quality of voice may be improved for individuals implanted in the sound-deprived ear, because they have an increased probability of using bimodal hearing. To evaluate this, behavioural and objective measures of binaural processing and benefits (e.g. localisation, speech in noise, binaural difference measured with brainstem responses) could be performed, as well as questionnaires evaluating the quality and benefits of bimodal (bilateral) compared with unilateral hearing.

The effect of a long-term sound deprivation on binaural processing may not be possible to assess with bimodal hearing. This is because a CI and a hearing aid deliver substantially different temporal and spectral auditory information to each ear. On the other hand, this effect may be more evident with bilateral cochlear implantation, which would allow for better control of the stimuli delivered to the bilateral auditory pathways. In this thesis, the 10 adults who received bilateral cochlear implantation received their first CI in the sound-deprived ear and their second in the aided ear some years later (manuscript 2). In this group, it was not possible to predict which ear would obtain greater monaural outcomes. It is possible that different results might have been found if a CI had first been placed in the aided ear, where this would have further enhanced the better ear. Specifically, this could have led to poorer outcomes in the later implanted sound-deprived ear. Simultaneous implantation would allow both ears to simultaneously adapt to the electrical signal, enabling further examination of the specific impact of a long-term monaural sound deprivation.
Auditory training could also contribute to outcomes of cochlear implantation in a sound-deprived ear, particularly when the auditory input in one ear is significantly better than in the other. It is possible that the auditory pathways and cortex adapt to the stronger auditory input received from either ear. Accordingly, specific auditory training of the weaker ear could strengthen the input from that ear and facilitate the use of binaural hearing. Testing this hypothesis would lead to a better understanding of cochlear implantation outcomes in relation to hearing experience and facilitate evidence-based practices with regards to rehabilitation programs following implantation. This study would involve auditory training with the CI alone for individuals using bimodal hearing who are able to recognise speech with their hearing aid alone. It would also involve training the second CI alone after sequential cochlear implantation. Although considerable training can be offered after a first CI, training after a second CI is often restricted and conducted in binaural conditions. This could explain the typically poorer outcomes obtained with a second CI when implantation is performed sequentially (c.f. Kühn-Inacker et al. 2004). To examine the contribution of controlled training or exposure, studies should be conducted with adults who have used their CI for a couple of years and reached a plateau in their outcomes. This would enable the identification of the specific impact of controlled exposure or training over the expected improvement in hearing abilities that is known to follow cochlear implantation. The impact of using the CI alone daily (passive learning) could be compared to the impact of auditory training with the CI alone (active learning). Although the type and magnitude of training that could optimise outcomes are unknown, a first step could be to verify if a varied and intense auditory training program with the weakest ear could improve outcomes with that ear and also the outcomes in the binaural condition. As discussed previously, specific outcome measures of auditory and cognitive processing would allow better identification of the source of improvement. If a significant improvement was found, research efforts could be placed on increasing the efficiency of the training programs (aiming at decreasing the costs and increasing the benefits).
8.5 Conclusion

Using different perspectives, methods and populations to study speech recognition performance after cochlear implantation in adults with long-term monaural sound deprivation, a strong pattern of results emerged: better hearing in one ear is related to better outcomes after implantation of either ear. In addition, the duration of sound deprivation in one ear was not shown to significantly contribute to speech recognition performance after implantation in that ear. In adults with hearing loss acquired post-linguistically, similar results can be obtained when implanting the better or the worse ear. However, poorer outcomes may be expected when implanting a long-term sound-deprived ear in adults with prelingual hearing loss, but outcomes do not appear related to the duration of the deprivation. Finally, implanting a sound-deprived ear increases the probability of gaining access to bimodal hearing, which potentially increases the functional benefits. These results may appear counter-intuitive, but corroborate the knowledge about neuroplasticity in unilateral deafness and cognitive hearing. While this new understanding may influence clinical practices, more research is needed to further understand the specific auditory and cognitive changes that occur with hearing asymmetries, and the best rehabilitation options for each individual.

Following his research on the effect of electricity on sensory function, Alessandro Volta predicted that all experiments relating to what he called the artificial electrical organ (...) will open a very wide field of reflection, and of view, not only curious, but particularly interesting to medicine. There will be a great deal to occupy the anatomist, the physiologist, and the practitioner (Volta 1800). This prediction was correct, and is still correct today; much in the field of cochlear implantation is yet to be learned.
References


Bergeron, F. (2012). Speech recognition in users of the most recent technologies from the four major cochlear implant manufacturers. *12th International Conference on Cochlear Implants and Other Implantable Auditory Prostheses.* Baltimore, USA.


References 140


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References 148


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# Appendix

## Table A.1. (manuscript 4) Pearson correlation matrix of Speech Recognition Scores (SRS) and possible predictive variables of outcomes in individuals implanted in a sound-deprived ear (n=70).

<table>
<thead>
<tr>
<th>SRS</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
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<th>6</th>
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<td>SRS</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1) age</td>
<td>-.27*</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2) Duration of sound deprivation in CI ear (years)</td>
<td>-.27*</td>
<td>.29*</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3) Duration of sound deprivation in CI ear (% of lifetime)</td>
<td>-.11</td>
<td>-.32**</td>
<td>.80**</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>4) Duration of bilat sign. deafness (years)</td>
<td>-.35**</td>
<td>.01</td>
<td>.01</td>
<td>-.01</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5) Duration of bilat sign. deafness (% of lifetime)</td>
<td>-.30*</td>
<td>-.12</td>
<td>-.04</td>
<td>.03</td>
<td>.97**</td>
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<tr>
<td>6) Use of contra hearing aid</td>
<td>-.13</td>
<td>.07</td>
<td>.21</td>
<td>.18</td>
<td>-.32**</td>
<td>-.32**</td>
<td>1</td>
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<tr>
<td>7) Implant Ear (right/left)</td>
<td>-.11</td>
<td>-.30*</td>
<td>.00</td>
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<td>-.05</td>
<td>-.01</td>
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* *p < 0.05, **p < 0.01

## Table A.2. (manuscript 5) Pearson correlation matrix of Speech Recognition Scores (SRS) and possible predictive variables of outcomes in individuals implanted in a sound-deprived ear (n=28).

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<th>6</th>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2) SRS pre-CI</td>
<td>.30</td>
<td>.28</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3) PTA CI ear</td>
<td>.13</td>
<td>.27</td>
<td>-.41*</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>4) PTA contra ear</td>
<td>-.00</td>
<td>.20</td>
<td>-.53**</td>
<td>.70**</td>
<td>1</td>
<td></td>
<td></td>
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<tr>
<td>5) Use of bimodal</td>
<td>-.10</td>
<td>.05</td>
<td>.39*</td>
<td>-.10</td>
<td>-.33</td>
<td>1</td>
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<td></td>
<td></td>
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<tr>
<td>6) Right or left CI</td>
<td>.21</td>
<td>-.13</td>
<td>.09</td>
<td>-.18</td>
<td>.04</td>
<td>-.09</td>
<td>1</td>
<td></td>
<td></td>
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<tr>
<td>7) Deprivation CI ear (years)</td>
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<td>-.65**</td>
<td>.10</td>
<td>.08</td>
<td>.09</td>
<td>-.03</td>
<td>-.06</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>8) Deprivation CI ear (% lifetime)</td>
<td>-.33</td>
<td>-.23</td>
<td>-.21</td>
<td>-.10</td>
<td>-.10</td>
<td>.00</td>
<td>-.05</td>
<td>.55**</td>
<td>1</td>
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<td>9) Bilat sig. HL (years)</td>
<td>-.61**</td>
<td>.055</td>
<td>-.57**</td>
<td>.19</td>
<td>.33</td>
<td>-.26</td>
<td>-.24</td>
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<td>.15</td>
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<td>10) Bilat sig. HL (% lifetime)</td>
<td>-.66**</td>
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<td>-.59**</td>
<td>.15</td>
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<td>-.21</td>
<td>-.19</td>
<td>-.02</td>
<td>.14</td>
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</table>

* *p < 0.05, **p < 0.01
Table A.3. (manuscript 5) Pearson correlation matrix of Speech Recognition Scores (SRS) and variables relating to the history of the hearing loss in individuals implanted in a sound-deprived ear (n=98).

<table>
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<th></th>
<th>1)</th>
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<th>5)</th>
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<td><strong>SRS</strong></td>
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<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1) Any severity of preling HL in CI ear</td>
<td>-.53**</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2) Any severity of preling HL in both ears</td>
<td>-.49**</td>
<td>.87**</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3) Severe preling HL in CI ear</td>
<td>-.49**</td>
<td>.75**</td>
<td>.70**</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>4) Severe preling HL in both ears</td>
<td>-.46**</td>
<td>.66**</td>
<td>.79**</td>
<td>.89**</td>
<td>1</td>
<td></td>
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<tr>
<td>5) Duration of sound deprivation in CI ear (years)</td>
<td>-.28**</td>
<td>.19*</td>
<td>.02</td>
<td>.12</td>
<td>.06</td>
<td>1</td>
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<tr>
<td>6) Duration of sound deprivation in CI ear (% of lifetime)</td>
<td>-.46**</td>
<td>.64**</td>
<td>.48**</td>
<td>.61**</td>
<td>.47**</td>
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<td>7) Duration of bilat sign. deafness (years)</td>
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<td>.37**</td>
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<td>.37**</td>
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<td>8) Duration of bilat sign. deafness (% of lifetime)</td>
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*p < 0.05, **p < 0.01