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Cognitive improvement after cochlear implantation in older adults with severe-to-profound hearing loss

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Table of contents

1 List of abbreviations

Abbreviation	Definition
ARHL	Age-related hearing loss
CANTAB	Cambridge Neuropsychological Test Automated Battery
CI	Cochlear Implant
dB	Decibel
dB HL	Decibel Hearing level
dB SPL	Decibel Sound pressure level
DS14	Type D questionnaire
FI	Fletcher Index
GDS	Geriatric Depression scale
HADS	Hospital Anxiety and Depression scale
HHIE	Hearing Handicap Inventory for the Elderly
HISQUI19	Hearing Implant Sound Quality Index
HUI	Health Utility Index
LIST	Leuven Intelligibility Sentences Test
MMSE	Mini-Mental State Examination
MoCA	Montreal Cognitive Assessment
NCIQ	Nijmegen Cochlear Implant Questionnaire
PTA	Pure Tone Average
QoL	Quality of Life
RBANS	Repeatable Battery for the Assessment of Neuropsychological Status
RBANS-H	Repeatable Battery for the Assessment of Neuropsychological Status for Hearing Impaired individuals
SNHL	Sensorineural hearing loss

SSQ12	Speech, Spatial, and Qualities of Hearing Scale
WHO	World Health Organization
WHOQOL-OLD	World Health Organization Quality of Life Assessment for elderly people

2 Abstract

Introduction: Hearing loss is a worldwide health problem that currently affects around 20% of the world population, and it is expected that these numbers will continue to increase. Untreated hearing loss can have a high impact on individuals' daily life, it can cause communication problems, social isolation, loneliness, frustration, and higher anxiety and depression rates. Furthermore, older adults with hearing impairment show an accelerated cognitive decline compared to normal-hearing individuals. Several hearing technologies are currently available to manage hearing loss, such as hearing aids and cochlear implants. Previous research indicated that these hearing technologies were not only beneficial for hearing abilities itself, as a positive effect on Quality of life and cognitive functioning was also observed one year after cochlear implantation.

Study design and participants: During this project the long-term effect of cochlear implantation on cognition and quality of life in elderly with severe-to-profound hearing loss was studied. All subjects included in the study were 55 years or older, have postlingual, bilateral, severe-to-profound hearing loss, and received a unilateral cochlear implant. Cognition was evaluated using the Repeatable Battery for the Assessment of Neuropsychological Status for Hearing Impaired Individuals (RBANS-H), and quality of life was evaluated using the following five questionnaires; Nijmegen Cochlear Implant Questionnaire (NCIQ); Hearing Implant Sound Quality Index (HISQUI); Speech, Spatial, and Qualities of Hearing Scale (SSQ12); Hospital Anxiety and Depression scale (HADS); and Type D questionnaire (DS14). Hearing abilities were also evaluated, using best-aided hearing thresholds and speech perception in quiet and in noise. All measurements; cognitive functioning, quality of life questionnaires, and audiometric assessments; were performed for each individual one month preoperatively, 12 months after cochlear implant activation, and annually thereafter until 48 months after cochlear implant activation.

Results: During this study 25 individuals are followed up at all time points. After cochlear implantation an improvement in hearing, cognition, and quality of life was observed. One year after cochlear implantation the total RBANS-H score (mean[SD], 92.78 [±15.08] vs 98.35 [±14.18])($p<0.001$) and the subdomain scores for "Immediate Memory" (94.13 [±18.75] vs 105.39 [±19.98]) ($p<0.001$), "Attention" (86.17 [±19.02] vs 91.57 [±15.35]) ($p=0.016$), and "Delayed memory" (97.91 [±14.51] vs 103.83 [±14.714]) ($p=0.006$) significantly improved. This effect stabilizes thereafter, and no further significant improvements are observed. A significant improvement was observed for the questionnaires related to hearing and listening abilities, including the NCIQ, HISQUI19, and SSQ12, one year after cochlear implant activation and remained stable thereafter. In addition, an effect was demonstrated for depression and anxiety scores. Type D personality traits; social inhibition and negative affectivity, also showed a considerable change after cochlear implant activation.

Conclusion: This study indicates a positive effect of cochlear implantation on hearing abilities, cognition, and quality of life one year after CI activation. In subsequent annual follow-up measurements, no further improvements were generally observed. These results confirm the importance of treating elderly with severe-to-profound hearing loss.

3 State of the Art Literature

3.1 The auditory system

Hearing, or auditory perception, is the process by which the ear transforms sound waves into electrical pulses, that are transferred to the brain, where they are interpreted as sounds (Plack, 2018). Our auditory system consists of both peripheral structures (e.g. outer, middle, and inner ear) and brain regions (e.g. auditory cortex)(Peterson et al., 2022).

Sound waves travel through a medium by moving molecules, which cause changes in air pressure within the environment. These vibrations reach the outer ear, i.e. auricle and external ear canal, which play a role in directing the sound waves into the tympanic membrane. Contact between the tympanic membrane and the pressure waves will result in vibrations of the membrane, these vibrations are transmitted to the middle ear bones, i.e. malleus, incus, and stapes (Figure 1). The auricle bones amplify the mechanical energy and transfer the movement to the oval window of the cochlea. The cochlea is a spiral-shaped fluid-filled tube and is divided into three cavities; i.e., scala vestibuli, scala media, and scala tympani. The upper and lower compartment, scala vestibuli and scala tympani, are filled with perilymph; a fluid with low potassium and high sodium concentration. These compartments are interconnected to each other at the apical end of the cochlea. The scala media is filled with endolymph; a fluid containing a high potassium concentration and a low sodium concentration. The Reissner membrane separates the scala media from the scala vestibuli, whereas the basilar membrane separates the scala tympani and scala media. On this basilar membrane, the organ of Corti is located, which contains the receptor cells, i.e., the inner and outer hair cells, the tectorial membrane covers these hair cells (Figure 2). The apical end of the hair cells contains stereocilia, this part of the cell is specialized in the reception of the signal and translates the mechanical energy into currents, whereas the basal side forms synapses with neurons. When sound waves reach the oval window of the cochlea, the vibrations pass through the scala vestibuli and scala tympani, also causing movement of the basilar membrane. This displacement of the basilar membrane results in a shear force between the stereocilia of the hair cells and the tectorial membrane. Due to the sliding movement between these membranes, the stereocilia are displaced. Depending on the bending direction this will result in opening or closing of the potassium channels. Opening of the channels leads to depolarization of the hair cells, resulting in the release of glutamate which will trigger action potentials in the spiral ganglion. Depending on the frequency a different part of the organ of Corti is stimulated, i.e. short waves created by higher frequencies activate hair cells at the base of the cochlea, whereas long waves caused by lower frequencies activate those at the apex of the cochlea. Thus, the organ of Corti translates the vibration waves into electrical pulses (Peterson et al., 2022, Amunts et al., 2012, Brown and Santos-Sacchi, 2013).

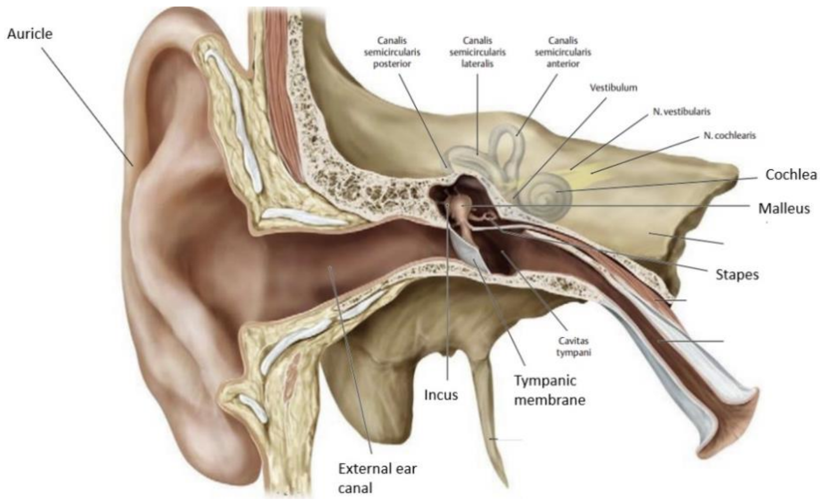

Figure 1: the auditory system, including the inner and outer ear (adapted from Schünke, 2010).

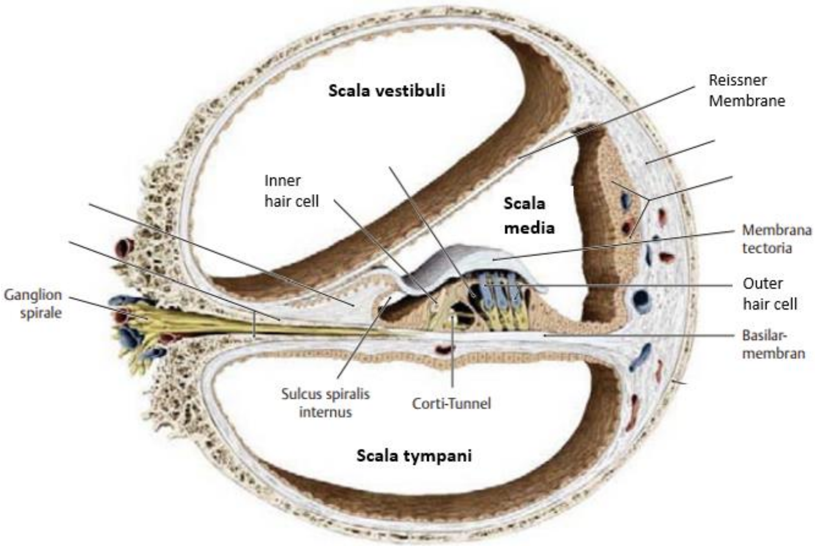

Figure 2: Cross section of the cochlea, illustrating the three cavities, i.e. scala vestibuli, scala tympani, and scala media or ductus cochlearis (adapted from Schünke, 2010)

Auditory information from the peripheral auditory system is sent to the auditory cortex via the brain stem and thalamus. The spiral ganglion, located in the cochlea, guides the action potentials via the cochlear nerve to the ventral and dorsal cochlear nuclei. On both sides of the brain stem, the information of the ventral cochlear nucleus is transmitted to the superior olivary complex. Via the lateral lemniscus, the vessels of the dorsal and ventral cochlear nuclei ascend towards the inferior colliculus, which is connected to the medial geniculate body of the thalamus. Finally, the thalamus sends the information to the auditory cortex, where the information is further processed to interpret sound (Figure 3) (Peterson et al., 2022, Nieuwenhuys, 1984, Schünke, 2010).

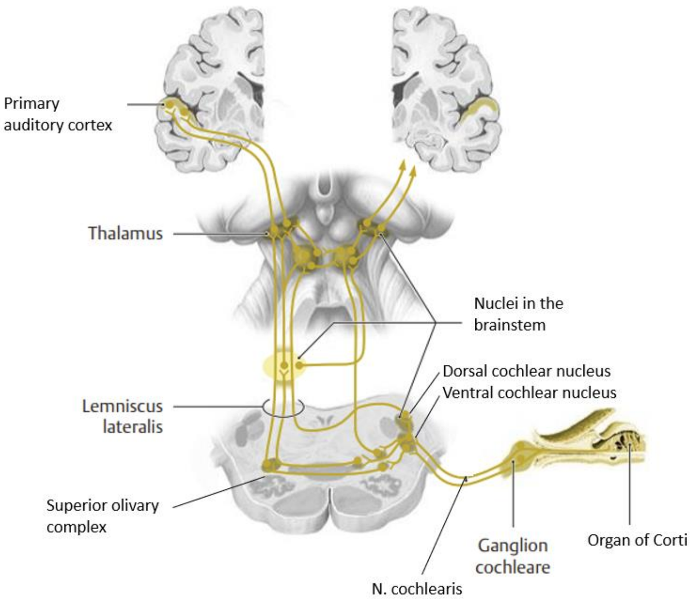

Figure 3: auditory pathway, starting in the organ of Corti and sending information to the primary auditory cortex (adapted from Schünke, 2010).

3.2 Hearing impairment

Hearing impairment currently affects around 20% of the world population. According to the World Health Organization (WHO), these numbers will continue to increase and it is expected that by 2050 1 in 4 individuals will have hearing problems. Hearing impairment is a common problem, especially in older adults as around 30% of the adults above the age of 60 have hearing loss. The prevalence of moderate or more severe grades of hearing loss increases with age (World Report on Hearing, 2021).

Pure tone audiometry and speech audiometry are the standard tools to evaluate patients' hearing abilities in clinical routine. Pure tone audiometry (ISO 8253-1:2010) measures hearing thresholds, i.e., the minimum sound level at which the ear can detect pure tones, in air-and bone-conduction pathways. These thresholds are evaluated within a range slightly broader than that of human speech, including frequencies ranging from 250 to 8000Hz. Pure tone audiometry allows to determine the severity, the type, and the configuration of hearing loss. Speech audiometry measures the speech recognition threshold, i.e. the lowest decibel hearing level (dB HL) at which the patient can correctly identify and repeat stimulus words or sentences in noise or in quiet (Tanaka et al., 2018, Kapteyn, 2011).

The WHO uses the 4 frequency pure tone average (PTA) to classify the severity of hearing loss. PTA is the average air-conduction hearing threshold at 500, 1000, and 2000Hz. In the 4 frequency PTA, 4000Hz is also included in the calculation. According to the WHO, hearing loss is classified as mild [20 to <35dB], moderate [35 to <50dB], moderately severe [50 to <65dB], severe [65 to <80dB], or profound [80 to <95dB] (Table 1) (World Report on Hearing, 2021).

Table 1: Classification of hearing loss (adapted from World Report on Hearing, 2021)

Grade/ classification	Hearing threshold in the better hearing ear in decibels (dB)
Normal hearing	< 20dB
Mild hearing loss	20 to < 35dB
Moderate hearing loss	35 to < 50 dB
Moderately severe hearing loss	50 to < 65 dB
Severe hearing loss	65 to < 80 dB
Profound hearing loss	80 to < 95dB
Complete or total hearing loss/ deafness	95 dB or greater

Hearing loss can be categorized in three different types of hearing loss, depending on the anatomical location of the cause; conductive hearing loss, sensorineural hearing loss (SNHL), and mixed hearing loss. Conductive hearing loss results from abnormalities in the outer and/or middle ear, e.g. obstruction, damage, or infection. Patients with this type of hearing loss will have normal bone-conduction thresholds, but air-conduction thresholds are elevated, resulting in an air-bone gap of 15dB or more. In patients with SNHL, the conversion of mechanical sound to neuroelectric signals in the inner ear and/or the auditory nerve is affected. In this type of hearing loss both the air-and bone conduction thresholds are elevated, with an air-bone gap of 10dB or less. Mixed hearing loss is the combination of conductive and SNHL, in which both air- and bone-conduction thresholds are elevated resulting in an air-bone gap of 15dB or more (Tanaka et al., 2018, Michels et al., 2019). Hearing impairment can also be linked to damage or dysfunction of the central auditory pathway, including the vestibulocochlear nerve, auditory brainstem, or auditory cortex. This central hearing impairment results in a more complex hearing disturbance and is the result of trauma, infarction, tumors, etc. (Zahnert, 2011).

Several risk factors exist that have an impact on hearing, however, the etiology often remains unknown. In many cases, genetic factors play an important role, but also a wide range of environmental factors have an effect on hearing abilities (Russ et al., 2018). A prominent and well-studied environmental risk factor is noise exposure.

Noise-induced hearing loss typically occurs gradually, starting with hearing loss in the high frequencies. Sudden hearing loss can occur after acoustic trauma. Additionally, hearing loss can be caused by injuries and damage to the head and auditory system, including head injuries, meningitis, otosclerosis, and otitis media, i.e. middle ear infection. Other risk factors include ototoxic medication, smoking, etc. (Russ et al., 2018, Uchida et al., 2005, Zhan et al., 2011). The most common sensory deficit in the elderly is age-related hearing loss (ARHL), also known as presbycusis. ARHL is a progressive, bilateral, symmetrical age-related SNHL. It is a complex disorder caused by the cumulative effects of aging on the auditory system, it involves genetic and environmental factors. Individuals with ARHL have a progressive decline of auditory function, such as increased hearing thresholds and poor frequency resolution (Bowl and Dawson, 2019, Schuknecht, 1955, Schuknecht and Gacek, 1993, Gates and Mills, 2005).

3.2.1 Impact on individuals life

Hearing loss can have a considerable impact on individuals' daily life. Untreated hearing impairment can cause communication problems, which will contribute to social isolation and loneliness. Furthermore, it can cause frustration, and previous research has also demonstrated that individuals with hearing loss show higher rates of anxiety and depression (Ciorba et al., 2012, Gopinath et al., 2012, Sung et al., 2016, Jayakody et al., 2018).

Moreover, several studies have shown an accelerated cognitive decline in older adults with peripheral hearing impairment compared to individuals with normal hearing. Lin et al., (2013) demonstrated that elderly with hearing loss have a 24% increased risk of cognitive impairment. This could mean that hearing loss is associated with an increased risk of dementia in later life (Valentijn et al., 2005, Lin et al., 2013, Gallacher et al., 2012, Lin et al., 2011, Ford et al., 2018). Dementia is a syndrome characterized by a significant chronic or progressive cognitive decline that impairs daily life and independent function. Dementia is a multifactorial disease, and several risk factors are likely to contribute, such as smoking, physical inactivity, midlife obesity, ageing etc. (Gale et al., 2018, Barnes and Yaffe, 2011, Baumgart et al., 2015). As previously mentioned, hearing loss might be a possible modifiable risk factor for the development of dementia (Lin et al., 2013, Valentijn et al., 2005, Gallacher et al., 2012, Lin et al., 2011).

The underlying relationship between cognition and peripheral hearing loss is not yet known, nevertheless, four hypotheses have been proposed and studied regarding this causal relationship: (1) common cause hypothesis, (2) cognitive load on perception hypothesis, (3) sensory deprivation hypothesis, and (4) information degradation hypothesis (Baltes and Lindenberger, 1997, Lindenberger and Baltes, 1994, Arlinger et al., 2009). The common cause hypothesis states that cognitive decline and hearing loss emerge from a similar factor or mechanism, such as genetic factors, environmental mechanisms, or the ageing brain. The second hypothesis, the cognitive load on perception hypothesis, suggests that due to cognitive decline seemingly 'simple' sensory tasks increase in cognitive complexity and demands. Therefore, cognitive capacity affects sensory processing. The sensory deprivation hypothesis states that peripheral hearing loss causes cognitive decline. This can be explained by the fact that long-term sensory difficulties may reduce intellectually stimulating interactions with the environment, which can eventually lead to a decrease in cognitive ability. The last hypothesis, the information degradation hypothesis, also suggests a similar causal relationship. It states that perceptual problems compromise cognitive performance. In contrast to the third hypothesis, the fourth hypothesis suggests that the impact on cognition is reversible. This implies that compensating for perceptual difficulties, for instance with a cochlear implant, may also improve cognitive performance. Previous studies already indicated that cochlear implantation attenuates cognitive decline in older adults (Völter et al., 2018, Mosnier et al., 2015).

3.2.2 Treatment for hearing loss

Currently, there is no cure or surgical treatment available to regenerate damaged hair cells. A broad range of therapeutic approaches regarding these possibilities are intensively studied nowadays; e.g., gene therapy, cell transplantation, and pharmaceutical therapy (Youm and Li, 2018, Hinton et al., 2021). Several hearing technologies are currently available to manage hearing loss, such as hearing aids and cochlear implants (CI). A conventional hearing aid is a noninvasive electronic device, worn behind or in the ear, that provides acoustic stimulation by amplifying sounds. A CI is a surgically implanted electronic device and consists of two parts: (1) an external part that is worn behind the ear and (2) an internal part that is surgically implanted. The external part contains microphones, a sound processor, and a transmitter. The microphones pick up sounds from the environment and the sound processor converts them into a digital signal. This signal is processed into a radio frequency signal, which is transmitted to the internal part. The radio frequency signal is decoded and converted into electric currents, these are sent along the electrode array in the cochlea, resulting in the stimulation of the auditory nerve, which transfers the signal to the brain (Figure 4). In essence, the device bypasses damaged parts of the ear, such as missing or damaged hair cells, and stimulates the auditory nerve directly. A CI can be used in individuals with profound hearing loss when a conventional hearing aid cannot be used, or when it has no or only limited benefit (Brodie et al., 2018, Zeng et al., 2008) (World Report on Hearing, 2021).

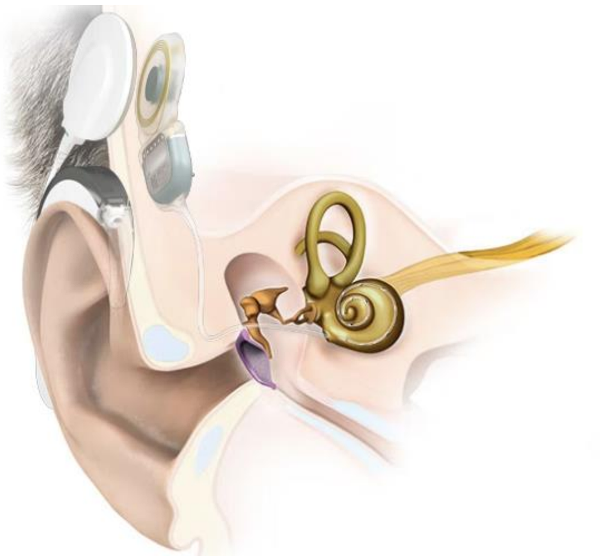

Figure 4: Cochlear implant (copyright: MED-EL, Innsbruck, Austria).

Adult cochlear implantation candidacy guidelines and criteria differ between countries, and international guidelines are limited (Buchman et al., 2020, Vickers et al., 2016). In Belgium, cochlear implantation is reimbursed by the *Belgische Rijksinstituut voor Ziekte- en Invaliditeitsverzekering*. The criteria for unilateral CI in adults with bilateral severe-to-profound hearing loss are the following; (1) average unaided air conduction threshold is 70dB or higher in the best hearing ear for at least 3 of the following frequencies: 500, 1000, 2000, and 4000Hz, (2) threshold of peak V in the brainstem evoked response audiometry is at least 75dB normal hearing level, (3) speech recognition score in quiet and in unaided condition is 50% or less at 70dB sound pressure level (dB SPL) in speech audiometry in free field. In addition, the patient should not have any contraindications to the implantation or the use of the CI (Mertens et al., 2021a, Obyn et al., 2020). In Belgium, yearly around 500 individuals receive a CI (https://www.healthybelgium.be/en/medical-practice-variations/sensory-system/ears/cochlear-implant). The audio processor is activated approximately one month after surgical implantation of the internal part. Patients need to adapt to this new way of hearing, therefore auditory rehabilitation is recommended to obtain optimal results. During this auditory therapy, patients will learn how to detect, discriminate, identify, and interpret sound signals. It is a multidisciplinary process including psychological counseling, medical checks, several appointments with the audiologist for the fitting of the audio processor, auditory training with a speech therapist, etc. (Boothroyd, 2007).

3.2.3 Studying the benefits of hearing restoration

Several studies have shown the benefits of hearing restoration by using hearing technology, such as hearing aids and cochlear implantation. First of all, it will significantly improve audiological test results, including the PTA and speech perception, which has a positive effect on listening abilities, and prevents isolation from inability to communicate (Aimoni et al., 2016, Budenz et al., 2011, Claes et al., 2018b). Furthermore, it will have a beneficial effect on Quality of Life (QoL), cochlear implantation resulted in a more pronounced QoL improvement compared to conventional hearing aids (Brodie et al., 2018, Aimoni et al., 2016, Mosnier et al., 2015). In addition, many studies demonstrated a significant improvement in cognitive functioning after cochlear implantation (Mertens et al., 2021a, Claes et al., 2018a, Völter et al., 2018, Mosnier et al., 2015, Claes et al., 2018b).

3.2.3.1 Effect on hearing performance and QoL

Overall, hearing aids improve hearing performance, a considerable gain in hearing thresholds can be observed after cochlear implantation (Aimoni et al., 2016). Speech perception in quiet and in noise significantly improve after cochlear implantation. Bundenz et al., (2011) found that the largest improvement in speech perception scores occurred three months after cochlear implantation, and these scores remained more or less stable afterwards. Several recent studies confirm these findings, they found a significant change in speech perception in quiet and in noise 6 months after implantation, and these results remained stable (Budenz et al., 2011, Claes et al., 2018b, Mosnier et al., 2015). Speech recognition in noise, which is more challenging, was shown to be positively associated with improvement in cognitive functioning (Andries et al., 2023).

As briefly discussed earlier, hearing restoration will have a positive effect on QoL, this is demonstrated by several research groups using different types of questionnaires (Claes et al., 2018b, Mosnier et al., 2015, Aimoni et al., 2016, Völter et al., 2018, Mertens et al., 2021b, Sonnet et al., 2017). Currently, there is no standardized protocol available to investigate QoL, but questionnaires are commonly used. Some are specifically designed for a certain intervention, such as cochlear implantation (disease-specific questionnaires), while others are more general (generic questionnaires). The latter can be used to examine a person's general health status across different populations, types of diseases, etc. Different generic questionnaires are currently available; e.g. WHO Quality of Life Assessment for elderly people (WHOQOL-OLD), SF-36, Health Utility Index (HUI), etc. These tools include questions related to sensation, mobility, emotion, pain, etc. (Andries et al., 2021, Horsman et al., 2003). Nijmegen Cochlear Implant Questionnaire (NCIQ) and Hearing Implant Sound Quality Index (HISQUI19) are questionnaires specifically designed to investigate the self-perceived benefit of a CI. The NCIQ gives a total score, and a subdomain score for the following 6 subdomains; Basic sound perception, Advanced sound perception, Speech production, Self-esteem, Activity limitations, and Social interaction. The HISQUI19 also provides a total score, which classifies the self-reported sound quality into 5 classes (Hinderink et al., 2000, Amann and Anderson, 2014). Völter et al., (2018) used two different questionnaires to evaluate QoL after cochlear implantation, a generic QoL assessment tool namely the WHOQOL-OLD and the CI-specific NCIQ. A significant improvement in general QoL was observed at 6 months after cochlear implantation, especially for sensory function and autonomy-related questions. In addition, a significant improvement was observed across all the 6 subdomains of the NCIQ at 6 months after implantation. 12 months after implantation, no further improvements were seen on any of the questionnaires (Völter et al., 2018). Results obtained by other research groups for the NCIQ are consistent with those findings (Mosnier et al., 2015, Claes et al., 2018b, Völter et al., 2022b). HISQUI19 scores also improved 6 months after implantation, and no additional improvement was observed thereafter (Claes et al., 2018b).

3.2.3.2 Effect on cognition

Elderly with hearing loss have an increased risk of cognitive impairment, previous studies have shown that the use of CI attenuates this cognitive decline (Amieva et al., 2015, Völter et al., 2018, Aimoni et al., 2016, Mosnier et al., 2015, Mertens et al., 2021a). Mertens et al., (2021) performed a longitudinal controlled study to investigate the effect of CI on cognition. It is one of the only studies with regard to this topic that included both a control and intervention group. Individuals were matched according to the following criteria; age, education, cognition, and percentage of residual hearing in best ear. The Repeatable Battery for the Assessment of Neuropsychological Status for hearing impaired individuals (RBANS-H) was used to evaluate cognition one month before implantation and at a follow-up moment 14 months thereafter. This study showed that both the RBANS-H total score and the score of the subdomain "Attention" significantly improved one year after cochlear implantation compared to the control group without CI. Nevertheless, the cognitive results one year after implantation were still worse compared to individuals with normal hearing. In addition, cochlear implantation had a positive effect on QoL, specifically on sound quality, and self-perceived hearing outcomes (Mertens et al., 2021a). Results of similar studies are in line with those findings, they all demonstrated a significant improvement of the total cognitive score and of the cognitive domain "Attention" after cochlear implantation, even though they were not using the same cognitive assessment tool. Several studies also reported an improvement in the cognitive subdomains "Immediate memory" and "Long-term memory". However these studies did not include a control group, so they were not able to correct for possible practice effects (Claes et al., 2018b, Völter et al., 2018, Mosnier et al., 2015). Another recent study demonstrated that this positive effect of cochlear implantation on cognition is not only present in individuals with normal cognitive scores preoperatively but also in individuals with mild cognitive impairment (MCI) (Andries et al., 2023). However, other studies did not find any positive effect of hearing aids on cognition (Valentijn et al., 2005).

Few research groups investigated the long-term effect of CI on cognition. Studies that have been performed on this topic confirm previous findings, i.e., significant cognitive improvement one year after cochlear implantation, but they also showed that this effect stabilizes over time (Ohta et al., 2022, Völter et al., 2022b). Völter et al., (2022b) investigated the long-term effect of cochlear implantation on cognition using a computer-based neurocognitive assessment tool consisting of nine subtests covering different cognitive domains. Cognitive evaluation of the subjects took place at three timepoints; preoperatively, 12 months, and up to 65 months after cochlear implantation. A significant improvement was found between the first two timepoints on the following cognitive domains; attention, immediate memory, long-term memory, working memory, and verbal fluency. No further significant improvement was observed between 12 and 65 months (Völter et al., 2022b). Similar results were obtained by Ohta et al., (2022), they investigated the effect on cognition using the Mini-Mental State Examination (MMSE). They found a significant improvement in MMSE scores one year after implantation compared to preoperatively, but no significant difference was found comparing MMSE score one year after implantation and MMSE scores two years after implantation (Ohta et al., 2022). Mosnier et al., (2018) investigated the effect of cochlear implantation on cognition in individuals with MCI. Individuals were followed-up over the course of 7 years after implantation. They demonstrated that there was a low rate of progression to dementia in these individuals, since only 6% of the individuals with MCI before implantation progressed towards dementia (Mosnier et al., 2018).

A wide range of research has been conducted on this topic, but it remains difficult to compare these findings due to the use of different protocols; i.e., different tools are used to assess cognition, difference in follow-up period, etc. To be able to obtain conclusive results regarding the benefit of cochlear implantation on cognition, several methodological considerations must be taken into account (Valentijn et al., 2005). Claes et al. (2018a) clearly summarize some of the important bias risks with regard to studying this association. One very important aspect is the suitability of the cognitive test, the test needs to be appropriate to assess cognition in individuals with severe-to-profound hearing loss. This is important to avoid bias in the results caused by their hearing impairment, as items that are presented only aurally may not be well perceived or may be misperceived by the individual. Hence, modifications of the original assessment tools are essential to study the effect of cochlear implantation on cognition and not the increase in performance due to improved hearing (Claes et al., 2018a, Dupuis et al., 2015). To test the effect of cochlear implantation on cognition, cognition needs to be assessed multiple times during the follow-up period. Hence, there is a risk for practice effect, which can be avoided or minimized by using different test versions. Additionally, the choice of the statistical method plays a very important role(Claes et al., 2018a).

3.3 How to study cognition in individuals with hearing loss?

3.3.1 Cognitive assessment tools

Currently, several cognitive assessment tools exist, and depending on the research question and protocol one might be more appropriate compared to the other. The cognitive tests differ from each other with regard to the assessment time, and the cognitive domains they assess. It is important to keep in mind that not all tools are equally suitable to assess cognition in individuals with a hearing impairment. A commonly used tool in the screening and diagnosis of dementia is the MMSE. Some of the previously described studies used this tool to evaluate the effect of cochlear implantation on cognition, often in combination with other tests, e.g. Trail Making Test, clock-drawing test, verbal fluency, etc. Bias risk linked to hearing impairment can be avoided by providing visual, and written explanations to the subject (Mosnier et al., 2015, Ohta et al., 2022, Sonnet et al., 2017). The administration of the MMSE takes around 10 minutes. It assesses the following cognitive functions: orientation to time and place, short-term memory, attention and calculation, recall, language, and praxis. A maximum total score of 30 is possible, and a low score correlates with poorer cognitive abilities (Folstein et al., 1975). Montreal Cognitive Assessment (MoCA), is a brief cognitive screening tool to assess MCI. It shows whether or not there is a cognitive problem, but no information is given about severity or how well or poorly someone scores compared to others. The screening takes around 10 minutes, and assesses the following cognitive aspects: short-term memory, visuospatial abilities, executive functions, phonemic fluency, attention, concentration, working memory, language, and orientation to time and place. A total maximum score of 30 can be obtained, and a score of 26 or above is seen as normal. A drawback of this test is that it does not correct for normal cognitive aging (Nasreddine et al., 2005). For individuals with a hearing impairment, a modified version of the MoCA is available, the HI-MoCA. In the HI-MoCA the instructions are visually shown on a PowerPoint presentation (Lin et al., 2017). Nonverbal and computerized assessment tools are also available, such as the Cambridge Neuropsychological Test Automated Battery (CANTAB) (https://www.cambridgecognition.com/cantab). CANTAB allows to examine the cognitive level in individuals with a hearing impairment. It is possible to test different cognitive domains in the subject by using one of the available test batteries or create your own. CANTAB allows repeated testing, and the risk of practice effect can be eliminated with randomized stimuli and parallel modes. Another cognitive assessment tool that can be used to evaluate the effect of a CI on cognition is the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS). This tool assesses five different cognitive domains; “Immediate memory”, “Visuospatial/ Constructional”, “Language”, “Attention”, and “Delayed memory”. This entire test battery takes around 30 minutes and provides a total score as well as a score for each subdomain. The scoring system of the RBANS allows for correction for normal cognitive aging (Randolph et al., 1998). A modification of the original RBANS is available that can be used to assess cognition in individuals with a hearing impairment, this will be further explained in the section “*4.* Study design and methods*”* (Claes et al., 2016, Randolph, 2012).

3.3.2 Confounding factors in cognitive assessment

Cognition can be influenced by a variety of different factors, some can be considered normal and occur in healthy individuals while others are modifiable risk factors for dementia (Livingston et al., 2020). Decline in cognitive functioning is not only present in individuals with a pathologic brain disease, but also in healthy elderly. The normal ageing process is associated with changes in certain cognitive abilities, such as executive function, processing speed, visuospatial, etc. Interindividual differences are present in these age-related cognitive changes, but normal ageing does not affect daily life. When studying cognition, especially in elderly, it is important to consider and correct for these changes (Harada et al., 2013). Another important factor that influences cognition is education, previous research indicated that the number of years of formal education is positively associated with cognitive functioning later in life (Lövdén et al., 2020). Depression is associated with cognitive functioning; more severe depressive symptoms are linked to decreased cognitive performance. Some cognitive domains are more severely affected by depression, such as executive function, processing speed, etc. In addition, depression and dementia are interconnected with each other. Depression is a risk factor for dementia, but it is also part of the prodrome and early stages of dementia (Helvik et al., 2019, Livingston et al., 2020, McDermott and Ebmeier, 2009). The cognitive performance can also be affected by brain injury, previous research has shown that traumatic brain injury increases the risk of dementia (Nordström and Nordström, 2018, Livingston et al., 2020). Other modifiable risk factors for dementia, which may thus have an effect on cognition in general, are hypertension, smoking, obesity, diabetes, excessive alcohol consumption, social contact etc. When studying the effect of certain interventions on cognition, it is important to take these factors into account (Calvino et al., 2022b, Livingston et al., 2020)

3.4 Research objectives

Research Questions:

- What is the long-term effect of cochlear implantation on cognition in elderly with severe-to-profound hearing loss?
- What is the long-term effect of cochlear implantation on QoL in elderly with severe-to-profound hearing loss?

Hypothesis:

Based on previous studies, a positive effect of cochlear implantation on cognitive performance can be expected, especially on the subdomain ‘Attention’. A significant improvement of the RBANS-H subdomain scores for ‘Immediate memory’ and ‘Long-term memory’ can also be expected. Based on previous findings regarding the long-term effect of CI, it is expected that the increase in RBANS-H score stabilizes approximately 2 years after implantation. Similar results are expected regarding the effect of cochlear implantation on QoL, a significant improvement within the first year after implantation and no further changes thereafter.

Aim of the internship and master thesis

The overall aim of this master thesis is to investigate the long-term effect of cochlear implantation on cognition and QoL in adults above the age of 55 with severe-to-profound hearing loss.

A large dataset is used to draw valuable conclusions. The data collection started in March 2015 and is still ongoing. It includes 99 intervention subjects, but only a few controls. The first patients included in the dataset have currently been followed-up for 7 years after implantation. Some of the individuals that were first included in the control group are now part of the intervention group. Recruitment is still ongoing.

During the internship, I took part in various aspects of clinical research. This included making appointments with patients according to the schedule of the study, notifying patients of their appointment, and sending the questionnaires on time via mail. I also helped with the data collection, which included evaluation of cognition in the patients using the RBANS-H, scoring of the RBANS-H according to the defined criteria. In addition, I spent a large amount of time on completing the database in OpenClinica. When sufficient data regarding the aim of the master thesis was obtained, the data was extracted. Before statistical analysis was applied on this dataset, I removed incorrect data, completed missing data, and all data was combined in one file. Thereafter, the statistical analysis was performed using SPSS.

4 Study design and methods

4.1 Study design

The effect of cochlear implantation in elderly with severe-to-profound hearing loss will be investigated. The main focus will be on the long-term effect of cochlear implantation on cognition in elderly, but QoL and audiometric parameters will also be assessed. A prospective, longitudinal study is performed, and data is collected at different timepoints. The first data collection is 1 month pre-operatively, this will be the baseline (T0) measurement. One month after the implantation, the CI is activated and 12 months thereafter (T1) the parameters are assessed again. After this, the parameters are evaluated annually (T2, T3, T4) (Figure 5). In this study, the preoperative data (T0) is compared with the following post-activation data: 12 months (T1), 24 months (T2), 36 months (T3), and 48 months (T4).

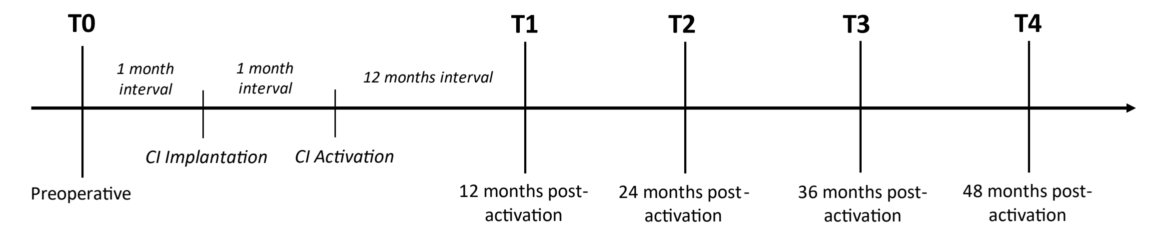

Figure 5: Overview of study design. T0, T1, T2, T3, and T4 are the different time points at which the parameters (RBANS-H, auditory battery, NCIQ, HISQUI19, SSQ12, HADS, DS14) are assessed. T0 corresponds with the baseline testing, this is 1 month prior to implantation. T1 is follow-up testing, which is done 12 months after CI activation, thereafter the testing is done annually. T2 is 24 months after activation, T3 is 36 months, and T4 is 48 months post-activation (adapted from Mertens et al., 2021).

Cognition will be assessed across the different time points using the RBANS-H, this cognitive assessment tool will be further explained in part "*4.1.2 Primary outcome measurement*". Secondary outcome measurements are also assessed across the different timepoints, these include audiological assessments and the following questionnaires: Nijmegen Cochlear Implant Questionnaire (NCIQ); Hearing Implant Sound Quality Index (HISQUI19); Speech, Spatial and Qualities of Hearing scale (SSQ12); Hospital Anxiety and Depression scale (HADS), and Type D questionnaire (DS14). The audiological test battery and the different questionnaires used in this study are explained in part "*4.1.3 Secondary outcome measurements*".

4.1.1 Subjects

The individuals included in the study are all at the age of 55 or above at baseline measurement. This age limit is based on previous research showing that 55 is the youngest mean age at which hearing impairment was linked to cognitive decline (Gallacher et al., 2012). The sample size calculation for the study is based on the RBANS-H total score, and available literature of similar studies is also considered. The calculation is done to investigate how many participants need to be included in the study to answer the research question. The following quantities are used for the estimation of the sample size: power of 80% using a paired t-test to detect a Cohen's d of 0,7 at a significance level of 0,05. A dropout is considered due to the duration of the study and the age of the study population. In previous studies a sample size of approximately 20 to 25 individuals in each group was used, this was sufficient to show a significant improvement of RBANS-H scores after cochlear implantation (Claes et al., 2016, Claes et al., 2018b, Mertens et al., 2021a).

The subjects included in the study are selected according to the following criteria, (1) aged 55 years or older, (2) postlingual, bilateral, severe-to-profound hearing loss (Table 1), (3) receiving a unilateral CI, and (4) their CI usage is more than 10 hours a day. Participants are excluded from the study in case they are not able to complete the test protocol due to additional impairments, such as uncorrected vision problems, and if other severe health issues occurred that might have an impact on the results. All subjects gave written informed consent to participate in this study.

4.1.2 Primary outcome measurement

RBANS is a neuropsychological assessment tool that is used to evaluate cognition in individuals. It can be used to access abnormal cognitive decline in older adults and as a neuropsychological screening battery for younger patients. The RBANS provides a score for five different cognitive domains, (1) "Immediate memory", (2) "Visuospatial/ Constructional", (3) "Language", (4) "Attention", and (5) "Delayed memory". The five cognitive domains are assessed via 12 subtests (Table 2). The entire test battery takes around 30 minutes (Randolph et al., 1998). To investigate cognition in the test subjects, the RBANS-H will be used, this is a modification of the original RBANS and is specially developed to examine cognition in individuals with hearing impairment (Claes et al., 2016, Randolph, 2012). In comparison to the original RBANS where the instructions are given orally, the RBANS-H provides an audiovisual presentation. Together with the standard oral instructions, written instructions are shown to the participant on an external screen. In addition, the stimuli in 4 of the 12 subsets (List Learning, Story Memory, Digit Span, and List Recognition) are presented simultaneously visually and orally. In essence, the RBANS-H is accompanied by a PowerPoint presentation with written instructions and stimuli of certain subsets are visually and orally presented (Claes et al., 2016).

The participants will be assessed with the RBANS-H at different time points during the study (Figure 5). It is important to avoid possible practice effects linked to this repeatable testing, therefore two different RBANS-H versions will be used during the study, RBANS-H A and B (Claes et al., 2018a).

Table 2: The five cognitive domains and twelve subtests of the RBANS (Claes et al., 2016)

Immediate memory	Visuospatial/Constructional	Language	Attention	Delayed memory
(1) List learning (2) Story memory	(3) Figure copy (4) Line Orientation	(5) Picture naming (6) Semantic fluency	(7) Digit Span (8) Coding	(9) List recall (10) List Recognition (11) Story Recall (12) Figure Recall

Immediate memory is assessed via two subtests, List Learning and Story Memory (Table 2). The first subtest consists of immediate recall of a 10-item list of semantically unrelated words. The words are presented orally and visually to the subject, the examiner reads the words aloud when they appear on the screen. After each learning trial the subject is asked to repeat as many words as possible. One point is given for each correct word. There are four learning trials for the wordlist, so a total score of 40 is possible. The second subtest is Story Memory. This test consists of immediate recall of a 12-item story, and there are two learning trails. Similar to the wordlist, the subject receives the information audio-visually. One point is given for each correct item, over the two learning trials a total score of 24 can be obtained (Claes et al., 2016, Randolph et al., 1998).

Visuospatial/Constructional Except for the instructions, that are presented on the screen, there are no further adaptations of the original RBANS with regard to the assessment of this cognitive domain. This index consists of two subtests, Figure Copy and Line Orientation (Table 2). In the first test the subject is asked to copy a geometric figure, this figure remains visually available while copying. The figure consists of 10 parts, each is evaluated for the accuracy of the shape and placement. Therefore, a 2-point score (accuracy and placement) is given for each part, and a total score of 20 points can be obtained. In the Line Orientation test a semi-circular pattern of numbered lines (1-13) is presented on the PowerPoint presentation, these lines are radiating out from a single point. Below this figure two lines of equal length are presented, these match the orientation of two lines from the figure above (Figure 6). The subject is asked to match these lines to the correct numbers of the semi-circular figure above. This is repeated for 10 items, each item consists of two lines and one point is given for each correctly matched line. Therefor a total score of 20 is possible on the Line Orientation test (Claes et al., 2016, Randolph et al., 1998).

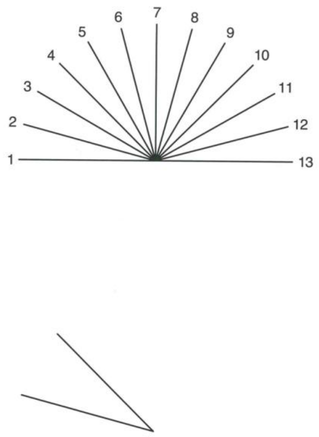

Figure 6: Line Orientation test.

Language The index Language also consists of two subtests: Picture Naming and Semantic Fluency (Table 2). In the Picture Naming test, 10 line drawings need to be named by the subject. For each correct naming one point is given. A semantic cue is given in case of an obvious misperception, e.g., when the line drawing is a trumpet, the semantic cue is 'a musical instrument'. In the Semantic Fluency test the participant is asked to name as many examples as possible from a given semantic category within 60 seconds, e.g., name as many fruits and vegetables, zoo animals, etc. For each example the subject will receive one point, with a maximal score of 40 (Claes et al., 2016, Randolph et al., 1998).

Attention The index Attention consists of the following two subtests: Digit Span and Coding (Table 2). In the RBANS-H, the string of numbers is shown on the screen and simultaneously read aloud by the examiner. After each string, the subject is asked to repeat the string in the same order. The first string has a length of two digits, and the length increases by one every time till the string has a length of nine digits. For each length two strings are provided, the second string is only read in case the first one is failed. A total score of 16 points can be obtained, there are eight (first) strings and two points can be obtained for each correct (first) string. In case the second string needs to be used, a maximum of one point can be obtained for this string when correct. When the participant is not able to correctly repeat the first and second string, the next strings consisting of more numbers are skipped. Coding is the second subtest of the index Attention. The subject is presented a page with symbols and a key is located at the top of the page. In the key, nine different symbols are each matched to a number. The subject is asked to fill in the correct numbers corresponding to each symbol within a time span of 90 seconds using this key. For each correct match within the given time, one point is given. A maximal score of 89 is possible (Claes et al., 2016, Randolph et al., 1998).

Delayed memory The last index, Delayed memory, consists of four subtests: List Recall, List Recognition, Story Recall, and Figure Recall (Table 2). In these subtests the participant needs to recall or recognize aspects of one of the previous tests. The first subtest, List Recall, involves recall of as many words as possible from the 10-item word list from the List Learning task. In this subtest one point is given for each correct word. In the List Recognition test the subject needs to recognize words from the 10-item word list from the List Learning task. This subtest consists of 20 words, 10 words of these are from the original list and 10 are not. The words are audio-visually presented word by word to the subject, and the subject is asked whether the word was on the original list or not. For each correct answer ("Yes, it was in the list", or "No, it was not in the list") one point is given, resulting in a maximal score of 20. The Story Recall subtest involves the recall of the story from the Story Memory test. The subject is asked to give as many details as possible from the story that was told earlier in the examination, for every correct item one point is given. In the last subtest of the Delayed Memory, the subject needs to recall the figure from the Figure Copy subtest. The subject is asked to draw as many elements of this figure as he/she can recall. The scoring is similar to the Figure Copy test, a 2-point score (accuracy and placement) is given for each part and a total score of 20 points can be obtained. The scores of the subtests List recall, Story recall and Figure recall are summed up (Randolph et al., 1998, Claes et al., 2016).

4.1.2.1 Score RBANS-H

For each subtest the total score is calculated such as previously described, this score will be scaled by age-group to a mean score of 100 with an associated standard deviation of 15. This scaling allows checking whether the different cognitive domains are normal according to the age of the individual. Hence, the scoring allows for correcting for normal cognitive ageing. A total scaled score for the RBANS can be derived from the sum of the scaled index scores of the individual cognitive domains, an example of a score form can be find in *8.1 Appendix*. This total score also has a normal mean of 100 and a standard deviation of 15. The scores can range from 40 to 160, a score of 40 corresponds with percentile <0.1 whereas a score of 160 corresponds with percentile >99.9 (Randolph et al., 1998).

4.1.3 Secondary outcome measurements

Together with the assessment of cognition, audiometric assessment and several questionnaires are done. These measurements are performed at baseline (T0) and annually after the activation of the CI (T1, T2, T3, T4) (Figure 5).

Audiometric assessment The audiometric test battery consists of pure tone audiometry, speech perception in quiet and in noise. Pure tone audiometry is measured in unaided and best-aided condition. Unaided pure tone audiometry is performed at 125, 250, 500, 1000, 2000, 3000, 4000, 6000, and 8000Hz. The aided air conduction thresholds are tested at the same frequencies. In case the subject has both a CI and a conventional hearing aid, aided thresholds are measured for each device separately and in best-aided condition. During the preoperative measurements, bone conduction is also tested, this is done at the following thresholds; 250, 500, 1000, 2000, 3000, and 4000Hz (ISO 8253-1, 2010) (Claes et al., 2016, Punte and Van de Heyning, 2013). Fletcher indexes (FI) are derived from the air conduction thresholds, Low FI corresponds with the average air conduction threshold at 500Hz, 1000Hz, and 2000Hz, whereas the High FI is calculated from 1000Hz, 2000Hz, and 4000Hz (Lamoré, 2018). Speech audiometry in quiet is also measured in unaided and aided condition. The Dutch NVA (*Nederlands Vereniging voor Audiologie*) list is used, each list contains 12 monosyllabic words of which one is a training example. The speech recognition score is the percentage of correctly identified phonemes, and it is tested at 65dB SPL (Claes et al., 2016, Bosman et al., 1995, Kapteyn, 2011). Speech perception is also assessed in noise, using the Leuven Intelligibility Sentences Test (LIST). In this test the noise level is fixed at 65dB SPL and 10 sentences of equal length are played aloud by a CD-player. Depending on the response of the subject, the level of the speech signal is changed: if the sentence is repeated correctly the speech signal is decreased by 2dB SPL and if the subject is not able to repeat the keywords correctly, the level is increased by 2dB SPL. The Speech Reception Threshold is calculated as the mean level of the five last sentences and the 11th (imaginary) item of the list. Lower scores on the speech perception in noise test indicate better performance (Claes et al., 2016, van Wieringen and Wouters, 2008).

Nijmegen Cochlear Implant Questionnaire (NCIQ) During this study the effect of cochlear implantation on several health-related QoL aspects is investigated. The NCIQ will be used, which is a Dutch self-assessment tool consisting of 60 questions. The questions are divided in the following principal domains: Physical, Psychological, and Social. These three principal domains consist of different subdomains, each subdomain covers 10 statements. The Physical domain consists of the subdomains, Basic Sound Perception, Advanced Sound Perception, and Speech Production. The Psychological domain consists of only one subdomain, namely Self-esteem. The last domain compromises two subdomains, Activity Limitations and Social Functioning. The subject needs to rate each statement on a 5-point Likert scale, ranging from “Never” to “Always” or from “No” to “Good”. In the questionnaire there is also a sixth response category “N/A” for items that are not relevant for them (Hinderink et al., 2000).

Hearing Implant Sound Quality Index (HISQUI19) Another parameter that is assessed during this study is the self-perceived level of auditory benefit of the CI users in everyday listening situations. This is done with the HISQUI19, which is a questionnaire that consists of 19 items and usually takes around 10 min. The subject needs to score the items on a 7-point Likert scale, and each response option is linked to a numerical value (never= 1 to always= 7). The total score of the HISQUI19 is the sum of all numerical values on the 19 items. The total score classifies the self-reported sound quality into 5 classes, "very poor" (score range below 30), "poor" (between 30-59), "moderate" (60-89), "good" (90-109), and "very good" (110-133) (Amann and Anderson, 2014, Mertens et al., 2015).

Speech, Spatial, and Qualities of Hearing Scale The study also includes a questionnaire to assess self-reported hearing disabilities. During this study the short form of the SSQ will be used, the SSQ12. This is a questionnaire that consists of 12 items, the subject gives a score ranging from 1 to 10 for each item. Lower scores are related to a higher level of hearing disability (Gatehouse and Noble, 2004, Noble et al., 2013).

Hospital Anxiety and Depression scale (HADS) In both groups symptoms of depression and anxiety are assessed, this is done with the HADS. It is a questionnaire consisting of 14 items, of these 7 are linked to the subscale "Depression" and 7 items are linked to "Anxiety". Anxiety and depression are scaled separately, a score below 7 indicates that there is no anxiety disorder or depression. A score between 8 and 10 indicates possible cases and a score above 11 are more definite cases with anxiety or depression symptoms (Zigmond and Snaith, 1983, Bjelland et al., 2002).

Type D questionnaire (DS14) The last secondary outcome measurement that is administered is the DS14 which is a tool to identify subjects with a type D personality. Individuals with this type of personality have the tendency towards negative affectivity and social inhibition. This means that the individuals tend to experience more negative emotions, such as anxiety, irritability, and they see things more negatively. Social inhibition refers to how individuals behave in social interaction, when they are with others they tend to feel more tense and insecure. Furthermore, they are more likely to inhibit the expression of certain emotions and behaviors to avoid disapproval by others. Individuals with Type D personality are more at risk for chronic distress and for a wide range of other health problems. The DS14 questionnaire assesses both traits of the Type D personality, 7 items are included for each trait. The subject rates each item on a 5-point Likert-scale ranging from 0 to 4. Individuals are classified as Type D personality in case both negative affectivity and social inhibition are higher or equal to 10 (Denollet, 2005).

4.2 Statistical analysis

IBM SPSS Statistics version 28 (IBM Corp., New York, NY) will be used for the statistical analysis. The changes in cognition and the secondary outcome measurements over time (T0 - T4) will be investigated. First a linear mixed model will be performed on the total RBANS-H score, RBANS-H sub scores, and the different questionnaires to investigate the evolution of the different outcome measurements over time. The following fixed factors are included in the linear mixed model; Timepoint (T0, T1, T2, T3 or T4), sex (male/female), and years of education. In the linear mixed model for the RBANS-H total score and sub scores the following fixed factors are also added; HADS anxiety score, HADS depression score, and RBANS-H version. In contrast to the RBANS-H scores, the QoL questionnaires are not corrected for age, therefor the fixed factor age is included in the linear mixed model for the QoL questionnaires. Afterward, post hoc pairwise comparisons will be performed on the data to identify clinically meaningful effects. To determine which statistical test will be used, data is first checked for normal distribution. In case the data is normally distributed a t-test is used for post hoc pairwise comparison, if not a nonparametric test variant is used, namely a Wilcoxon test, to identify meaningful effects. To determine the correlation between hearing restoration and cognitive improvement, the preoperative scores are subtracted from the postoperative score for the following measurements; RBANS-H total score, NVA score, LIST score, and both FI low and FI high score. Thereafter, a Spearman rank correlation test is performed to study the correlation between the improvement in cognitive score and the improvement in different audiometric assessment scores. The one-sided significance threshold is assessed to determine significance.

5 Results

Out of the 99 individuals included in the study, we were able to select 25 individuals for whom measurements were available across all timepoints. 30 individuals participated in the study for 4 years or more after cochlear implantation, but at T2 one subject was not able to participate in any of the measurements and at T3 four individuals did not participate in any of the measurements. Some individuals did not participate in the cognitive test or questionnaires at a particular timepoint, these individuals were also excluded for the statistical analysis of that specific outcome measure (Figure 7). Details for the specific tests will be explained in more detail in the designated section. An overview of the characteristics of the participants at baseline is shown in Table 3.

Table 3: Overview of the participants characteristics at baseline (preoperatively)

Variable	Number (%)	
Number of subjects	25	
Age in years, mean	69,8	
Formal education in years, mean[a]	10,4	
Sex		
Male	16 (64)	
Female	9 (36)	
Unaided PTA best ear preop, mean, dB[b]	90	
Cause	**Ipsilateral**[c]	**Contralateral**[c]
Hereditary	2 (8)	2 (8)
Meningitis	1 (4)	1 (4)
Noise induced	0 (0)	1 (4)
Otosclerosis	2 (8)	2 (8)
Ototoxicity	1 (4)	1 (4)
Trauma	1 (4)	1 (4)
Unknown	16 (64)	15 (60)
Meniere's disease	1 (4)	1 (4)
Chronic otitis media	1 (4)	1 (4)
Ear implanted		
Right	13 (52)	
Left	12 (48)	
Hearing aid use		
Bilateral	9 (36)	
Unilateral	14 (56)	
No	2 (8)	
Retired		
Yes	22 (88)	
No	3 (12)	

[a] *Formal education is counted from the age of 6, elementary school*
[b] *PTA is the average hearing sensitivity at 500Hz, 1000Hz and 2000Hz*
[c] *ipsilateral: cause of hearing loss on the implanted side, contralateral indicates the other side*

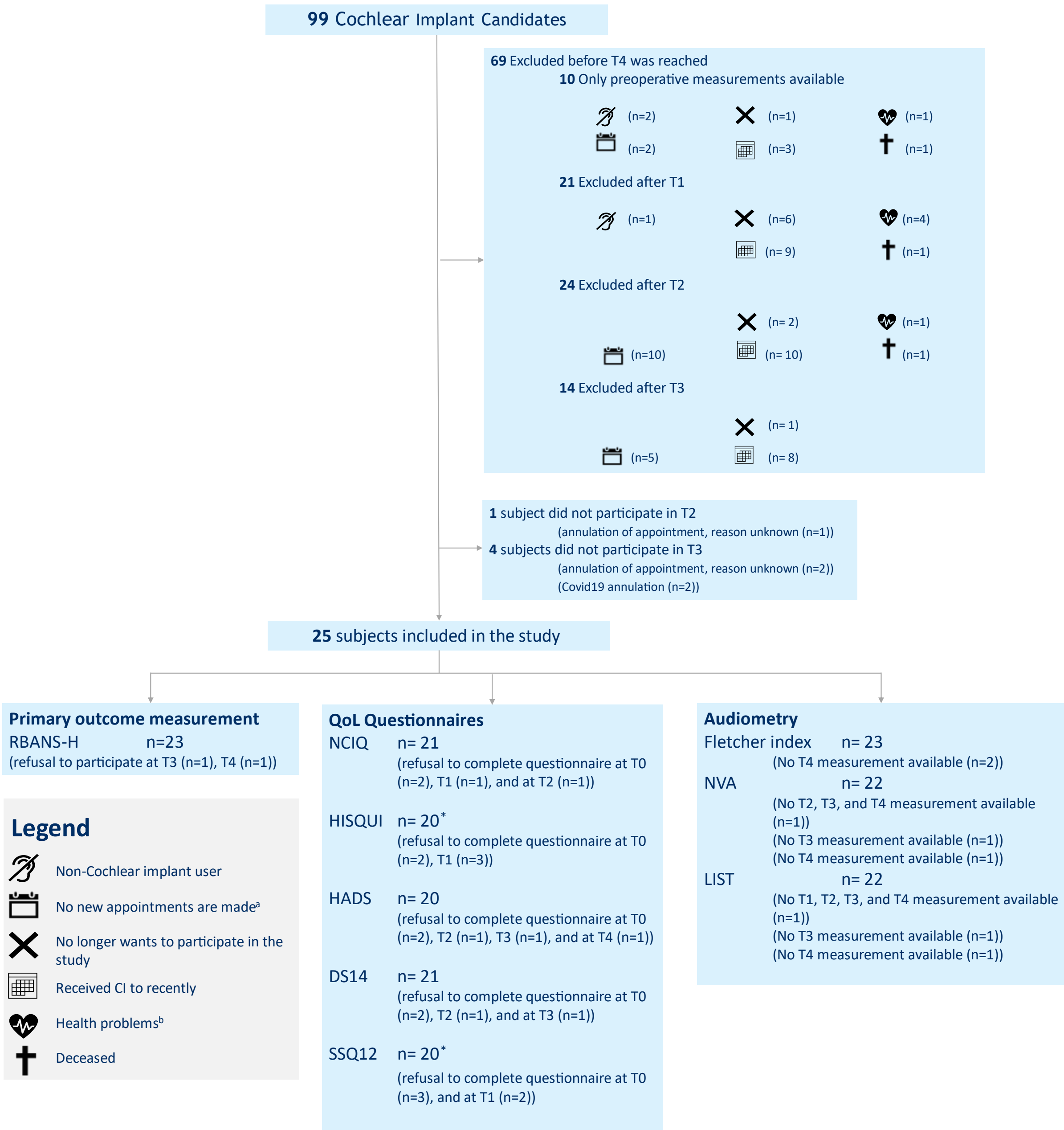

Figure 7: Flowchart of the study population. 99 subjects participate in the study, of these only 25 subjects are included for 4 years or more and participated at all timepoints. For some individuals certain tests were not performed, therefore a slightly different amount (n) of data is used for the statistical analysis. (These tests are only compared between T0 and T1, because the sample size over 4 years was less than 20 subjects, [a] reasons differ between subjects, e.g. Covid19 annulation, sickness, repeatedly canceling the appointment, etc., [b] include health problems that prevented the subject from participating or could have a significant effect on test results, including dementia, cancer, psychiatric disorder, stroke, etc.,)*

5.1 Primary outcome measurement

5.1.1 RBANS-H

Some individuals preferred not to participate in the cognitive test, or were not able to participate due to illness. Therefore, two more individuals are excluded for the primary outcome measurement, one subject did not participate in the cognitive test at T3, another subject did not participate at T4. This results in a sample size of 23 subjects for the RBANS-H total score and for the RBANS-H subdomains. Despite this missing data, the sample size was still of adequate size to make valuable conclusions. Data for both the RBANS-H total score, as well as the subdomains is normally distributed, therefore a parametric t-test is used to determine significant differences.

The linear mixed model including the following fixed factors; timepoint, sex, years of education, HADS anxiety score, HADS depression score, and RBANS-H version; showed only a significant association between timepoint and RBANS-H total score. In addition, the subdomains of the RBANS-H showed no association with the factors sex, years of education, HADS anxiety score, HADS depression score, and RBANS-H version. The following cognitive subdomains showed a significant association with the factor Timepoint; "Immediate Memory", "Visuospatial Memory", and "Delayed Memory". An improvement in the overall cognitive score, and for three subdomains is observed when comparing the data before and 12 months after cochlear implantation using a t-test. Preoperatively the mean RBANS-H score was 92.78 (± 15.08) and significantly improved to a mean value of 98.35 (±14.18) 12 months after implantation ($p<0.001$). Thereafter no further significant changes are observed in the RBANS-H total score, indicating that the effect of cochlear implantation on cognition stabilizes approximately one year after implantation (Figure 8a). Additionally, index scores for the 5 different cognitive subdomains were compared over time. The index scores of the subdomains "Visuospatial" and "Language" did not show any significant changes over time, indicating that cochlear implantation had no effect on these cognitive domains. A significant difference was observed for the following subdomains; "Immediate memory" ($p<0.001$), "Attention" ($p=0.016$), and "Delayed memory" ($p=0.006$), comparing T0 and T1. The index score for "Immediate memory" improved from a mean score of 94.13 (± 18.75) preoperatively to a mean score of 105.39 (±19.98) at T1. The "Attention" index scores improved significantly with mean scores improving from 86.17 (±19.02) at T0 to 91.57 (±15.35) at T1. The fifth subdomain, "Delayed memory", considerably improved from a mean score of 97.91 (±14.51) to 103.83 (±14.714) 12 months after implantation. After T1, none of the cognitive subdomains showed a significant change in index score.

In summary, a significant improvement was observed for the RBANS-H total score and for the subdomains "Immediate memory", "Attention", and "Delayed memory", comparing the RBANS-H scores preoperatively and 12 months after CI activation. After T1 no further significant improvement was observed, indicating that the results stabilize 12 months after CI activation (Figure 8).

Moreover, no significant correlation was found between the improvement in RBANS-H score and improvement in hearing abilities, namely FI scores, speech recognition in quiet and in noise, using a Spearman rank correlation test.

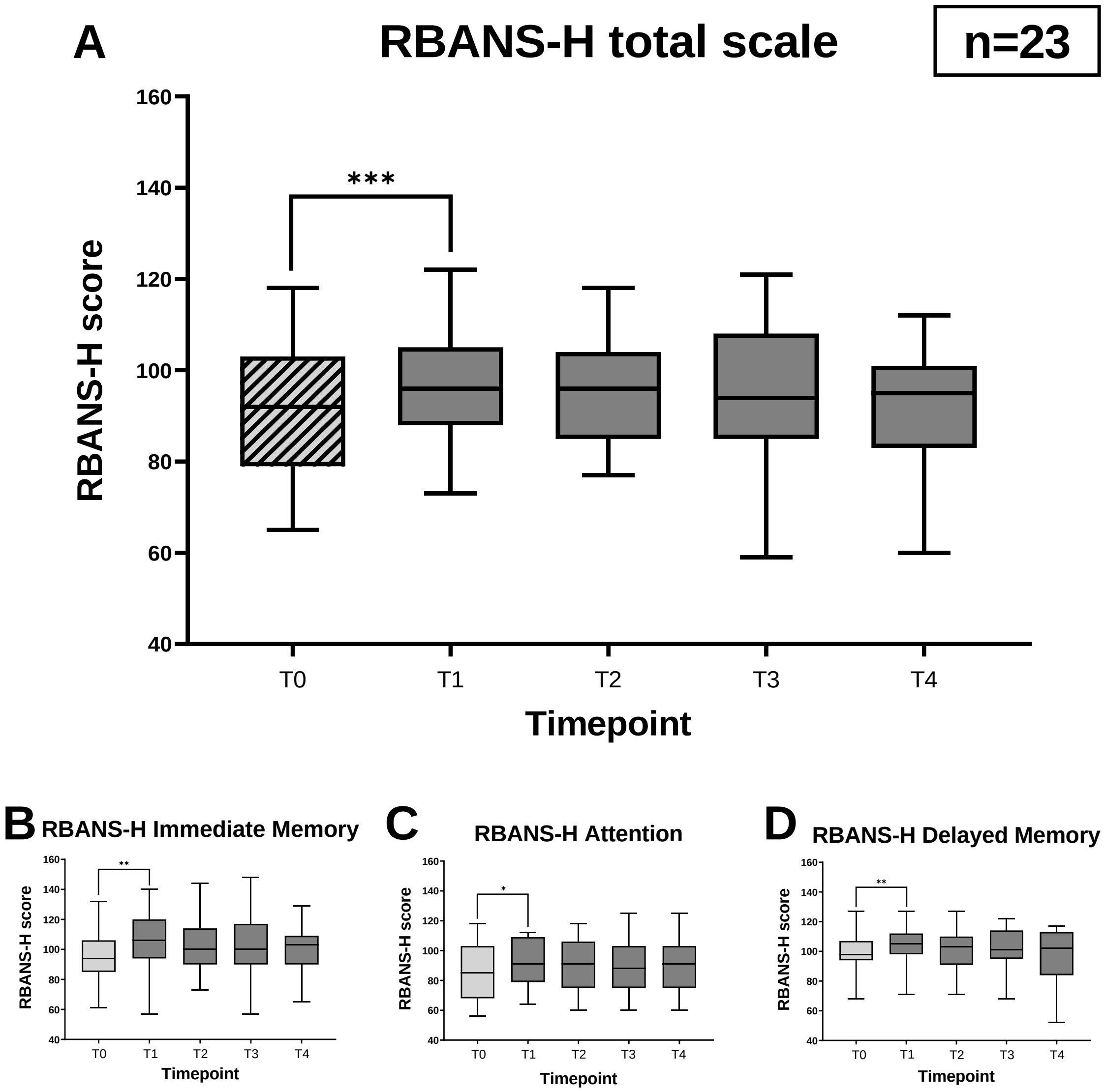

Figure 8: Cognitive outcome measurements, boxplots of the RBANS-H total score and index scores over the different timepoints (T0, T1, T2, T3, and T4). Boxplots represent minimum, 1st quartile, median, 3rd quartile, and maximum of the RBANS-H score (A) RBANS-H total score, a significant improvement is observed comparing T0 and T1 (p<0.001) using a t-test. (B) Immediate Memory index score of the RBANS-H shows a significant improvement comparing T0 and T1 (p= 0.002). (C) Attention index score of the RBANS-H, a significant improvement between T0 and T1 (p=0.016) is observed. (D) Delayed Memory index score of the RBANS-H, a significant change is present when comparing T0 and T1 (p=0.006). (indicates p < 0.05, ** indicates p < 0.01, and *** indicates p < 0.001)*

One year after cochlear implantation, an increase in total RBANS-H score was observed in 19 individuals (83%). In the years after cochlear implantation, some individuals further progresses while other show a decline in cognitive scores. Overall most individuals show an improvement in cognitive scores in the years after implantation, comparing T0 and T4, 12 individuals (52%) showed an improvement, 10 individuals show a slight deterioration in score, and the others remained stable. Before implantation, 30% of the individuals had a RBANS-H percentile between 25 and 75. Four years after implantation this increased to 61% of the individuals with a RBANS-H score within this range. Figure 9 clearly demonstrates the change in RBANS-H percentile over the different timepoints for the individuals.

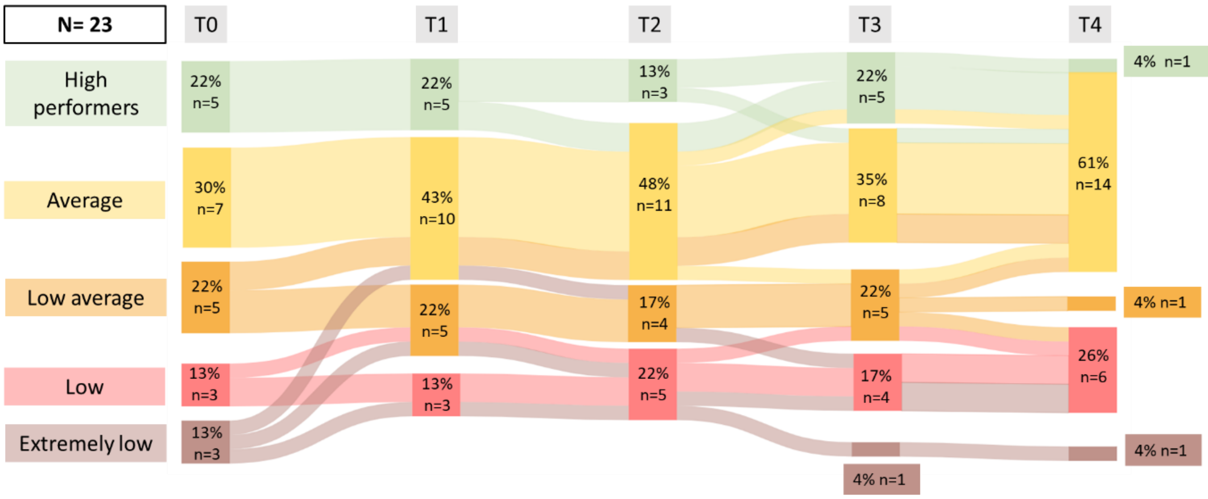

Figure 9: Sankey diagram shows the evolution of the cognitive level of the individuals over time. Individuals are divided in the following 5 groups depending on their percentile on the RBANS-H score preoperatively; High performers (percentile ≥ 75), Average (percentile >25 and <75), Low average (percentile ≥16 and <25), Low (percentile <16 and >2), and Extremely low (percentile ≤2).

5.2 Secondary outcome measurements

5.2.1 QoL: Questionnaires

5.2.1.1 NCIQ

Despite the fact that the questionnaires were sent to the subjects on time, some individuals preferred not to fill in the questionnaire or only a small part of the questionnaire. Preoperatively NCIQ was missing for two individuals, at T1 for one individual, and at T2 also for one subject. This results in a sample size of 21 subjects for the NCIQ, the data is normally distributed.

Linear mixed model analysis showed only an association with timepoint, and no association was found for the factors age, sex, and years of education. An improvement is seen for both the NCIQ total score and the subdomain scores when performing pairwise comparison with preoperative and 12 months postoperative scores. The NCIQ total score improved from a mean score of 34.23 (±12.65) at T0 to 61.83 (±15.27) at T1, t-test indicated this improvement significant (p<0.001). After T1 no more significant changes were observed in the total NCIQ score (Figure 10a). Additionally, all the subdomains of the NCIQ are significantly improved after cochlear implantation (p<0.001). The subdomain scores; Basic Sound Perception (mean (±SD), 22.33 (±18.48) vs 61.60 (±16.77)), Advanced Sound Perception (20.38 (±14.88) vs 49.20 (±15.59)), Speech Production (54.39 (±21.68) vs 72.02 (±17.90)), Self Esteem (39.76 (±19.16) vs 64.26 (±21.34)), Activity Limitations (36.32 (± 19.52) vs 66.73 (± 21.67)), Social Interaction (32.92 (± 15.87) vs 57.55 (± 17.27)); increased 12 months after cochlear implantation, the subdomains Basic Sound Perception and Self Esteem remain stable thereafter. The other subdomains showed a small decrease in score, but there is still a significant improvement compared to T0 (Figure 10 b-f).

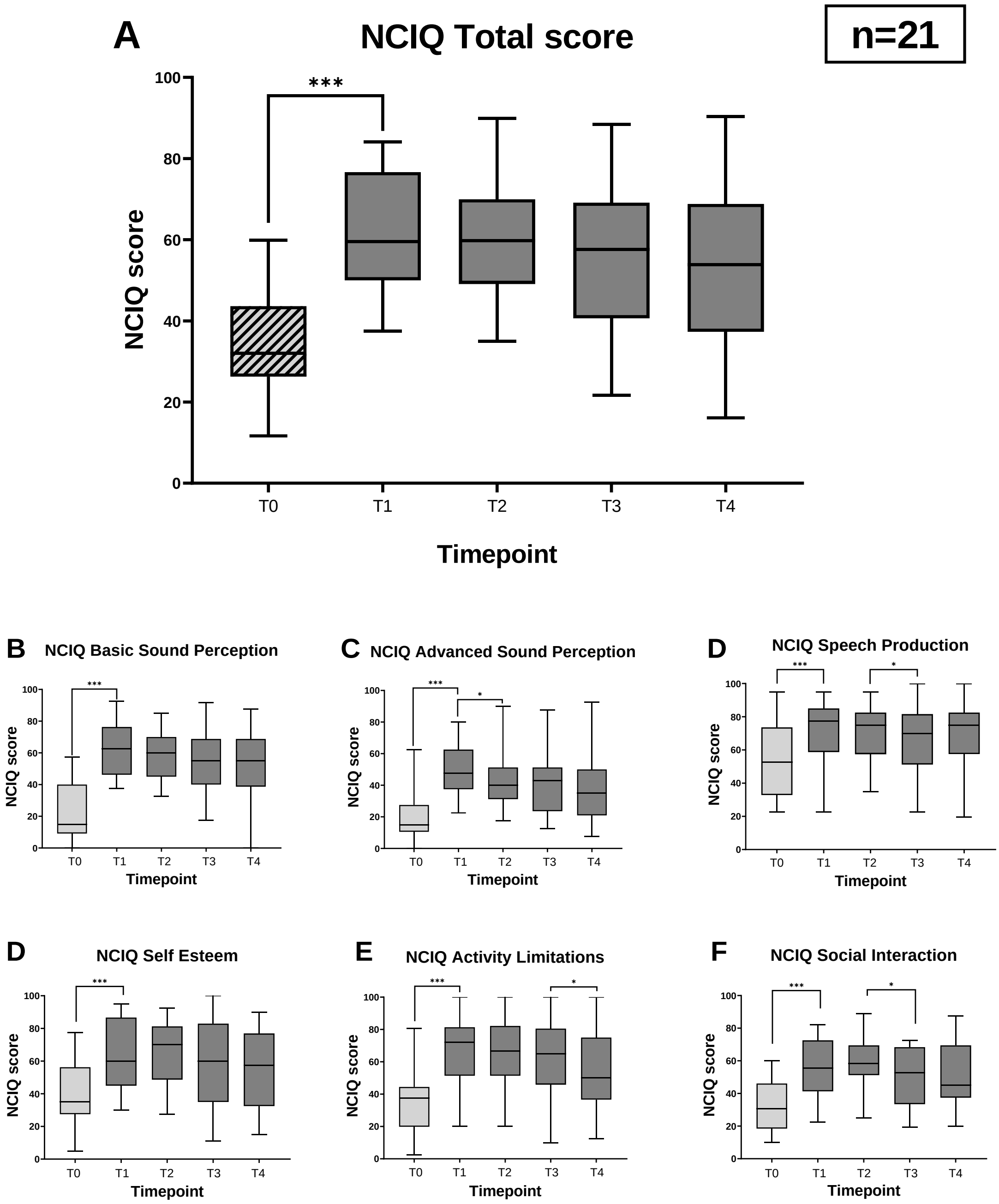

Figure 10: NCIQ scores presented as boxplots at the different timepoints. Boxplots represent minimum, 1st quartile, median, 3rd quartile, and maximum of the NCIQ score. (A) NCIQ total score, significant difference comparing T0 and T1 (p<0.001). (B) NCIQ Basic Sound Perception score, significant improvement one year after cochlear implantation in comparison to preoperatively (p<0.001). (C) NCIQ Advanced Sound Perception score, comparing T0 and T1 a significant improvement is present (p<0.001), comparing T1 and T2 a small decline can be observed (p=0.022). (D) NCIQ Speech Production, significant improvement comparing T0 and T1 (p<0.001), and a small decline can be observed between T2 and T3 (p=0.036). (D) NCIQ Self Esteem, significant improvement 12 months after CI activation (p<0.001). (E) NCIQ Activity Limitations score, improvement comparing T0 and T1 (p<0.001) but a small decline comparing T3 and T4 (p=0.020). (F) NCIQ Social Interaction score, improvement comparing preoperatively and 12 months postoperatively (p<0.001), and a small change after T2 (p=0.019). (indicates p < 0.05, ** indicates p < 0.01, and *** indicates p < 0.001).*

5.2.1.2 HISQUI19

The HISQUI19 questionnaire is the only questionnaire filled in on the computer during the appointment in the clinic, and not send by mail to the subject. These questionnaires were often not completed by the subject, resulting in a too small sample size (n=10) to investigate the long-term effect. Therefore, the effect of cochlear implantation on the HISQUI19 score is only investigated one year after CI activation. It was possible to compare the HISQUI19 score of 20 individuals preoperatively and at T1, these scores were normally distributed. Linear mixed model analysis, with the following fixed factors; age, sex, preop years of education, and timepoint; only showed a significant association between HISQUI19 score and Timepoint. Posthoc comparison showed a significant improvement in HISQUI19 score after cochlear implantation (p<0.001). Preoperatively the mean HISQUI19 score was 31.85 (± 9.65), this score increased to a mean total score of 65.15 (±13.95) 12 months after CI activation (Figure 11). Before implantation 8 subjects (40%) reported their sound quality as "very poor" and 12 (60%) reported their sound quality as "poor". After implantation all subjects reported their sound quality as "poor" (35%) or "moderate" (65%), and none remained in the first category ("very poor").

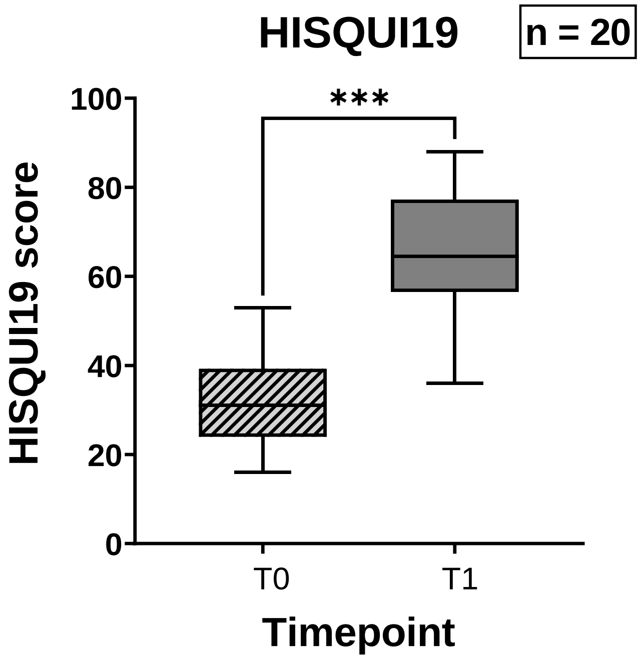

*Figure 11: Boxplots of the HISQUI19 total score preoperatively and at T1, boxplots represent minimum, 1st quartile, median, 3rd quartile, and maximum score. A significant improvement is present when comparing T0 and T1 (p<0.001) (*** indicates p < 0.001).*

5.2.1.3 SSQ12

Sample size of individuals for whom SSQ12 questionnaires are available for all timepoints was too small, therefore the effect of cochlear implantation is only studied at T0 and T1. Preoperatively the SSQ12 was missing for three individuals, and at T1 two individuals did not fill in this questionnaire, resulting in a sample size of 20 individuals when studying the effect of CI one year after activation. The SSQ12 results are not normally distributed according to the Shapiro-Wilk test, therefore a Wilcoxon Test is used to check for a significant effect of cochlear implantation on the SSQ12 score. A significant effect is observed when using a Wilcoxon test comparing SSQ12 score at T0 and at T1 (p<0.001), a similar effect was found when using a t-test (p<0.001). Preoperatively a total mean score of 1.42 (±1.11) is observed, this score significantly improved to a mean score of 3.64 (±1.59) one year after CI activation (Figure 12).

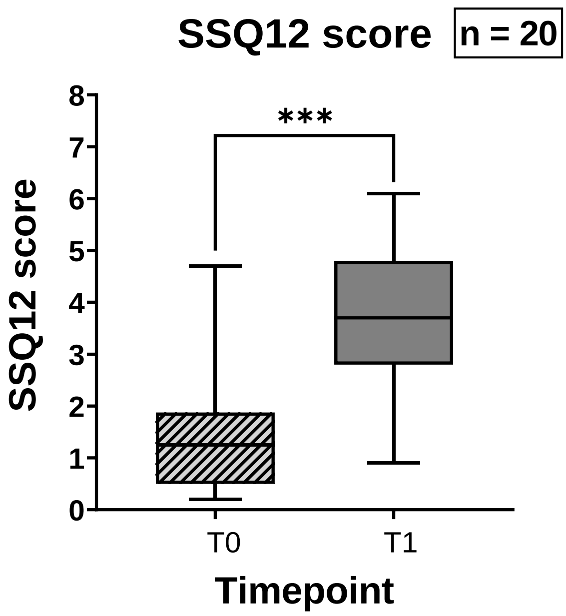

*Figure 12: SSQ12 score before cochlear implantation and 12 months after CI activation presented as a boxplot. Boxplots represent minimum, 1st quartile, median, 3rd quartile, and maximum score. A significant effect is present when comparing T0 and T1 (p<0.001)(***indicates p<0.001).*

5.2.1.4 DS14

Type D personality questionnaires were missing for two subjects preoperative, for one at T2, and for one subject at T3. This resulted in a total of 21 subjects for whom DS14 questionnaire were available for all timepoints. Both Negative affectivity and Social inhibition scores are normally distributed. Linear mixed model analysis showed only a significant association between timepoint and Negative affectivity score, and timepoint and Social inhibition score. The fixed factors, age, sex, and years of education did not show any association with Negative affectivity score or Social inhibition score. A significant improvement in both scores is present when comparing preoperative measurement and T1, one year after CI activation no further improvement is seen in neither of the personality D traits. The Negative affectivity score decreased from a mean value of 10.65 (±7.09) preoperatively to 6.85 (±7.18) at T1 (p=0.004). Social inhibition score decreased from a preoperative mean value of 16.15 (±7.90) to a mean value of 11.05 (±7.39) 12 months after CI activation (p=0.003)(Figure 13a,b). In case both type D personality traits have a score equal or greater than 10, then the individual has Type D personality. Preoperatively 8 subjects (38%) have type D personality according to the DS14 questionnaire, this amount of subjects reduced to 6 subjects (29%) one year after CI activation (Figure 13c).

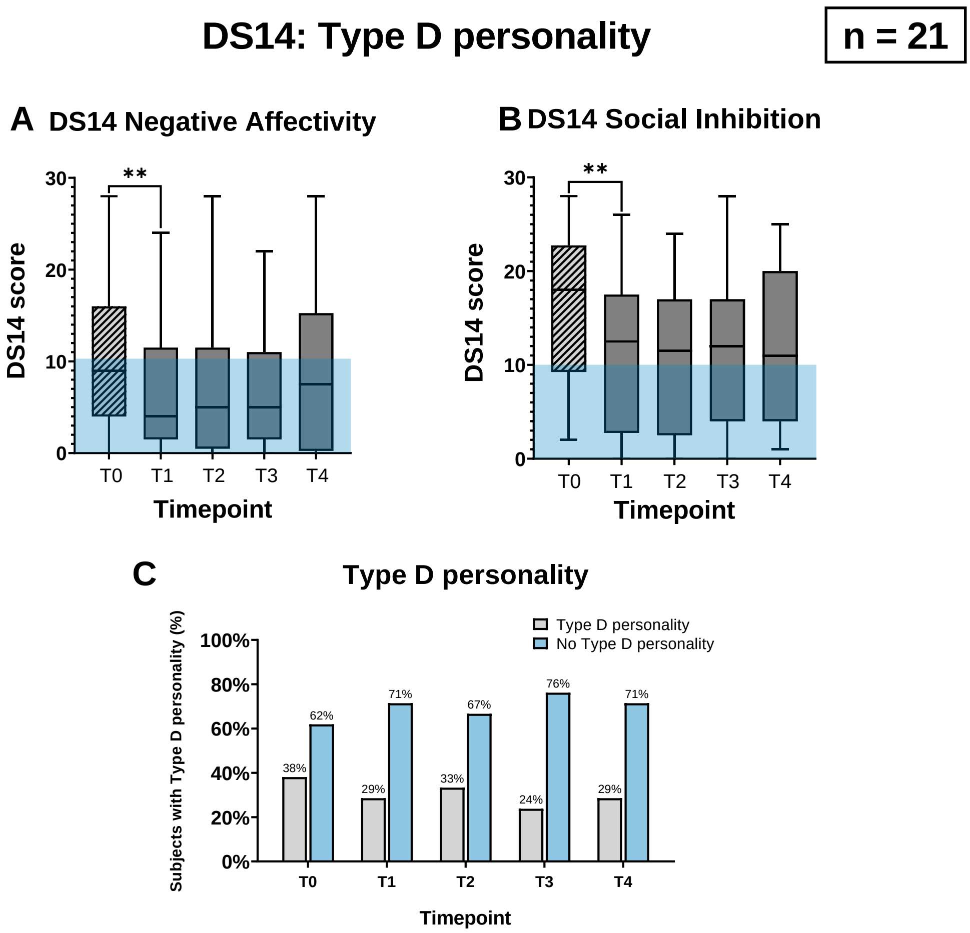

*Figure 13: DS14 scores are presented as boxplots over the different timepoints. Boxplots represent minimum, 1st quartile, median, 3rd quartile, and maximum score. The area marked in blue represents scores below 10, so no Negative Affectivity or Social inhibition. (A)This figure illustrates the DS14 Negative Affectivity score, here a significant improvement is present when comparing T0 and T (p=0.004). (B) DS14 Social inhibition score, a significant change is present when comparing T0 and T1 (p=0.003). (C) percentages of individuals with type D personality at each timepoint (** indicates p < 0.01).*

5.2.1.5 HADS

HADS questionnaire was not completed by two subjects at T0, and at T2, T3 and T4 one subject refused to complete the HADS questionnaire. Resulting in a sample size of 20 subjects for the statistical analysis of the HADS questionnaire. HADS Anxiety and Depression scores are not normally distributed according to the Shapiro-Wilk test, therefor a Wilcoxon test is used to check for a significant effect of cochlear implantation on anxiety and depression. Anxiety score showed a significant decrease one year after CI activation using a Wilcoxon test (p=0.008), score changed from 6.60 (±3.82) at T0 to 4.50 (±3.27) at T1, thereafter no further significant changes are observed. In the depression score a significant decrease is observed comparing T0 and T1 using a Wilcoxon test (p<0.001), preoperatively a score of 7.10 (±3.70) is observed and one year after implantation this score decreased to 4.40 (±3.75) (Figure 14).

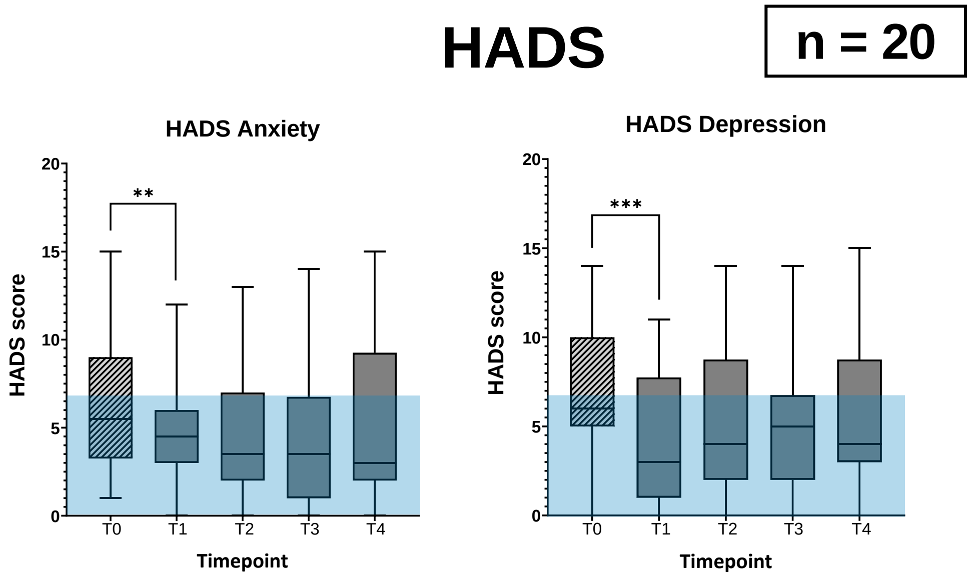

*Figure 14: HADS scores represented as boxplots, these represent minimum, 1st quartile, median, 3rd quartile, and maximum of the HADS score. Scores below 7 (blue area) indicate there is no anxiety or depression. Left figure shows the anxiety score of the HADS, here a significant change is observed comparing T0 and T1 (p=0.008). The right figure shows the depression score of the HADS at the different timepoints, here a significant change in score is observed comparing T0 and T1 (p<0.001) (** indicates p < 0.01, and *** indicates p < 0.001).*

5.2.2 Audiometry

5.2.2.1 Fletcher index

Audiological measurements are only missing for two individuals at T4, resulting in a sample size of 23 for whom measurements are available at all timepoints (T0-T4). The best Low and High FI are calculated for each individual at every timepoint, and these are used to compare over the different timepoints. The best-aided hearing condition preoperatively is used to compare the situation after cochlear implantation, hence for some individuals the FI score preoperatively is measured with a conventional hearing aid. The data of both the Low FI and High FI are normally distributed. Linear mixed model analysis showed a significant association between timepoint and both FI's. The fixed factors; age and years of education also showed an association with Low FI and High FI, with regard to sex no association was found. As expected, a considerable effect of cochlear implantation on hearing performance is observed. A significant improvement is shown when comparing Low FI and High FI preoperatively and at T1 using a t-test (p<0.001), thereafter no further changes are seen. Preoperatively the mean Low FI score was 73.13 (±22.76)dB, this reduced to a mean value of 41.46 (±5.30)dB at T1. A similar improvement is seen in the High FI score, at T0 the mean value was 81.87 (±22.18)dB and this improved to High FI mean value of 39.53 (±4.96) (Figure 15).

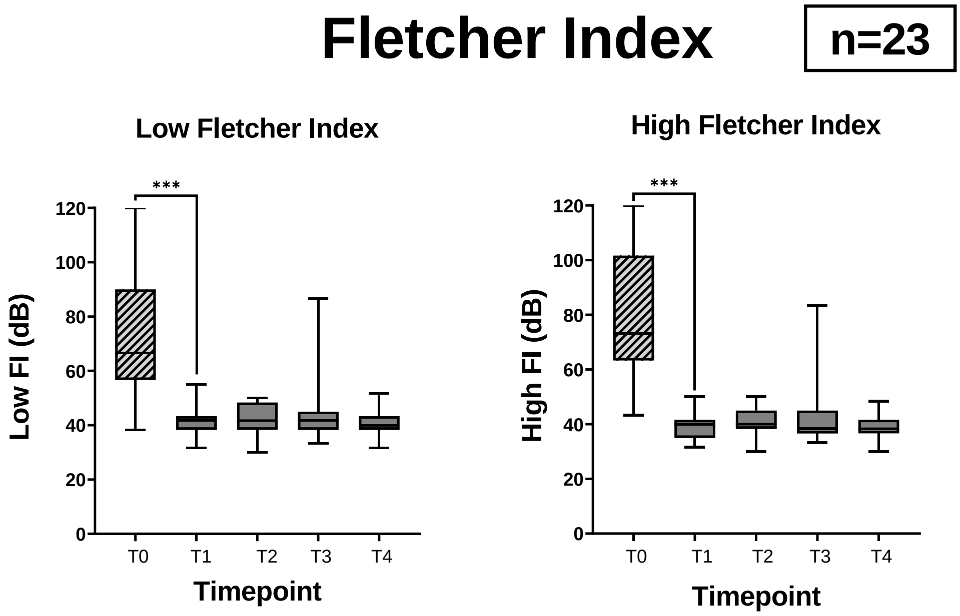

*Figure 15: Fletcher indexes are presented as boxplots over the different timepoints. Boxplots represent minimum, 1st quartile, median, 3rd quartile, and maximum of FI. Figure at the left shows the Low FI (average air conduction threshold at 500Hz, 1000Hz, and 2000Hz), whereas the figure at the right shows the High FI (average air conduction threshold at 1000Hz, 2000Hz, and 4000Hz). Both the Low FI and High FI show a significant improvement one year after CI activation (*** indicates p<0.001).*

5.2.2.2 Speech recognition in quiet and in noise

For some individuals the speech recognition in quiet and in noise was not measured. Speech recognition in quiet scores are missing for one subject at T2, T3 and T4, for one subject at T3, and for one subject at T4. Speech recognition in noise scores are missing for one subject at all postoperative measurements, for one subject at T3 and for one at T4. A sample size of 22 subjects was used for both the Speech recognition in quiet and in noise, and both NVA scores and LIST scores did not show normal distribution. One year after cochlear implantation a significant improvement in speech recognition in quiet, but also in noise is observed using a Wilcoxon Test($p<0.001$). Preoperatively the mean score on the NVA list was 27.04 (±26.64)%, and this score increased to a mean value of 77.27 (±12.44)%. For the Speech recognition in noise a maximal score of 20dB SNR can be obtained by the individual, higher scores on the LIST indicate worse performance. Preoperatively the mean score on the LIST was 17.90 (±4.93), one year after implantation this score significantly changed to a mean value of 6.30 (±5.29). Thereafter, only a change in LIST score is seen when comparing T1 and T2 using a Wilcoxon test ($p=0.005$) (Figure 16).

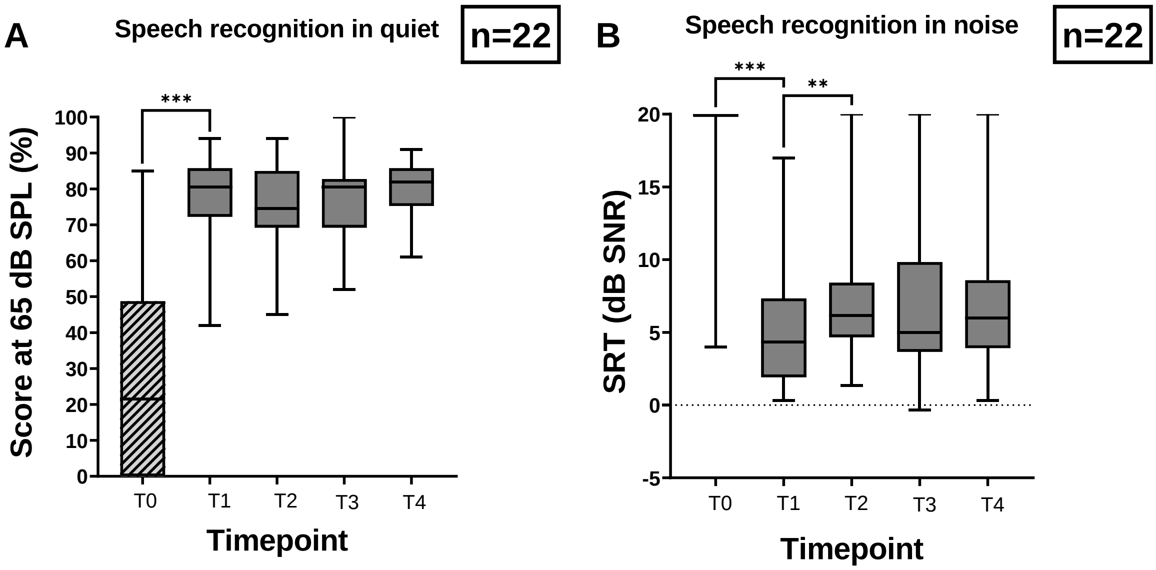

Figure 16: Speech recognition score in quiet and in noise represented as boxplots over the different timepoint. Boxplots represent minimum, 1st quartile, median, 3rd quartile, and maximum. (A) Speech recognition in quiet, measured using the NVA, showed a significant improvement one year after cochlear implantation (p<0.001). (B) Speech recognition in noise, measured using the LIST, showed a significant improvement one year after implantation (p<0.001). Thereafter a small change in score is observed when comparing T1 and T2 (p=0.005).

6 Discussion

6.1 Primary outcome measurement: Cognition

In this prospective longitudinal study, a significant improvement was demonstrated in the RBANS-H total score and on the following 3 cognitive subdomains; Immediate Memory, Attention, and Delayed Memory; 12 months after cochlear implant activation compared to preoperatively. No further significant improvement in cognitive functioning was seen in subsequent years. These findings are in line with previous publications, but it remains difficult to compare research on this topic due to the differences in study design. Such as previously described (“3.3.1 *Cognitive assessment tools*”), a wide range of cognitive assessment tools are currently available and each has its benefits and drawbacks. When comparing different studies on the effect of cochlear implantation on cognition, a difference in the selection of cognitive assessment tools is observed. Some studies use a screening tool for MCI or dementia (e.g., MoCA or MMSE), while others use a more comprehensive test battery consisting of multiple tests to assess each cognitive domain separately (e.g. RBANS-H, CANTAB, or ALAcog). Nevertheless, in the majority of studies an improvement in overall cognitive functioning was observed using different cognitive evaluation tools, for example MMSE (Mosnier et al., 2015), RBANS-H (Claes et al., 2018b, Mertens et al., 2021a), multimodular computer-based test battery (ALAcog)(Völter et al., 2018, Völter et al., 2022b), etc. Sonnet et al., (2017) made use of the MMSE, a screening test for dementia, but was not able to identify a meaningful effect of cochlear implantation on global cognitive functioning (Sonnet et al., 2017). This can be explained by the fact that screening tests are less sensitive and only differentiate between normal and abnormal cognitive functioning. However, other studies did find a significant improvement in cognitive functioning one year after cochlear implantation using the MMSE (Ohta et al., 2022, Mosnier et al., 2015). Most studies provided written instruction to the subject during the cognitive assessment to avoid improvement in cognitive performance linked to improvement in hearing. When comparing the effect of cochlear implantation on the cognitive subdomains some minor differences can be observed between the studies. Since there was no consensus in the selection of cognitive tests to examine different cognitive domains, comparing results is difficult. Some studies used the RBANS-H, which is corrected for age and investigates five different cognitive domains. While other studies made their own selection of cognitive tests. Despite those differences in assessment tools, various studies indicate a significant improvement in similar cognitive domains. A study by Völter et al., (2018) found significant improvements in executive functions such as attention, inhibition and working memory. Additionally, for delayed recall, and long-term memory a significant change was observed (Völter et al., 2018). Studies by Claes et al., (2018b) and Mertens et al., (2021a) made use of the RBANS-H, making it more easy to compare our results. In their studies they found significant effects in the same cognitive domains, namely “Attention”, “Immediate memory”, and “Delayed memory” one year after CI activation. Mertens et al., (2021a) were able to investigate the effect of cochlear implantation on cognition using both a control and intervention group. After correction for the improvement found in the control group, only a significant improvement was observed in the total RBANS-H score and the subdomain “Attention” (Mertens et al., 2021a).

In our study the practice effect is minimized by using two different versions of the RBANS-H, namely RBANS-H version A and B which are equivalent to each other. However, previous studies mentioned that the use of two RBANS-H versions is not sufficient to completely eliminate practice effects (Mertens et al., 2021a, Claes et al., 2018a). In our study, the risk of a practice effect is even higher as cognition is evaluated five times in the subjects. A study design including a control group which is assessed at similar timepoints as the intervention group is required to measure practice effect, and correct for it. From a scientific point of view, the ideal study design is a randomized control design. This means that CI candidates are randomly assigned to either the control or intervention group. Such a research design is far from ethical in this situation, as subjects who meet the criteria to receive a CI would then be excluded from the treatment. A more plausible solution is the use of a matched control group, where intervention and control individuals are matched for important characteristics such as gender, mean age, duration of formal education, cognitive functioning, etc., However, it remains difficult to recruit individuals in the control group given the positive effects of the CI. Some reasons why an individual may not receive a CI and might be included in the control group are the following: the subject is still on a waiting list or did not meet the reimbursement criteria for cochlear implantation, participant has a health condition which does not allow anesthesia or the ear anatomy did not allow cochlear implantation, or simply because the individual prefers not to undergo surgery (Claes et al., 2018a, Mertens et al., 2021b). After 2019, reimbursement criteria for cochlear implantation were less strict in Belgium, making more people eligible for a CI (Obyn et al., 2020). Which is very positive from a health perspective, but on the other hand complicates the recruitment of a control group of sufficient size. In addition to using a control group, another possible solution to reduce the practice effect is using more versions of the RBANS-H. Unfortunately currently only two RBANS-H versions are translated and validated in Dutch, and such as previously mentioned, the use of multiple versions of the cognitive test will not eliminate the risk for practice effect completely.

This study included individuals with a different cognitive level preoperatively, varying from high performers to individuals with a very low cognitive score or even MCI. Hence, it is not clear whether all individuals indeed suffered from a cognitive decline preoperatively due to perceptual difficulties. Individuals with a poor cognitive score preoperatively seem to improve more compared to individuals that already had a normal or high score before cochlear implantation. A study by Mosnier et al., (2015) describes the effect of cochlear implantation on cognition in a group of individuals with a poor cognitive score preoperatively, and in individuals with the best cognitive performance. They observed an improvement in cognitive functioning after cochlear implantation in over 80% of the subjects who had a low cognitive score before implantation. Subjects with high cognitive score preoperatively remained stable after cochlear implantation, and around 24% showed a slight decline (Mosnier et al., 2015). Another study investigated the effect of cochlear implantation in individuals with MCI preoperatively, they found a clinically meaningful improvement in cognitive score after implantation (Andries et al., 2023). Based on our findings and these other studies, it seems that the greatest effect on cognition is present in individuals with a lower score preoperatively, and that the effect is less pronounced in the high performers. Nevertheless, solid evidence is lacking as most studies investigate only the poor performers or the group of poor and high performers as a whole. In order to make valuable conclusions regarding the difference in cognitive evolution, the effect of cochlear implantation on cognition needs to be investigated in a group of poor performers, and high performers.

In the section “*3.2.1. Impact on individuals life*” different hypotheses regarding the effect of hearing loss on cognition are described. Results from this study point in the direction of the Information degradation hypothesis, this hypothesis states that perceptual difficulties cause cognitive decline and that this decline is reversible. During this thesis we observed an improvement in cognitive performance after compensating for hearing problems using a CI. Nevertheless, no clear correlation was found between the improvement in cognition and hearing thresholds, or speech recognition in quiet or noise in this study. Another recent study was able to show a negative correlation between improvement in speech recognition in noise and cognitive improvement in individuals with MCI preoperatively (Andries et al., 2023). However, several studies concur with our findings, and found no clear correlation (Völter et al., 2022b, Mosnier et al., 2018, Völter et al., 2022a, Knopke et al., 2021, Ohta et al., 2022). The correlation found in the study by Andries et al., (2023), and not in the others may be linked to the fact that only individuals with MCI were included in this study (Andries et al., 2023).

In addition to the lack of a control group in this study, there are some other limitations and considerations that should be taken into account in future research. An important aspect to consider is the fact that individuals receive auditory rehabilitation after cochlear implantation, which may have a positive effect on cognitive functioning. It is difficult to predict to what extent the improvement in cognitive functioning is linked to the CI itself or to the auditory rehabilitation. In addition, a small sample size of 23 participants is used to study the effect of cochlear implantation on cognition. This sample size is in line with the calculations, namely a sample of at least 19 subjects is needed to obtain 80% power using a paired t test to detect a Cohen’s d of 0.7 at a significance level of 0.05. Nevertheless, a larger study group to investigate the effect of cochlear implantation on cognition on the long-term must remain a goal in future research. Cognition is a complex aspect to study, as it is influenced by a broad range of different factors (Livingston et al., 2020, Calvino et al., 2022b). During this study only a few confounders are taken into account, including age, sex, years of formal education, anxiety and depression, but none of these showed a significant association with the RBANS-H score. Certain medical conditions, or the use of medication could also have affected the cognitive functioning in the participants. This is especially important since the study population consists of individuals aged 55 or older, and these are more prone to certain health conditions and many of them use medication.

6.2 Secondary outcome measurements

One year after cochlear implantation a significant improvement was observed in all scores on the QoL questionnaires. Thereafter the results stabilize for most questionnaires, unfortunately we were not able to analyze HISQUI19 and SSQ12 scores after T1.

Both the NCIQ and HISQUI19 are commonly used questionnaires in the field of cochlear implantation. These questionnaires are specifically designed to investigate the effect of cochlear implantation on several health-related QoL aspects and auditory benefit. The NCIQ is a self-assessment tool developed to quantify health-related QoL aspects in CI users. This questionnaire contains questions about different situations across the following 6 subdomains; Basic sound perception, Advanced sound perception, Speech production, Self-esteem, Activity limitations and Social interaction (Hinderink et al., 2000). The HISQUI19 investigates the auditory benefit, it contains questions relating to sound quality and complex listening situations. It contains for instance, items related to distinguishing between different voices/ speakers, identifying music sound, sound localization, talking on the phone, etc., (Amann and Anderson, 2014). Such as can be expected, both the NCIQ and HISQUI19 show an improvement after cochlear implantation, and this effect is similar in other studies. During this study a significant improvement is seen in the NCIQ total score and across all six subdomains one year after cochlear implantation, this is in line with results from previous literature (Völter et al., 2018, Claes et al., 2018b, Mosnier et al., 2015). One year after cochlear implantation the NCIQ results stabilize, and no further improvement is observed in the majority of studies (Völter et al., 2022b, Mosnier et al., 2018). Several studies reported a significant improvement in self-reported hearing one year after cochlear implantation using the HISQUI19 questionnaire (Mertens et al., 2021a, Claes et al., 2018b). In our study, the HISQUI19 was the only questionnaire filled in on a computer during the appointment in the hospital. Response rate on this questionnaire was low, and a sample of 20 individuals or more for the different timepoints was not achieved. Therefore, the effect of cochlear implantation on the HISQUI19 score is only investigated preoperatively and 12 months after CI activation. Possible causes of this low response rate on the HISQUI19 may be the length of the appointment, as many elderly do not want to stay to fill in an extra questionnaire, the accessibility to a computer at the hospital, ability to work with a computer, etc. Unfortunately, the main reason remains unclear and possible solutions to solve the low response rate should be explored. Possible solutions for this low response rate include; send the HISQUI19 questionnaire to the subjects together with the other QoL questionnaires via mail, give the subjects a code to access and fill in the questionnaire via their home computer before or after the hospital appointment. This last solution will not work for all elderly as some of them do not own a computer or have difficulties handling a computer.

The SSQ12 investigates the self-reported level of hearing disability, it is developed for the use in clinical research and rehabilitation settings. It includes items relating to speech, localization of sounds, and qualities of hearing such as ease of listening, identification/recognition, signal segregation, clarity, etc., (Noble et al., 2013, Gatehouse and Noble, 2004). Several studies observed a significant increase in SSQ12 score after cochlear implantation, meaning a lower level of hearing disability is reported by the individuals (Mertens et al., 2021a, Claes et al., 2018b, Calvino et al., 2022a). In this study the response rate on the SSQ12 is low compared to the other questionnaires, only 13 individuals filled in the questionnaire for all the timepoints which was considered too low for statistical analysis. Therefore, this questionnaire was only investigated preoperatively and at 12 months after CI activation. Although the SSQ12 is send to the subject along with the other questionnaires via mail, the response rate is low. This may be related to the difference in format of the questionnaire: while the other questionnaires consist of several response options, the SSQ12 consists of a scale ranging from 0 to 10 on which the patient has to indicate his/her answer.

A possible limitation is that the questionnaires related to hearing, namely NCIQ, HISQUI19, and SSQ12, are not designed to specifically investigate elderly, a possible alternative or additional questionnaire might be the Hearing Handicap Inventory for the Elderly (HHIE). This questionnaire explores the emotional and social consequences of hearing loss in elderly, and it may be used to investigate the self-perceived hearing handicap. It consists of 25 items with three possible answers: “yes”, “sometimes” and “no”. Compared to the questionnaires already included in the protocol, the HHIE focusses more on social and psychological aspects of hearing impairment in elderly (Ventry and Weinstein, 1982).

In addition to these QoL aspects related to hearing, anxiety and depression were also examined in this study using the HADS questionnaire. One year after CI activation a significant improvement was found for both anxiety and depression. The tools to investigate anxiety and depression differ between studies. Some studies selected a specific questionnaire to investigate depression, such as the Hamilton Depression Scale (Sonnet et al., 2017), while others used the HADS which investigates both anxiety and depression (Calvino et al., 2022a, Claes et al., 2018b, Mertens et al., 2021a). Moreover, it may be useful to consider the use of a depression scale specifically designed for the elderly, such as the Geriatric Depression scale (GDS). No consensus was found in published results on depression and anxiety. Some studies found a significant decrease in depression rates one year after cochlear implantation using GDS questionnaire (Choi et al., 2016) or HADS questionnaire (Calvino et al., 2022b). Nevertheless, many other studies did not find a significant improvement in depression rates using GDS questionnaire (Mosnier et al., 2015, Völter et al., 2022b), HADS questionnaire ((Mertens et al., 2021a), or Hamilton Depression scale (Sonnet et al., 2017). Moreover, one study found a significant effect 6 months after cochlear implantation using the HADS questionnaire, but these results did not remain significant 12 months after CI activation (Claes et al., 2018b). Hence, most studies did not found a significant effect after cochlear implantation, or only saw a significant improvement in the first months after cochlear implantation. A possible explanation might be that individuals are in general very happy with their CI in the first months, but later on they may face the limitations of the CI resulting in no significant decrease one year after cochlear implantation. Depression and anxiety are also linked to a variability of other factors, such as for instance other diseases, household situation, family relationships, etc., these might have an effect on the results.

The last secondary outcome measurement, type D personality, also showed a significant improvement after CI activation. This was investigated using the DS14, and an effect was seen on both type D personality traits, namely social inhibition and negative affectivity. Individuals with type D personality are more susceptible for symptoms of anxiety and depression, chronic stress, lower levels of self-esteem, well-being, etc. Hearing loss predicts poorer outcomes for some of these factors to which type D personalities are more vulnerable than the general population, such as anxiety and depression, etc., (Andries et al., 2022a, Cosh et al., 2019, Ciorba et al., 2012). The decrease in type D personality traits after cochlear implantation may be explained by the positive effect on daily life activities, mental health, and communication (Sonnet et al., 2017, Andries et al., 2022a). Despite this positive effect of cochlear implantation on Type D personality traits, there is still a higher rate of type D personality after cochlear implantation compared to the general population. Preoperatively 38% of the individuals are categorized as type D personalities, this decreases to 29% one year after CI activation. In the general population around 21% of the individuals have a type D personality (Denollet, 2005). Our findings are consistent with prior research investigating Type D personality after cochlear implantation using both a control and intervention group. A study by Andries et al., (2023) was specifically dedicated to investigate type D personality in CI users, this study included 76 CI users and 21 severely hearing impaired controls without CI. A study by Mertens et al., (2021a) was dedicated to investigate different outcome measurements after cochlear implantation, this study included 24 subjects in the intervention group and 24 individuals in the control group. Both studies found a significant change in type D personality traits in the intervention group, but not in the control group (Andries et al., 2022a, Mertens et al., 2021a).

Similar limitations are present when studying the effect of cochlear implantation on QoL, as we discussed earlier with studying the effect of cochlear implantation on cognition, including sample size, absence of a control group, and effect of certain confounders. Another important consideration is the absence of generic questionnaires in this study. While the NCIQ and HISQUI19 only address specific hearing-related issues, a generic questionnaire would provide a view of the general health status of individuals. However, a study by Andries et al., (2022) revealed that the HUI, a generic questionnaire, might underestimate health related QoL changes after cochlear implantation (Andries et al., 2022b). Sonnet et al., (2017) used a generic questionnaire, namely WHOQoL-OLD, to investigate the QoL before and after cochlear implantation. They found no significant increase in the global WHOQoL-OLD results after CI, but a significant improvement on the sensory ability domain was observed (Sonnet et al., 2017). Another consideration is the fact that all questionnaires are developed for the general population, and no specific questionnaires were used to evaluate elderly. Moreover, the following questionnaires used in this study were not specifically validated for CI users; SSQ12, HADS, and DS14; so they may not be able to detect important health relates QoL factors related to cochlear implantation.

Cochlear implants are used to treat hearing loss in individuals with severe-to-profound hearing loss for whom hearing aids do not provide sufficient benefit. Therefore, it is expected that hearing abilities will improve after CI activation. This is demonstrated in previous studies, and confirmed by this study. An improvement in both pure tone thresholds, and speech recognition in quiet and noise is observed. The self-reported improvement, evaluated with NCIQ, HISQUI19, and SSQ12; corresponds to the more objective audiometric measurements. Hence, both the audiometric assessment and the self-reported assessment tools indicate that cochlear implantation clearly improves hearing abilities.

6.3 Conclusion

The results of this study indicate a positive effect of cochlear implantation on cognition, QoL, and hearing abilities one year after CI activation. In subsequent annual follow-up measurements, no further improvements were generally observed. This means that subjects are already experiencing benefits from a CI one year after implantation, not only in terms of hearing but also cognition and QoL improve. These positive effects remain stable in the following years. Hearing loss has a major impact on individuals' daily life, it can cause communication problems, social isolation, loneliness, higher rates of anxiety and depression, etc. Hence, this study points to the importance of treating severe-to-profound hearing loss in elderly, as a CI can reduce the negative effects of hearing loss in several domains. Cochlear implantation will improve hearing abilities, which will result in an improvement in several QoL aspects. In addition, this study shows that treating hearing loss with a CI improves cognitive functioning, and might reduce the risk of dementia in later life. Future research should be encouraged using a control group and a larger sample size. In addition, there is a need for a standardized, multidimensional study protocol to assess cognition and QoL before and after cochlear implantation, which would facilitate comparisons across different international studies and institutes.

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8 Appendix

8.1 RBANS-H scoring form

Subject ID	HEAR_COG_ . _ . . _ . . . .

SCORE CONVERSION PAGE

	Total score	Total score	Index score
I. Immediate memory			
1. List learning			
2. Story memory			
II. Visuospatial-Constructional			
3. Figure copy			
4. Line orientation			
III. Language			
5. Picture naming			
6. Semantic fluency			
IV. Attention			
7. Digit span			
8. Coding			
V. Delayed memory			
9. List recall			
10. List recognition			
11. Story recall			
12. Figure recall		sum	

Sum of index scores

Percentile

Total scale

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