Cochlear implantation in adults with early-onset deafness

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Cochlear implantation in adults with early-onset deafness

PROEFSCHRIFT

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volgens het besluit van het College van Decanen,
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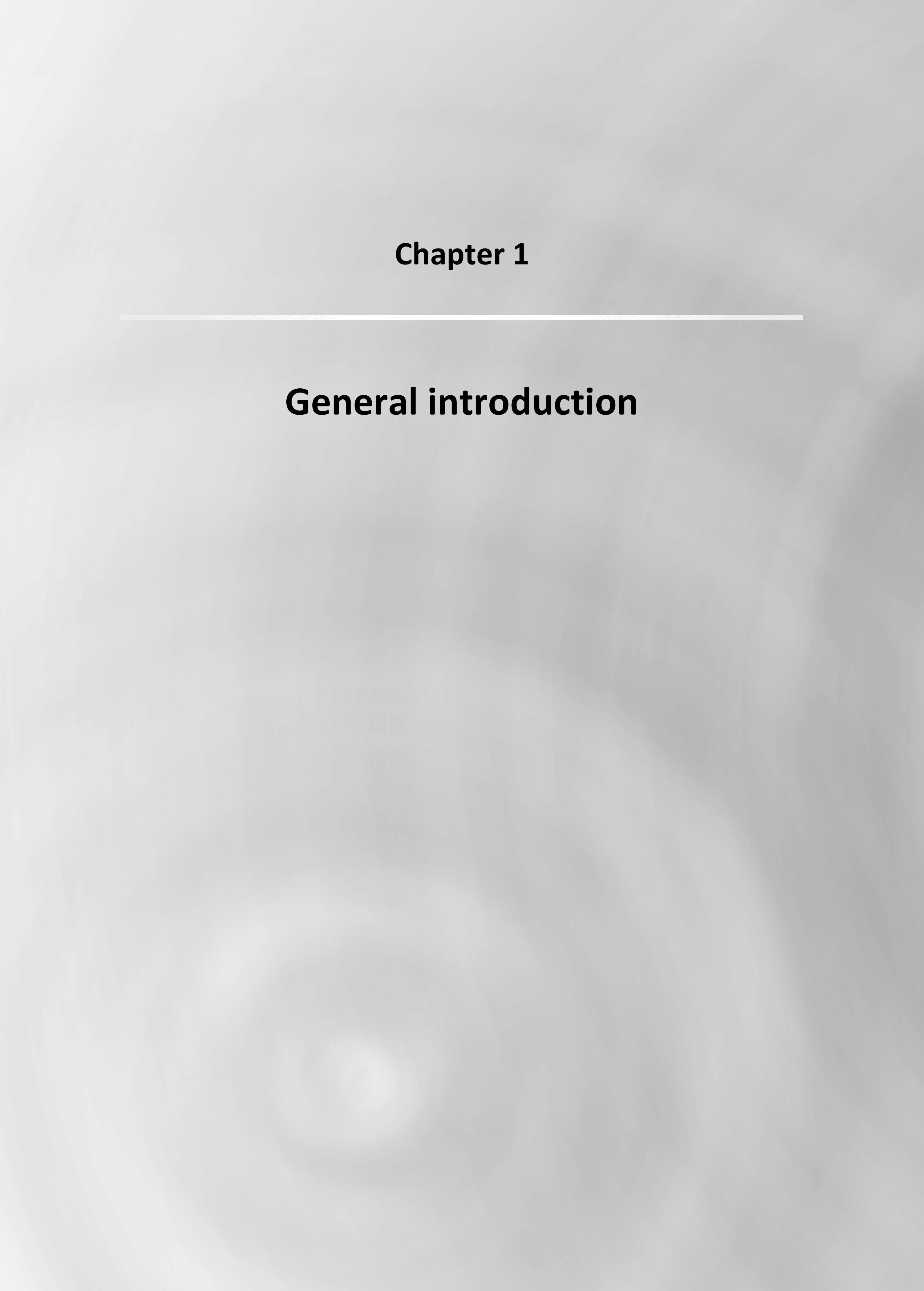
List of Abbreviations

AMDT	Amplitude Modulation Detection Threshold
BM	Basic Map
CI	Cochlear Implant
CL	Current Level
CNC	Consonant Nucleus Consonant
EM	Experimental Map
EDDL	Electrode Discrimination Difference Limen
MCL	Most Comfortable Loudness
MTS	Monosyllable Trochee Spondee
NCIQ	Nijmegen Cochlear Implant Questionnaire
pps	pulses per second
PF	Prognostic Factor
PTA	Pure Tone Average
PW	Pulse Width
rpo	ripples per octave
SDC	Smallest Detectable Change
SEM	Standard Error of Measurement
ST	Speech Tracking
TMTF	Temporal Modulation Transfer Function
UCL	Uncomfortable Loudness
VAS	Visual Analogue Scale
wpm	words per minute

Chapter 1

General introduction



BACKGROUND

The first commercially available cochlear implant systems in the 1980’s of the previous century were mostly single-electrode devices that used an analogue conversion of sound to electrical current (e.g. House/3M device). When this new technique was applied in adult patients with an early, prelingual[1] onset of deafness, it became clear that this group reacted differently to electrical stimulation than patients with a late, postlingual[2] onset of deafness: early deaf patients described odd, tactile sensations or vibrations in and around their head which, very gradually, sometimes following months of stimulation, changed into a sensation which resembled “hearing” (Eisenberg, 1982). With further development of cochlear implant systems, the auditory advancements of early-deafened, adult subjects remained very limited compared to those of postlingually deafened adults (Skinner et al., 1992; Snik, Makhdoum, Vermeulen, Brokx, & van den Broek, 1997; Waltzman, Cohen, & Shapiro, 1992). On the other hand, early studies also reported clear positive effects of cochlear implantation in this patient group, such as better sound-awareness, increased independence, and improved communication skills (Hinderink, Mens, Brokx, & van den Broek, 1995; Zwolan, Kileny, & Telian, 1996). With the most recent cochlear implant processing techniques, some subjects are able to attain open set speech understanding, but large intersubject variability (Bosco et al., 2013; Caposecco, Hickson, & Pedley, 2012; O'Gara, Cullington, Grasmeder, Adamou, & Matthews, 2016; van Dijkhuizen, Beers, Boermans, Briaire, & Frijns, 2011) and significant differences with postlingually deafened subjects (Kraaijenga et al., 2016; Moon et al., 2012) remain.

In this introduction we continue with a short explanation of how a modern cochlear implant works, followed by what the consequences of an early-onset deafness are for central auditory development. Thereafter we introduce some of the issues we face regarding cochlear implantation in the early-deafened, adult population, and how this thesis aimed to address them.

MECHANISM OF A COCHLEAR IMPLANT

A cochlear implant is an electronic device that is able to restore hearing in patients with severe sensorineural hearing loss, by means of directly stimulating the auditory nerve fibres in the cochlea. It is made up of an external and an internal part (see Figure 1). The internal part containing the receiver/stimulator and electrode array is implanted surgically, with the electrode array being meticulously placed in the cochlea. The external part, containing the sound processor and transmitter, encodes the sound received by the

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[1] Onset before the end of the language acquisition period, generally considered about 4-6 years

[2] Onset after the end of the language acquisition period, generally considered about 6 years

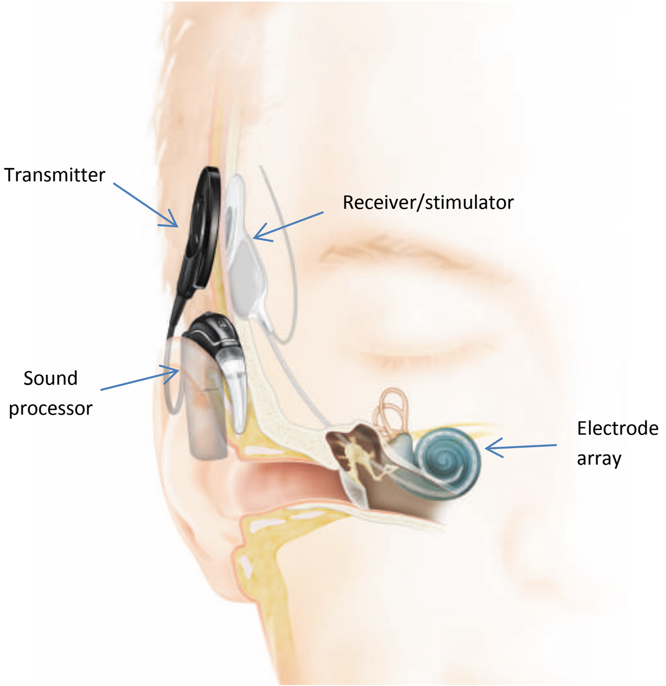

Figure 1. External and internal part of a Cochlear Implant (Copyright Cochlear Limited)

sound processors' microphone. This digital code is transferred from the transmitter to the internal receiver/stimulator, which in its turn converts it to very fast electrical impulses which are sent to the electrode array. These electrical impulses stimulate the auditory nerve fibres in the cochlea, which transfer the signals further to the brain, following the same pathways as in normal hearing. The various auditory nuclei in the brain then translate these impulses into meaningful sounds.

The "language" which is used to translate the sound into a digital code is called the sound processing strategy (see Figure 2 for an overview). Nowadays all sound processing strategies split up the sound picked up by the microphone based on its frequency content, by means of so-called band pass filters. In that way, low-frequency sounds can be transmitted to electrodes located towards the apex (the tip) of the cochlea (e.g. BPF1 in Figure 2), and high-frequency sounds to electrodes at the base (outer end) of the cochlea (e.g. BPF4), following the natural tonotopy[3] of this auditory structure.

After the sound is filtered into several frequency bands (usually between 12-22, depending on CI brand), the temporal fine structure of the acoustic waves is discarded,

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[3] Tonotopy: spatial organization of anatomic regions in a way that neighbouring frequencies are represented by fysically neighbouring areas; is present throughout the auditory system

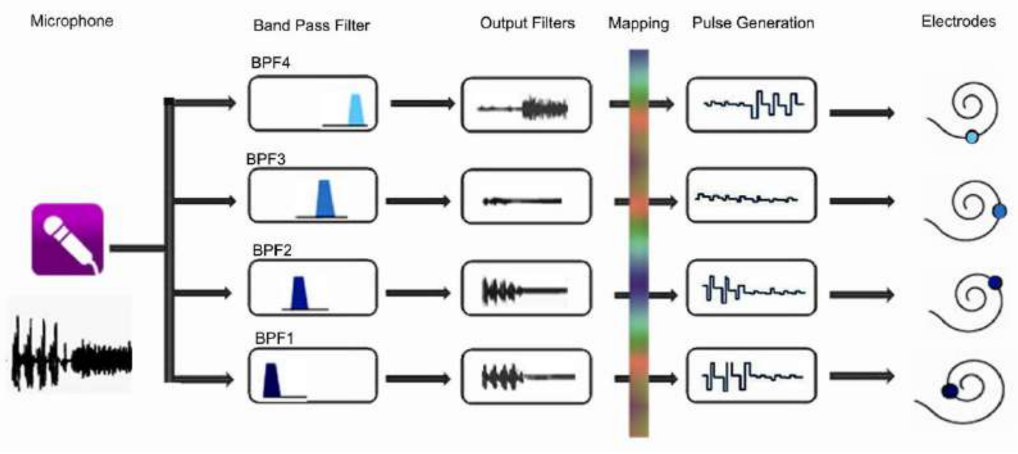

Figure 2. Block diagram of the sound processing of a Cochlear Implant (figure by JPL Brokx)

leaving only the slowly varying temporal envelope. In the next phase, the output is modified in terms of a number of parameters that are individually set for each patient (e.g. the current level that is needed to attain a comfortably loud stimulation). This process is called “mapping”. The resulting signal is then used to model fast electrical pulse trains which are passed on to the electrodes.

As a result of this sound processing, information on the frequency content of the acoustic signal is mainly available through the place of stimulation in the cochlea and temporal information is mainly present in the envelope of the CI signal. The terms *spectral* and *temporal resolution or processing ability* will return on several occassions throughout this thesis, and can be defined as the ability to resolve the frequency components, respectively the changes in auditory information over time, of an acoustic signal.

CONSEQUENCES OF AUDITORY DEPRIVATION ON AUDITORY DEVELOPMENT

When exposition to auditory information is absent or reduced in early childhood, this has widespread consequences for the maturation of the auditory system. On one hand it has been shown that the connections of the bottom-up auditory pathway, transferring incoming sounds from the auditory nerve fibres in the cochlea through the various auditory nuclei in the brainstem to the auditory cortex, remain at least partly functional in congenital deafness. This allows early-deafened subjects to at least “perceive” sounds when they receive a cochlear implant later in life (Kral, Yusuf, & Land, 2017). On the other hand, early auditory experience is necessary for the functional development of mainly the auditory cortex. For example, small babies are sensitive to all elementary features of sounds in any language. By the age of 1, however, they become specialised in those acoustic features that allow them to distinguish phonemes in their own mother tongue and at the same time, they become insensitive to the non-distinctive features. In that way “auditory objects” are formed: perceptions related to hearing which allow one to categorize the acoustic environment, such as a phonemic categories. In case of early and continued auditory deprivation, a neuronal network incapable to form these auditory objects is developed. When cochlear implantation is performed later in life in an individual with early-onset deafness, the auditory system is thought to no longer have the high synaptic plasticity that allows for this type of bottom-up driven learning (Kral, 2007).

Studies in electrically stimulated congenitally deaf animals have also shown that there is a deviant activation pattern within the primary auditory cortex and a reduced activity of the deeper cortical layers (Kral, 2007). These deep layers are assumed to play a central role in integrating bottom-up, sensory information with top-down information coming from higher-order cortical areas, such as information on active auditory objects. In an experienced brain it is assumed that conflicts between the bottom-up and top-down information streams, i.e. between the sensory input and the brain’s expectations, are the driving force behind adult learing (Kral et al., 2017). In case of auditory deprivation, the main hypothesis is that there is a functional decoupling between higher-order and primary auditory areas (Kral, 2007; Kral & Sharma, 2012), which prevents learning based on these modulating top-down influences, also when auditory input is restored through a cochlear implant.

In addition it has been shown that, secondary to early auditory deprivation and the lack of sufficient auditory input to the higher-order auditory cortex, cross-modal plasticity can occur: the higher order auditory areas are recruited to participate in the functioning of other sensory modalities, such as vision (Kral et al., 2017; Sharma, Campbell, & Cardon, 2015). The extent to which this occurs might be related to the success of hearing restoration through a cochlear implant: Buckley and Tobey (2011) observed a strong correlation between the amount of visual cross-modal reorganisation and speech understanding scores with CI in a group of late-implanted, prelingually deaf subjects. The results of studies investigating the effect of auditory deprivation and subsequent cochlear implantation on cortical auditory evoked potentials (CAEPs), point to the existence of a sensitive period for normal auditory development, which closes at about 7 years of age (Sharma et al., 2015).

In conclusion, when a cochlear implant reintroduces auditory stimulation in early-deafened patients after the ‘’sensitive period’’ has closed, i.e. in adolescence or adulthood, the auditory system is unable to adapt sufficiently to the new input and poor outcomes are to be expected. It needs to be noted, however, that most of the early-deafened subjects in this thesis have not been completely deprived from auditory stimulation during their development, e.g. due to stimulation of their residual hearing with hearing aids and/or a slightly older age at onset of deafness. As a result, the extent of the effects of auditory deprivation as described here might be somewhat reduced in those subjects.

PROBLEM STATEMENT

A cochlear implant user needs to be able to extract and process at least part of the spectral and temporal information that is present in the signal delivered by the sound processor, in order to recognize sounds and understand speech in daily life. As described previously, the development of the auditory system alters when auditory stimulation is absent or limited early in life. A substantial part of the limitations in auditory speech understanding experienced by early-deafened CI users, can therefore be traced back to the deviant functioning of especially central auditory structures. Much less known, however, is to what extent these early-deafened CI users also have problems on a peripheral level, extracting the relevant spectral and temporal information from the CI signal. Most research efforts focus on how póstlingually deaf CI users perform on measures of spectral and temporal processing (Anderson, Nelson, Kreft, Nelson, & Oxenham, 2011; Won, Drennan, Nie, Jameyson, & Rubinstein, 2011). Only a few studies have specifically investigated spectral and temporal processing abilities of early deaf patients (Busby & Clark, 1996, 2000; Busby, Tong, & Clark, 1993), generally revealing poorer performance when compared to postlingually deaf patients. An important question is therefore to what extent early-deafened subjects are able to perceive and understand the “language” of the cochlear implant, which allows them to extract the necessary speech cues. More extensive investigation of the spectral and temporal processing abilities of these patients can tell us more on which aspects of sound processing are potentially causing difficulties, and whether changing certain aspects of how the sound is delivered to the early-deafened ear, might help to overcome them.

Clinicians working with early-deafened, late-implanted CI users in the field know from general experience that most of these patients have little chance of becoming star performers, defined in terms of open-set, auditory only speech understanding outcomes. They also know that the variation between patients in terms of outcomes is high and that there is a risk for some patients to become non-users, whereas others will be very satisfied despite only limited auditory improvements. Since the majority of cochlear implant clinics have only limited numbers of adult CI users with an early-onset deafness, it is difficult to set out clear implantation criteria for new candidates, taking into account both auditory and subjectively experienced outcomes. The latest review on outcomes of this specific population of CI users already dates back to 2004 (Teoh, Pisoni, & Miyamoto, 2004a), thus not incorporating results from studies performed in the last 10-15 years with the most recent technologies. More extensive and up-to-date knowledge on expected outcomes can aid in determining implantation criteria, and is also highly relevant for patient counselling, ensuring realistic expectations. Ideally it would be possible to predict outcomes based on factors that are already known pre-implantation, and thus determining which individuals are likely to benefit most from cochlear implantation. A number of, sometimes large-scale, studies predicting outcomes of postlingually deafened

CI users have been performed in recent years (Blamey et al., 2013; Holden et al., 2013; Lazard, Vincent, et al., 2012; Roditi, Poissant, Bero, & Lee, 2009). For early-deafened subjects such studies are rare, given the much smaller number of implantations. It can also not simply be assumed that the factors important in predicting outcomes of postlingually deafened CI users are the same as for early-deafened CI users, given for instance the implications of early onset deafness on auditory development and the variation in early auditory rehabilitation in this population. It would therefore be useful to see whether the outcomes of the available studies can be combined to provide us with useful insights on which factors are important outcome predictors for early-deafened CI users.

Finally, when predicting or measuring performance with a cochlear implant, the golden standard is to look at open-set, auditory word or sentence recognition, traditionally in quiet, but more recently also in noise. Part of the early-deafened CI users will have chance-level performance on these auditory tests, also after implantation (Caposecco et al., 2012; Heywood, Vickers, Pinto, Fereos, & Shaida, 2016). However, this does not necessarily imply that these patients do not obtain any auditory benefit from the CI stimulation: the traditional tests may simply not be sensitive enough to detect very small changes in auditory perception or enhancements in lip reading. It would thus be useful to see whether there are other, non-traditional tests capable of capturing much smaller changes in auditory performance. From another angle, clinical experience shows that auditory benefit and patient satisfaction do not necessarily go hand in hand. It is therefore interesting to find out in which auditory quality of life areas changes occur after implantation, and whether these changes are also present in patients not obtaining clear gains on traditional auditory tests.

AIMS OF THIS THESIS

In this thesis we aimed to investigate auditory processing abilities in relation to CI fitting, to optimise outcome measurement and to increase knowledge on outcome predictors of cochlear implantation in adult patients with an early onset of deafness.

The following research questions were addressed:

What are the temporal processing abilities of early-deafened CI users, and is there a relation with speech understanding?

In *Chapter 2* we measured temporal processing abilities of both pre- and postlingually deafened CI users by means of their sensitivity to sound-field sinusoidal amplitude modulations. The resulting Amplitude Modulation Detection Thresholds (AMDTs) at different modulation frequencies form a Temporal Modulation Transfer Function (TMTF), which was compared between early- and postlingually deafened CI users. It was hypothesized that early-deafened CI users would perform less good than postlingually deafened CI users.

Speech perception measures for both patient groups were correlated with the mean AMDT per modulation frequency, the mean AMDT, the attenuation rate of the TMTF and the surface area under the TMTF in order to investigate the possible relationship between performance on the measure for temporal processing and speech understanding skills with CI.

Do early-deafened CI users have limited access to spectral information, and if so, can this be optimised in order to improve performance?

We hypothesized in *chapter 3* that early-deafened CI users would have difficulties to discriminate between stimulation given on different electrodes, and that this limits their access to the spectral information encompassed in the stimulation pattern of the CI. We measured electrode discrimination difference limens, i.e. the minimal distance between two electrodes that is needed to perceive them as different, for the entire electrode array in a group of 6 early-deafened CI users.

Further in *chapter 3*, results of the electrode discrimination testing were used in order to create an experimental CI fitting containing only discriminable electrodes. Performance with the subjects' clinical fitting was compared to performance with the experimental fitting after an adjustment period of 4 weeks. Performance measurements included tests for speech understanding, both in quiet and in noise, a listening effort test and a spectral ripple discrimination test, which is a measure of spectral resolution. Subjective appreciation of both fittings was assessed by means of a Visual Analogue Scale (VAS) and a questionnaire.

What are the postoperative outcomes of early-deafened, late-implanted CI users in terms of auditory performance and (hearing-related) quality of life?

Relevant data with respect to this study aim were first of all gathered through an extensive search of the literature: *chapter 4* presents the results of a systematic review including 38 studies that have outcomes on either open- or closed-set speech understanding, audiovisual benefit or subjective benefit. Study outcomes on the relevant outcome domains were extensively analysed, taking into account the results of the thorough quality assessment which identified a number of issues that might have impacted the presented results. Secondly, *chapter 6* presents the results of a prospective study, with auditory outcomes of 27 early-deafened CI users up to 3 years after implantation.

As a first subquestion, we wondered **whether it is possible to capture limited changes in auditory performance after cochlear implantation by means of outcome measures that are better adapted to early-deafened CI users?** Therefore, outcomes in the poorer performing subjects of *chapter 6* were assessed not only by a traditional open-set word test, but additionally by means of the conversation-like speech tracking test (De Filippo & Scott, 1978), as well as the closed-set monosyllable-spondee-trochee (MTS) test (Erber & Alencewicz, 1976).

As a second subquestion, we were interested **whether benefits for auditory-related quality of life are related to the auditory benefits of early-deafened subjects?** *Chapter 6* also presents the pre- and postimplantation results on a subjective questionnaire that was developed specifically for early-deafened CI users. The relation between subjectively experienced and auditory benefits was assessed by means of calculating correlations between postoperative changes on the questionnaire and changes on the auditory tests.

Which patient-related factors can predict the postoperative speech understanding outcomes of early-deafened, late-implanted CI users?

In *chapter 5* we present the second part of our systematic review*,* in which 13 studies with a clear prognostic study goal were identified, investigating a multitude of potential prognostic factors. The outcomes of these studies were combined and analysed in light of potential sources of bias, in order to determine the most promising prognostic factors for speech understanding outcome in this population.

For the study group in *chapter 6*, we equally investigated which of 8 patient-related factors were related to the 1 year postoperative word recognition scores. The factors showing a significant relation in the simple linear regression analysis, were included in the subsequent multivariable regression analysis, resulting in a final multiple regression model.

Chapter 2

Amplitude modulation detection and speech recognition in late-implanted prelingually and postlingually deafened CI users

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ABSTRACT

Objectives: Many late-implanted prelingually deafened cochlear implant (CI) patients struggle to obtain open-set speech understanding. Since it is known that low-frequency temporal-envelope information contains important cues for speech understanding, the goal of this study was to compare the temporal-envelope processing abilities of late-implanted prelingually, and postlingually deafened CI users. Furthermore, the possible relation between temporal processing abilities and speech recognition performances was investigated.

Design: Amplitude modulation detection thresholds (AMDTs) were obtained in 8 prelingually and 18 postlingually deafened CI users, by means of a sinusoidally modulated broadband noise carrier, presented through a loudspeaker to the CI user's clinical device. Thresholds were determined with a 2-down-1-up 3-interval oddity adaptive procedure, at 7 modulation frequencies. Phoneme recognition (Consonant-Nucleus-Consonant) scores (% correct at 65 dB SPL) were gathered for all CI users. For the prelingually deafened group, scores on 2 additional speech tests were obtained: (1) a closed-set monosyllable-trochee-spondee (MTS) test (% correct scores at 65 dB SPL on word recognition and categorization of the suprasegmental word patterns), and (2) a speech tracking test (number of correctly repeated words per minute) with texts specifically designed for this population.

Results: The prelingually deafened CI users had a significantly lower sensitivity to amplitude modulations than the postlingually deafened CI users, and the attenuation rate of their TMTF was greater. None of the prelingually deafened CI users were able to detect modulations at 150 and 200 Hz. High and significant correlations were found between the results on the amplitude modulation detection test and CNC phoneme scores, for the entire group of CI users. In the prelingually deafened group CNC phoneme scores, word scores on the MTS test, and speech tracking scores correlated significantly with the mean AMDT of the modulation frequencies between 5 and 100 Hz and with almost all separate amplitude modulation thresholds. High correlations with these speech measures were also found for the attenuation rate of and the surface area below the TMTF. In postlingually deafened CI users, CNC phoneme scores only correlated significantly with the 100- and 150-Hz amplitude modulation thresholds, as well as with the attenuation rate of and surface area below the TMTF.

Conclusions: Prelingually deafened CI users were less sensitive to temporal modulations than postlingually deafened CI users, and the attenuation rate of their TMTF was steeper. For all CI users, subjects with better amplitude modulation detection skills tended to score better on measures of speech understanding. Significant correlations with low modulation frequencies were found only for the prelingually deafened CI users and not for the postlingually deafened CI users.

INTRODUCTION

While many cochlear implant (CI) users have excellent speech recognition in quiet (Dorman & Spahr, 2006), part of this population still struggles (Lazard, Giraud, Gnansia, Meyer, & Sterkers, 2012; Santarelli, De Filippi, Genovese, & Arslan, 2008; Teoh et al., 2004a). Most of them are late-implanted prelingually deafened patients, i.e. with an onset of deafness before the end of the language acquisition period. Important information for speech recognition is present in temporal cues up to about 50 Hz: normal-hearing subjects can achieve nearly perfect speech recognition using slow temporal cues (<20 Hz), combined with limited spectral information (Friesen, Shannon, & Cruz, 2005; Shannon, Zeng, Kamath, Wygonski, & Ekelid, 1995). Since temporal cues seem to be important, and long-term auditory deprivation induces changes along the entire auditory pathway (Teoh, Pisoni, & Miyamoto, 2004b), the present study was conducted to compare the temporal processing abilities of prelingually and postlingually deafened CI users, and to assess whether these abilities are related to speech recognition performance.

A powerful approach to determine the temporal processing abilities of CI users is to measure the sensitivity to sinusoidal amplitude modulations. The amplitude modulation detection threshold (AMDT), expressed as the smallest modulation depth that can be detected, measured at several modulation frequencies, results in a temporal modulation transfer function (TMTF). In normal-hearing subjects and postlingually deafened CI users the TMTF has a low-pass filter characteristic, i.e. high sensitivity at low modulation frequencies and decreasing sensitivity with increasing modulation frequency (Bacon & Viemeister, 1985; Dau, Kollmeier, & Kohlrausch, 1997; Shannon, 1992; Viemeister, 1979).

A range of studies on amplitude modulation detection in CI users reported the effects of stimulation rate (Arora, Vandali, Dowell, & Dawson, 2011; Galvin & Fu, 2005, 2009; McKay & Henshall, 2010; Pfingst, Xu, & Thompson, 2007), stimulation site (Garadat, Zwolan, & Pfingst, 2012; Pfingst et al., 2007), stimulation mode (Galvin & Fu, 2005; Pfingst, 2011), stimulus duration (Luo, Galvin, & Fu, 2010), stimulus level (Galvin & Fu, 2005, 2009; Pfingst et al., 2007), and loudness growth (McKay & Henshall, 2010) on AMDTs. In most of these studies the electrical stimulus was presented directly to one or more electrodes using computer-controlled stimulation, bypassing the clinical sound processor. Recently however, Won, Drennan, et al. (2011) and Gnansia et al. (2014) conducted studies in which stimuli were presented in sound-field to the sound processor of postlingually deafened CI users. This approach assesses the sensitivity to amplitude modulations in a clinical setting, including both the processors' signal processing and the subjects' individual maps. Won, Drennan, et al. (2011) showed that the TMTFs of CI users measured in free-field, have the same low-pass filter shape as the TMTFs of CI users measured with electric stimulation directly at one electrode. When they compared the sound-field TMTFs of the postlingually deafened CI users to the sound-field TMTFs of normal hearing and hearing-impaired subjects as obtained by Bacon and Viemeister (1985), Won et al. (2011)

found a lower general sensitivity to amplitude modulation and a steeper slope for the CI users compared to the 2 other groups.

Almost all studies regarding temporal processing mentioned so far, investigated the amplitude modulation detection abilities of postlingually deafened CI users. However, for prelingually deafened CI users the shape of the TMTF is not well characterized. One study, by Busby et al. (1993), obtained electric TMTFs of 3 prelingually deafened CI users. All 3 subjects showed a lower sensitivity to amplitude modulation, and for one of these subjects the shape of the TMTF differed from the low-pass filter characteristic; this TMTF had a characteristic of 2 band-pass filters.

Temporal information in speech, e.g. syllabicity, rhythm, manner of articulation, voicing, stress, and intonation, is present in the envelope and periodicity of an acoustic waveform (Rosen, 1992). It is therefore not surprising that several studies have found a correlation between amplitude modulation detection abilities and speech recognition performance for postlingually deafened CI users. Cazals, Pelizzone, Saudan, and Boex (1994) found that the rejection rate, which they defined as the difference between the AMDT at the 400- and at the 71-Hz modulation frequency, measured at the most apical electrode, correlated with average performance for vowel and consonant recognition administered at 70dBA. Fu (2002) found highly significant correlations between mean electric AMDTs (for a 100 Hz modulation, averaged over several stimulation levels) and both vowel and consonant recognition scores. In a study by Luo, Fu, Wei, and Cao (2008), mean electric AMDTs (averaged for 20-Hz amplitude modulation across 5 stimulation levels) were significantly correlated with Chinese tone, consonant, and sentence recognition scores. Arora et al. (2011) found that mean AMDTs (obtained with vowel-like stimuli presented via direct audio input to a research processor), predicted sentence in noise outcomes at 65 dB SPL. These mean AMDTs were determined by averaging across the 50- and 100-Hz modulation frequencies and various stimulation rates, presented at an acoustic level that when processed through the processor, produced electrical stimulation levels close to the subjects' electrical most comfortable level (MCL). Won et al. (2011) found significant correlations between the mean AMDTs, averaged over 7 modulation frequencies ranging from 10 to 300 Hz, and both consonant-nucleus-consonant (CNC) monosyllabic phoneme scores and speech reception thresholds (SRTs) in noise. When looking at the individual modulation frequencies, significant correlations were found only for the higher modulation frequencies (from 75 Hz onwards for the CNC scores and from 150 Hz onwards for the SRTs in noise). In addition, Won et al. (2011) found that the attenuation rate, i.e. the slope, of the sound-field TMTF, which is defined as the b-component of the exponential function, $AMDT\ (f_{mod}) = -ae^{bf_{mod}}$ fitted through the AMDTs from 10 to 200 Hz, correlated with both CNC scores in quiet and speech reception thresholds (SRTs) in noise. Given that the attenuation rate is mainly determined by the AMDTs at higher modulation frequencies, the results of Won et al. (2011) suggest that CI users with better thresholds for high modulation frequencies obtain better speech understanding scores. In a recent study of Gnansia et al. (2014), sound-field AMDTs measured at a low modulation frequency of 8 Hz also correlated significantly with vowel and consonant identification scores in quiet. In noise, no significant correlations were found (Gnansia et al., 2014). Since in all these studies only postlingually deafened CI users were tested, it is unknown whether a correlation exists between amplitude modulation detection measures and speech performance scores for prelingually deafened CI users.

The first goal of the present study is to compare the sound-field AMDTs of prelingually deafened CI users with the sound-field AMDTs of postlingually deafened CI users. It is hypothesized that prelingually deafened CI users perform more poorly than postlingually deafened CI users on the temporal modulation detection tests. The second goal of this study is to assess the possible relation between temporal processing abilities, measured with AMDTs, and speech recognition scores for the entire group of CI users, and for the prelingually and postlingually deafened CI users separately.

MATERIALS AND METHODS

Subjects

Both prelingually (n=8) and postlingually (n=18) deafened CI users participated in this study. All subjects were Dutch native speakers with oral communication as their primary mode of communication. Some of the prelingually deafened CI users were also familiar with Dutch sign language. All CI users were unilaterally implanted after the age of 18 years and had minimally one year experience with the CI. The age at onset of deafness for the prelingually deafened subjects can be found in Table 1. Note that 3 of the prelingually deafened subjects had an onset at 2 or 3 years of age, and might therefore be considered perilingually rather than prelingually deafened. For convenience of comparison however, it was preferred to use the term “prelingual” for all subjects with an onset of deafness before the end of the language acquisition period. The duration of the moderate to profound hearing loss of both the pre- and postlingually deafened CI users is also listed in Table 1, together with information about the age at implantation, etiology and implant type. The duration of hearing loss was referred to as the time up to the implantation date, from when the PTA of the best ear was at least 60 dB HL or, if this information was not available, the time from when the subject had started to wear hearing aids bilaterally. The use of human subjects was approved by the local Medical Ethical Committee.

Setup

The acoustic stimuli were presented in a sound-treated booth through a speaker (Klein + Hummel O 110 D) positioned 1 m in front of the subjects. The APEX 3 program (developed at ExpORL-K.U.Leuven (Francart et al. 2008)), run on a laptop, was used to present the stimuli in an adaptive procedure. All subjects listened to the stimuli presented in the

Table 1. Subject Characteristics

Subject	Age (yr)	Age at Onset of Deafness (yr)	Duration of Hearing Loss (yr)	Age at Implantation (yr)	Etiology	Implant Type
PRE01	49	3	42	45	Meningitis	HiRes 90k
PRE02	67	2	63	65	Meningitis	HiRes 90k
PRE03	47	Congenital	40	40	Rubella	HiRes 90k
PRE04	74	0.7	70	71	Meningitis	Nucleus CI512
PRE05	73	Congenital	71	71	Unknown	CONCERTO
PRE06	65	3	58	61	Meningitis	HiRes 90k
PRE07	40	Congenital	37	37	Unknown	HiRes 90k
PRE08	62	0.3	58	59	Meningitis	HiRes 90k
POST01	66	/	35	58	Hereditary	HiRes 90k
POST02	73.5	/	9	64	Hereditary + noise exposure	Nucleus 24R
POST03	72	/	22	53	Otosclerosis	HiRes 90k
POST04	66	/	10	61	Otosclerosis	Nucleus 24RE
POST05	73	/	15	69	Ménière’s Disease	Nucleus 24RE
POST06	74	/	39	68	Unknown	HiRes 90k
POST07	61	/	26	55	Otosclerosis	Nucleus 24RE
POST08	79	/	15	74	Hereditary	Nucleus 24RE
POST09	58	/	8	55	Sudden deafness	SONATA
POST10	65	/	23	62	Unknown	HiRes 90k
POST11	56	/	17	52	Hereditary	Nucleus 24RE
POST12	44	/	15	34	Meningitis	Nucleus 24 R
POST13	80	/	/	75	Otosclerosis	Nucleus 24RE
POST14	57	/	29	52	Unknown	HiRes 90k
POST15	65	/	15	62	Temporal Bone Fracture	SONATA
POST16	66	/	2	61	Progressive Familiar	HiRes 90k
POST17	60	/	20	53	Hereditary motor and sensory neuropathy	HiRes 90k
POST18	70	/	23	66	Chronic Otitis Media	Nucleus 24RE

sound-field with their own sound processor and with the clinical map of their own preference.

Stimuli

Stimuli were generated digitally in MATLAB (The Mathworks, Inc.) with a sampling frequency of 44.100 Hz. A broadband noise carrier was created, which was limited by a fourth-order band-pass filter with cut-off frequencies of 80 and 8500 Hz.

Sound pressure level verification was performed at the position of the head to assure linearity of the setup system. The average sound pressure level of the unmodulated stimulus was 65 dB SPL. The broadband noise carrier was sinusoidally amplitude modulated by the following equation: $y(t) = f(t)[1 + m_i sin(2\pi f_m t)]$*]*, where $y(t)$ is the stimulus, $f(t)$ is the broadband noise carrier, m_i is the modulation depth and $f_m$the modulation frequency. Seven modulation frequencies were used: 5, 10, 50, 75, 100, 150, and 200 Hz. To compensate for acoustic intensity increment due to the amplitude modulation, the modulated signal was divided by the long-term average power of the sinusoidally modulated waveform, $1 + (m_i^2/2)$, to equalize the RMS values of the stimuli. Both the modulated and unmodulated stimuli were gated on and off with 30-ms linear ramps. Stimulus duration was 500 ms and 1000 ms for an additional test condition administered to a limited number of subjects.

Procedure

AMDTs were obtained using a 2-down-1-up, 3-interval oddity, adaptive forced-choice procedure, tracking the 70.7% point of the psychometric function (Levitt, 1971). The stimulus duration as well as the interstimulus duration was 500 ms. Subjects were instructed to choose the stimulus which they perceived as being different from the other two.

The initial modulation depth was -2 dB re 100% amplitude modulation and the initial step size was 4 dB. After 2 reversals the step size was reduced to 2 dB. In a single run 8 reversals were obtained, and the average of the last 6 reversals was used to determine the modulation detection threshold. After completing the runs for all 7 modulation frequencies in a randomized order, the entire session of 7 runs was repeated in order to check for reproducibility. The average of these 2 sessions was taken as the final measure of the modulation detection threshold per modulation frequency. A pause was planned at least once between each session of 7 runs, in order to reduce the possible influence of diminished concentration and fatigue.

Speech Tests

For both the pre- and the postlingually deafened CI users, phoneme scores on an open-set Dutch monosyllabic (CNC) word test (Bosman & Smoorenburg, 1995) were gathered at 65 dB SPL. In this test, the phoneme recognition score is measured as a percentage correct. The scores were obtained from the last yearly clinical evaluation of the subject.

Since prelingually deafened CI users generally score poorly on standard open-set word tests, 2 more simple speech tests were also administered to this group. The monosyllable-trochee-spondee (MTS) test, adapted from Erber and Alencewicz (1976), is a Dutch 12-item closed-set word identification test, where each word is presented twice. Word scores (entire word should be correct) and suprasegmental scores (number of correct syllables per presented word and the stress pattern of the word should be correct) were gathered as a percentage correct for administration at 65 dB SPL. The speech tracking test, with texts designed specifically for prelingually deafened CI users (Boons & Debruyne, 2011), is an open-set sentence identification test where a number of additional cues (e.g. repeating parts of the sentence, allowing lip reading) is given to the subject in a predetermined order. The amount of time the subject needs to repeat the entire text is used to calculate the score, expressed as the number of words per minute. Speech tests were administered during one of the 2 visits.

Data Analysis

Normality of AMDTs was checked with the Shapiro-Wilk test. Non-parametric tests were applied in cases of non-normality, which occurred at higher modulation frequency data because of floor effects, and for the attenuation rate data because of outliers. Floor values occurred when modulations were undetected by the participant; in these cases a value of zero was assigned.

To check reproducibility, Spearman correlation coefficients between the first and second measurements of all AMDTs were obtained. A mixed-model was estimated to compare the AMDTs of prelingually and postlingually deafened CI users over the 7 modulation frequencies. Additional analyses included independent *t* tests and Mann-Whitney *U* tests, depending on normality, to compare the different modulation frequencies pairwise.

Both groups were further compared with respect to the attenuation rate and the surface area below the TMTF. The attenuation rate relates to the shape of the entire TMTF and the surface area below the TMTF relates to the gain (overall sensitivity to amplitude modulation) and shape of the TMTF, whereas the AMDTs only describe the sensitivity to temporal modulations at individual frequencies. The attenuation rate of the TMTF is, as in Won (2011), defined as the b-component of an exponential function fitted through the data: $AMDT\ (f_{mod}) = -ae^{bf_{mod}}$, with $AMDT$ the absolute amplitude modulation detection threshold in dB re 100% modulation. Here, a is the intercept, b the attenuation rate, and f_{mod} the modulation frequency in Hz. The mean fit through the data of both the prelingually and postlingually deafened CI users is plotted in Figure 1. The surface area below the TMTF is calculated as the integral of the exponential function $AMDT\ (f_{mod}) = -ae^{bf_{mod}}$. An independent *t* test or Mann-Whitney *U* test was used to compare the attenuation rate and the surface area below the TMTF between both groups, depending on normality. Bonferroni adjustments occurred separately for the 7 modulation frequencies and the 3 overall AMDT outcome parameters.

One-sample *t* tests were performed to investigate the difference between the AMDTs obtained in this study for the postlingually deafened CI users and the mean AMDT values reported by Won et al. (2011).

Since floor effects occurred for higher modulation frequencies, Spearman's rank correlation coefficient was used to describe relations between speech performance scores and individual AMDTs, mean AMDTs, the attenuation rate of the TMTF, and the surface area below the TMTF. This was done for the total group of CI users and for the pre- and postlingually deafened CI users separately. A Bonferroni adjustment for multiple comparisons was added per group for the 7 modulation frequencies and also for the 3 overall AMDT outcome parameters.

Finally, additional measurements were done with 1000-ms stimuli in all prelingually and 8 of the postlingually deafened CI users. To compare the results obtained with both stimulus lengths, a paired sample *t* test or Wilcoxon Signed Rank test was used, depending on normality.

RESULTS

Spearman correlation coefficients of the 2 AMDT measurements for each of the 7 modulation frequencies ranged from 0.86 to 0.99, providing evidence of reproducibility. In Figure 1, the mean sound-field AMDTs of the prelingually and postlingually deafened CI users are plotted against the modulation frequency, resulting in sound-field TMTFs. The mean exponential fits of both groups are shown as thin lines in the figure. For comparison, mean sound-field TMTFs of 24 postlingually deafened CI users (Won, Drennan, et al., 2011) and of 4 normal-hearing listeners (Viemeister, 1979) are displayed. The low-pass filter shape of the TMTFs of those other studies can also be observed in the mean TMTFs of the prelingually and postlingually deafened subjects tested in this study: sensitivity to amplitude modulation decreased with increasing modulation frequency.

A significant difference was found between the mean sound-field AMDT of the prelingually and postlingually deafened CI users (*F* = 8.69, df = 1, 24, *p* = 0.007), indicating that prelingually deafened CI users are less sensitive to amplitude modulations than postlingually deafened CI users. Analysis of the different modulation frequencies showed a significant difference ($p < 0.05$) between both groups for the modulation frequencies 5 to 150 Hz, but not for the 200-Hz modulation frequency, as can be seen in Table 2. After Bonferroni correction for multiple comparisons, however, only the difference for the 100-Hz modulation frequency remained significant. When comparing the numbers relating to the shape of the TMTF, a significant difference was found between pre- and postlingually deafened CI users with respect to the attenuation rate (*p* = 0.021), and the surface area below the TMTF (*p* = 0.003); the latter remained significant after Bonferroni correction (see also Table 2).

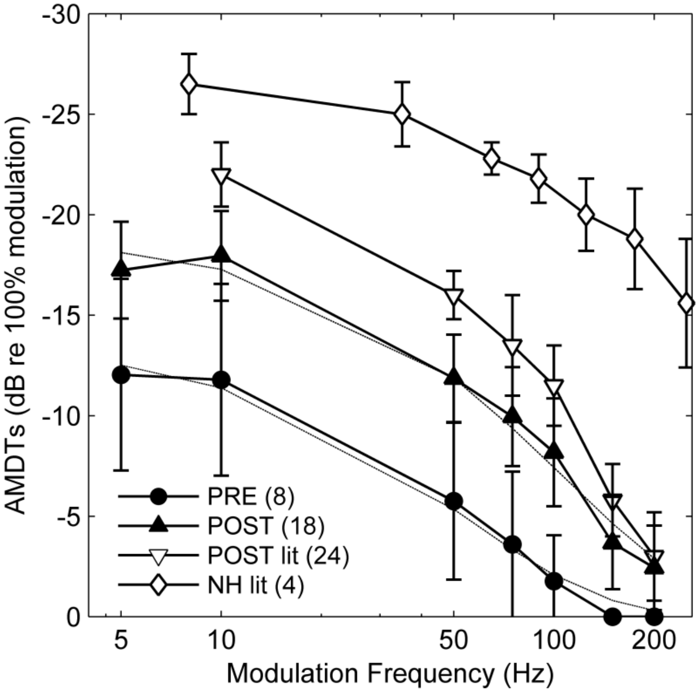

Figure 1. TMTFs based on the mean sound-field AMDTs of the 8 prelingually deafened CI users (circles) and the 18 postlingually deafened CI users (triangles) measured in this study, as well as 24 CI users (reverse triangles, data adapted from Won et al. (2011)), and 4 normal-hearing listeners (diamonds, data adapted from Viemeister (1979)). Error bars indicate the 95% confidence interval; the thin lines are the mean exponential fits for the prelingually and postlingually deafened CI users measured in this study.

Table 2. Group Comparisons of Amplitude Modulation Detection Thresholds

	Prelingual (Mean ± SD)	Postlingual (Mean ± SD)	*p*
5 Hz	-12.04 ± 6.88	-17.24 ± 5.21	0.044*
10 Hz	-11.79 ± 6.88	-17.95 ± 4.82	0.015*
50 Hz	-5.75 ± 5.63	-11.86 ± 4.70	0.008*
75 Hz	-3.60 ± 5.22	-9.96 ± 5.33	0.009*
100 Hz‡	-1.77 ± 3.29	-8.18 ± 5.81	0.006*†
150 Hz‡	0.00 ± 0.00	-3.67 ± 4.98	0.013*
200 Hz‡	0.00 ± 0.00	-2.43 ± 4.56	0.08
mean AMDT	-7.0 ± 4.71	-10.8 ± 6.05	0.007*
attenuation rate, b‡	-0.039 ± 0.029	-0.012 ± 0.005	0.021*
surface area	543 ± 485	1636 ± 881	0.003*†

Amplitude Modulation Detection Thresholds expressed in dB re 100% Modulation

*: significant with α < 0.05

†: significant after Bonferroni correction

‡: Mann-Whitney U test was used instead of independent-samples t-test

The individual sound-field TMTFs of the prelingually deafened CI users are shown in Figure 2. Two prelingually deafened CI users (PRE01 and PRE04) scored in the range of the postlingually deafened CI users, while one of the subjects (PRE02) was unable to distinguish modulated from unmodulated stimuli at any of the 7 modulation frequencies. In addition, none of the prelingually deafened CI users were able to detect amplitude modulations at modulation frequencies of 150 and 200 Hz. Three of the 8 subjects (38%) were able to detect amplitude modulations at 75 Hz and 2 of the 8 (25%) at 100 Hz, as shown in Figure 3. When a subject was unable to detect amplitude modulations at a certain modulation frequency, the threshold was reported as 0 dB re 100% modulation. Of the 18 postlingually deafened CI users in this study, the percentage of subjects that was able to distinguish modulated from unmodulated stimuli decreased with increasing modulation frequency: 89% of subjects could detect modulations at 100 Hz, 61% at 150 Hz and 44% at 200 Hz (see Figure 3). The mean sound-field TMTF of the postlingually deafened CI users in this study indicated a lower overall sensitivity to amplitude modulation when compared to the mean sound-field TMTF of the 24 CI users tested by Won, Drennan, et al. (2011), as can be seen in Figure 1. Significant differences between both groups were found for the modulation frequencies 10 to 100 Hz (*p* < 0.05). AMDTs at 5 Hz could not be com-pared since this modulation frequency was not tested by Won et al. (2011). No significant differences were found between the AMDTs at the modulation frequencies 150 and 200 Hz.

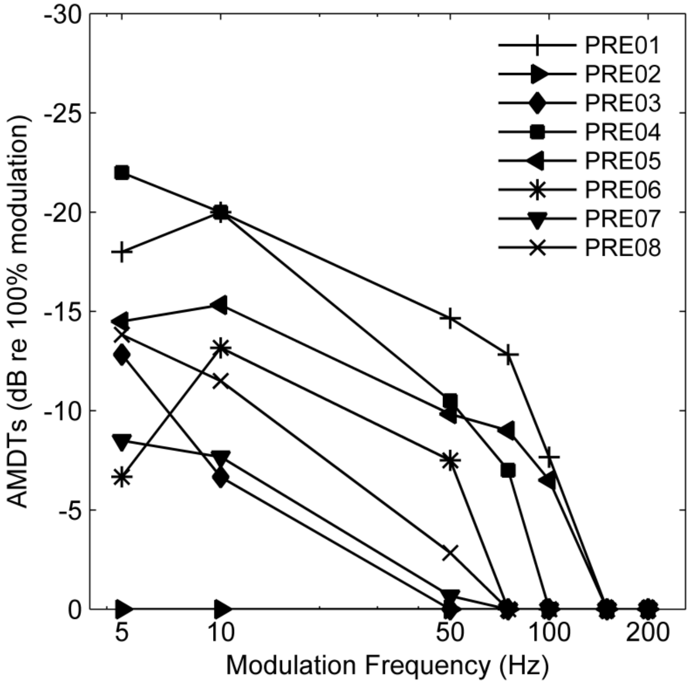

Figure 2. Individual freefield TMTFs of 8 late implanted prelingually deafened CI users.

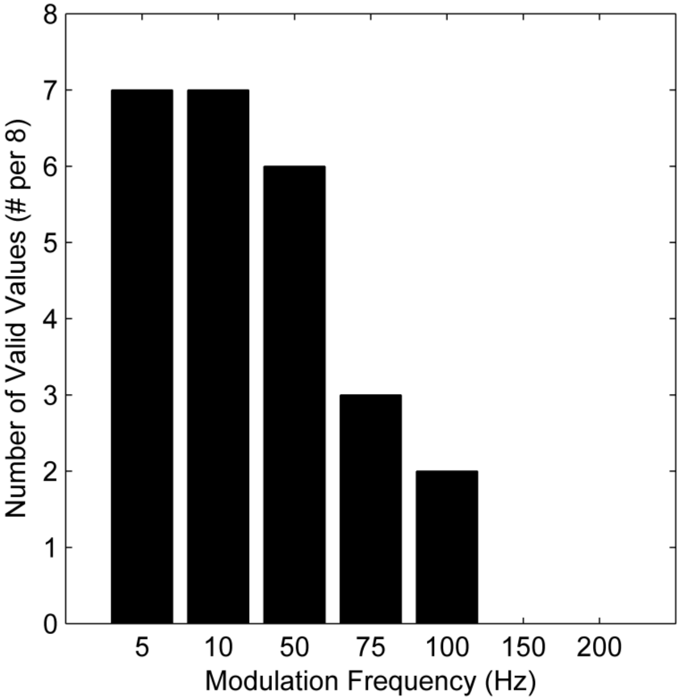

Figure 3. The number of late implanted prelingually deafened CI users that were sensitive to that modulation frequency.

Table 3 presents correlations (Spearman's Rho) between the temporal modulation detection abilities and various speech scores (CNC phoneme scores, MTS words scores, MTS suprasegmental scores, and speech tracking), for the prelingually and postlingually deafened group, as well as for the total group of subjects. The means and standard deviations of the speech tests are also given for each group. Note that for the MTS-test and the speech tracking test, scores are only available for the prelingually deafened CI users.When looking at all the CI users tested in this study, the correlations between the CNC phoneme scores and the thresholds for the individual modulation frequencies, the mean AMDT, the attenuation rate of and the surface area below the TMTF, were significant ($p < 0.05$), as can be seen in the last column of Table 3. After Bonferroni correction for multiple comparisons, only the correlations with the 5-, 10-, and 200-Hz modulation frequencies were no longer significant.

For the prelingually deafened CI users separately, significant correlations ($p < 0.05$) were found between the individual modulation frequencies 5, 10, 50, 75, and 100 Hz and CNC phoneme scores, MTS word scores, and speech tracking scores. Correlations with MTS suprasegmental scores were not significant, except for the 100-Hz modulation frequency. The mean AMDT of this group was significantly correlated with all speech measures (see Table 3). Finally, the attenuation rate of the TMTF and the surface area below the TMTF

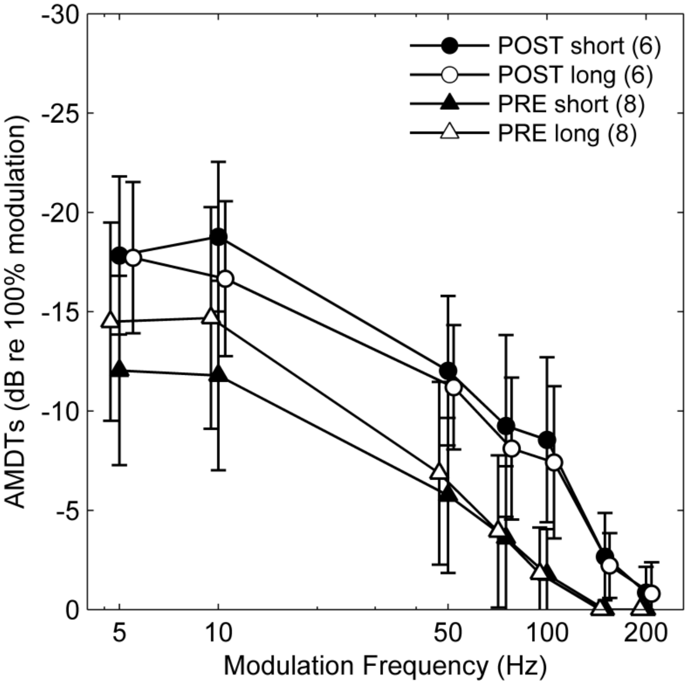

Figure 4. Mean free field TMTFs obtained with short stimuli (filled symbols) and long stimuli (open symbols) of 8 prelingually (circles) and 6 postlingually deafened CI users (triangles). Error bars indicate the 95% confidence interval.

were significantly correlated with all speech measures, except for the correlation between the attenuation rate and the MTS suprasegmental score. Only a limited number of correlations remained significant after the correction for multiple comparisons was applied (see Table 3).

When looking at the postlingually deafened CI users, significant correlations were found between CNC phoneme scores and the 100- and 150-Hz modulation frequencies, as well as the attenuation rate of the TMTF. These correlations remained significant after Bonferroni correction (see Table 3).

In Figure 4, the graphs represent the mean TMTFs for the 8 prelingually and 6 of the 18 postlingually deafened subjects, in 2 test conditions: a short (500 ms) versus a long (1000 ms) stimulus duration. The prelingually deafened CI users demonstrated a higher sensitivity to 5-Hz ($p = 0.005$, significant after Bonferroni correction) and 10-Hz ($p = 0.011$, significant with $p < 0.05$) amplitude modulations obtained with the 1000-ms stimuli in comparison to the 500-ms stimuli. For the 6 postlingually deafened CI users, there was no significant difference for the pairwise comparisons between AMDTs obtained with 500- or 1000-ms stimuli at any modulation frequency.

Table 3. Spearman's Rho (r_s) Correlations Between Measures of Sound-Field Amplitude Modulation Detection and Speech Perception Scores (Mean ± SD; *range*)

	Prelingual				**Postlingual**	**All**
	MTS – word (57 ± 35%) *0 – 100%*	MTS – suprasegmental (80 ± 17%) *52 – 100%*	Speech Tracking (26 ± 13 words/min) 16 – 56 words/min	CNC (28 ± 34%) *0 – 94%*	CNC (68 ± 20%) *23 – 99%*	CNC (56 ± 32%) *0 – 99%*
AMDT at 5 Hz	-0.786* (*p* = 0.021)	-0.548 (*p* = 0.160)	-0.714* (*p* = 0.047)	-0.862*^{c} (*p* = 0.006)	-0.347 (*p* = 0.159)	-0.512* (*p* = 0.008)
AMDT at 10 Hz	-0.826* (*p* = 0.011)	-0.635 (*p* = 0.091)	-0.743* (*p* = 0.035)	-0.829* (*p* = 0.011)	-0.150 (*p* = 0.553)	-0.478* (*p* = 0.013)
AMDT at 50 Hz	-0.838*† (*p* = 0.009)	-0.659 (*p* = 0.076)	-0.790* (*p* = 0.020)	-0.855*† (*p* = 0.007)	-0.277 (*p* = 0.266)	-0.601*† (*p* = 0.001)
AMDT at 75 Hz	-0.791* (*p* = 0.019)	-0.627 (*p* = 0.096)	-0.873*† (*p* = 0.005)	-0.930*† (*p* = 0.001)	-0.371 (*p* = 0.130)	-0.645*† (*p* = 0.000)
AMDT at 100 Hz	-0.764* (*p* = 0.027)	-0.764* (*p* = 0.027)	-0.764* (*p* = 0.027)	-0.814* (*p* = 0.014)	-0.612*† (*p* = 0.007)	-0.740*† (*p* = 0.000)
AMDT at 150 Hz	-	-	-	-	-0.621*† (*p* = 0.006)	-0.624*† (*p* = 0.001)
AMDT at 200 Hz	-	-	-	-	-0.316 (*p* = 0.202)	-0.410* (*p* = 0.037)
mean AMDT	-0.929*† (*p* = 0.001)	-0.762* (*p* = 0.028)	-0.833*† (*p* = 0.010)	-0.913*† (*p* = 0.002)	-0.395 (*p* = 0.104)	-0.673*† (*p* = 0.000)
attenuation rate, *b*	-0.821* (*p* = 0.023)	-0.750 (*p* = 0.052)	-0.857*† (*p* = 0.014)	-0.778* (*p* = 0.039)	-0.589*† (*p* = 0.010)	-0.715*† (*p* = 0.000)
surface area	0.905*† (*p* = 0.002)	0.786* (*p* = 0.021)	0.786* (*p* = 0.021)	0.875*† (*p* = 0.004)	0.407 (*p* = 0.094)	0.688*† (*p* = 0.000)

*: significant with $\alpha < 0.05$

†: significant after Bonferroni correction

DISCUSSION

The TMTF of Prelingually and Postlingually Deafened CI Users

The first goal of the study was to compare the sound-field AMDTs of prelingually and postlingually deafened CI users. The absolute sensitivity of prelingually deafened CI users to amplitude modulation was significantly lower than that of the postlingually deafened CI users. The modulation frequency where the difference remained significant, even after correction for multiple comparisons, was 100 Hz. This might be interpreted as such that below 100 Hz, the prelingually deafened CI users are still reasonably capable of detecting amplitude modulations, as can also be found in Figure 3. At 100 Hz, their performances start to decline very quickly, whereas most of the postlingually deafened CI users still perform adequately. Above 100 Hz, however, CI users in both groups start to have great difficulties, resulting in smaller group differences again. In addition, both the attenuation rate of the TMTF and the surface area below the TMTF differed significantly between both groups. Although not meeting the stricter criterion for multiple comparisons, it does point to a trend that the slope of the TMTF of the prelingually deafened CI users is steeper, thus that performances in this group declined more rapidly towards the higher modulation frequencies.

These findings are in agreement with Busby et al. (1993), who found lower sensitivity to electrical amplitude modulation in 3 prelingually deafened CI users than in 4 postlingually deafened CI users. A likely explanation is that the changes along the entire auditory pathway, due to the early onset and long-term auditory deprivation (Teoh et al., 2004b), contributed to a reduced sensitivity to amplitude modulation in prelingually deafened CI users.

The individual TMTFs of 2 prelingually deafened CI users (PRE01 and PRE04), as can be seen in Figure 2, lay within the 95% - confidence interval of the postlingually deafened CI users, while one subject (PRE2) was unable to distinguish any of the modulated stimuli from the unmodulated stimuli. In Table 1 it can be seen that there are no striking differences between the etiologies of these subjects. A possible explanation for these interindividual differences could be that better performing prelingually deafened CI users had a larger amount of residual hearing (mostly at low frequencies) preoperatively, or had this during a longer period in their lives. Residual hearing, especially at 500 Hz, and age at onset of severe to profound hearing loss are both good predictors for CI outcome (Blamey et al., 2013; Lazard, Vincent, et al., 2012). To evaluate this theory, the mean preoperative hearing thresholds of the 8 prelingually deafened CI users in this study at 250 and 500 Hz, were compared to their mean AMDT, but no significant correlation was found. Also, no correlation between the mean AMDT and the age at onset of deafness was found for the prelingually deafened CI users.

The individual sound-field TMTFs of the prelingually deafened CI users in this study all had a low-pass filter characteristic. The band-pass filter shape of the TMTF, as found in one prelingually deafened CI user by Busby et al. (1993), was not found in this study. However, for some subjects the AMDT at the 5-Hz modulation frequency was lower than at the 10-Hz modulation frequency. A similar observation was done by Viemeister (1979), who found lower modulation sensitivity for short stimulus durations (250 and 500 ms) in combination with slow modulation frequencies (< 8 Hz) in normal-hearing listeners, for a gated broadband noise carrier. When they applied continuous stimuli with the same durations and modulation frequencies, the sensitivity was comparable with the threshold at the 10-Hz modulation frequency again. The authors hypothesize that the effect might be due to interferences from the gating, which consequently “mask” some of the modulations. More recently, there are no studies where a gated broadband noise stimulus was used in combination with modulation frequencies below 10 Hz (except for Gnansia (2014), but no TMTF was determined there).

The sound-field AMDTs of the 18 postlingually deafened CI users were compared to those of the 24 CI users evaluated by Won et al. (2011), as shown in Figure 1. At the 10- to 100-Hz modulation frequencies, the measured AMDTs in this study were significantly worse than those of Won et al. (2011). Since it is known that preoperative factors, such as duration of severe to profound hearing loss, duration of moderate hearing loss (up to the onset of severe to profound hearing loss), and the PTA of the better ear have a significant influence on speech performance with CI (Blamey et al., 2013; Lazard, Vincent, et al., 2012), it was investigated whether such differences between the subjects in this study and the subjects in the study of Won et al. (2011) could account for the lower sensitivity to modulations found in this study. Although no information about the preoperative residual hearing of the subjects of Won et al. (2011) is available, there is no reason to assume that preoperative PTAs would be different between both groups. The CNC scores of both groups could not be compared, since phoneme scores were measured in this study and word scores by Won et al. (2011). The duration of the moderate to severe hearing loss before implantation could be compared, although no details are given by Won et al. (2011) as to how the “duration of hearing loss” is defined. It was found that the “duration of hearing loss” of the subjects in the study of Won et al. (2011), was significantly shorter (p = 0.033) than of the subjects in this study. This shorter duration of hearing loss could contribute to the better AMDTs found by Won et al. (2011).

Another difference between both studies lies in the adaptive procedure: in this study a 3AFC procedure was used, versus a 2AFC procedure in Won et al. (2011). It is known that with a 2AFC procedure, threshold estimates show a larger variability due to smaller values of the sensitivity index d’ (Hacker & Ratcliff, 1979; Leek, Hanna, & Marshall, 1992). Although this might have contributed to the significant differences that were found, it cannot explain them.

Finally, whereas in this study stimuli of 500 ms were used, Won et al. (2011) used stimuli of 1000 ms. The reason why the shorter duration might have an influence pertains to the effect of short, gated carriers on low-frequency slow-rate modulation (Viemeister, 1979), as mentioned above. For the prelingually deafened CI users, the improvement of the sensitivity to 5- and 10-Hz modulations for 1000-ms stimuli compared to 500-ms stimuli, might be an illustration of this phenomenon. The additional measurements that were done with 1000-ms stimuli in 6 of the postlingually deafened CI users, however, showed that the longer stimulus duration had no effect. It is not clear why this effect was found only for the prelingually deafened CI users, but it must be concluded that stimulus duration did most likely not contribute to the differences with the results of Won et al. (2011).

The Relation between Sensitivity to Amplitude Modulation and Speech Performance

The second goal of the present study was to determine the possible relation between the ability to detect amplitude modulations and speech recognition scores, for the entire group as well as for prelingually and postlingually deafened CI groups separately.

When looking at all CI users from both groups together, all correlations with CNC phoneme scores and AMDT parameters were significant. For the individual modulation frequencies 5, 10 and 200 Hz, the correlations were no longer significant after multiple comparisons correction, which is consistent with the weak correlations that are found for these modulation frequencies in the postlingually deafened group.

In the group of prelingually deafened CI users, the MTS word scores, the speech tracking scores, and the CNC phoneme scores had high and significant correlations with the separate modulation frequencies (5, 10, 50, 75, and 100 Hz), the mean threshold across modulation frequencies and the measures relating to the shape of the TMTF. Even though not all separate correlations met the strict multiple comparisons criterion, the high correlation coefficients suggest a relation between the variables. This may indicate that this group was able to utilize modulations in the speech envelope up to 100 Hz for the identification of segmental information (CNC phoneme scores and MTS word scores), and running speech (speech tracking). Correlations with the MTS suprasegmental scores were less high and mostly not significant, which may be partly due to ceiling effects, since suprasegmental scores were generally high (up to 100%) and the standard deviation was smaller than that of the other speech scores.

For the postlingually deafened CI users, significant correlations were found between the CNC phoneme scores and AMDTs at the higher modulation frequencies of 100 Hz, 150 Hz, and with the attenuation rate and the surface area below the TMTF, but not with individual AMDTs at 5, 10, 50, 75, or 200 Hz, or the mean AMDT. This was unexpected, given that it is known from literature with normal hearing subjects that especially low-frequency temporal cues contain important information for speech recognition when spectral cues are limited. Moreover, additional temporal information above approximately 20 Hz does not even seem to be used as long as minimal spectral cues are available (Friesen et al., 2005; Shannon et al., 1995). Also in contrast with this finding is the fact that mainly the slowly-varying envelope, with frequency components up to about 250 Hz, is encoded in current commercial cochlear implant sound processing strategies (McDermott, McKay, & Vandali, 1992; Vandali, Whitford, Plant, & Clark, 2000).

The presence of a ceiling effect for the low modulation frequencies in this subject group, which could give rise to the absence of correlations, is not very likely since the standard deviations for these results were not particularly smaller for the postlingually deafened CI users (see Table 2).

Looking at the literature, however, these findings in the postlingually deafened group are in agreement with the results of Won et al. (2011), who found significant correlations between CNC phoneme scores and the AMDTs at higher modulation frequencies (75 to 300 Hz) but not with AMDTs at low modulation frequencies (10 and 50 Hz). Also in agreement with this study, they found significant correlations between the attenuation rate and CNC phoneme scores, where the attenuation rate, the *b*-component of the exponential fit, was primarily determined by the AMDTs at higher modulation frequencies (i.e. 200 and 300 Hz). The latter is also the case for the data in this study, where correlations with the attenuation rate were only significant for the modulation frequencies 50 to 200 Hz. Taken together, our current results and the study of Won et al. (2011) both suggest that when CI users have better amplitude modulation detection skills at higher modulation frequencies, they attain better speech understanding scores. Though only a 100-Hz modulation frequency was measured, and stimulation was done directly at the electrodes, Fu (2002) found highly significant correlations between the mean AMDT (averaged over various stimulus levels) and vowel and consonant recognition scores. On the other hand, a number of studies found correlations with lower modulation frequencies. Also using electric stimulation, Luo et al. (2008) found a significant correlation between AMDTs at both the 100-Hz and 20-Hz modulation frequency and consonant- and sentence recognition scores, but not vowel recognition scores. Recently, Gnansia et al. (2014) found a significant correlation between sound-field AMDTs at a modulation frequency of 8 Hz and consonant and vowel identification scores.

Further Considerations

Sound-field Stimulation

The sound-field TMTF can be seen as a representation of temporal performance in the daily life situation, when the CI is used. It describes the characteristics of the auditory system combined with the CI, including speech coding strategy and individual map settings. Since the attack time of a noise reduction system is relatively long compared to the stimulus duration, no effect of this feature is assumed. Compression is another factor that could affect the AMDT, however, Won et al. (2011) tested the influence of AGC on AMDTs in 7 CI users and did not find significant effects at 65 dB(A). In general though, it is difficult to control the modulation depth without stimulating directly at the electrode(s), especially when different speech coding strategies and different individual map settings are used.

Intensity and Loudness Cues

In this study, it is unlikely that intensity cues were used by the subjects to detect amplitude modulations, since a compensation for intensity increase coming with amplitude modulation was executed, as described in the methods section. However, it is possible that loudness cues were used, since loudness is more related to the peak-intensity than the RMS of the signal (Fraser & McKay, 2012; McKay & Henshall, 2010). This could give the subject an additional cue to choose between modulated and unmodulated stimuli.

Loudness balancing and roving are ways to compensate for possible loudness cues. In research regarding amplitude modulation, the effect of these interventions has been investigated. McKay and Henshall (2010) performed loudness balancing of 250- and 500-Hz modulated stimuli and measured loudness differences. The effect on AMDTs was not measured. They concluded that modulated stimuli were perceived as louder than unmodulated stimuli. Fraser and McKay (2012) measured the effect of balancing and roving in 4 CI users. For the low modulation frequency (50 Hz), 2 out of 4 CI users showed worse AMDTs after balancing and roving. For the higher modulation frequencies (300-600 Hz), this effect was found in 3 out of 4 subjects. Galvin, Fu, Oba, and Baskent (2014) measured AMDTs at 10 and 100 Hz in nine CI users, with and without a novel method to control for possible loudness cues. In an adaptive task, the stimuli were balanced and global roving was applied. The AMDTs were generally worse with this method, but controlling for loudness cues did not affect the general finding that AMDTs became worse when the modulation frequency increased. In another study with 5 CI users, Chatterjee and Oberzut (2011) found that there was a small but significant effect of roving (without loudness balancing) on the overall gain of the TMTF. The shape of the TMTF, however, was unaffected. On the other hand, Won et al. (2011) found that roving had no significant effect on AMDTs, as measured for modulation frequencies of 10, 100, and 200 Hz in 2 CI users. In conclusion, it was found that when applying roving, AMDTs were generally worse, but the overall shape of the TMTF was not affected. For sound-field stimulation though (see Won et al., 2011), these findings have not yet been confirmed.

In the current study, loudness balancing between the modulated and unmodulated stimuli was not performed. This task would be very difficult for the prelingually deafened CI users, especially for the low modulation frequencies, where changes in loudness are clearly noticeable during the stimulus. However, when no balancing is performed, an even larger amount of roving should be applied in order to correct for possible loudness cues, especially when modulation depths are larger than -15.92 dB re 100%, which is >16% (Chatterjee & Oberzut, 2011). The latter occurs for most of the modulation frequencies of the prelingually deafened CI users (Figure 2). Since in this study neither roving nor loudness balancing was applied, the AMDTs might overestimate the sensitivity to amplitude modulations due to loudness cues, and this for the whole range of modulation frequencies. This means that there is a small, but unlikely, chance that the real AMDTs, and thus also the gain of the TMTFs, might be lower. In addition, this effect of loudness cues could be different for each subject group. If this were the case, this would have an impact on the results discussed in the previous sections, regarding the lower sensitivity of the prelingually deafened CI users to amplitude modulations, and the correlations between the speech measures and the individual and mean AMDTs. However, since it is also known that the shape of the TMTF would not be affected, this would not change the results where the main parameter was the attenuation rate. In other words, the significant difference that was found between the attenuation rate of the TMTF of the postlingually and prelingually deafened CI users, and the high correlations between the attenuation rate and various speech measures in all groups, would not likely have been influenced by loudness cues.

CONCLUSIONS

This study measured the temporal processing abilities of both prelingually and postlingually deafened CI users by means of the sensitivity to sound-field sinusoidal amplitude modulations of a broadband noise. It was found that prelingually deafened CI users were less sensitive to amplitude modulations than postlingually deafened CI users, and that their performance degraded more quickly with increasing modulation frequency.

High correlations were found between temporal modulation detection and speech recognition ability in both pre- and postlingually deafened CI users. Better modulation detection thresholds that degraded less quickly when the modulation frequency increased, were related to better speech understanding scores. For postlingually deafened CI users, such correlations were not found between modulation frequencies below 100 Hz and speech recognition. Although this has been observed in literature before, it is not clear what causes this effect, given that primarily slowly varying temporal cues are used for speech recognition.

Finally, although the influence of loudness cues on the absolute levels of the AMDTs cannot be ruled out, the significant correlations that were equally found with the shape-dependent measures of the TMTF, point to the authenticity of these findings.

Chapter 3

Fitting prelingually deafened adult cochlear implant users based on electrode discrimination performance

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ABSTRACT

Objective: This study investigated the hypotheses that (1) prelingually deafened CI users do not have perfect electrode discrimination ability and (2) the deactivation of non-discriminable electrodes can improve auditory performance.

Design: Electrode discrimination difference limens were determined for all electrodes of the array. The subjects' basic map was subsequently compared to an experimental map, which contained only discriminable electrodes, with respect to speech understanding in quiet and in noise, listening effort, spectral ripple discrimination and subjective appreciation.

Study Sample: Subjects were six prelingually deafened, late implanted adults using the Nucleus cochlear implant.

Results: Electrode discrimination difference limens across all subjects and electrodes ranged from 0.5 to 7.125, with significantly larger limens for basal electrodes. No significant differences were found between the basic map and the experimental map on auditory tests. Subjective appreciation was found to be significantly poorer for the experimental map.

Conclusions: Prelingually deafened CI users were unable to discriminate between all adjacent electrodes. There was no difference in auditory performance between the basic and experimental map. Potential factors contributing to the absence of improvement with the experimental map include the reduced number of maxima, incomplete adaptation to the new frequency allocation, and the mainly basal location of deactivated electrodes.

INTRODUCTION

Prelingually deafened patients who receive a cochlear implant (CI) in adulthood, after many years of severe hearing impairment or auditory deprivation, constitute a very specific group of cochlear implant users. In the early years of cochlear implantation, results from this population were not very promising, with subjects experiencing very limited benefit with respect to speech understanding (Snik et al., 1997; Tong, Busby, & Clark, 1988; van den Broek, Admiraal, Brokx, Mens, & Spies, 1992). With advancements in speech processing strategies, these subjects have generally become more successful CI users, albeit with large inter-individual differences (Caposecco et al., 2012; Teoh et al., 2004a). In view of this substantial variability in outcome, the current study attempted to optimize cochlear implant performance for prelingually deafened subjects by means of individually adapted cochlear implant fitting.

When looking at the underlying auditory processing abilities of this patient population, it is clear that the long-term auditory deprivation of these subjects has influenced the development of the auditory pathways. A long period of profound deafness will severely reduce the number of spiral ganglion cells on a peripheral auditory level. A clear relation between the number of surviving spiral ganglion cells and clinical performance with a cochlear implant has not yet been shown, however (Fayad & Linthicum, 2006; Xu, Kim, Snissarenko, Cureoglu, & Paparella, 2012). Anomalies in this part of the auditory system alone can therefore not fully explain the limited results for most prelingually deafened, late-implanted CI users. It is more likely that this can be explained by aberrant development of the auditory brainstem and, most of all, the auditory cortex. Studies in children using cochlear implants (Gordon et al., 2011) and animal models (Butler & Lomber, 2013) have shown that the subcortical nuclei of the auditory brainstem require auditory input for further maturation; a sophisticated tonotopy, for instance, does not develop (Butler & Lomber, 2013). Synaptic activity in the primary auditory cortex will deviate substantially from normal including less activation of the deeper cortical layers (Kral, 2007). These deep layers are usually responsible for cognitive modulation, integrating descending (top-down) input from higher-order cortical layers, and also project back to subcortical structures. Based on animal studies, Kral (2007); Kral, Tillein, Heid, Hartmann, and Klinke (2005) hypothesized that a functional decoupling between the primary auditory cortex and higher cortical layers occurs when auditory input is not restored before the end of a sensitive period which, in humans, is thought to lie around 7 years of age (Sharma, Nash, & Dorman, 2009). This may lead to an auditory system that is incapable of forming auditory objects, which is a requirement for attributing meaning to incoming auditory stimuli (Kral, 2013). In addition, cross-modal reorganization may occur, with mainly higher order auditory structures being recruited by other sensory modalities such as vision (Kral, 2007). This phenomenon is illustrated by Buckley and Tobey (2011), who showed that higher activation in the auditory cortex in response to peripheral visual movements was correlated with lower speech understanding scores in CI users with a prelingual onset of deafness. In conclusion, differences in auditory processing may explain the reduced speech understanding performance as compared to postlingually deafened CI users.

Given the irreversible consequences of long-term auditory deprivation in prelingually deafened CI users, arranging the speech signals through the processing strategies might facilitate the reception and processing in the compromised auditory structure. Due to the filterbank system of CI processing, which relies on cochlear tonotopy, the exact pattern of stimulated sites along the array contains potentially important information for speech understanding. It is hypothesized in this study that it is difficult for prelingually deafened CI users to discriminate between stimulation given on different electrodes, and that this limits their access to the spectral information encompassed in the stimulation pattern. These difficulties might be due to a reduced neural survival on a peripheral level, with different electrodes stimulating largely the same neurons, as well as to a less precise development of tonotopy throughout the auditory system. Additionally, the auditory cortex might encounter more difficulties in translating the incoming neural signals into distinct, auditory percepts. The ability to discriminate between stimulation given at different sites in the cochlea can be evaluated by means of electrode discrimination testing. In postlingually deafened cochlear implant users, (near) perfect discrimination was found when stimulation was given at C-level (Chatterjee & Yu, 2010; Laneau & Wouters, 2004; Zwolan, Collins, & Wakefield, 1997). To our knowledge, two studies have specifically tested the electrode discrimination abilities of prelingually deafened CI users. In the first study (Busby & Clark, 1996), 50% discrimination limens of six subjects for an apical, mid and basal electrode ranged from 0.5 to over 7 electrodes. In the second study, average limens across 3 electrode positions targeting 70.7% correct, varied from 0.68 to 5.36 electrodes in a group of 16 young subjects (Busby & Clark, 2000).

Electrode discrimination results and speech understanding have been found to correlate in some, but not all studies investigating this relationship (Busby & Clark, 2000; Henry, McKay, McDermott, & Clark, 2000; Zwolan et al., 1997). However, these studies did not use up-to-date speech coding strategies. More recently, studies using spectral ripple discrimination tests generally found good correlations between discrimination thresholds and speech understanding (Drennan, Anderson, Won, & Rubinstein, 2014; Jones, Won, Drennan, & Rubinstein, 2013; Won, Drennan, & Rubinstein, 2007). Spectral ripple discrimination relies on complex spectral pattern analysis, and therefore is expected to require good electrode discrimination skills. Moreover, a number of studies have shown no further improvement in speech understanding with more than about 7 to 12 active electrodes (Friesen et al., 2005; Shannon, Cruz, & Galvin, 2011). Our objective was therefore to determine whether speech understanding performance of prelingually deafened CI users would improve when only mutually discriminable electrodes were selected for use in cochlear implant fitting. Selectively turning off electrodes related to "ineffective sites" in order to improve speech perception is referred to as the "site selection strategy" (Pfingst, Burkholder-Juhasz, Zwolan, & Xu, 2008). To our knowledge, only two studies have tested speech recognition in postlingually deafened subjects using an experimental cochlear implant program containing only discriminable electrodes. In a study by Zwolan et al. (1997), seven out of nine subjects showed improvement with the experimental map. It is important to note that these subjects made use of the MPEAK strategy, an F0F1F2-based strategy encoding the fundamental frequency (F0), first (F1) and second (F2) formant, no longer used nowadays. A study by Saleh, Saeed, Meerton, Moore, and Vickers (2013) found significant improvements in speech perception scores for 16 of 25 postlingually deafened subjects, using an experimental program that contained either only discriminable or the two-thirds most discriminable electrodes.

The first goal of the present study is to determine electrode discrimination difference limens for the entire electrode array in a number of prelingually deafened, late-implanted adult cochlear implant users. It is hypothesized that a number of electrodes have less than perfect discrimination limens, with subjects not being able to discriminate between stimulation on adjacent or even further removed electrodes. The second goal is to investigate whether changing CI fitting based on the electrode discrimination results, can lead to improved speech understanding, listening effort, spectral ripple discrimination and subjective appreciation in this patient population.

METHODS

Subjects

The six subjects in this study met the following inclusion criteria: onset of deafness/severe hearing loss before or at the age of 4 years, unilateral implantation with a Nucleus cochlear implant, a minimum of 1 year experience with their implant, Dutch native language, oral communication as primary mode of communication, age at implantation >16 years, age at inclusion >18 years and < 80 years and normal reading skills. Four subjects used a Nucleus CP810 processor, one used a CP910 processor and one a Freedom processor. Their PTA (pure-tone average of 500, 1000 and 2000 Hz) for the contralateral ear ranged from 92 to 115 dB HL. Table 1 presents the subjects' main characteristics. The Medical Ethical Committee of the Maastricht University Medical Center granted approval for the study protocol.

Electrode discrimination testing

Prior to electrode discrimination measurements, thresholds (T-levels), most comfortable loudness (MCL) levels, and uncomfortable loudness (UCL) levels were determined for a number of electrodes, and loudness level was balanced between electrodes. Deactivated electrodes in the map that subjects used in daily life, were not included in the experiments.

Stimuli were pulse trains with a duration of 1 s, a rate of 900 pulses per second (pps), pulse width (PW) 25 or 50 µs with a 8 µs interphase gap. 900 pps was also the clinically used rate for all subjects. T-levels were determined on five electrodes spread over the array and interpolated for the remaining electrodes. The MCL-level was measured on the most central electrode of the array. Initial MCL-levels for the remaining electrodes were set at the same percentage of the dynamic range (between T- and UCL-level) as the central electrode. UCL-levels were determined for all active electrodes of the array. For both the MCL- and UCL-levels a loudness scale containing five steps (almost inaudible, soft, medium, loud, too loud) was used, with the MCL-level corresponding to "medium" and the UCL-level to "too loud".

All electrodes were loudness balanced pairwise for loudness with their neighboring electrode. The most central electrode of the array was chosen as a starting point in order to minimize the drift in loudness towards the ends of the array. Neighboring electrodes were chosen because they are easier to balance due to the small differences in sound quality and because it was important for the discrimination task that nearby electrodes were well balanced. In each run, the current level (CL, as clinically applied by Cochlear^{TM}) of the reference electrode was kept constant and the level of the comparison electrode was varied adaptively in a 1 up – 1 down procedure (Levitt, 1971). The starting level for each comparison electrode and the first, central, reference electrode was the initial, previously determined, MCL-level. Each trial consisted of two intervals, one on the reference electrode and one on the comparison electrode, using the same stimuli as described above, with an interstimulus interval of 1 s. The subject judged which of both stimuli was louder after each trial. The level of the comparison electrode was then adapted accordingly in the next trial. A step size of 5 CL was applied with the stimulation level on any electrode maximized at the predetermined UCL-level. The run was terminated after six reversals; the average of the last four reversals was used to calculate a "balanced level". Two runs were conducted per electrode pair and the average balanced level of both runs was used as the new fixed level of the reference electrode for the next pairwise comparison. It is possible that small differences in loudness may remain between "balanced" stimuli; therefore, loudness roving was adopted to prevent the effect of loudness from systematically impacting the results (see below).

Electrode discrimination testing was performed using a 2-down-1-up 3-interval oddity adaptive procedure (Levitt, 1971), converging to the 70.7% correct point on the psychometric function. In other words, a difference limen of 1 electrode would indicate that the subject could correctly discriminate adjacent electrodes with an accuracy of 70.7%. Loudness roving was applied to each interval of the stimulus presentation, the magnitude being calculated per subject, based on the principles of Dai and Micheyl

(2010)[4]. In each trial, the subject was presented with three stimuli in random order: two on the same, fixed (reference) electrode and one on the other (comparison) electrode. The interstimulus interval was 0.5 s. The electrode number of the comparison electrode was varied adaptively in a 2-down-1-up manner. At the beginning of the procedure the comparison electrode was five electrode numbers more basal (for electrode numbers 7 to 22) or apical (for electrode numbers 1 to 6) than the reference electrode. The switch from a basal to an apical direction resulted in some overlap, in particular in the vicinity of reference electrode numbers 6 and 7. For S5, the distance at the beginning of the procedure was increased, to maximally nine electrodes, due to discrimination difficulties. The procedure started with a step size of two electrodes for the first two reversals, and a step size of one electrode for the remaining four reversals. The average of the last four reversals was used as the result of the run. When the subject showed a perfect performance between adjacent electrodes (100% accuracy), the reversals in the procedure would be between the same and the neighboring electrodes, leading to an average difference limen of 0.5. Two runs were performed for each reference electrode. The electrode discrimination difference limen (EDDL) was then calculated as the difference between the reference electrode number and the average of both runs.

Creating the experimental map

An experimental map (EM) was programmed, starting from the subjects' basic map (BM) used by the subject in daily life. Using the results of the electrode discrimination testing, electrodes were deactivated so that all remaining electrodes were mutually discriminable for the subject. If there was more than one possible deactivation pattern, the number of deactivated electrodes was kept as low as possible with the remaining electrodes spread optimally over the array. In case of contradictory discrimination in apical versus basal direction, the best discrimination result was used. The Frequency Allocation Table (FAT) was redistributed over the remaining electrodes using the "recalculate" option of the Custom Sound™ software[5]. Since this induces a shift of the tonotopic representation of the frequency map, subjects were given a habituation period of four weeks with the EM. At the end of the study, the processor was reprogrammed according to the subjects' preference.

The ACE strategy was applied in the BM of all subjects, with the number of maxima set to eight. In the EM, the ratio between maxima and number of electrodes was kept at the

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[4] For our adaptive procedure, the roving range was calculated as the averaged difference between the balanced levels of the two runs of all electrode pairs, which is an estimation of the amount of error after the balancing procedure, divided by .69. If, for example, the average difference between the results of run 1 and run 2 for a subject was 4 CL, the roving range R needed to be at least 5.8 ≈ 6 CL. This roving range was then applied on each side of the balanced loudness level of each electrode: if the balanced MCL-level was 150 CL, the loudness was randomly roved between 147 and 153 CL for that electrode.

[5] With this algorithm, the channel frequency boundaries are redistributed in a way that they increase linearly up to 1 kHz and logarithmically above 1 kHz, with relatively narrow apical channels and broader basal channels.

Table 1. Subject Characteristics

Subject	Cause of deafness	Onset of deafness	Experience with CI (yrs)	Age at Implantation (yrs)	Procesor type	Implant Type
S1	LVAS	Congenital	6	28	Nucleus CP810	Nucleus CI 24 RE (CA)
S2	Unknown	Congenital	11	49	Nucleus CP810	Nucleus CI 24 R (CS)
S3	Meningitis	Age 3	2	34	Nucleus Freedom	Nucleus CI 24 RE (CA)
S4	LVAS	Congenital	7	29	Nucleus CP810	Nucleus CI 24 R (CA)
S5	Meningitis	Age 4	3	53	Nucleus CP910	Nucleus CI 24 RE (CA)
S6	Cytomegalovirus	Unknown	3	27	Nucleus CP810	Nucleus CI 512

LVAS = Large Vestibular Aquaduct Syndrome

Table 2. Electrode discrimination difference limen (EDDL) results, and parameters of the BM and EM per subject

Subject	# Active electrodes BM	# Maxima BM	Range of EDDL	Mean EDDL	# Active electrodes EM	Deactivated electrode numbers	# Maxima EM	Active Smartsound™ options
S1	16	8	0.5 – 4.75	≤1.36	12	22,20,3,1*(*19,17,11,10,8,6*)	6	Zoom, ADRO, ASC
S2	22	8	0.5 – 2.875	1.17	17	11,9,6,4,2	6	ADRO
S3	22	8	0.5 – 3.5	1.24	16	18,11,7,5,3,1	6	ADRO
S4	22	8	0.5 – 5.875	2.02	12	21,17,11,9,8,6,5,4,2,1	5	ADRO, ASC
S5	22	8	1.125 – 7.125	3.88	8	22,20,18,16,15,13,11,10,9,7,6,5,3,2	4	ADRO, ASC, SNR-NR, WNR
S6	22	8	1 – 5.25	2.18	9	21,18,16,14,12,11,9,8,6,5,3,2,1	4	ADRO

BM = Basic Map, EM = Experimental Map, ADRO = Adaptive Dynamic Range Optimization, ASC = Autosensitivity Control;
*these electrode numbers were already deactived in the BM of S1

original level, thereby reducing the number of maxima, with a minimum of four. This reduction of the maxima was preferred in an attempt to emphasize spectral contrasts, given that the number of electrodes available for stimulation was reduced. If SmartSound™ options were used, they were programmed in combination with the EM as well, since denying subjects the use of their favourite SmartSound™ options could have a negative impact on their acceptance of the new map. Only during the spectral ripple discrimination test, which is described below, SmartSound™ options were deactivated. All remaining parameters were left unaltered in the EM, except when subjects indicated that the EM was louder or softer, in which case a general adjustment of C-levels was allowed.

Evaluation procedures

Tests on speech understanding, listening effort, spectral resolution and a questionnaire addressing subjective appreciation were administered to compare the EM with the BM in a repeated-measures design with 2 visits, separated by a four week habituation period with the EM.

Speech understanding tests

Phoneme scores in % correct on an open set, Dutch, monosyllabic (CNC) word test (Bosman & Smoorenburg, 1995) were collected at 75, 65 and 55 dB SPL. A Dutch open-set sentence test (LIST) (van Wieringen & Wouters, 2008) was administered in quiet at 65 dB SPL. If the score in quiet was larger than 50%, administration of the LIST was done in noise as well, using an adaptive procedure. If, on the other hand, the average score on the LIST in quiet was lower than 50%, or if the result on the LIST in noise was worse than 10 dB SNR, a closed-set Dutch number test (LINT) (van Wieringen & Wouters, 2008) was added to the test battery. If the score on the LINT in quiet was greater than 50%, administration was also performed in noise. In addition, LIST and LINT scores were determined as the average of three adaptive runs.

Listening effort test

If the LIST or LINT had been administered in noise, a subjective test of self-reported listening effort was added to assess more subtle differences in speech perception, at a supra-threshold level. Such differences might be experienced by subjects, but are likely to remain undetected when using only standard speech recognition tests. In this test, the subject needed to indicate listening effort on a 13-point scale, ranging from “no effort” to “very much effort”. The speech material used was either the LIST or the LINT, depending on the subject, presented at 6 different signal-to-noise ratios (-6, -3, 0, +3, +6 and +9 dB). The signal-to-noise ratio as determined with the BM was taken as the reference (0) and was left unchanged in the second session with the EM.

Spectral ripple discrimination test

In the spectral ripple discrimination test, the subject was asked to discriminate between a spectrally rippled noise stimulus (a noise with sinusoidal variations in amplitude along the frequency axis) and the same stimulus shifted in phase (positions of the spectral peaks and valleys reversed). The spectral ripple discrimination test is considered to be a test of spectral resolution, which is supported by the correlations with other measures of spectral resolution, including spatial tuning curves (Anderson et al., 2011) and measures of channel interactions (Jones et al., 2013; Won, Jones, Drennan, Jameyson, & Rubinstein, 2011). Our hypothesis was that spectral resolution, as assessed with the ripple discrimination test, improves with the experimental map. This is based on the reasoning that when indiscriminable electrodes are deactivated and all channels elicit different percepts, small differences in the spectral pattern across channels can be readily discerned.

For the spectral ripple stimuli, a Gaussian broadband noise carrier was used (120 – 7680 Hz), spectrally modulated on a log-frequency axis, as in Anderson et al. (2011). Ripple densities of 0.125, 0.176, 0.250, 0.354, 0.500, 0.707, 1.000, 1.414, 2.000, 2.828, 4.000, 5.657 and 8.000 ripples/octave (rpo) were created, with the peaks equally spaced on the log-frequency axis. The spectral modulation depth was held constant at 30 dB. The starting phase was 0° for the standard and 180° for the inversed stimuli. The duration of the stimuli was 500 ms, including a 30 ms Gaussian rise/fall time. Stimuli were presented in sound-field at 60 dB SPL and a ± 4 dB random level rove was added to avoid the influence of loudness cues. A psychophysical experiment was used to find the spectral ripple discrimination threshold per subject, which is the highest ripple density at which the subject can still discriminate two spectrally rippled stimuli with inverse positions of the peaks and valleys. Two standard and one inverse stimuli were presented per trial, in a 2-down-1-up 3-interval oddity adaptive procedure (Levitt, 1971). Each run started with a ripple density of 0.176. The mean of the last six out of ten reversals was used to establish the threshold, averaged over three runs.

It is known that for ripple densities above 2.000 ripples per octave, the ripple pattern is no longer clearly represented in the processor's output (Croghan, Krishnamoorthi, & Smith, 2013). Spectrogram analysis of our own physical measurements confirmed this, as can be seen in Figure 1 for ripple densities 1.000, 2.000 and 4.000 rpo. We therefore did not expect subjects being able to discriminate between phase-inversed ripples when ripple densities were high.

Questionnaire

Subjective appreciation of both the BM and the EM was evaluated with a questionnaire consisting of 17 questions regarding primary sound processing, sense of safety and ease of communication. The questionnaire was completed at the beginning of each session and concluded with a Visual Analogue Scale asking subjects to score their general appreciation of the program, whether it be BM or EM. In the second session subjects designated which program they preferred (BM, EM or no preference).

Materials

The determination of T-, MCL- and UCL-levels was performed using the subjects' own speech processor and Cochlear's clinical software Custom Sound™. For the loudness balancing and electrode discrimination testing, individual electrodes were stimulated with a L34 research processor in combination with Cochlear NIC research software and the APEX test platform (Francart, van Wieringen, & Wouters, 2008). All words, numbers and sentences were administered in sound-field through a single speaker (Klein + Hummel O 110 D), positioned 1 m in front of the subject, connected to a laptop. The subjects used their own speech processor without a contralateral hearing aid. The APEX 3 test platform (Francart et al., 2008) was used to present the LIST and LINT stimuli. The listening effort test used the Oldenburg Measurement Applications software package, developed by Hörtech Oldenburg (www.hoertech.de). Stimuli for the spectral ripple discrimination test were created using MATLAB (The MathWorks, Inc.).

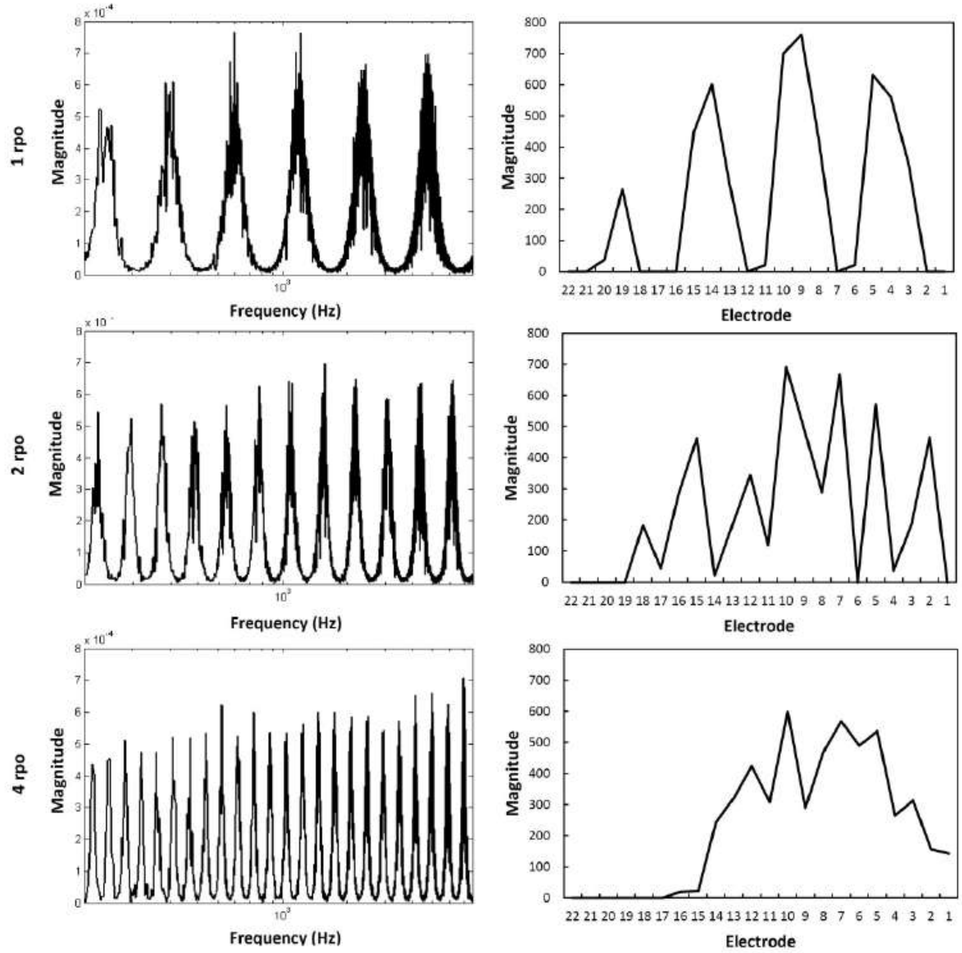

Figure 1. Spectra of the spectral ripple input stimulus (left) and output spectra of a CI with 22 active electrodes (right), for ripple densities 1.000, 2.000 and 4.000 rpo.

RESULTS

Electrode discrimination testing

All 22 electrodes were active in the clinical map of five of the six subjects. For subject 1 (S1), six electrodes could not be used for testing due to impedance problems. Pulse widths of 25 µs were used, except for subject 5 (S5), where the pulse width was changed to 50 µs due to out of compliance issues. The MCL of the central electrode, which was electrode number 12 for all six subjects, was on average 73% (range 63-79%) of the dynamic range between T- and UCL-levels. Good test-retest reliability was indicated by the intraclass correlation coefficients (ICC) for agreement, which ranged from .744 to .968 for the two runs of the electrode discrimination test. The range of the electrode discrimination difference limens (EDDLs), as well as the mean EDDL per subject, are presented in Table 2.

Difference limens ranged from 0.5 to 7.125 over all subjects and reference electrodes. Subjects' average EDDLs ranged from 1.17 for the best (S2) to 3.88 for the worst performer (S5). For S1, the average value is preceded by a "≤" sign since there were a large number of deactivated electrodes contributing to an artificially increased average.

For each subject, the EDDLs are displayed in Figure 2. When the last four reversals are alternately on the reference and adjacent comparison electrode, the resulting difference limen is 0.5 (i.e., perfect discrimination). A striking similarity between the discrimination patterns of all subjects except S1, were smaller EEDLs for the apical and mid-electrodes, and larger EDDLs for more basally located electrodes. When dividing reference electrodes into apical (electrodes 16-22), middle (electrodes 8-15) and basal (electrodes 1-7) and calculating the average EEDL for S2 to S6, mean EEDLs were 1.16, 1.86 and 3.3 for the apical, middle and basal categories respectively. S1 was excluded due to the large number of missing values. A one-way repeated measures ANOVA indicated that that the mean difference limen was significantly affected by electrode category (F= 18,84, df = 2,8, *p* = .001). Pairwise comparisons with a Bonferroni correction revealed significant differences between apical and basal (*p* = .034), and between middle and basal (*p* = .024), but not between apical and middle (*p* = .149).

Comparing the basic and experimental map

The parameters of the basic map (BM) and the experimental map (EM) per subject can be found in Table 2. The number of deactivated electrodes based on the electrode discrimination results ranged from 4 (S1) to 14 (S5). The number of maxima was reduced for all subjects, with a reduction to four maxima for S5 and S6. For five out of six subjects the EM sounded softer than the BM; C-levels were therefore increased in live-mode by 3 to 7 CL for these subjects.

Speech understanding tests

Individual subject and group median results for both the BM and the EM on the CNC monosyllabic word test are presented in Figure 3. Although median scores were slightly

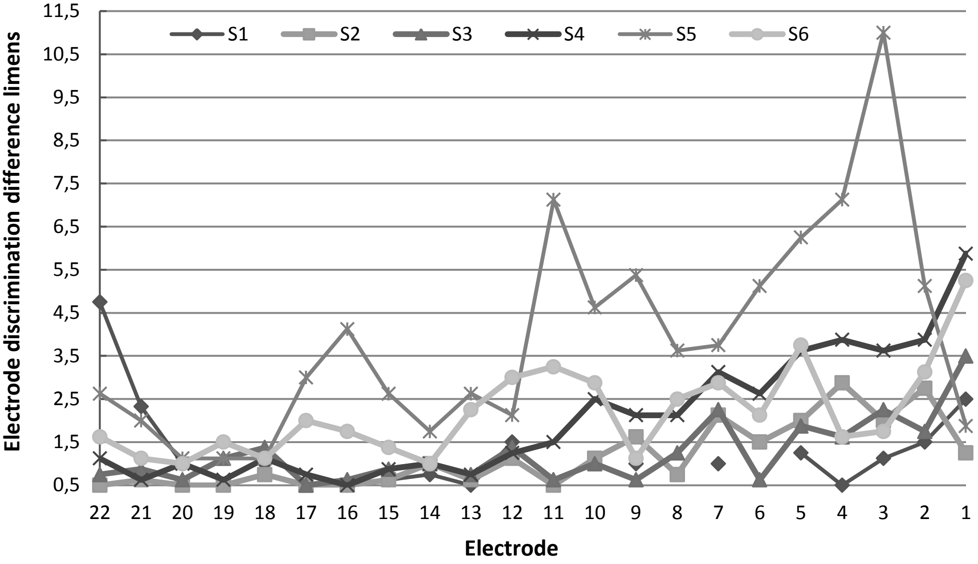

Figure 2. The electrode number of the reference electrode is represented on the X-axis; the electrode discrimination difference limen is displayed on the Y-axis. Reference electrode number 22 on the left is the most apical electrode; reference electrode number 1 is the most basal electrode. In case of perfect discrimination EDDLs would be 0.5 (lower boundary).

lower with the EM for the 75 and 65 dB administration levels, these differences were not statistically significant according to the Wilcoxon signed-rank test (*p* = .893, *p* = .463 and *p* = .074 for the 55, 65 and 75 dB administration levels, respectively).

The LIST was administered in quiet to all subjects except S5, for whom the test was too difficult. The LINT in quiet was also administered to S2, S4, S5 and S6. Subject mean and group median results for both maps are presented in Figure 4. The Wilcoxon signed-rank test revealed no significant difference between the scores obtained with the BM or the EM for the LIST (*p* = .414) or LINT (*p* = 1.0) in quiet. In order to analyze possible differences between BM and EM on an individual subject level, the smallest detectable change (SDC) in test score was calculated[6]. It represents the minimal change in score for this change to be real, that is, not due to measurement error. Based on the results of the five subjects on the LIST in quiet, the SDC was 12.4%. As can be seen in Table 3, only the difference score of S2 was statistically significantly larger than the SDC, indicating a lower recognition score when wearing the EM. On the LINT in quiet, none of the difference scores between BM and EM reached the SDC of 11% (see Table 3).

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[6] The Smallest Detectable Change (SDC) is calculated as 1.96 * √2 * SEM. The standard error of measurement (SEM) is based on the square root of the error variance of the ICC model for consistency, and divided by three given that there are three repeated measures.

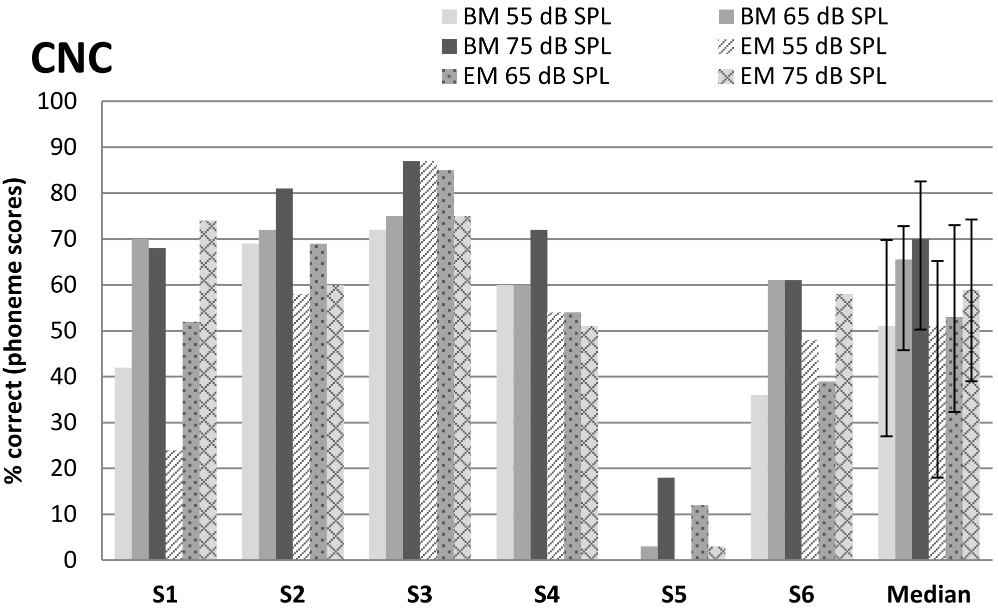

Figure 3. Individual and group median phoneme scores on the CNC test for the 6 subjects, with the BM and the EM, at 55, 65 and 75 dB SPL. Error bars for the median represent the interquartile range.

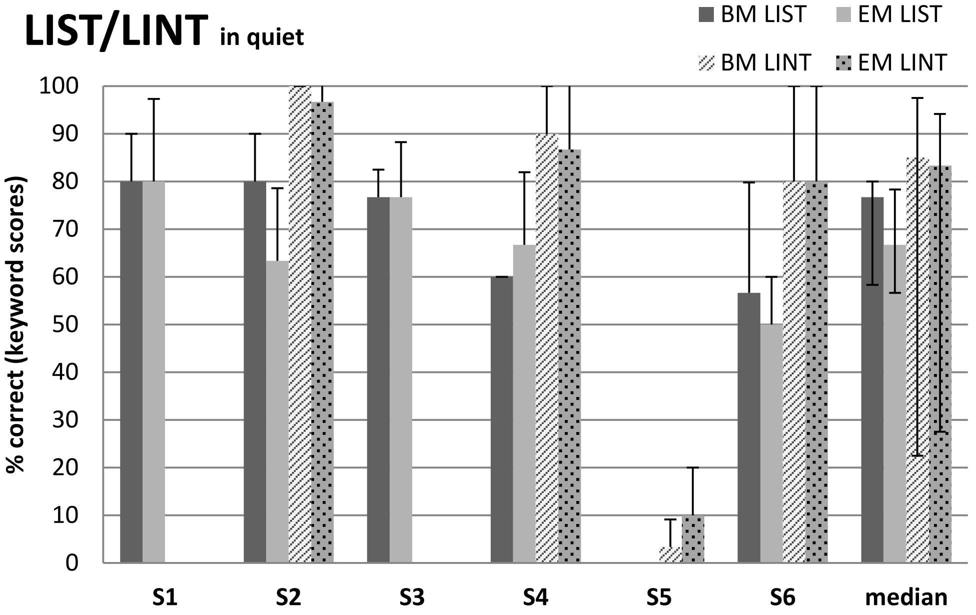

Figure 4. Subject mean and group median % correct scores on the LIST and/or LINT in quiet for all subjects, with the BM and the EM. Error bars represent 1 SD for the subject means and the interquartile range for the group median scores.

Table 3. Individual difference scores averaged over 3 measurements

Subject	LIST silence (%)	LINT silence (%)	LIST noise (dB SNR)	LINT noise (dB SNR)	Spectral ripple (rpo)
S1	0	NA	1.75*	NA	-0.09
S2	-16.67*	-3.33	-	4.42*	-0.65*
S3	0	NA	1.78*	NA	-0.19
S4	6.66	-3.33	-	-4.66*	0.05
S5	NA	6.67	NA	NA	-0.03
S6	-6.66	0	-	0.87	-0.31*

A negative sign before the number indicates a decrease in test score from BM to EM (NA = test not administered, - = no usable result , * = significant difference based on the SDC as calculated with the data from the subjects in this study)

On the LIST in noise, only two (S1 and S3) of the five tested subjects obtained a signal-to-noise ratio better than 10 dB SNR. The LINT in noise was therefore administered to S2, S4 and S6 instead. S5 was not able to perform a test in noise. Individual results with the BM and EM on either the LIST or LINT in noise can be seen in Figure 5. For S1 and S3, results were slightly better with the EM, with difference scores larger than the smallest detectable change of 1.17 dB SNR (Table 3). This is lower than the 1.8 dB SNR obtained for a group of 17 postlingual CI users (unpublished data), indicating that the slightly better scores for S1 and S3 do not represent a clinically relevant improvement. On the LINT in noise, an improvement greater than 1.5 dB was obtained by S2 and S4, with S2 performing significantly better and S4 significantly worse for the EM. For S6 there was no significant difference. For the LIST in noise, calculation of the SDC was based on the results of just three subjects.

Listening effort test

The listening effort test was administered to all subjects except S5. There was no difference between the BM and the EM for either for the total listening effort averaged over the six signal-to-noise-ratios (p = .68) or for any of the separate signal-to-noise-ratios, indicating no change in listening effort in noise.

Spectral ripple discrimination test

The spectral ripple test was administered to all six subjects. The individual discrimination thresholds ranged from 0.303 to 1.823 rpo for the BM and from 0.267 to 1.167 rpo for the EM as can be seen in Figure 6. The median threshold was 0.925 rpo with the BM and 0.855 rpo with the EM, this difference not being statistically significant (Wilcoxon signed-rank test, p = .075). On an individual subject level, the result with the EM was statistically significantly worse for both S2 and S6, for whom the SDC was 0.26 rpo (see Table 3).

Questionnaire

Questionnaire scores obtained for the BM and the EM did not differ (*p* = .225, Wilcoxon signed-rank test). The EM was attributed a statistically significantly lower score for the Visual Analogue Scale (*p* = .042, Wilcoxon signed-rank test). Three out of six subjects indicated “no preference” regarding the BM or EM programs, while two preferred the BM and one the EM.

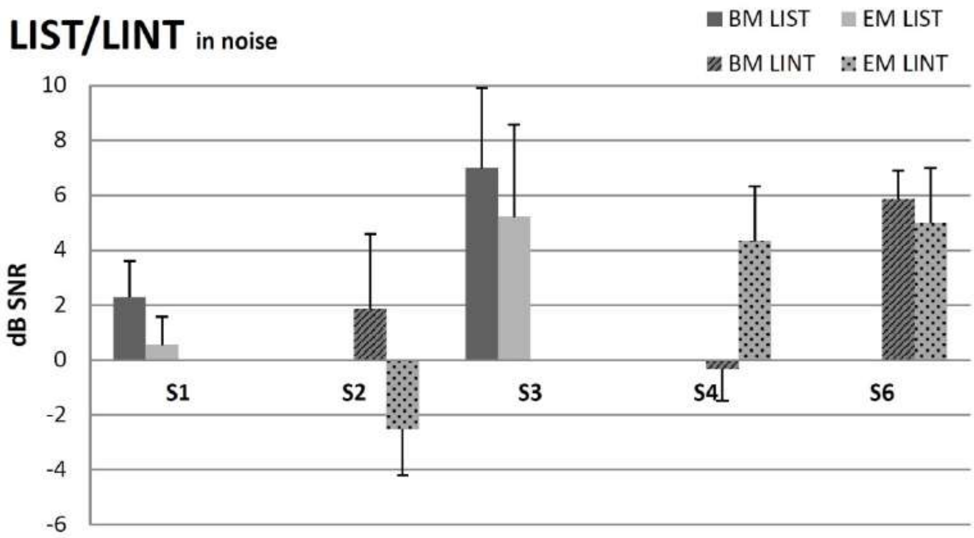

Figure 5. Subject mean scores in dB SNR on the LIST or LINT in noise, for all subjects except S5. Error bars represent 1 SD.

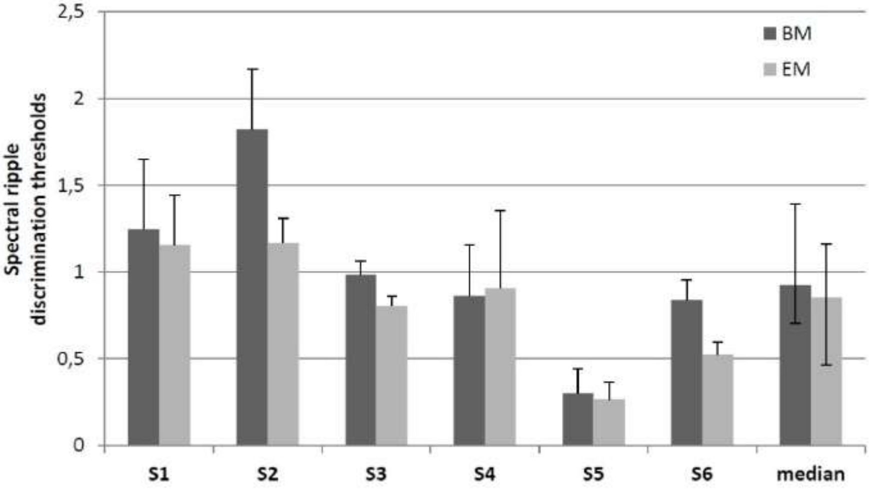

Figure 6. Subject mean and group median ripple discrimination thresholds for the BM and the EM. Error bars represent 1 SD for the subject mean and the interquartile range for the group median scores.

DISCUSSION

The absolute electrode discrimination difference limens (EDDLs) found in this study concurred with those found in other studies with prelingually deafened subjects (Busby & Clark, 1996, 2000). Although four out of our six subjects obtained a difference limen of 0.5 for at least one reference electrode, the observed range in difference limens (0.5 to 7.125) confirms that in many cases adjacent and even further separated electrodes cannot be discriminated by this group of CI users. A limitation of the adaptive method used to determine the EDDL however, is that it assumes that discrimination improves when electrodes are further apart, which is not always necessarily the case, for instance, when there is a tip fold-over of the electrode array.

A striking observation in this study is the clearly poorer performance for the basal reference electrodes. This pattern was also found by Zwolan et al. (1997) in their three early deafened subjects, Henry et al. (2000) for postlingually deafened subjects, and in a pitch discrimination study by Kwon and van den Honert (2006). However, Busby and Clark (2000) did not observe a poorer performance basally, although electrode number 8 was the most basal reference electrode tested. A plausible explanation may be that most of our subjects did not like the sharp, often unpleasant sensation caused by stimulation of the basal electrodes, hampering discrimination tasks for these electrodes. Secondly, it may be that during the loudness balancing procedure, a drift occurred towards the basal electrodes. In this way, balanced levels could have become gradually softer, again due to the sharp sensation of stimulation on these electrodes, which in turn made discrimination more difficult. Thirdly, it is known that the amount of surviving spiral ganglion cells diminishes with a long period of profound deafness (Hardie & Shepherd, 1999). As suggested by Pfingst et al. (2008), the number and condition of the activated neurons might be inferior at “ineffective” sites. It can be hypothesized that there are likely to be less surviving spiral ganglion cells in the basal region of the cochlea, where duration of deafness can be expected to be the longest for most subjects with prelingual extensive hearing loss.

For the sample as a whole, no significant differences were found between the two maps on either the CNC test or the LIST in silence. Sample comparison of the BM and EM could not be made for the speech tests in noise. At the individual subject level some significant differences were found between BM and EM, albeit not always in the same direction. Given that the SDC calculations were based on a small number of subjects, they were likely smaller than the true SDC's, as was illustrated for the LIST in noise. Hard conclusions can therefore not be drawn. This together with the fact that subjects did not experience a change in the amount of effort they needed to listen to and understand sentences or numbers in noise may be an indication that our findings are due to chance, and that there is no difference in speech understanding between the basic and the experimental map.

The findings of the present study are not in agreement with those by both Zwolan et al. (1997), and more recently Saleh et al. (2013), who found significant improvements on tests of speech understanding, for at least some of their subjects, when the map contained only discriminable electrodes. There are a number of possible explanations for this lack of concordance.

First, the use of the MPEAK strategy by Zwolan et al. (1997) compromises comparison to results obtained with current speech processing strategies, like ACE. The MPEAK strategy specifically encodes F1 and F2 by stimulating individual electrodes; therefore it makes sense that by enlarging the contrast between the electrodes used for the representation of F1 and F2, speech understanding scores improve.

Second, it might be that the reduction of the number of maxima in the present study had a negative influence on performance with the experimental map. Plant, Whitford, Psarros, and Vandali (2002) found that varying the number of maxima between 6 and 16 had little effect on speech understanding in silence, but that a 6-maxima program was significantly worse in noise. It has also been described by Qazi, van Dijk, Moonen, and Wouters (2013) that "wrong maxima selection" is likely to occur when listening to speech in noise with the ACE strategy, with a large portion of maxima being occupied by noise. The reduction in number of maxima could therefore have influenced our results in noise, but not in silence. It can be assumed that this factor did not have an effect on the results by Saleh et al. (2013), since they used a variety of speech processing strategies, and did not mention a reduction of maxima for the Nucleus® users.

Moreover, the prelingually deafened subjects in the present study might not have been completely adjusted to the altered frequency allocation consequent to the deactivation of electrodes. Zwolan et al. (1997) applied the default frequency allocation available in the software for both maps, but given the use of the MPEAK strategy this redistribution is likely to have had fewer consequences, and a positive effect of the experimental map could occur even without an adjustment period. In the more recent study by Saleh et al. (2013) it is not mentioned how the frequency allocation is changed, although it can be assumed that re-allocation was automatically implemented by the CI software of the various brands. In their study, just as in the present one, subjects were given one month to adapt to the experimental program since it is known that changes in frequency allocation require an adjustment period. Fu, Shannon, and Galvin (2002) found that three months of experience with a map that had a severely shifted frequency allocation was not enough to attain the original level of speech understanding of three experienced CI listeners. A model was developed based on these results, which suggested that these subjects were not able to completely alter their internal representations or "phoneme labels", in favor of the new situation (Sagi, Fu, Galvin, & Svirsky, 2010). In the current study, some subjects explicitly reported that the EM required an adjustment with respect to how everything sounded. It is possible that prelingually deafened CI users generally

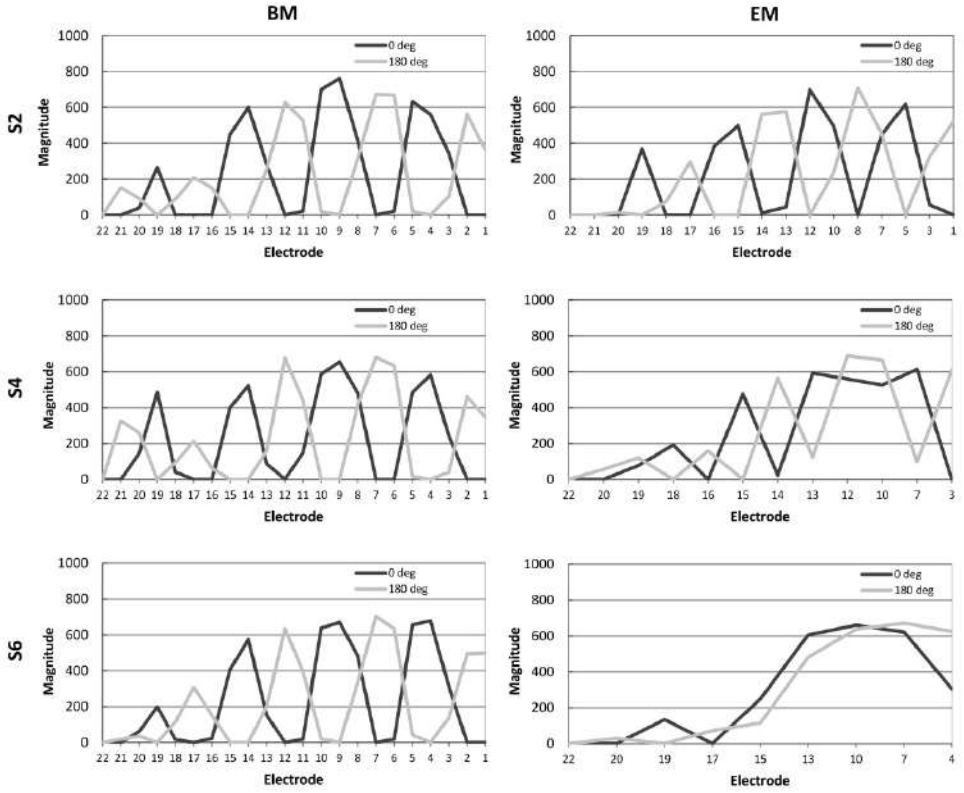

Figure 7. Output spectra for the 1 rpo spectral ripple stimuli obtained for the BM (left) and EM (right) of S2 (top), S4 (middle) and S6 (bottom).

require more time to form stable internal representations of sounds, especially given their limitations on a central auditory level, and that the one month adaptation period in this study was not sufficient to adjust to the albeit limited frequency shift.

The fourth factor that might have limited the potential improvement with the EM in this study, is related to the fact that deactivated electrodes were mainly located in the basal part of the array. This improved resolution mainly in the high-frequency region, whereas fine spectral resolution is more important for low to mid-frequencies (McKay, 2005). Also, Henry et al. (2000) only found a significant correlation between electrode discrimination abilities and speech information only up to 2680 Hz. Details regarding the deactivation pattern were not provided by Saleh et al. (2013).

Spectral ripple discrimination thresholds also did not differ between the BM and the EM. At the individual subject level, S2 and S6 even performed significantly worse with the EM. Our hypothesis that a map consisting of discriminable channels leads to better performance on a test of spectral resolution was therefore not confirmed. We wondered whether this could be explained by the reduction in the number of electrodes. Shifted channels are broader in the EM than in the BM and contain a larger frequency range.

When ripple density increases, there is an increased possibility that both a peak and a valley fall into the same frequency band, thus reducing the number of peaks and valleys and flattening the output spectrum. This was verified by measuring the electrode outputs of spectral ripple stimuli with different ripple densities presented in sound field to a Nucleus® sound processor that contained the exact maps of our subjects. A Nucleus® Freedom™ implant emulator was used for the recordings and data were analyzed with MATLAB (The MathWorks, Inc.). An illustration of the differences between the basic and experimental maps of S2, S4 and S6, who had a relatively decreasing number of active electrodes in their EM, can be seen in Figure 7 for the 1 rpo stimulus: the output spectrum is increasingly flattened with the EM for S2 to S6, when the number of active electrodes becomes smaller. The flattening generally occurred at lower ripple densities when the map contained less than 22 active electrodes. We obtained an estimation of the amount of available contrast for both BM and EM, per subject and per ripple density. We wanted to see if possible differences in the amount of contrast between the BM and EM, could be related to the subjects' actual ripple discrimination performance. We did this by calculating the difference between outputs of the phase-shifted stimuli and averaging them over the electrodes according to the method described by Croghan et al. (2013); see Figure 8. For S2 and S6 a significant difference in performance between the BM and EM was found on the ripple test. The majority of reversals in the adaptive procedure of S6 occurred at 0.707 rpo with the EM, while for the BM the stimulus with 0.707 rpo was mostly discriminated correctly. It can be seen in Figure 8 that the average difference between the output spectra for the phase-shifted stimuli was smaller for the EM, and declined more rapidly from 0.5 rpo onwards for the EM, whereas it remained constant for the BM. This may explain the worse performance by S6 for the EM. At the same time, S2 also performed worse for the EM, although there were no clear differences between BM and EM at 1.414 rpo, which is the density S2 could almost never discriminate in the adaptive procedure for the EM. No significant difference was found between ripple thresholds of S4, whereas a smaller contrast with the EM is clearly visible in Figure 8, starting from 0.707 rpo. For the remaining subjects S1, S3 and S5, the ripple densities where reversals occurred during the adaptive procedure were well below the ripple densities where the output spectrum became seriously disturbed. Therefore, we conclude that the amount of available spectral contrast available in the spectral ripple stimuli, and the reductions herein with the EM, could not be related to the ripple discrimination results.

Finally, the fact that there were no significant differences between BM and EM for the questionnaire concurs with the other results. For the Visual Analogue Scale, the EM rated statistically significantly lower than the BM which may be attributable to the required adjustment to the sound quality of the EM. Or it might be simply because our subjects did not feel as comfortable with the new map as with the old one, reflecting the adjustment to the internal representations of (speech) sounds.

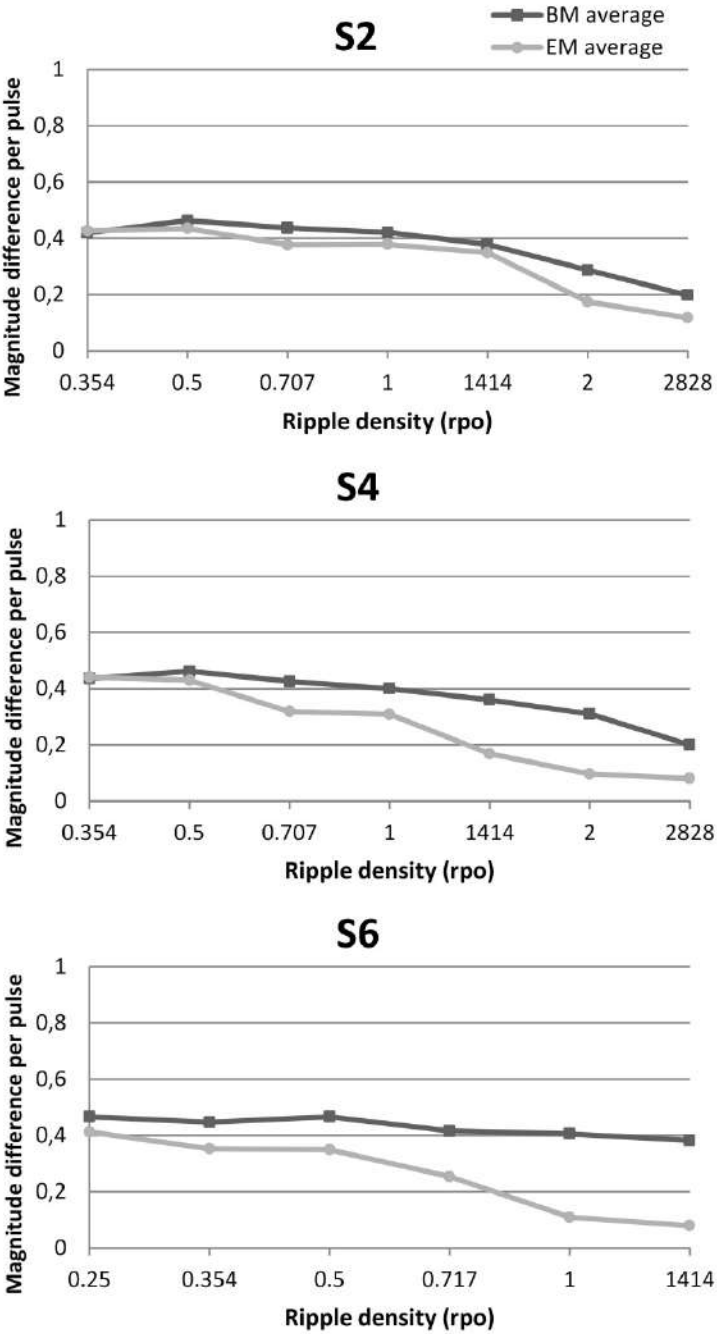

Figure 8. Average difference between output spectra of the phase-shifted stimuli of increasing ripple densities, ranging from 0.354 to 2.828 rpo for S2 and S4, and from 0.25 to 1.414 rpo for S6. The dark grey line represents the contrasts measured with the BM, the light grey line represents the contrasts measured with the EM.

CONCLUSIONS

In this study, the electrode discrimination abilities of six prelingually deafened CI users were investigated. The electrode discrimination difference limens ranged from 0.5 to 7.125 over all subjects and reference electrodes, confirming our first hypothesis that subjects were not able to discriminate between all adjacent electrodes. Across-site variations were observed, with significantly larger limens for basally located electrodes. Based on these findings, an experimental map containing only discriminable electrodes was devised to test our second hypothesis, which was whether such a map could improve auditory performance. However, this experimental map did not appear to be superior to the basic map for any of the subjects, on tests of speech understanding in quiet and in noise, spectral ripple discrimination or listening effort. Moreover, subjects generally preferred the basic to the experimental map. Our second hypothesis was therefore not confirmed. Factors that may have influenced the observed outcomes were (1) the reduction in the number of maxima in the experimental map, (2) the possibility that the adaptation period of four weeks was too short for these prelingually deafened subjects to become accustomed to the altered frequency allocation, and (3) the fact that a large proportion of the deactivated electrodes were located in the basal region of the cochlea, where fine spectral resolution is less important.

The current study was based on the results of only six subjects, hereby limiting generalizability. Besides testing more subjects, the following recommendations for future studies can be made: use electrode discrimination performance to adjust CI fitting, avoid reducing the number of maxima (in case of the ACE strategy) and create a good balance of deactivated electrodes along the array. It may also be advisable to extend the adaptation period with the new map, or to perform the experiment in a cohort of recently implanted prelingually deafened adults, who have not yet become accustomed to a particular frequency allocation.

Chapter 4

Systematic review on late cochlear implantation in early deafened adults and adolescents. Part 1: clinical effectiveness

Under review

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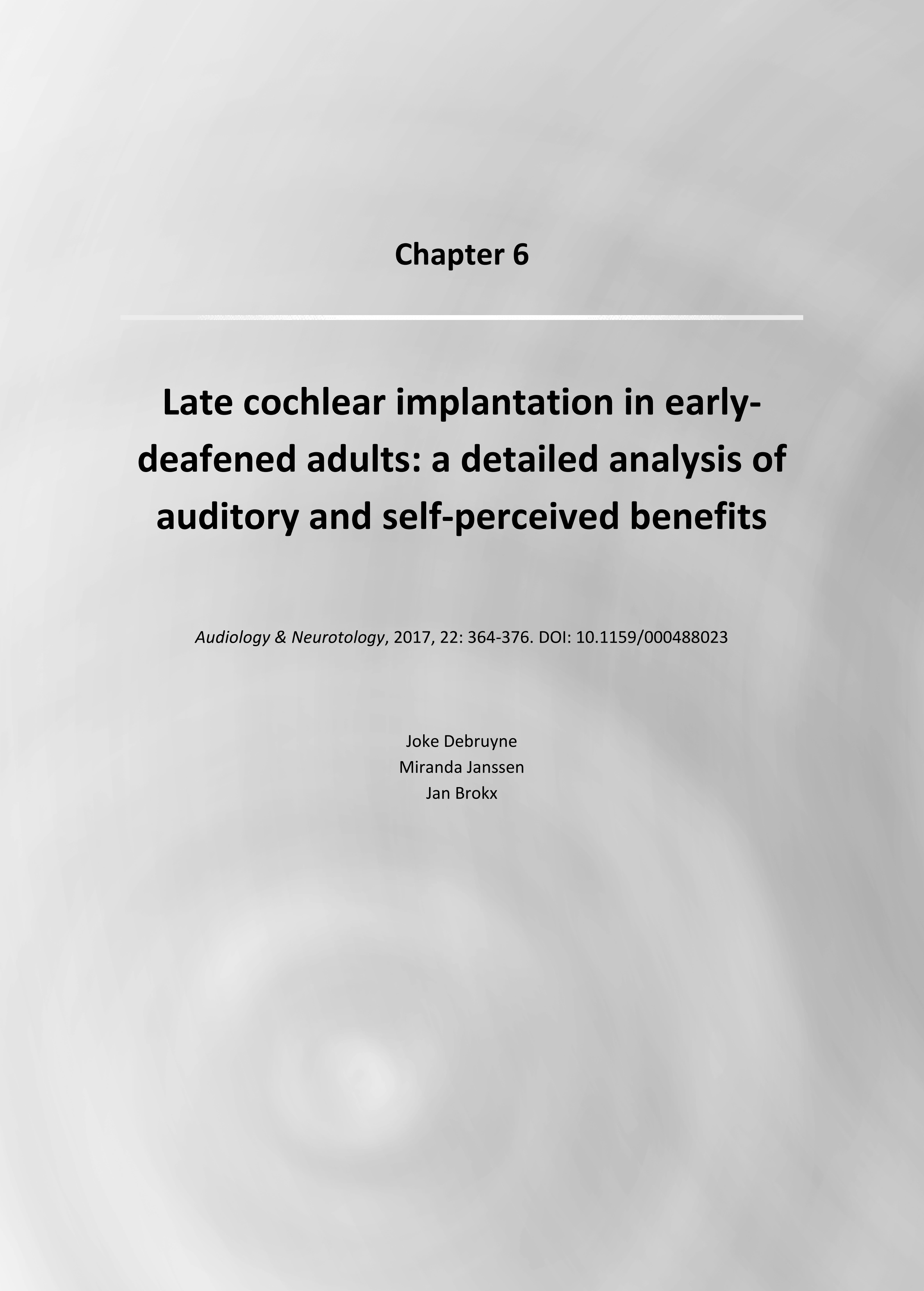
Miranda Janssen
Jan Brokx

Chapter 5

Systematic review on late cochlear implantation in early deafened adults and adolescents. Part 2: predictors of performance

Under review

Joke Debruyne
Miranda Janssen
Jan Brokx



Chapter 6

Late cochlear implantation in early-deafened adults: a detailed analysis of auditory and self-perceived benefits

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ABSTRACT

Objectives: It is known that early-deafened cochlear implant (CI) users are a very heterogeneously performing group. To gain more insight into this population this study investigated (1) postoperative changes in auditory performance over time based on various outcome measures, focusing on poor performers, (2) self-perceived outcomes, (3) relations between auditory and self-perceived outcomes and (4) preimplantation factors predicting postoperative outcomes.

Methods: Outcomes were assessed prospectively in a group of 27 early-deafened, late-implanted CI users, up to three years post-implantation. Outcome measures included open-set word and sentence recognition, closed-set word recognition, speech tracking and a questionnaire on self-perceived outcomes. Additionally, the relative influence of eight preimplantation factors on CI outcome was assessed with linear regression analyses.

Results: Significant improvements were found for auditory performance measures and most of the questionnaire domains. Significant changes on the closed-set word test, speech tracking and questionnaire were also found for a subgroup of poor performers. Correlations between auditory and self-perceived outcomes were weak and non-significant. Preoperative word recognition and preoperative hearing thresholds, both for the implanted ear, were significant predictors of postoperative outcome in the multivariable regression model, explaining 63.5% of the variation.

Conclusions: Outcome measurement in this population should be adjusted to the patients' individual performance level and include self-perceived benefit. There is still a need for more knowledge regarding predictors of CI outcomes in this group, but the current study suggests the importance of the preoperative performance of the ear to be implanted.

INTRODUCTION

In the early years of cochlear implantation, adults with an early onset of deafness, i.e. before (prelingual) or during (perilingual) language development, displayed very limited benefit on speech understanding tests (Skinner et al., 1992; Snik et al., 1997; Waltzman et al., 1992). Consequently, they were often considered poor cochlear implant (CI) candidates. At the same time, studies reported that, in spite of these poor outcomes, satisfaction rates were high (Hinderink et al., 1995; Kaplan et al., 2003; Peasgood et al., 2003; Zwolan et al., 1996). As speech coding strategies evolved towards SPEAK, CIS and ACE from the late 90's onwards, studies showed that more beneficial results were possible for prelingually deafened adults (Schramm et al., 2002; Waltzman & Cohen, 1999; Waltzman et al., 2002). A number of recent studies have demonstrated significant postoperative improvement in the mean scores of this group of CI users on various speech understanding tests (Bosco et al., 2013; Caposecco et al., 2012; Klop et al., 2007; Rousset et al., 2016; Santarelli et al., 2008; Shpak et al., 2009; van Dijkhuizen et al., 2011; Yang et al., 2011). Nevertheless, there are still large interindividual differences, with part of the early-deafened population obtaining scores slightly above or at 0% when speech understanding is assessed using open-set words or sentences. In this study we argue that this does not necessarily mean that these CI users do not gain any auditory benefit from their CI, but rather that the tests used to evaluate performance might not be sensitive enough to detect more modest contributions of the implant to speech perception. In 2012, Caposecco et al. (2012) showed that while 18 of 38 CI users with early-onset hearing loss were unable to attain more than 30% open-set speech discrimination postoperatively, they were all able to at least discriminate suprasegmental cues with their CI. Two other studies showed that poor performing, prelingually deafened CI users were able to integrate auditory information from the cochlear implant with visual speech information, obtaining higher scores in the audiovisual condition (Craddock et al., 2016; Moody-Antonio et al., 2005). These studies demonstrate the importance of including the ability to use suprasegmental and audiovisual cues when evaluating the benefit of cochlear implantation in this patient group. In this study we wanted to investigate this further, by means of examining the added value of two non-traditional outcome measures to capture small, but relevant auditory benefit. Although recent studies have shown significant advancements in mean speech understanding scores for early-deafened CI users, it is still unclear when these subjects reach their maximum, or so-called performance plateau. Postlingual CI users generally do not show further improvement after 1 year or even 6 months of CI use (Lenarz, Sonmez, Joseph, Buchner, & Lenarz, 2012). However, some studies assessing early-deafened CI users over time found that auditory performance continued to improve beyond 6 months or even 1 year post-implantation (Santarelli et al., 2008; Shpak et al., 2009; Zeitler et al., 2012), whereas other studies observed no further increases beyond the 1 year evaluation moment (van Dijkhuizen et al., 2016; Waltzman et al., 2002) or even earlier (Teoh et al., 2004a). This knowledge is important in order to guide patient expectations, and it may also influence how to design post-implant rehabilitation. In addition to the evaluation of two non-traditional outcome measures, the current study therefore compares outcomes at regular intervals, up to three years post-implantation.

There is increasing agreement that the impact of cochlear implantation should not only be evaluated with respect to changes in speech understanding performance, but also with respect to self-perceived changes in quality of life. High user satisfaction rates have consistently been reported in studies on early-deafened CI users, even in subjects with almost negligible gain in auditory performance (Bosco et al., 2013; Caposecco et al., 2012; Hinderink et al., 1995; Kaplan et al., 2003; Peasgood et al., 2003; Zwolan et al., 1996). A number of studies have evaluated quality of life before and after implantation and found significant postoperative improvements, mainly in hearing-related quality of life questionnaires (Klop et al., 2007; Most, Shrem, & Duvdevani, 2010; Schramm et al., 2002; Straatman et al., 2014; van Dijkhuizen et al., 2011), but also in hearing-related domains of general health status questionnaires (Klop et al., 2007; Straatman et al., 2014). Questionnaires like the Nijmegen Cochlear Implant Questionnaire (NCIQ) (Hinderink et al., 2000) are able to detect postoperative improvements for early-deafened CI users. Nevertheless it must be kept in mind that such questionnaires were developed to evaluate the benefit for postlingually deafened CI users and may therefore be less appropriate for early-deafened CI users with respect to, for example, the wording of questions (e.g. complexity) or the situations that are addressed (e.g. telephone use). In this study, the questionnaire applied is designed specifically to evaluate self-perceived benefit in early-deafened cochlear implant users. Moreover, the possible relation between self-perceived benefit, and auditory benefit will be investigated, since they are both relevant in defining and measuring “successful implantation”. It is pertinent to ask whether both outcome types provide the same information since this might affect patient counseling and possibly implant indications. Studies investigating this specific relation are scarce, however. In 2011, van Dijkhuizen et al. only found a significant correlation between speech perception outcomes and the subdomain “advanced sound perception” of the NCIQ, whereas both Peasgood et al. (2003) and Straatman et al. (2014) found no significant correlations between auditory outcome measures and scores on the Glasgow Benefit Inventory. Additionally, Straatman et al. (2014) found no significant correlations between phoneme benefit scores and the generic HUI3 (Feeny et al., 2002), or the postoperative changes on the NCIQ. The authors hypothesized that prelingually deafened adults, in contrast to postlingually deafened adults, might be satisfied with just minimal improvements in hearing abilities.

So far we discuss here the significance of optimally measuring the outcome of cochlear implantation in this specific patient group. Another objective of this study is directed toward predicting preoperatively which patients will become good and/or satisfied cochlear implant users. Relevant patient characteristics can vary in many ways: the communication mode in which the patient has been raised, whether the hearing loss had a pre- or perilingual onset, the amount of residual hearing, whether or not hearing aids have been used, etc. It would be very useful to know which of these preimplantation factors are related to postoperative outcomes. The results of studies performing correlation analysis or multiple regression analysis in groups of prelingual CI users have been ambiguous. Study samples are often small and a wide range of patient factors are considered that are not uniformly defined across studies. Although not conclusive over all studies, significant relations have been found between CI outcome and patient's own speech intelligibility (van Dijkhuizen et al., 2016), communication mode (Caposecco et al., 2012; Rousset et al., 2016; Yang et al., 2011; Zeitler et al., 2012) and preoperative speech understanding scores (Caposecco et al., 2012; Kraaijenga et al., 2016; Rousset et al., 2016; van der Marel et al., 2015; Yang et al., 2011). At the same time, duration of deafness (Caposecco et al., 2012; Kraaijenga et al., 2016; van der Marel et al., 2015; van Dijkhuizen et al., 2016; Yang et al., 2011) and etiology (Kraaijenga et al., 2016; Zeitler et al., 2012) do not seem to be related to CI outcomes in this patient group.

In summary, the current study had four objectives. The first was to examine in detail postoperative changes in auditory performance in a group of late-implanted, early-deafened adult CI users. For this purpose, both standard open-set word and sentence recognition tests were used pre- and postoperatively, as well as two less commonly used tests, hereafter referred to as "non-traditional" tests. The first of these two tests is speech tracking (De Filippo & Scott, 1978), which evaluates changes in the best-aided, audiovisual communicative abilities. The second is the monosyllable-trochee-spondee test (Erber & Alencewicz, 1976), which assesses changes in closed-set, (suprasegmental) word recognition. It was hypothesized that these non-traditional tests could demonstrate clear postoperative changes in subjects who show no or only limited improvements on the standard open-set auditory tests. We also wanted to determine if and when auditory performance reaches a plateau in this patient population. Therefore measurements were done up to 3 years post-implantation. A second objective was to implement and evaluate a questionnaire that would be sensitive to the specific, self-perceived advancements of early-deafened CI users. The third study objective was to evaluate the relation between changes in auditory performance and changes in the subjective evaluation questionnaire. The final and fourth aim was to identify which preimplantation factors are related to postoperative speech understanding scores with the CI. The investigated preimplantation factors were: preoperative pure-tone-average hearing loss (PTA) in the better ear, preoperative PTA in the implanted ear, preoperative best-aided word recognition score, preoperative word recognition score in the implanted ear, communication mode at implantation, hearing aid use at implantation, preoperative hearing aid use in the implanted ear and age at onset of deafness (pre- vs. perilingual).

MATERIALS AND METHODS

Participants

This article presents prospective data, gathered since 2010, on 27 adult early-deafened cochlear implant users who received an implant at the Maastricht UMC+. The Medical Ethical Committee of the MUMC+ deemed that the study fulfilled ethical requirements since it was an extension of regular patient care. All subjects who met the following criteria were included in the study: unilateral implantation, acquisition of deafness or severe hearing impairment at or before the age of four years and implantation in adulthood (>18 years). In order to receive a CI at the Maastricht UMC+, early-deafened subjects additionally needed to be sufficiently motivated and receptive to auditory communication. There were no further exclusion criteria. Only subjects who had at least 1 year experience with the CI were included.

Twenty-seven subjects met the inclusion criteria. The mean age at implantation of was 45 years (range: 20-71 years). A prelingual onset of deafness or severe hearing loss, defined as an age at onset of ≤12 months, was found in 22 or 81% of subjects; the remaining five (19%) had a perilingual onset (>12 but <48 months). Nineteen subjects (70%) were oral communicators, the remaining eight (30%) used a combination of oral and manual communication. All but four subjects (85%) were using at least one hearing aid at the time of the implantation and 18 subjects (67%) were wearing a hearing aid in the ear that was subsequently implanted. An overview of relevant subject characteristics and a number of summary statistics can be found in Table 1. All subjects had followed the extensive rehabilitation program which is the standard post-implant care at the Maastricht UMC+, and all but one were regular users of their device. The latter subject, S15, became a non-user after 1 year of CI use because she could not become accustomed to the sound of the implant. The post-implant follow-up time was 3 years for 14 subjects, 2 years for four subjects and 1 year for the remaining nine subjects (mean 2.2 years). Complications occurred neither during CI surgery nor during the postoperative rehabilitation period.

Outcome measures

The preoperative pure-tone-average hearing loss (PTA) at 0.5, 1 and 2 kHz was calculated for each subject, both for the implanted ear and for the best ear (see Table 1). Open-set word recognition was evaluated in free field at 65 and 75 dB SPL by means of the phoneme score on the Dutch, monosyllabic, consonant-nucleus-consonant (CNC) word test (Bosman & Smoorenburg, 1995). The maximum percentage correct was gathered in the best-aided auditory-only condition (with one or two hearing aids preoperatively; postoperatively in the condition used in daily life: either CI alone or CI + contralateral hearing aid) and additionally in the CI-alone condition.

Table 1. Overview of subject characteristics

Subject number	Sex	Age at CI (yrs)	Cause of HI	Age at onset of HI (mo)	Communi-cation mode at CI	HA use at CI	HA use at CI (implanted ear)
1*	M	30	Unknown	0	Oral + manual	yes	yes
2	F	72	Unknown	0	Oral	yes	yes
3*	M	27	Unknown	0	Oral	yes	yes
4*	F	21	Meningitis	4	Oral + manual	no	no
5	F	71	Unknown	0	Oral + manual	yes	yes
6	F	63	Measles	36	Oral	yes	yes
7	M	33	Meningitis	5	Oral	yes	yes
8	M	25	Unknown	0	Oral	yes	yes
9	M	48	Rubella	0	Oral	yes	yes
10*	F	51	Unknown	0	Oral	yes	yes
11	M	61	Meningitis	24	Oral	yes	yes
12	F	51	Unknown	0	Oral	yes	yes
13	M	49	Perinatal asphyxia	0	Oral	yes	yes
14*	F	35	Meningitis	29	Oral + manual	no	no
15*	F	26	Meningitis	12	Oral + manual	no	no
16*	F	50	Rubella	0	Oral	yes	no
17	F	46	Rubella	0	Oral	yes	no
18	F	61	Head trauma	48	Oral	yes	yes
19	F	65	Unknown	0	Oral + manual	yes	no
20	F	57	Rubella	0	Oral	yes	yes
21	F	33	Pendred syndrome	0	Oral	yes	yes
22	M	40	Perinatal asphyxia	0	Oral	yes	yes
23*	M	62	Unknown	0	Oral	yes	no
24*	F	31	Ear infections	24	Oral + manual	no	no
25	F	55	Unknown	0	Oral	yes	yes
26	F	20	Pendred syndrome	0	Oral + manual	yes	yes
27*	M	44	Unknown	0	Oral	yes	no
Summary / mean	**37% M 63% F**	**45**	**NA**	**81% prelingual 19% perilingual**	**70% Oral 30% Oral + manual**	**85% yes 15% no**	**67% yes 33% no**

Subjects with an asterisk (*) belong to the poor performing group. (CI = Cochlear Implantation, yrs = years, HI = Hearing Impairment , mo = months, HA = Hearing Aid, PTA = Pure Tone Average at 0,5; 1; 2 kHz)

Table 1. *Continued*

Subject number	Pre-op PTA (implanted ear, dB HL)	Pre-op PTA (best ear, dB HL)	Speech coding strategy	Implant type	Follow-up time post CI (yrs)
1*	105	95	ACE	Nucleus CI 422(SRA)	2
2	97	92	ACE	Nucleus CI 422(SRA)	2
3*	97	97	ACE	Nucleus CI 422(SRA)	3
4*	118	118	ACE	Nucleus CI 24RE(ST)	3
5	103	102	FS4	CONCERTO	3
6	100	83	FSP/FS4	CONCERTO	1
7	105	105	ACE	Nucleus CI 24RE(CA)	3
8	97	97	FS4	CONCERTO	3
9	115	107	ACE	Nucleus CI 422(SRA)	2
10*	105	105	ACE	Nucleus CI 422(SRA)	3
11	95	95	HiRes-P	HiRes 90k Adv HiFocus ms	1
12	115	115	ACE	Nucleus CI 24RE(CA)	3
13	97	92	HiRes Optima-S	HiRes 90k Adv HiFocus ms	1
14*	117	117	ACE	Nucleus CI 11+11+2M	3
15*	120	102	ACE	Nucleus CI 24RE(CA)	1
16*	118	112	ACE	Nucleus CI 422(SRA)	1
17	98	88	FS4	CONCERTO	3
18	85	67	HiRes Optima-S	HiRes 90k Adv HiFocus ms	1
19	110	97	ACE	Nucleus CI 422(SRA)	3
20	112	105	ACE	Nucleus CI 422(SRA)	1
21	93	93	ACE	Nucleus CI 422(SRA)	3
22	110	110	ACE	Nucleus CI 422(SRA)	3
23*	115	113	ACE	Nucleus CI 422(SRA)	1
24*	112	108	HiRes-S	HiRes 90k HiFocus 1J	1
25	97	83	HiRes-S Fid 120	HiRes 90k HiFocus 1J	3
26	93	93	ACE	Nucleus CI 422(SRA)	2
27*	118	117	ACE	Nucleus CI 422(SRA)	3
Summary / mean	**105**	**100**	**NA**	**NA**	**2,2**

The second open-set test was a Dutch sentence recognition test, with a variable volume setting according to the subjects' preference, administered in the best-aided, auditory-only condition. The result is expressed as a syllable score. The third test, speech tracking (ST), is a structured, “conversation-like” task that combines sentence identification with auditory comprehension (De Filippo & Scott, 1978). The amount of time needed to repeat a text which is read live and out loud to the subject, determines the score, expressed as the number of words per minute (#wpm). The speech tracking test was administered in the best-aided, auditory-visual condition. The texts used were specifically designed for early-deafened, Dutch CI users (Boons & Debruyne, 2011). In poor performers, the monosyllable-trochee-spondee (MTS) test (Erber & Alencewicz, 1976) was used as a test for closed-set (suprasegmental) word recognition. This 12-item test assesses both word identification (word score) as well as identification of suprasegmental cues (suprasegmental score). Administration of the MTS-test was at 65 dB SPL in the best-aided, auditory-only condition. If no hearing aids were worn in the preoperative condition of the open-set word, sentence or MTS-test, or if the test was not administrable, a score of 0% was assigned.

A questionnaire to assess subjective outcomes was constructed specifically for early-deafened CI users. The questionnaire consists of five subscales: primary sound processing, sense of safety, ease of communication, social aspects of hearing and self-confidence. Appendix A contains information regarding the development and subsequent reliability analyses. The translation of the questionnaire is presented in Appendix B.

Auditory tests were administered preoperatively, 6 months, and 1 year postoperatively. For some subjects they were also administered at 2 and 3 years postoperatively, according to available follow-up time. Subjects also completed the questionnaire dedicated to early-deafened CI users at each of these evaluation moments, except at 6 months postoperatively.

Data analysis

To evaluate the postoperative changes in auditory performance up to 3 years post-implantation (first study objective), with decreasing subject numbers over time, multilevel linear regression modeling was performed. The applied covariance structure chosen was based on likelihood ratio testing and the Bayesian information criterion (BIC). Auditory performance changes over a specific time period were then evaluated with pairwise comparisons. Bonferroni-Holm adjustments of the standard α-value of 0.05 were made in case of multiple comparisons. If the sample size was small, which was the case when considering a subgroup of subjects, the non-parametric Wilcoxon signed-rank test was applied to pairwise comparisons. Descriptive statistics of the difference or change scores between preoperative and 1 year postoperative measurements were also obtained.

For the questionnaire (second study objective), the number of subjects with available data decreased with follow-up time. Missing responses on questionnaire items were replaced if, for a patient, the amount of missing values was ≤50% for a subscale. In case of >50% missing values, the subject was excluded from further analysis of that particular subscale. Multiple imputation (MI) was used to generate 40 datasets. These datasets were then analyzed separately, and finally a single (pooled) MI estimate and its standard error were calculated by combining the estimates and standard errors obtained from each completed dataset using “Rubin’s rules” (Little & Rubin, 2002; Rubin, 1987). The imputation method was determined by the “automatic” method in SPSS multiple imputation. Multilevel linear regression analyses with a compound symmetry covariance structure were performed to assess the course of the subscale sum scores and total sum score of the questionnaire over the different time periods. In case of multiple comparisons, p-values were again Bonferroni-Holm corrected, with alpha ≤.05 being considered statistically significant.

To evaluate the relation between results on the questionnaire and speech performance tests (third study aim), Spearman’s correlation coefficients were calculated given the small sample size and since some variables did not display a normal distribution. Correlations were calculated between the difference scores (1 year post- vs. preoperative) on both the CNC word test and the ST-test on one side and the changes in outcome 1 year post-implantation on the total score and subscale scores of the questionnaire, on the other.

For the fourth study objective, the bivariate relations between preimplantation factors and the 1 year postoperative CNC word recognition score with CI, were first explored with simple linear regression. Multivariable regression analysis, using a backward method, was then performed with those variables that were significant in the simple linear regression analysis. During the backward regression analysis, non-significant preimplantation factors were sequentially removed (removal criterion: p <.10). In the final model there were then no more variables that met the removal criterion. The final model is presented with estimated coefficients, along with the “adjusted” R2, which is how much of the total variation in word recognition 1 year postoperative can be explained by the model, adjusted for the number of variables included. All analyses were performed using SPSS 22.0.

RESULTS

Study objective 1: changes in auditory performance

Figures 1A, B and C show the individual and mean observed scores of the 27 subjects on the word recognition, sentence recognition and ST-tests, respectively. Multilevel analysis showed a significant effect of the time of measurement for word recognition (F(4, 19.41) = 5.139, p = .005), sentence recognition (F(4, 21.89) = 4.525, p = .008) and the ST-test (F(4, 78.31) = 12.076, p < .0001). After Bonferroni-Holms’ correction, pairwise comparisons

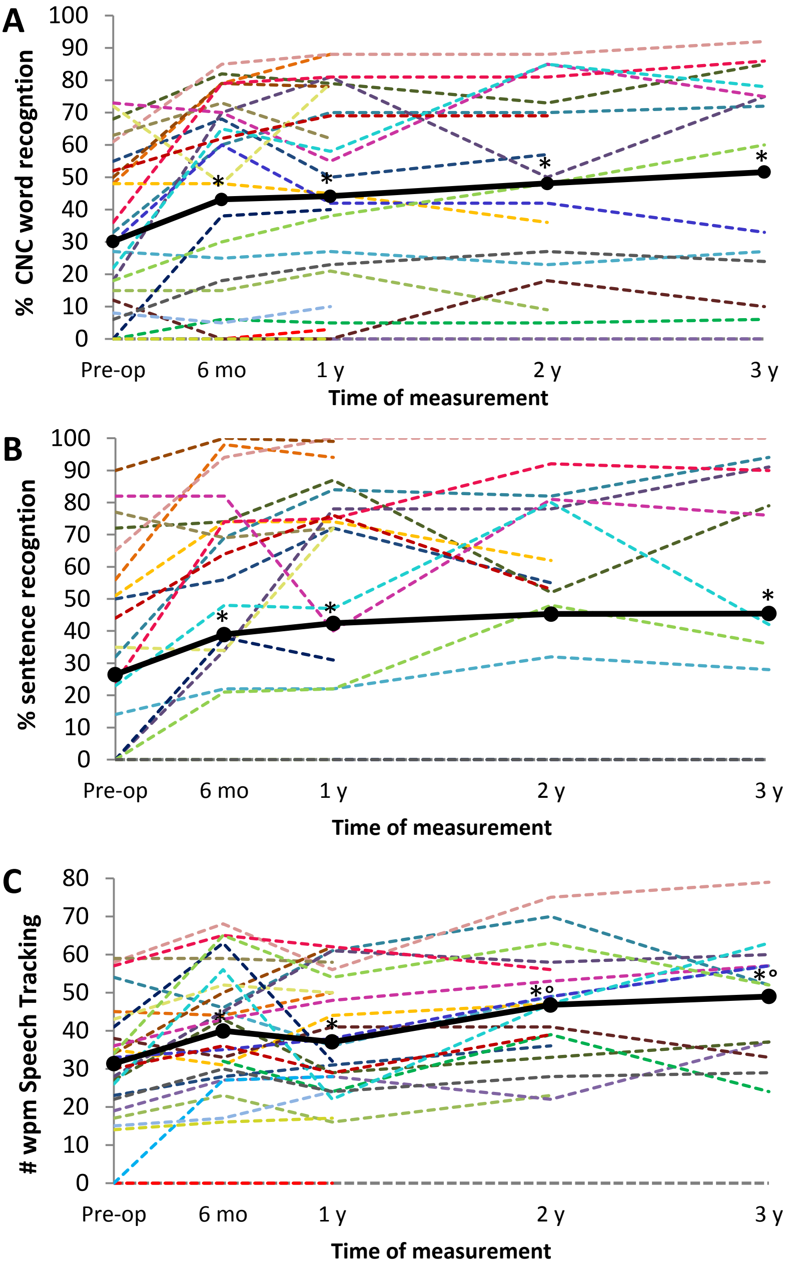


Figure 1. Individual (striped lines) and mean (thick line) observed scores on the CNC word recognition (A), sentence recognition (B) and ST-test (C) for n=27. Preoperative, 6 month, 1, 2 and 3 year postoperative observed mean scores were respectively 30.2, 43.2, 44.2, 48.1 and 51.6% for the CNC word scores (A); 26.5, 38.9, 42.4, 45.3 and 45.4% for the sentence recognition scores (B) and 31.4, 39.9, 37.0, 46.8 and 49 words per minute for the ST-test (C). For respectively 3, 10 and 1 subject(s), data points remain at 0 in figure A, B and C. Significant differences after Bonferroni-Holm's correction are indicated with * when compared to the preoperative situation and with ° when compared to the 1y postoperative situation.

revealed significantly higher scores for all postoperative measurements when compared to the preoperative situation, and this on all three tests, with the exception of the 2y postoperative measurement of the sentence recognition test (p = .07 after correction). On the ST-test, significant improvements were found 2 and 3 years postoperatively compared to the 1y postoperative situation. No further differences were found between the postoperative measurements on any of the tests.

Although postoperative improvements were found for the entire subject group, the scores of a number of subjects remained very low, for some even at 0%. Table 2 shows the preoperative and 1 year postoperative scores of the individual subjects for the different outcome measures. The changes in score from pre-op to 1y post-op were added as difference scores. Subjects whose scores remained below 30% on the open-set word recognition test are labeled "poor performers" and marked with an asterisk in both Table 1 and Table 2. The 30% criterion applied was the same as that by Arisi et al. [2010] and Caposecco et al. [2012]. If the difference score of an individual subject in Table 2 was ≤ 5% / ≤ 5 wpm, the result was considered to be stable (no change). Inspection of individual scores reveals that only five subjects (S7, S12, S13, S18 and S22) show an improvement for all three tests, i.e., open-set word recognition, sentence recognition and speech tracking. Seven more subjects (S2, S5, S6, S8, S9, S25 and S26) show an improvement on two of the three tests, and have a stable score on the third. Subject 21 showed improvement on two tests, but there was no speech tracking score available. None of these in total 13 subjects belong to the group of earlier defined "poor performers". The remaining subjects who neither show improvements on at least two out of three tests nor belong to the poor performers are S11, S17, S19 and S20. The performance of both S11 and S19 is more or less the same before and after cochlear implantation. S11 performs well, both preoperatively with two hearing aids, as well as 1 year postoperatively with hearing aid and CI. S19 displays a small improvement on postoperative word recognition, while scores for sentence recognition and speech tracking remain unchanged. For S17 and S20 we see a discrepancy in their results, with improvements on two of the three tests, but declines on the third. When looking at the poor performers (n=10), it can be seen that only S1 and S27 show an improvement on open-set word recognition, of 6 and 17% respectively. S10, on the other hand, performs 12% worse postoperatively. For the remaining poor performers (S3, S4, S14, S15, S16, S23 and S24), phoneme scores on the open-set CNC word test remain stable. Only one of the poor performers (S3) improves more than 5% on the sentence recognition test and many obtain a 0% score, due to the test not being administrable. In contrast, scores on the speech tracking and particularly the MTS test show a much greater variation, with improvements for some subjects (S3, S4, S14, S15, S16, S23 and S27) and stable results or even slight declines for others (S1, S10 and S24).

In Figure 2, as well as at the bottom of Table 2, the mean observed scores of the 10 poor performing subjects are presented. S14 was excluded from the ST-test because there was

Table 2. Individual subject scores

Subject number	Open-set word recognition (%)			Sentence recognition (%)			Speech tracking AV (#wpm)			MTS wordscore(%)			MTS suprasegmental score (%)		
	Pre-op	**1y post**	**Difference score**	**Pre-op**	**1y post**	**Difference score**	**Pre-op**	**1y post**	**Difference score**	**Pre-op**	**1y post**	**Difference score**	**Pre-op**	**1y post**	**Difference score**
1*	15	21	6	0	0	0	17	16	-1	48	52	4	88	64	-24
2	55	50	-5	50	72	22	23	31	8						
3*	27	27	0	14	22	8	28	36	8	48	92	44	88	96	8
4*	0	0	0	0	0	0	19	28	9	0	4	4	0	56	56
5	68	79	11	72	87	15	27	29	2						
6	48	88	40	56	94	38	45	50	5						
7	33	70	37	32	84	52	54	61	7						
8	61	88	27	65	100	35	58	56	-2						
9	48	45	-3	51	74	23	35	44	9						
10*	12	0	-12	0	0	0	38	41	3	32	12	-20	56	52	-4
11	63	62	-1	77	72	-5	59	58	-1						
12	18	81	63	0	78	78	28	61	33						
13	50	78	28	90	99	9	34	62	28						
14*	0	5	5	0	0	0	/	24	/	0	16	16	0	56	56
15*	0	3	3	0	0	0	0	0	0	0	8	8	16	48	32
16*	0	0	0	0	0	0	0	28	28	0	28	28	0	64	64
17	73	55	18	82	40	-42	36	48	12						
18	72	79	7	35	72	37	43	50	7						
19	30	42	12	0	0	0	33	38	5						
20	0	40	40	0	31	31	41	32	-9						
21	36	81	45	24	75	51	57	/	/						

Table 2. *Continued*

Subject number	**Open-set word recognition (%)**			**Sentence recognition (%)**			**Speech tracking AV (#wpm)**			**MTS wordscore(%)**			**MTS suprasegmental score (%)**		
	Pre-op	**1y post**	**Difference score**	**Pre-op**	**1y post**	**Difference score**	**Pre-op**	**1y post**	**Difference score**	**Pre-op**	**1y post**	**Difference score**	**Pre-op**	**1y post**	Difference score
22	18	38	20	0	22	22	34	54	20						
23*	8	10	2	0	0	0	15	24	9	24	32	8	48	68	20
24*	0	0	0	0	0	0	14	17	3	48	40	-8	68	68	0
25	22	58	36	23	47	24	26	22	-4						
26	52	69	17	44	76	32	30	29	-1						
27*	6	23	17	0	0	0	22	24	2	8	68	60	20	92	*72*
Mean of all subjects	**30,2**	**44,2**		**26,5**	**42,4**		**31,4**	**37,0**							
Mean of bad perfor-mers	**6,8**	**8,9**		**1,4**	**2,2**		**17**	**23,8**		**20,8**	**35,2**		**38,4**	**66,4**	

Preoperative and 1 year postoperative scores are presented, as well as the difference score between both evaluation moments. Mean scores are given for all subjects and for the subgroup of bad performers (n=10, indicated with * behind the subject number). (AV = Auditory-Visual condition, #wpm = number of words per minute, MTS = Monosyllable Trochee Spondee)

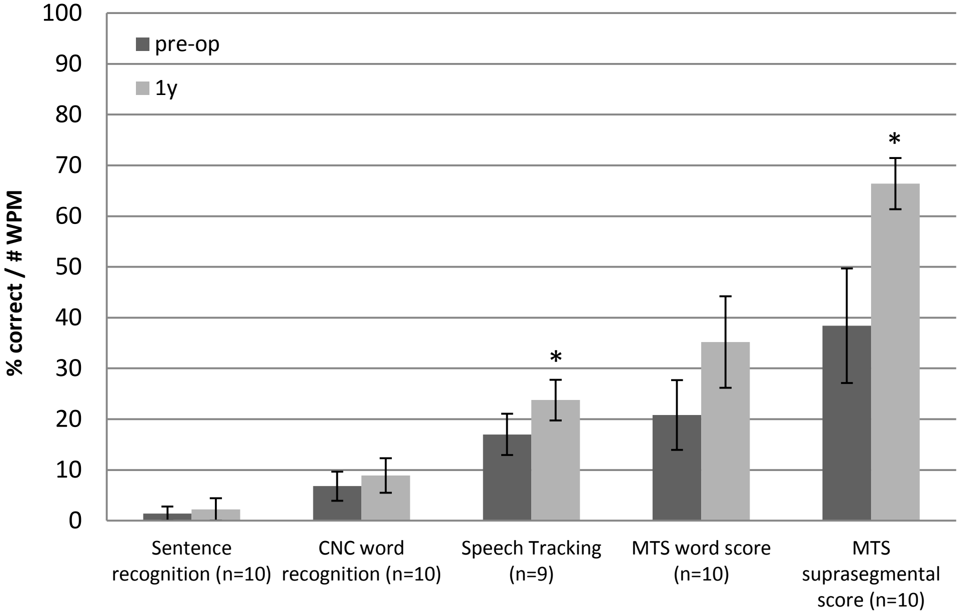


Figure 2. Preoperative and 1 year postoperative results of the poor performing group. Error bars represent the standard error of the mean. Asterisks (*) indicate a significant difference compared to the preoperative situation.

no preoperative measurement. A statistically significant improvement from a mean pre-op score of 38.4 to a mean post-op score of 66.4% was found for the suprasegmental score on the MTS-test (p = .038). For the word score on the MTS-test, the improvement from a mean pre-op score of 20.8% to 35.2% post-op was non-significant (p = .092). On the ST-test, a small but significant improvement from a mean of 17 wpm pre-op to a mean of 23.8 wpm post-op (p = .017) was seen. There was no improvement in the mean open-set word and sentence recognition scores after 1 year of CI use.

Study objective 2: self-perceived benefits

Questionnaire scale scores were obtained at pre- and 1 year postoperative for 16 to 20 subjects (depending on the subscale) and at 2 and 3 year postoperative for 13-14, respectively, 11 subjects (see Figure 3). Multilevel analysis found significant improvements at 1y postoperative compared to preoperative for the total questionnaire score and each of the separate subscales except for “social aspects of hearing”. The largest mean improvements were seen for primary sound processing (from 47.4% pre-op to 69.4% 1y post) and sense of safety (from 40.8% pre-op to 62.4% 1y post); the total score improved from 53.2% preoperatively to 63.9% 1 year postoperatively. On the long term, scores remained significantly higher than preoperatively for the total questionnaire and for the subscales "primary sound processing" and "ease of communication". This was not the case for "self-confidence" (at 2 and 3y post-op) and "sense of safety" (at 3y post-op). Total

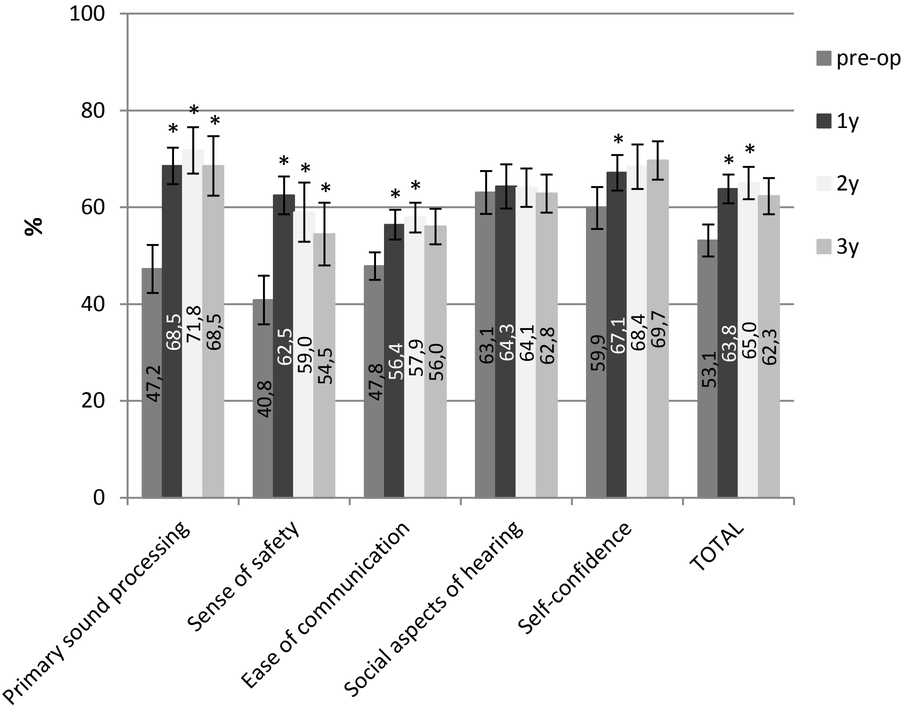


Figure 3. Mean observed scores (expressed in %) on the questionnaire for the 5 separate subscales and the total questionnaire. Error bars represent the standard error of the mean. N is 16 to 20 for the pre-op and 1y post-op measurement, 13 to 14 for the 2y post-op measurement and 11 for the 3y post-op measurement. Asterisks (*) indicate a significant difference after Bonferroni-Holms' correction, compared to the preoperative situation.

questionnaire scores were available for five of the 10 poor performing subjects and showed a significant improvement of almost 11% 1 year post-op (z=-2.023, p = .043).

Study objective 3: relations between auditory and self-perceived benefits

Correlation analyses of the changes in auditory performance with the changes on the questionnaire 1 year postoperatively, revealed very weak to weak, nonsignificant correlations. Spearman correlations between the questionnaire (subscales and total questionnaire) and the difference scores on open-set word recognition are positive and range between .09 and .38 (n=16 to 20); correlations between difference scores on the questionnaire and ST performance are close to zero (range: -.08 and .12, n=14 to 20).

Study objective 4: predictive value of preimplantation factors on speech recognition scores

Simple regression analysis indicated that six of the eight preimplantation factors were significant predictors for the 1 year postoperative CNC word recognition scores (left side of Table 3). Inclusion of these six factors as independent variables in a backward

Table 3. Regression analyses

	Simple regression			
	B	**SE B**	**β**	***p***
Pre-op PTA (better ear)	-1.396	0.368	-0.605	*.000*
Pre-op PTA (implanted ear)	-2.145	0.379	-0.750	*.000*
Pre-op CNC word recognition (best-aided)	0.759	0.162	0.685	*.000*
Pre-op CNC word recognition (implanted ear)	0.828	0.205	0.629	*.000*
Hearing aid use at implantation: yes/no	-38.957	13.416	-0.502	*.004*
Hearing aid use at implantation (implanted ear): yes/no	-37.278	9.006	-0.638	*.000*
Pre vs. perilingual onset of deafness	3.945	14.167	0.056	*.391*
Communication mode at implantation: Oral vs. Oral + manual	-18.026	11.519	-0.299	*.065*
	Multivariable regression			
	B	**SE B**	**β**	***p***
Pre-op PTA (better ear)	NS			
Pre-op PTA (implanted ear)	-1.670	0.382	-0.584	*.000*
Pre-op CNC word recognition (best-aided)	NS			
Pre-op CNC word recognition (implanted ear)	0.472	0.176	0.359	*.013*
Hearing aid use at implantation: yes/no	NS			
Hearing aid use at implantation (implanted ear): yes/no	NS			

Values for the unstandardized regression coefficient (B), standard error (SE) of B, standardized regression coefficient Beta (β) and the significance values *p* are given for the regression of CNC word recognition score with CI only, 1y post implantation, on 8 investigated preimplantation factors. For the simple regression the standardized coefficients β represent the correlations between the preimplantation factors and the outcome variable. For the multivariable regression, two preimplantation factors remained as significant predictors in the final model after backward analysis. The adjusted R^2 for the final model was .635. (PTA= Pure Tone Average at 0,5;1;2 kHz, NS = Not Signficant), n=27

regression procedure resulted in a model including preoperative PTA (*p*< .0001) and preoperative CNC word recognition score (*p*= .013), both for the implanted ear, as predictors of the CNC word recognition score with CI 1 year postoperative (right side of Table 3) with an explained variation of 63.5%. The backward analyses performed are presented in Appendix C.

DISCUSSION

Study objective 1: changes in auditory performance

The first aim of this study was to evaluate the postoperative change in auditory performance of a group of early-deafened, late implanted adult CI users by means of both traditional (open-set word and sentence recognition) and non-traditional (speech tracking (ST) and the monosyllable-trochee-spondee test (MTS)) tests, administered in the best-aided condition. A limitation concerning both the sentence recognition and ST-test, is that they are not validated. Results of the multilevel analysis showed a significant effect of the time of measurement for all three tests. Due to the relatively small number of subjects, which moreover decreased with follow-up time, these results do need to be interpreted with caution. Compared to the pre-operative situation, significant improvements were present already after 6 months of CI use. The only exception was the 2 year postoperative measurement of the sentence recognition test, which lost its statistical significance after correction for multiple comparisons. Since no drop in performance was observed 2 year postoperatively (see Figure 1B), this lack of statistical significance might be explained by the reduction in statistical power due to a smaller sample size for that measurement. The fact that the change 3 years postoperatively once again attained statistical significance, even though the observed score remained the same with an even smaller sample size, is presumably due to the higher estimation of the mean, as predicted by the multilevel model. The mean word recognition scores of 44.1% (range 0-88%) and mean sentence recognition scores of 42.4% (range 0-100%) at the 1 year postoperative measurement are comparable to those found in other studies, although it is unclear for some of these studies whether the reported scores were obtained with CI only or in the best aided condition (Caposecco et al., 2012; Klop et al., 2007; Santarelli et al., 2008; van Dijkhuizen et al., 2011; Yang et al., 2011; Zeitler et al., 2012). Consistent with literature, we found extremely large differences between individual word and sentence recognition scores (see Figures 1A and 1B).

Until now, there has been no literature reporting speech tracking for this patient group. Besides being administered in the best-aided condition, the ST-test was performed with the aid of visual cues, bringing it more in line with everyday life communication. Although the absolute improvements were small for most subjects, the improvement was significant at the group level. Given that most of the subjects in this study were excellent lip readers, these apparently small changes are most likely explained by the fact that the added value of the CI becomes apparent in conjunction with the best communicative situation (e.g. lip reading). Results therefore show that it can be demonstrated that cochlear implantation can improve communication speed, when measured in a test situation that is as close to real life communication as possible.

Another part of our first study objective was to see how performance on various tests evolved in the course of time. It is clear from Figure 1 that the largest changes occurred from pre-op to 6 months post-op, for all three tests. No significant improvements were found thereafter, except for 2y and 3y post-op versus 1y post-op on the ST-test (fig. 1C), although these may be attributable to the small decrease in performance 1 year postoperatively. Our results therefore conform to those on postlingual adults and do not support the hypothesis purported by Santarelli et al. (2008) that prelingually deafened CI users might show improved results in the long-term due to remaining plasticity in the auditory cortical areas.

Descriptive analysis of the individual pre- and 1y postoperative scores (Table 2) show that, of the 17 subjects that obtained more than 30% open-set word recognition 1 year post implantation, 13 showed a clear improvement on at least two out of the three tests including open-set word recognition, sentence recognition and speech tracking. Two subjects (S11 and S19) scored the same before and after implantation, and two (S17 and S20) had mixed results, for which we have no explanation. On the other hand, the 10 subjects that scored below 30% word recognition 1y post-op, generally showed no improvement on open-set word or sentence recognition. One could draw the conclusion that there is no measurable auditory benefit of cochlear implantation in these subjects. However, when taking the results of the non-traditional outcome measures – speech tracking and particularly MTS – into account, new information is added which allows us to distinguish between subjects that do show a measurable benefit with their CI and those who don't. Some subjects who are considered to be unsuccessful CI users do obtain auditory benefits. While no significant improvements were found for the open-set word and sentence recognition test, the suprasegmental score on the closed-set MTS-test and the number of correctly repeated words per minute on the ST-test, did show significant improvements. Our hypothesis, that non-traditional auditory measures are more suitable than traditional open-set, auditory-only speech tests to detect true auditory gains in poor performing subjects, is thus confirmed. It can be therefore be advised to gear the choice of speech tests to the performance level of the subject, considering both standard and less traditional tests for an optimal monitoring of outcomes.

It is interesting to note that all four subjects who did not wear hearing aids preoperatively, belong to the poor performing group. These subjects did wear hearing aids during childhood but stopped wearing them as adolescents, presumably due to limited benefit. However, if we further compare the characteristics of those poor performing subjects that show no postoperative improvement on any of the tests with those that do, there are no clear differences to be found in terms of communication mode, age at implantation or hearing aid use.

Study objective 2: self-perceived benefits

Subjective experience after CI should be an integral part of the evaluation protocol. A limitation of the questionnaire used in this study, which was specifically designed for the early-deafened group of CI users, is of course the lack of sufficient validation. Results on the questionnaire revealed that subjective scores were significantly higher post-implantation for the subscales "primary sound processing", "sense of safety" and "ease of communication". Other studies that assessed hearing-related quality of life before and after implantation in this patient group also found significant postoperative improvements when using the NCIQ (Klop et al., 2007; Straatman et al., 2014; van Dijkhuizen et al., 2011), PIPSL (Schramm et al., 2002) or a number of self-reporting questionnaires (Most et al., 2010). In our study there was no effect of the CI on the subscale "social aspects of hearing", and the effect on "self-confidence" was only significant at 1y post-op. The subscale "social aspects of hearing" contains questions like "Do you like to go to parties or meetings?" and "How often do you feel left out by others?". A likely explanation for the absence of a significant change in this subscale may be the early onset of deafness. The subjects in this study had been participating in social situations with a severe hearing impairment for their entire lives, which is also illustrated by the relatively high pre-op scores in this subscale so that noticeable changes in this area are unlikely. The same reasoning may explain the slight changes found in the subscale “self-confidence”. Other studies failed to find significant postoperative improvements for subscales related to self-confidence or self-esteem (Klop et al., 2007; Most et al., 2010), or found slightly smaller changes (Straatman et al., 2014). Although it is hard to compare the content of the different questionnaires, it makes sense that the subscale “self-esteem” of the NCIQ also encompasses questions that are related to the subscale “social aspects of hearing” of the current study.

Study objective 3: relations between auditory and self-perceived benefits

Auditory gains on either CNC word recognition or speech tracking did not appear to be related to benefit scores on the questionnaire. This might in part be attributable to the fact that there were significant improvements in the questionnaire scores for the subgroup of poor performers. Our results are in agreement with Straatman et al. (2014), although van Dijkhuizen et al. (2011) did find some significant correlations, but only with the subscale “advanced sound perception” of the NCIQ. This appears to indicate that in early-deafened CI users, quality of life benefit scores are generally independent of auditory gains. When judging whether an implantation is successful, both types of outcome measures should thus be taken into account, since they evaluate distinctly different aspects of cochlear implantation rehabilitation. A so-called “poor” performer might experience subjective benefits without improvement on open-set speech tests. Also, the fact that a correlation with the advancements on the speech tracking test was not found, which – in contrast to the open-set word test - did show postoperative benefits even in the poor performing group, suggests that self-perceived changes are not related to the improvements in day-to-day communication skills. It would be interesting to investigate further the relation between subjective outcomes and, for instance, the MTS-test in a larger group of poor performers.

Study objective 4: predictive value of preimplantation factors on speech recognition scores

Two of the eight investigated preimplantation factors remained in the final multiple regression model: the preoperative CNC word recognition score and the preoperative PTA, both for the implanted ear, together explaining 63.5% of the variation in postoperative speech understanding with CI. This result needs to be interpreted with caution however, given that the regression analyses were based on data of only 27 subjects. Two recent studies also performed multiple regression analysis in groups of respectively 58 and 43 early-deafened subjects (Kraaijenga et al., 2016; Rousset et al., 2016). In the study by Kraaijenga et al. (2016), the preoperative best-aided word recognition score, and not the score of the ear to be implanted as in our study, was found to be the only significant predictor of the 1y post-op word recognition scores, and explained 31% of the variation. In that same study, the preoperative PTA of the CI-ear, which was the second significant factor in our model, correlated significantly with the outcome variable but lost its significance in the subsequent multivariable analysis. In the study by Rousset et al. (2016), the preoperative phoneme score of the ear to be implanted could, together with a standard score for receptive language abilities, account for 26.3% of the variation in postoperative speech perception scores. In their study, the PTA of the implanted ear, however, did not have a significant correlation with the outcome measure. Given that the word recognition score of the implanted ear was a significant predictor in both Rousset et al. (2016) as in the current study, it seems worthwhile to include this factor in future studies.

While only two preimplantation factors remained as significant predictors in our final model, there were four more preimplantation factors correlating significantly with the outcome measure: preoperative best-aided CNC word recognition, preoperative PTA of the better ear, hearing aid use at implantation (yes/no) and hearing aid use at implantation in the implanted ear (yes/no). As mentioned previously, the preoperative best-aided word recognition score was a significant predictor in the multivariable regression model of Kraaijenga et al. (2016). van der Marel et al. (2015) equally observed a significant correlation with preoperative phoneme scores. On the other hand, van Dijkhuizen et al. (2016) (after Bonferroni correction) and Zeitler et al. (2012) did not find a significant correlation with preoperative CNC scores. Similarly to the preoperative CNC scores, our study found the preoperative PTA of the implanted ear to be a significant predictor, whereas the significant correlation of the preoperative PTA of the better ear was dropped in the backward multiple regression modeling procedure. Both preimplantation factors regarding hearing aid use at implantation, were also dropped in the backward procedure. In 2012, Caposecco et al. found that the time without an aid in the implant ear (at implantation) was a significant predictor, while van Dijkhuizen et al. (2016) found no significant correlation between postoperative speech perception and hearing aid use.

Finally, two of the eight preimplantation factors did not show a significant correlation with our outcome measure: communication mode at implantation and pre- vs. perilingual onset of deafness. The first is somewhat surprising, given that advantages for oral communicators are seen in most (Caposecco et al., 2012; Rousset et al., 2016; Yang et al., 2011; Zeitler et al., 2012), yet not all previous studies (van Dijkhuizen et al., 2016). The factor regarding pre- vs. perilingual onset of deafness has only been assessed by Caposecco et al. (2012). In contrast to our results, this study did find a significant relation between the progressivity of the hearing loss and sentence recognition scores with CI.

CONCLUSION

This study showed that early-deafened but late implanted adult CI users obtained significant auditory improvements, mainly within the first six months after implantation. It was found that, on average, auditory performance of poor performing subjects increases but this can only be captured by using specific tests like speech tracking or tests assessing more suprasegmental features of speech. On an individual subject level, these new outcome measures add valuable information and allow for more differentiation between poor performing subjects. The current results emphasize the importance of using a different test battery for the auditory evaluation of this group of CI users.

An instrument assessing subjective experiences after CI should be an integral component of the evaluation protocol, given that individually experienced benefit is not fully captured by the auditory tests.

Postoperative performance with CI could be explained to a large part by two preimplantation factors: preoperative PTA and preoperative CNC word recognition, both of the implanted ear. Studies in larger groups of early-deafened patients could contribute further to understanding the role that preimplantation factors have on CI outcome in this population.

APPENDIX A: Reliability analysis of the subjective questionnaire

As a first step in the development of the questionnaire used in this study, structured interviews using open questions were performed with a number of early-deafened CI users, to identify the domains on which these CI users experienced changes after their implantation. These findings were used to formulate questions covering aspects of hearing and communication, social and psychological functioning. Questions were intuitively divided in five subscales: primary sound processing, sense of safety, ease of communication, social aspects of hearing and self-confidence. The original questionnaire contained 55 questions, with a 5-point Likert response scale for each question. For computation of the scores on the questions, the answer categories were transformed, with never/not at all = 0, occasionally/somewhat = 25, regularly/more or less = 50, usually/for the most part = 75 and always/completely = 100. For 20 questions which were phrased in opposite form (questions number 3, 4, 5, 8, 9, 14, 15, 16, 18, 25, 27, 29, 31, 36, 37, 40, 43, 44, 45, 47), the transformation was reversed.

The results of the 20 subjects that completed the questionnaire 1 year postoperatively were used to perform a reliability analysis. First, three questions which had more than 15% missing values (left blank or “not applicable”), were considered not to be relevant for this patient population and were left out in further analysis. Subjects that had missing values for more than 25% of the questions in a certain subscale were equally excluded from the reliability analysis of that particular subscale. Remaining missing values were imputed 40 times for each subscale, using multiple imputation, presupposing the missing mechanism is Missing At Random (MAR), which means that the probability of an observation being missing does not depend on unobserved measurements. Cronbach’s alpha was calculated for each of the 40 imputed datasets. Questions that, if left out, increased the average Cronbach’s alpha over the 40 data sets by at least .02, were excluded from that subscale of the questionnaire. This resulted in a final questionnaire containing 50 questions in five subscales: primary sound processing (8 questions), sense of safety (5 questions), ease of communication (12 questions), social aspects of hearing (12 questions) and self-confidence (14 questions). Values of Cronbach’s alpha were .83, .57, .77, .92 and .86 respectively. The final questionnaire can be found in Appendix B.

APPENDIX B: Subjective questionnaire for early-deafened CI users (translated from Dutch by a native English speaker)

		Never	Occasionally	Regularly	Usually	Always	N/A
1.	Can you hear soft sounds (such as running water, twittering birds, the clock ticking) in quiet surroundings?	☐	☐	☐	☐	☐	☐
2.	Is it easy for you to express your own opinion?	☐	☐	☐	☐	☐	☐
3.	Do you have to concentrate to follow a conversation?	☐	☐	☐	☐	☐	☐
4.	Do you feel ignored by others?	☐	☐	☐	☐	☐	☐
5.	Are you sometimes relieved when a conversation is over?	☐	☐	☐	☐	☐	☐
6.	Can you recognize everyday sounds in your home?	☐	☐	☐	☐	☐	☐
7.	Do you like to go to parties or meetings?	☐	☐	☐	☐	☐	☐
8.	Do you feel like you are worth less than other people?	☐	☐	☐	☐	☐	☐
9.	Do you sometimes need to have things repeated in a conversation?	☐	☐	☐	☐	☐	☐
10.	Are you happy about the things you can do and what you actually do?	☐	☐	☐	☐	☐	☐
11.	Can you hear the phone ringing in the same room?	☐	☐	☐	☐	☐	☐
12.	Are colleagues and acquaintances considerate towards you?	☐	☐	☐	☐	☐	☐

	Never	Occasionally	Regularly	Usually	Always	N/A
13. Are strangers able to understand what you are saying?	☐	☐	☐	☐	☐	☐
14. Are you nervous when you need to speak in a group?	☐	☐	☐	☐	☐	☐
15. How often do you feel alone?	☐	☐	☐	☐	☐	☐
16. Do conversations sometimes end soon because they are tiresome?	☐	☐	☐	☐	☐	☐
17. Can you hear cars and motorbikes approaching when you are outside?	☐	☐	☐	☐	☐	☐
18. Are you embarrassed by your hearing problems?	☐	☐	☐	☐	☐	☐
19. Are you at ease in a group?	☐	☐	☐	☐	☐	☐
20. Can you hear the difference between clinking silverware and clapping hands?	☐	☐	☐	☐	☐	☐
21. Are you able to perform your daily chores/work?	☐	☐	☐	☐	☐	☐
22. Is it easy for you to initiate a conversation with someone you do not know well?	☐	☐	☐	☐	☐	☐
23. Can you hear the doorbell?	☐	☐	☐	☐	☐	☐
24. Is it easy for you to meet new people?	☐	☐	☐	☐	☐	☐
25. Do you try to hide your hearing problems?	☐	☐	☐	☐	☐	☐
26. Can you hear the difference between the voice of a man and a child?	☐	☐	☐	☐	☐	☐

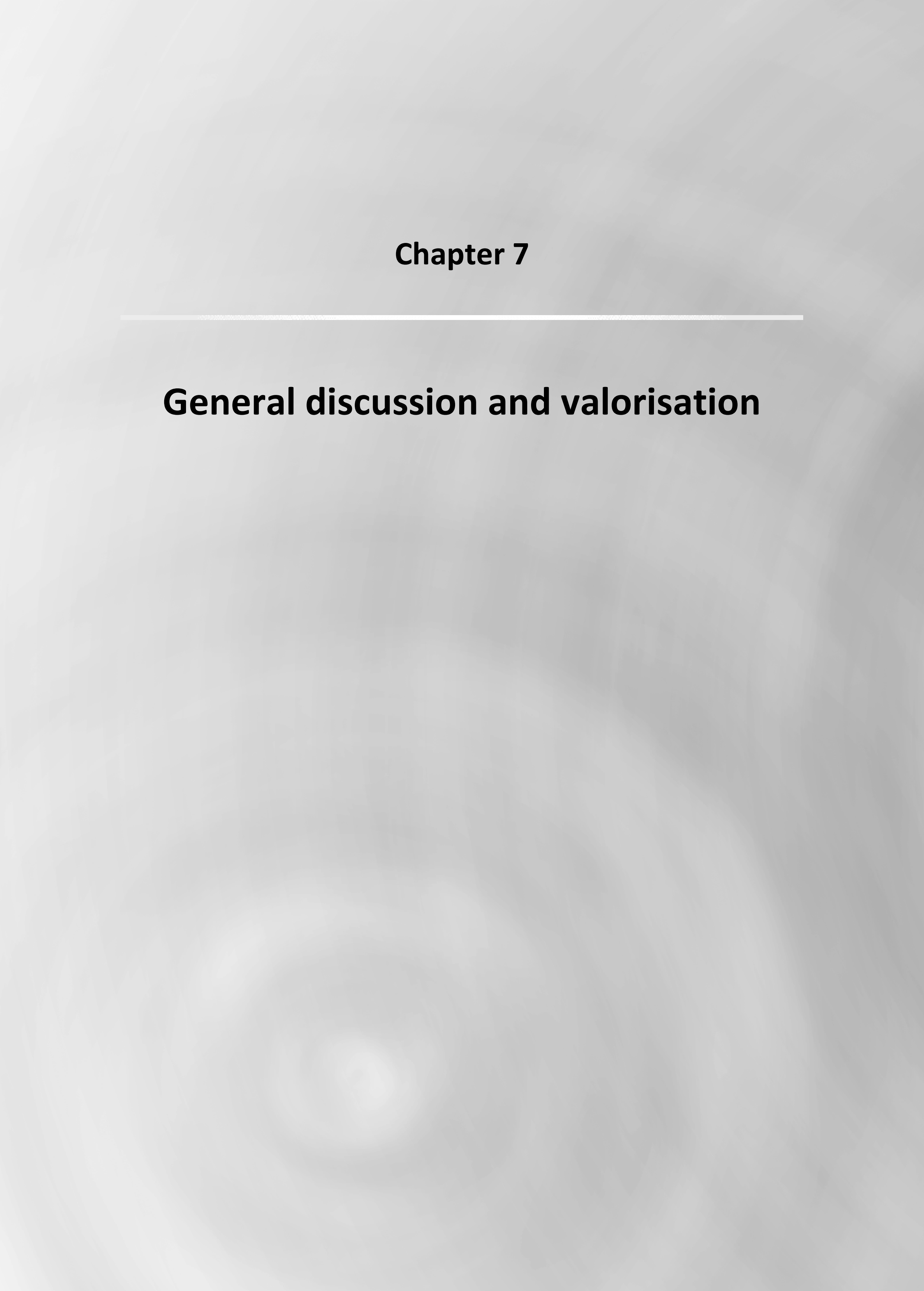
		Never	Occasionally	Regularly	Usually	Always	N/A
27.	How often do you feel depressed?	☐	☐	☐	☐	☐	☐
28.	Do you like being in a group of people?	☐	☐	☐	☐	☐	☐
29.	Do misunderstandings sometimes occur during conversation?	☐	☐	☐	☐	☐	☐
30.	Can you hear someone calling your name from another room?	☐	☐	☐	☐	☐	☐
31.	Does it bother you that you are deaf/hearing impaired?	☐	☐	☐	☐	☐	☐
32.	Do friends and family show consideration for you?	☐	☐	☐	☐	☐	☐
33.	Can you recognize the voice of someone you know well in a quiet room?	☐	☐	☐	☐	☐	☐
34.	Do you think you are successful?	☐	☐	☐	☐	☐	☐
35.	Can you hear the voice of the person next to you in a quiet room?	☐	☐	☐	☐	☐	☐
36.	Is it embarrassing for you to have to say something in a group?	☐	☐	☐	☐	☐	☐
37.	How often are you tense or tired at the end of the day?	☐	☐	☐	☐	☐	☐
38.	Do you think your opinion is important?	☐	☐	☐	☐	☐	☐
39.	Can you hear the difference between music and the news on the radio?	☐	☐	☐	☐	☐	☐
40.	How often do you feel stressful?	☐	☐	☐	☐	☐	☐

	Never	Occasionally	Regularly	Usually	Always	N/A
41. Can you hear someone calling your name in a quiet room?	☐	☐	☐	☐	☐	☐
42. Do you like to talk to others?	☐	☐	☐	☐	☐	☐
43. Are you worried that others cannot understand you?	☐	☐	☐	☐	☐	☐
44. How often do you feel left out by others?	☐	☐	☐	☐	☐	☐
45. Do you need to read lips to understand someone?	☐	☐	☐	☐	☐	☐
46. Can you hear whether a car is far away or close by?	☐	☐	☐	☐	☐	☐
47. Does it bother you when you cannot understand someone?	☐	☐	☐	☐	☐	☐
48. Can you hear loud sounds (such as traffic, a dog barking, door slamming,…)?	☐	☐	☐	☐	☐	☐
! The answer categories of the following 2 questions are different!	Not at all	Somewhat	More or less	For the most part	Completely	N/A
49. You are talking to one person in a <u>quiet</u> room. You can see that person's lips. Can you understand this person?	☐	☐	☐	☐	☐	☐
50. You are talking to one person at a party or meeting (<u>busy</u> surroundings). You can see that person's lips. Can you understand this person?	☐	☐	☐	☐	☐	☐

APPENDIX C: Overview of the backward multivariable regression analysis

Preimplantation factors	**B**	**SE B**	**β**	***p***
Model 1				
Pre-op PTA (better ear)	-0.535	0.709	-0.232	*.460*
Pre-op PTA (implanted ear)	-0.982	0.934	-0.343	*.305*
Pre-op CNC word recognition (best-aided)	-0.129	0.318	-0.116	*.690*
Pre-op CNC word recognition (implanted ear)	0.561	0.308	0.426	*.084*
Hearing aid use at implantation: yes/no	-10.022	13.150	-0.129	*.455*
Hearing aid use at implantation (implanted ear): yes/no	-3.423	12.113	-0.059	*.780*
Model 2				
Pre-op PTA (better ear)	-0.564	0.686	-0.244	*.420*
Pre-op PTA (implanted ear)	-1.052	0.880	-0.368	*.245*
Pre-op CNC word recognition (best-aided)	-0.165	0.285	-0.148	*.570*
Pre-op CNC word recognition (implanted ear)	0.604	0.263	0.459	*.032*
Hearing aid use at implantation: yes/no	-11.831	11.231	-0.153	*.304*
Model 3				
Pre-op PTA (better ear)	-0.399	0.614	-0.173	*.522*
Pre-op PTA (implanted ear)	-1.019	0.865	-0.356	*.251*
Pre-op CNC word recognition (implanted ear)	0.509	0.202	0.387	*.020*
Hearing aid use at implantation: yes/no	-10.411	10.792	-0.134	*.345*
Model 4				
Pre-op PTA (implanted ear)	-1.508	0.418	-0.527	.001
Pre-op CNC word recognition (implanted ear)	0.449	0.178	0.341	.019
Hearing aid use at implantation: yes/no	-10.203	10.651	-0.132	.348
Model 5				
Pre-op PTA (implanted ear)	-1.670	0.382	-0.584	.000
Pre-op CNC word recognition (implanted ear)	0.472	0.176	0.359	.013

Adjusted R^2=.595 for Model 1, .613 for Model 2, .625 for Model 3, .634 for Model 4 and .635 for Model 5 (= final model)



Chapter 7

General discussion and valorisation

The aim of the current thesis was to expand current knowledge regarding cochlear implantation in a very specific patient group: adults or adolescents with an onset of deafness in early childhood. In the different chapters of this thesis we presented data on the outcomes of this patient group with CI and on the factors that might influence these outcomes, either patient-related or related to the fitting and coding of the electrical signal.

Defining the target group

One of the difficulties we came across in the course of this thesis was how to define and demarcate our specific target group of patients. In the different chapters they are referred to as congenitally, prelingually, perilingually, as well as early-deaf(ened) patients. Where the first three terms each refer to a different age at onset, “early” is a more comprehensive term, generally referring to any age at onset before the end of the language acquisition period. Although the term “prelingual deafness” has been used quite broadly in literature to indicate an onset before the age of 4 or even 6 years (Santarelli et al., 2008; Teoh et al., 2004a; van Dijkhuizen et al., 2016), and has also been used in that sense in *chapters 2 and 3* of this thesis, it is actually defined as an onset before the beginning of the language acquisition period.

The differentiation of patients based on age at onset is important, as it is presumed that even minimal auditory exposure affects auditory development compared to no auditory exposure at all (Kral, 2007), but at the same time it is practically unfeasible as the medical and audiological information required to make such a differentiation is usually lacking, especially in patients born before the introduction of new born hearing screening. Even the clinical classification of a patient as “early” deaf, the term we adopted in *chapters 4, 5 and 6*, is mostly based on the combined information obtained from a number of sources such as available medical files and audiograms from the past, presence of deaf speech, type of education received, and recall of family members on the onset of the hearing impairment.

An important aspect adding further variability to our target group is that not only the age, but also the degree and configuration of the hearing loss are often unknown for patients born several decades ago. Taken together, our target group of early-deafened patients is necessarily diverse, the use of strict definitions being unfeasible, primarily due to the lack of sufficient information on the hearing history of many patients.

From another angle, the demarcation of our target group is equally determined by the age at which cochlear implantation is performed. The main issue is whether subjects implanted as adolescents or adults, with a comparable onset of deafness, can be seen as one group or not. From what implantation age onwards is it reasonable to say that the influence of the early onset of the hearing impairment outweighs the influence of the age at implantation? Is there for example a difference between early-deafened subjects implanted at age 12 vs. 25, based on their age at implantation? In the review in *chapter 5*, we concluded that age at implantation is very likely not related to CI outcomes in adults with early onset of deafness, whereas in adolescents this relation does need further investigation. This implies that, until this is further clarified, the better option would be to separately analyse outcomes of early-deafened adolescents and adults if the aim is to see how these subjects perform as a group. This is also the case in *chapters 2, 3 and 6* of this thesis, where all subjects were implanted after the age of 18 years. On the other hand, based on evidence from N1 and P1 potentials, Sharma et al. (2015) showed that “in all likelihood, the sensitive period ends by age 7 years, resulting in a re-organized auditory cortex that is unable to effectively process the stimulation provided by the cochlear implant”. The reasons why the outcome of CI would be different for adolescents and adults, as sensitive periods are closed in both cases, is an additional question that would then have to be addressed. Potentially other factors such as education and early hearing aid rehabilitation could explain the difference, rather than the younger age itself.

Optimizing fitting parameters

C*hapters 2 and 3* of this thesis revolve around how technical aspects of cochlear implant signal processing, such as fitting parameters and properties of the CI signal, might affect outcomes in our target group of CI users. Current cochlear implant processing generally employs a “one size fits all” approach with respect to most fitting parameters, such as stimulation rate, number of stimulated electrodes, frequency allocation, etc. Although these default settings work well for most postlingual CI users, they are not necessarily optimal for early-deafened CI users who have developed a completely different auditory system due to their early onset of auditory deprivation. We therefore hypothesized that a more individualised approach towards fitting could improve performance, with psychophysical measures of certain signal processing aspects being used to change fitting parameters.

In *chapter 2* we measured amplitude modulation detection thresholds (AMDTs) to assess temporal processing abilities of both pre- and postlingually deafened CI users. This method is commonly used since the CI processor equally applies amplitude modulations to the envelope of the fast electrical pulse trains that are delivered to the electrodes. We were able to demonstrate that the amplitude modulation detection abilities of the early-deafened group were significantly poorer than those of the postlingually deafened group, especially for fast modulations. In addition, AMDTs were significantly correlated with speech recognition measures, also for the early-deafened subjects. If this relation were to be a causal one, a better detection of amplitude variations over time could potentially lead to better speech understanding. Consequently, it would be interesting to investigate whether improving the transmission of these temporal cues by means of changes to the speech processing strategy, could lead to improved speech recognition. So far, however, research efforts focusing on the effects of changing stimulation rate and/or stimulation level, which both influence the transmission of temporal cues, have not been successful at finding consistent and significant improvements on temporal or speech processing abilities (overview in Brochier, McDermott, and McKay (2017)). Since these studies are generally performed in postlingually deafened CI users, and we found that temporal processing was significantly poorer for the average early-deafened CI user, it would be interesting for future studies to investigate these relations specifically in an early-deafened subject group. In addition, as our study showed that the ability to detect slow modulations was related to speech understanding performance in this group, those subjects having most difficulty detecting these slow modulations are also the ones for which it would be most interesting to investigate the effect of changing these parameters.

Where *chapter 2* focuses on the processing of temporal cues, *chapter 3* gives attention to the coding of spectral parameters, related to the place of stimulation. In *chapter 3* we first measured spectral processing through the ability to perform electrode discrimination, and then attempted to optimize the processing of spectral cues by means of deactivating all non-discriminable electrodes. A clear advantage of the adapted fitting on outcomes could not be found, however. In addition to the limited number of subjects, the influence of a number of other parameters that were changed along with the deactivation of electrodes could not be ruled out, and gives rise to further investigation.

In *chapter 3*, the limited number of subjects unfortunately did not allow for an investigation of the relation between spectral discrimination performance and speech understanding outcomes with CI, but other studies have been able to demonstrate such a relation, also in prelingually deafened adults (Busby & Clark, 2000; Gifford et al., 2018). The presence of such a relation suggests that an optimization of the coding of spectral cues could have a positive impact on speech understanding outcomes as well. The success of studies, including our own, attempting to improve spectral resolution by means of deactivating electrodes that poorly encode speech information, is however mixed (Henshall & McKay, 2001; Saleh et al., 2013; Vickers, Degun, Canas, Stainsby, & Vanpoucke, 2016; Zwolan et al., 1997).

A recent study by Sagi and Svirsky (2018) offers new explanations for why purely removing the poorest encoding electrodes from the fitting map might not be the best solution. By means of extensive mathematical modelling, they were able to demonstrate that the main limiting factor in previous studies is the fact that the criteria used to deactivate the poorest encoding electrodes do not take the distribution of speech information over the remaining electrodes into account. Their results show that the benefit in speech recognition was significantly greater when an electrode deactivation pattern was used that maximizes the discrimination of speech cues (“model-optimized”), compared to a deactivation pattern that simply removes the poorest encoding electrodes (“best electrodes”). For the poorer performing group in this study (electrode discrimination difference limens between 0 and 4 electrodes), which is most representative for our study group of early-deafened CI users, maximum improvements were demonstrated for the model-optimized approach when 11 out of the 22 electrodes remained active.

A recurring bottleneck, both in our study (*chapter 3*) as in the model of Sagi and Svirsky (2018), is that complete adaptation to each new combination of electrodes is required in order to attain a maximal score for this combination. Presuming however, that subjects are able to completely adapt given sufficient time, these new insights demonstrate that combining a measure for identifying poorly discriminating electrodes with a model approach focusing on optimally transferring speech information, has significant potential for improving outcome. This is an interesting line of research which requires further exploration in our target group, although the time-consuming measurements might be a practical obstacle to find sufficient numbers of subjects willing to participate.

Measuring outcome: a different perspective

In *chapters 2 and 3* we focused on how technical aspects of CI processing are related to speech understanding outcomes in the group of early-deafened CI users. In *chapter 6* however, one of the aims was to explore how we should measure outcome in our target group in the first place. Traditional outcome measures for CI users mainly include open-set word and sentence recognition tests in quiet, evolving towards measures in noise as performance of the average, postlingual CI user improves, as illustrated by the recommendations of the New Minimum Speech Test Battery (MSTB) for adult cochlear implant users (Auditory Potential, 2011). This shift towards more complex outcome measures tends to forget that a significant proportion of adult CI users, especially in the early-deafened group, still struggles to obtain any open-set speech recognition benefit at all (Caposecco et al., 2012; Heywood et al., 2016; O'Gara et al., 2016; Rousset et al., 2016). In *chapter 6* our subject group of 27 early-deafened subjects obtained a mean 1 year post-operative CVC word recognition score of 44.2%, which corresponds with the range of outcomes (20-49%) of the studies reviewed in *chapter 4*. Out of the 27 subjects in our subject group, however, 7 obtained no more than 10% and 10 subjects scored less than 30% on this open-set CVC word test. This latter group of 10, the so-called “poor performers”, did show significant benefit on a closed-set measure of suprasegmental cues as well as on a measure of speech tracking, assessing the general ease of communication. Part 1 of our systematic review (*chapter 4*) equally found measures of closed-set speech understanding to be valuable and although there were no studies included that assessed speech tracking, there is a similarity with tests assessing auditory-visual communication. The latter tests showed significant benefits in almost all studies, pointing to the capability of early-deafened subjects to combine new, auditory information from the CI with visual information obtained through lip reading, thus obtaining a higher level of speech understanding. Our recommendation therefore is to substitute traditional outcome measures of speech understanding with closed-set measures and measures assessing the combination of auditory and visual information in this patient population, especially in poor performers. To this end, we are currently working on an extended validation of the (Dutch) texts used for the speech tracking test we implemented in this population, in order to improve their clinical usefulness.

In addition, it was shown in *chapter 6* that the early-deafened subject group, but also the subgroup of poor performers, showed significant benefit on the questionnaire on subjective benefit, the latter despite the absence of a significant improvement on open-set speech understanding. Very positive outcomes for hearing-related quality of life were confirmed in *chapter 4*. In general, changes in subjective experience after cochlear implantation were most clear for domains related to sound perception, sense of safety and communication, but were less obvious with respect to social life or self-esteem, which we believe might be due to the long-standing nature of the subjects' hearing impairment. The questionnaire used in *chapter 6*, which was specifically developed to be used in our target population, fulfils the need for a questionnaire that takes the particularities of this patient group into account. On the other hand, the limited number of subjects it was submitted to unfortunately did not allow for an extensive validation. This is an issue that should be further addressed prior to a wider use of the questionnaire. Finally, the lack of a strong relation between subjective benefit on one hand and speech perception outcome on the other, emphasizes that a subjective measure of outcome is indispensable in our target population to obtain a truthful assessment of outcome.

Predicting performance

The second part of the systematic review presented in *chapter 5* identified three variables as having good potential in predicting (speech understanding) outcomes in the early-deafened population; one of those, the preoperative word recognition score, was one of two remaining significant predictors in the multiple regression analysis performed on our own study group as well (*chapter 6)*. The two other variables that were identified as good predictors in *chapter 5*, i.e. preoperative speech intelligibility and communication mode in childhood, were not incorporated in our own analysis. This can mainly be attributed to a lack of data on these variables as they are not systematically assessed in our CI-candidates. Inversely the second significant predictor of our own regression analysis, pre-operative hearing thresholds of the ear to be implanted, was not clearly related to outcomes in the studies of the review; the thresholds of the better ear showed more predictive potential. The small number of subjects our multiple regression analysis was based on inevitably limits the generalizability of the observed outcomes. There is clearly a need for research in larger groups of early-deafened subjects, which at the same presents a major challenge given the relatively small proportions of early-deafened CI users implanted in most clinics. A multicentre study, as has been performed in postlingually deafened CI users (Blamey et al., 2013), could potentially provide an answer to this problem.

Apart from sample size issues, the major limitations observed in *chapter 5* which should be taken into account by future studies, were the lack of clear definitions of the included variables, as well as inappropriate statistical analysis. Attention also needs to be paid to the choice of predictors to include. Until now, the focus of most studies - including our own - has been on demographic factors concerning hearing history and the implantation itself. The combination of these factors has never been be able to explain much more than about 60% of the variation in speech understanding outcome in this population, with a great deal of variables mainly explaining the same variation (*chapter 6*, Caposecco et al., 2012; Kraaijenga et al., 2016; O'Gara et al., 2016; van Dijkhuizen et al., 2011).

Recently, Pisoni et al. (2017) suggested that the missing predictors should be sought in measures of underlying cognitive processing, at least in postlingually deaf adults. In that respect, Kral et al. (2016) suggest that the limited auditory experience during the development of early-deafened subjects not only disturbs the perception of spoken language and development of the auditory system itself, but also affects the development of neurocognitive functions such as concept formation and executive functioning, and results in altered connections between the auditory system and other brain systems. Individual variability in the development of neural circuits in response to auditory deprivation is thought to contribute to the observed variability in outcomes with a cochlear implant later on. Subjects, who are for instance better at integrating top-down information streams with the incoming auditory cues, are more likely to become better performers. These ideas can be extended to the population of late-implanted but early-deafened CI users: the extent to which these higher-order neurocognitive functions have been developed might be determined by the amount of auditory input in early childhood (which is related to the exact age at onset of deafness, the amount of residual hearing and the adequacy of early hearing aid rehabilitation), along with the aforementioned individual variability. It would thus be an interesting area for further investigations to assess if and which measures of neurocognitive functioning could be used within our target population, and whether they are valuable as predictors in multiple regression analyses.

Finally, when taking in mind that a measure for auditory-visual speech recognition is often a more relevant way to assess outcome in early-deafened CI users (*chapter 4 and 6)*, it would equally be interesting for future studies in our target population to find relevant predictors for such an auditory-visual outcome measure, instead of just focusing on auditory-only benefits. As the ability to integrate these communication modes potentially requires different skills, the relevant predictors might differ as well.

Reflecting on implantation criteria

Although cochlear implantation in patients with early-onset deafness remains controversial within the Deaf community, especially when it concerns young children (Sparrow, 2010), it was not within the scope of this thesis to go further into this debate. With respect to early-deafened adults we believe that it is a personal choice for every individual to sign up, or not, for cochlear implantation. As the technique of cochlear implantation was not yet applied on a large scale in the Netherlands until the late 90's, parents of children born deaf or severely hearing impaired before that time did not have the possibility to choose for a cochlear implant, as is the case nowadays.

The results presented in *chapters 4, 5 and 6* urge us to reflect on the implantation criteria for those early-deafened adults who are interested in increasing their access to the hearing world and are now candidates for cochlear implantation. A very interesting observation was that the evidence so far does not strongly support the notion that subjects showing large changes in hearing-related quality of life are also the ones obtaining significant speech understanding improvements. Although more research is definitely required, a strong correlation between auditory gains and subjective benefits could be found neither in our study group nor in the review. In addition, the anticipated gain in auditory-only speech understanding with CI is generally limited, whereas it was also demonstrated that when subjects are evaluated with assessment methods targeted to their level of auditory functioning, benefits often do arise, but they might be on domains other than open-set speech understanding.

Based on these observations, we suggest that implantation criteria in this population should not only look at the expected level of auditory-only speech understanding, but also include alternative domains of potential benefit including auditory-visual speech recognition and hearing-related quality of life.

Summary

Cochlear implantation has become a well-established treatment option in postlingually deafened patients, with most of them obtaining good results on traditional tests for speech recognition. When early-deafened patients receive a cochlear implant in (late) adolescence or adulthood, however, speech recognition results are often not so favorable. The added value of a CI in this patient group therefore remains unclear and subject to discussion. This is reflected by the doubts of many CI clinics whether or not to implant early-deafened, adult or adolescent CI-candidates. More knowledge of both the expected outcomes with a CI within this group, and the factors that might influence them, is therefore of great importance for candidacy decisions. This thesis addressed a number of important issues related to cochlear implantation in this very specific subject group, from factors relevant in determining pre-implant candidacy (*chapters 4, 5 and 6*), over aspects related to CI signal processing and fitting (*chapters 2 &* 3), to optimization of outcome assessment (*chapter 6*). The ultimate goal was to gain more insight into the field of cochlear implantation in the early-deafened but late-implanted patient population, in order to improve patient selection and (the assessment of) cochlear implant outcome.

The general introduction in *chapter 1* starts with a brief description of the mechanism of a cochlear implant, explaining the relation with spectral and temporal processing. It continues with an overview of how auditory deprivation in early childhood affects the development of the auditory system. It then describes a number of issues and problems related to cochlear implantation in this population, and the corresponding research questions that emerged out of these, which we aimed to answer in the different chapters of this thesis.

Chapter 2 evaluates the extent to which both early-deafened and postlingually deafened adult CI users are able to process temporal envelope cues. Since these cues are present also in the CI signal, it was equally of interest to us whether the ability to process them is related to speech recognition outcomes. We reported worse amplitude modulation detection tresholds (AMDTs) - a measure of temporal processing - for the early-deafened subjects compared to a postlingually deafened group. None of the early-deafened subjects were able to detect very fast (>100 Hz) modulations. In addition, better speech recognition scores were obtained in subjects having better amplitude modulation thresholds that degraded less quickly with increasing modulation frequency. Another difference between both subject groups was that significant correlations between the detection of slow modulations and speech recognition were present only for the early-deafened but not for the postlingual group, the reason for which currently remains unclear.

In *chapter 3,* the spectral processing abilities of a small group of early-deafened CI users were investigated by means of an adaptive electrode discrimination testing procedure.

Results showed that subjects are not able to perceptually discriminate between all adjacent electrodes, especially when electrodes are located in the basal region of the cochlea. The obtained outcomes were subsequently used to create an adapted cochlear implant fitting containing only discriminable electrodes and subjects were given four weeks to adjust to this new fitting. Results revealed no significant differences between the subjects' basic fitting and the new, experimental fitting, with respect to speech recognition performance (in quiet or noise), listening effort or spectral ripple discrimination. Subjective appreciation was generally worse for the experimental fitting. A number of factors related to the creation of the experimental map, more specifically the reduction of the number of maxima, the adaption period of (only) 4 weeks and the mainly basal location of the deactivated electrodes, which is a region less relevant for speech understanding, might explain the lack of an improvement with the experimental map.

Chapters 4 and 5 present a systematic review on cochlear implantation in early-deafened, late-implanted adolescent and adult CI users. In *chapter 4* we focus on postoperative outcomes and in *chapter 5* on factors that are predictive of these outcomes. The systematic search yielded 1449 unique articles. Further selection identified 38 studies meeting the eligibility criteria for part 1, and 13 studies that were prognostic in nature and thus relevant for part 2. In *chapter 4* we reported significant improvements for open-set speech recognition in the majority of the included studies, and observed significant improvements for measures assessing closed-set and auditory-visual speech understanding as well as hearing-related quality of life in almost all studies involved. In *chapter 5*, the synthesis of a vast variety of potential prognostic factors, assessed in the included studies, revealed three factors with good predictive potential: communication mode (mainly in childhood), preoperative speech intelligibility, and preoperative speech recognition scores. Furthermore, suggestions were made for a number of other factors that are worth further investigation.

Quality assessment of the studies included in the review also revealed several methodological weaknesses and sources of bias which might have impacted the observed outcomes, albeit to an unknown extent. Main issues included inadequate statistical testing, often related to the limited sample size, lack of information on relevant study aspects, such as measurement methods of prognostic factors, and variation between the included study groups due to unspecified implantation- and study inclusion criteria.

The prospective study presented in *chapter 6*, which included 27 early-deafened adults that received a cochlear implant, demonstrated significant improvements in auditory performance in accordance with the results of the review, as well as self-perceived benefits on a questionnaire that was specifically developed for this population of CI users. An interesting result was that a subgroup of poor performers, i.e. subjects failing to show an improvement on open-set speech recognition tests, did obtain signifcant benefit when assessed with measures targeted to their level of performance (such as closed-set tests and speech tracking). A correlation between objective and subjective outcome measures could not be found. This emphasizes the need for a subjective evaluation of outcomes also in this patient group, as measures of speech understanding do not seem to fully capture the indvidually experienced benefit after cochlear implantation. In the last study objective of *chapter 6,* two factors were identified that were able to explain 63.5% of the variation in outcomes of the included subjects, i.e. preoperative PTA and preoperative CNC word recognition (both of the implanted ear). Where the latter was found to be relevant in *chapter 5* as well, the first was not, demonstrating the need for further research especially in larger subject groups.

In the general discussion (*chapter 7*) the main findings of this thesis are discussed in light of their implications for the clinical field, and suggestions for further research are presented. A number of difficulties concerning the definition of our patient group of interest, are discussed. Suggestions are made as to how fitting parameters can be further explored and, when integrated with for instance mathematical modeling, potentially improve outcomes. In order to better predict performance with CI in our patient group, research in larger study groups is needed and new prognostic factors - such as those revealing underlying cognitive processes - should be investigated. We conclude that a cochlear implant in early-deafened, late-implanted adults and adolescents generally has a positive outcome. However, less traditional outcome measures, which focus on the patients' individual performance level and take subjective benefit into account, are required to reveal the true impact of a cochlear implant for these patients.

Nederlandse samenvatting

In dit proefschrift staat de patiënt centraal die vanaf geboorte doof of op zeer jonge leeftijd doof geworden is, én pas (laat) in de adolescentie of op volwassen leeftijd een cochleair implantaat (CI) heeft gekregen. Bij cochleaire implantatie wordt een kleine elektrode-drager chirurgisch ingebracht in het slakkenhuis van de patiënt. Wanneer dit inwendige implantaat verbinding maakt met een uitwendige geluidsprocessor, zorgt dit systeem ervoor dat akoestische signalen omgezet worden in een reeks elektrische pulsen. Deze elektrische pulsen stimuleren de auditieve zenuwuiteinden in het slakkenhuis, die ervoor zorgen dat het signaal verder geleid wordt tot in de hersenen en zo uiteindelijk “gehoord” wordt door de patiënt. Bij postlinguaal dove volwassenen - dit zijn patiënten waarbij het gehoorverlies is ontstaan ná het einde van de spraak-taalontwikkeling - is cochleaire implantatie een veel voorkomende behandelingsmethode geworden. Het merendeel van deze patiënten behaalt dan ook goede tot zeer goede resultaten op traditionele tests voor spraakverstaan. Dit staat in contrast met de resultaten die worden behaald door vele vroeg-dove volwassenen. De meerwaarde van een CI bij deze patiëntengroep staat dan ook nog regelmatig ter discussie. Dit zien we ook terug in de twijfels die veel CI centra hebben over het al dan niet implanteren van vroeg-dove, volwassen CI-kandidaten. Meer kennis over zowel de te verwachten resultaten met een CI bij deze patiëntengroep, als van de factoren die deze resultaten mee bepalen, is daarom van groot belang bij de patiëntenselectie.

In dit proefschrift wordt ingegaan op een aantal thema’s die allemaal gerelateerd zijn aan cochleaire implantatie bij vroeg-dove volwassenen. Zo wordt onderzocht welke factoren relevant kunnen zijn bij het preoperatief bepalen van wie een geschikte CI-kandidaat is (*hoofdstukken 5 & 6*), hoe de verwerking van het CI-signaal en het fitten van de geluidsprocessor geoptimaliseerd kunnen worden (*hoofdstukken 2 & 3*), en welke uitkomstmaten het meest geschikt zijn om de uiteindelijke prestaties met een CI te evalueren (*hoofdstukken 4 & 6*). Het uiteindelijke doel van het proefschrift is om de bestaande kennis op het gebied van cochleaire implantatie bij vroeg-dove, maar laat geïmplanteerde patiënten te vergroten, en hiermee de patiëntenselectie en (het in kaart brengen van) de prestaties met een CI te verbeteren.

De inleiding in *hoofdstuk 1* start met een korte beschrijving van het werkingsmechanisme van een cochleair implantaat. Ten behoeve van de hoofdstukken 2 en 3 wordt ingegaan op begrippen als spectrale en temporele verwerking. Vervolgens wordt uitgelegd hoe auditieve deprivatie op zeer jonge leeftijd de ontwikkeling van het hele auditieve systeem beïnvloedt. Hierbij worden ook een aantal problemen en nieuwe ideeën besproken met betrekking tot cochleaire implantatie bij deze patiëntengroep. Tenslotte worden de hieruit voortvloeiende onderzoeksvragen, die we in de verschillende hoofdstukken van dit proefschrift trachten te beantwoorden, gepresenteerd.

Hoofdstuk 2 brengt in kaart in welke mate zowel vroeg-dove als postlinguaal dove volwassen CI-gebruikers in staat zijn om temporele eigenschappen van een geluid te verwerken. Omdat er ook temporele aspecten aanwezig zijn in de omhullende van een CI-signaal, was een belangrijke onderzoeksvraag of de mate waarin een CI-patiënt deze aspecten kan verwerken gerelateerd is aan zijn of haar resultaten op het gebied van spraakverstaan. De mate van temporele verwerking werd gemeten met behulp van een test voor amplitude-modulatiedetectie. Onze resultaten lieten zien dat de gevonden drempels op deze test minder goed waren voor vroeg-dove patiënten dan voor postlinguaal dove patiënten. Bij de groep vroeg-dove patiënten was tevens niemand in staat om heel snelle modulaties (>100 Hz) te detecteren. Zowel binnen de vroeg-dove als binnen de postlinguaal dove patiëntengroep werd een significante correlatie gevonden tussen de resultaten op de amplitudemodulatiedetectietest en de spraakverstaanscores met het CI. Een opvallend verschil was dat signficante correlaties tussen spraakverstaanscores en het detecteren van langzame modulaties enkel binnen de vroeg-dove groep gevonden werden. Waarom dit niet het geval was binnen de postlinguaal dove groep is onduidelijk.

In *hoofdstuk 3* worden de spectrale verwerkingsmogelijkheden van een kleine groep vroeg-dove CI-dragers onderzocht aan de hand van een adaptieve testprocedure voor elektrodediscriminatie. De resultaten laten zien dat de onderzoekspatiënten niet in staat waren om alle naast elkaar liggende elektroden van elkaar te onderscheiden. Dit was met name het geval bij de elektroden die zich in het basale deel van de cochlea bevinden. De uitkomsten van de testprocedure werden vervolgens gebruikt om een aangepaste instelling van het CI te creëren, die enkel discrimineerbare elektroden bevat. De proefpersonen kregen 4 weken de tijd om aan deze aangepaste instelling te wennen. Bij metingen na deze gewenningsperiode werden er geen significante verschillen gevonden wat betreft spraakverstaan (in stilte of in ruis), luisterinspanning, of discriminatie van spectrale “ripples” (een test voor spectrale resolutie) tussen de standaard instelling en de nieuwe, experimentele instelling. De subjectieve appreciatie was in het algemeen in het nadeel van de experimentele instelling. Mogelijke verklaringen voor het uitblijven van een verbetering met de experimentele CI-instelling zijn een te korte gewenningsperiode, de reductie van het aantal maxima bij de experimentele instelling en het feit dat het merendeel van de uitgeschakelde elektroden zich in het basale deel van de cochlea bevonden, hetgeen een minder relevante regio is voor spraakverstaan.

Hoofdstukken 4 en 5 presenteren ieder een deel van een systematische review bij vroeg-dove, laat-geïmplanteerde adolescente of volwassen CI-dragers. In het eerste deel (*hoofdstuk 4*) ligt de focus op de postoperatieve resultaten; in het tweede deel (*hoofdstuk 5*) staan de factoren die een potentieel voorspellende waarde hebben voor deze resultaten centraal. Het systematisch zoeken in de literatuur leverde 1449 unieke artikels

op. De daarop volgende selectie identificeerde 38 studies die voldeden aan de vooropgestelde inclusiecriteria voor deel 1, en 13 studies met een prognostische onderzoeksopzet die relevant waren voor deel 2. In *hoofdstuk 4* rapporteren we significante verbeteringen voor het open set spraakverstaan bij de meerderheid van de geïncludeerde studies. Patiënten scoorden ook significant hoger op testen voor gesloten set en auditief-visueel spraakverstaan na implantatie, alsook voor de gehoorgerelateerde kwaliteit van leven. In *hoofdstuk 5* wordt een grote verscheidenheid aan potentieel voorspellende factoren besproken. Er worden drie factoren geïdentificeerd met goed voorspellend potentieel, namelijk: de wijze van communicatie (met name in de kindertijd), de preoperatieve spraakverstaanscores en de preoperatieve verstaanbaarheid van de eigen spraak van de patiënt. Verder worden er suggesties gedaan met betrekking tot welke andere factoren verder onderzocht dienen te worden in toekomstige studies.
Een evaluatie van de kwaliteit van de geïncludeerde studies liet diverse methodologische zwakheden en mogelijke bronnen van bias zien, die mogelijk invloed hebben gehad op de geobserveerde resultaten. De belangrijkste problemen hadden te maken met inadequate statistische testmethodes (vaak gerelateerd aan de beperkte grootte van de onderzoeksgroep), het ontbreken van relevante studie-informatie (zoals bij de meetmethode van voorspellende factoren) en variatie tussen de geïncludeerde studiegroepen van de diverse studies ten gevolge van niet-gespecificeerde implantatie- en inclusiecriteria.

De prospectieve studie bij 27 vroeg-dove CI-patiënten die gepresenteerd wordt in *hoofdstuk 6* laat - net zoals de review - significante postoperatieve verbeteringen zien qua auditieve prestaties. Een significante verbetering werd ook gevonden wat betreft subjectief ervaren voordelen, gemeten met een vragenlijst die specifiek ontwikkeld werd voor deze populatie van CI-gebruikers. Een interessante bevinding was dat een deelgroep van slechte presteerders, d.w.z. een groep van patiënten die geen verbetering liet zien qua open set spraakverstaan, toch significant vooruitging wanneer zij onderzocht werd met testen die beter aangepast waren aan hun niveau van auditief functioneren (zoals gesloten set tests en “speech tracking”). Verder kon er geen correlatie gevonden worden tussen objectieve en subjectieve uitkomstmaten. Dit geeft aan dat het van belang is ook een subjectief evaluatie-instrument te gebruiken bij vroeg-dove CI-gebruikers, gezien de resultaten op de objectieve spraakverstaantesten los lijken te staan van de individueel ervaren voordelen. In het laatste deel van *hoofdstuk 6* werden twee factoren geïdentificeerd die samen 63.5% van de variatie in uitkomsten van de geïncludeerde CI-gebruikers konden verklaren, namelijk de preoperatieve gehoordrempel en de preoperatieve CVC woordherkenningsscore (in beide gevallen van het geïmplanteerde oor). Waar de preoperatieve spraakverstaanscore ook in *hoofdstuk 5* een significante voorspeller bleek te zijn, was de preoperative gehoordrempel dat niet. Dit toont aan dat er nood is aan verder onderzoek, met name in grotere patiëntengroepen.

In de algemene discussie (*hoofdstuk 7*) worden de belangrijkste bevindingen van dit proefschrift besproken in het kader van hun mogelijke implicaties voor het klinische werkveld en worden er suggesties voor verder onderzoek gepresenteerd. Enkele moeilijkheden waarmee we geconfronteerd werden bij het definiëren van onze patiëntengroep worden hier besproken. Verder worden er suggesties gedaan hoe bepaalde parameters van de CI-instelling verder onderzocht kunnen worden en hoe deze, indien geïntegreerd met bepaalde wiskundige modellen, mogelijk tot verbeterde resultaten kunnen leiden. Om de prestaties met een CI binnen onze patiëntengroep beter te kunnen voorspellen is met name meer onderzoek in grotere groepen nodig en dienen nieuwe voorspellers (zoals diegene die onderliggende cognitieve processen in kaart brengen) onderzocht te worden. Concluderend kunnen we stellen dat een cochleair implantaat bij vroeg-dove, laat-geïmplanteerde adolescenten en volwassenen doorgaans tot een positief resultaat leidt. Echter, de traditionele auditieve tests zijn voor deze groep veel minder geschikt. Het gebruik van aangepast testmateriaal, aangevuld met een instrument gericht op het in kaart brengen van subjectief ervaren voordelen, is van belang bij het bepalen van wat een CI voor deze groep van patiënten betekent.

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Curriculum Vitae

Joke Debruyne werd geboren op 21 juli 1984 te Asse, België en groeide op in Sint-Amands, aan de Schelde. Na het doorlopen van haar middelbare school aan de Onze-Lieve-Vrouw Presentatie te Bornem, waar zij de richting Moderne Talen – Wiskunde volgde, startte zij in 2002 met de opleiding Logopedische & Audiologische Wetenschappen aan de Katholieke Universiteit Leuven (KULeuven, België). Zij koos voor de afstudeerrichting audiologie en behaalde in 2006 haar masterdiploma met grote onderscheiding. Voor haar masterthesis, die handelde over auditieve discriminatie bij kinderen met ontwikkelingsstotteren, ontving zij van de docenten de Outstanding Master Thesis Award. In 2007 vervolledigde zij haar opleiding met een diploma van de academische lerarenopleidng en een postgraduaat hoortoestelaanpassing. Tijdens het laatste jaar van haar opleiding liep zij gedurende 3 maanden stage bij het audiologisch centrum van het Maastricht UMC+ en ging hier kort na haar afstuderen aan de slag. Als master audioloog staat zij in voor de audiologische zorg binnen het volwassenteam. Naast haar klinische werkzaamheden startte zij met een promotietraject onder begeleiding van dr. ir. Jan Brokx en prof. dr. Bernd Kremer (Maastricht UMC+), en met de externe steun van prof. dr. ir. Tom Francart (KULeuven), hetwelke resulteerde in dit proefschrift.

List of publications

1. De Ruiter, A.M., **Debruyne, J.**, Chenault, M.N., Francart, T., Brokx, J.P.L. (2015). Amplitude Modulation Detection and Speech Recognition in Late-Implanted Prelingually and Postlingually Deafened Cochlear Implant Users. *Ear Hear*, 36(5), 557-66.
2. **Debruyne, J.**, Francart, T., Janssen, A.M., Douma, K., Brokx, J.P. (2016). Fitting prelingually deafened adult cochlear implant users based on electrode discrimination performance. *Int J Audiol*, 56(3), 174-185.
3. **Debruyne, J.**, Janssen, M., Brokx, J. (2017). Late Cochlear Implantation in Early-Deafened Adults: A Detailed Analysis of Auditory and Self-Perceived Benefits. *AudiolNeurootol*, 22(3), 364-376.
4. Vaerenberg B, Smits C, De Ceulaer G, Zir E, Harman S, Jaspers N, Tam Y, Dillon M, Wesarg T, Martin-Bonniot D, Gärtner L, Cozma S, Kosaner J, Prentiss S, Sasidharan P, Briaire JJ, Bradley J, **Debruyne J**, Hollow R, Patadia R, Mens L, Veekmans K, Greisiger R, Harboun-Cohen E, Borel S, Tavora-Vieira D, Mancini P, Cullington H, Ng AH, Walkowiak A, Shapiro WH, Govaerts PJ. (2014). Cochlear implant programming: a global survey on the state of the art. *ScientificWorldJournal*, 2014:501738