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Single Sided Deafness

consequences for children's language development & intervention via early cochlear implantation

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Single Sided Deafness - consequences for children's language development & intervention via early cochlear implantation.

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Abstract

Children with single sided deafness (SSD), a congenital severe to profound sensorineural unilateral hearing loss ≥ 80 dB HL, constitute a patient group for which there is no standard care. It is widely acknowledged, however, that these children experience direct and indirect consequences of the one-sided sensory deprivation. In normal hearing, (NH) information of sound reaching the two different ears is integrated: interaural time and level differences are used to identify and separate sound sources. In children with SSD, this binaural hearing is absent and therefore the ability to localize sound sources and to understand speech in noisy situations is hampered. Moreover, several behavioral studies have shown that deficient auditory processing in children with SSD negatively affects language and cognitive development. Also, greater listening effort and difficulties in traffic, sports and in social settings are often reported and can have quite a large impact on daily life.

The main aim of the first part of the present doctoral research was to contribute to the knowledge about the difficulties children with unaided SSD experience with regard to neurocognitive skills and hearing abilities in daily life. In our first study, we therefore compared task performance of the clinical sample of 5-15 year old Dutch-speaking children with SSD of the university hospital in Leuven (n=21) to that of age- and gender matched NH peers (n=42). We specially focused on a detailed insight of the language difficulties experienced, which was not present in the literature. We assessed morphology, syntax and vocabulary and not only looked at test scores but also analyzed the error patterns of the children. We also assessed short term memory and working memory by means of digit span tasks, and documented the impact of SSD on the children's daily life by means of a questionnaire. Our results showed that at group level, the children with unaided SSD performed significantly lower than the NH peer control group on the language tests of morphology, syntax and vocabulary. Mostly the correct use of the past participle and pronouns appeared more difficult, formulating sentences more often went wrong by making mistakes in grammar and semantics, and more often pictures were named with a word that was too general or that only sounded like the target word. Performance for both groups was similar for short term memory and working memory. Results furthermore showed that in daily life, the children with SSD experienced problems in spatial hearing and in understanding speech in noisy situations, and the effort they have to put into listening and in understanding speech was considerably greater than in NH children. In conclusion, the outcomes of our first study thus suggest that there is a difference

for hearing in everyday life situations and language development when having one versus two good ears. Hence, there is a need for intervention to optimize auditory perception.

Untreated SSD leads to cortical reorganization that continues with increasing duration of SSD. Therefore, it is advised that treatment is provided within an early critical period. This is to prevent overrepresentation of the hearing ear in the auditory system and biased input to higher order cortical areas, and to possibly restore cortical organization. The main aim of the second part of the present doctoral research was to set up a longitudinal study focused on the effectiveness of cochlear implantation as a possible remediation for very young children with SSD. This is the only rehabilitative option that offers the potential to partially restore binaural hearing when implanted early in life, as it captures sound on the impaired side and transmits it to the brain via electrical stimulation of the auditory nerve. Research is required to determine the evidence for this in order to provide appropriate rehabilitation.

Over the course of the PhD project, 14 children with SSD ear have received a CI (provided by Cochlear Ltd). Importantly, children were very young at implantation (8-26 months of age, mean, SD). The children are followed up twice a year during their first 4 to 5 years with a CI, and possibly beyond. Whereas previous studies only describe auditory outcomes and subjective benefit, we also assess the benefit of a CI with regard to the development of language and cognition. Care was taken to develop a protocol that consists of standardized behavioral tests and parent questionnaires and is tailored to the specific age of the child. Furthermore, study is novel because performance of the implanted children is compared to that of two control groups of children with SSD but no CI or with bilateral normal hearing.

In our second study, we focused on the outcome measures for the assessment of receptive and expressive communication in infants under the age of 2. In the first two years of life, assessment is rather challenging because language is still limited. We selected one behavioral test, the Bayley-III-NL, and one parent questionnaire, the N-CDI, and used the LENA system to assess quantity of speech by the child and the adults in its environment. We aimed to investigate whether these three different types of outcomes together would provide a good description of a child's communicative development. Data of 27 children with NH or with SSD with or without a CI were analyzed. We observed positive relationships between the Bayley-III-NL behavioral test, N-CDI questionnaire and LENA system outcomes of children under the age of 2. Furthermore, Bayley-III-NL language comprehension and language production scores and the LENA estimates of quantity of speech by adults around the child and interaction between child and adults seemed predictive of later linguistic outcomes (between 24 and 36 months). This supports construct validity of the Bayley-III-NL language tests and emphasizes the importance of interaction with and language input to the child for its linguistic development. We concluded that the chosen methods are relevant outcome measures for very young children to assess communicative skills and language environment and that they are complementary to each other.

In our third study we presented data of the first 6 implanted children of the CICADE study who were 2 years of age or older at the moment of writing (~5;6 years (1 child), 3;6 (1 child), 2;6 (3 children) and 2;0 (1 child)). Outcomes of language comprehension, expressive vocabulary, morphosyntactic skills, cognitive information processing and hearing abilities in daily life were compared to those of 12 children of the SSD_noCI group and 19 of the NH peers. In general, we expect that improvements with CI could be much more subtle for our participants with SSD than for bilaterally deaf children. Moreover, while our children had to be implanted at a very young age due to the narrow window of opportunity, potential benefits may only become prevalent after some time. Despite the young age and limited language, the current data showed that the SSD_CI group seemed to perform largely in line with the NH controls on tests of language, whereas results of the SSD_noCI group were more diverse. Compared to the SSD_CI group, scores of a larger part of the SSD_noCI children were lower than those of the NH controls. For some of the SSD_noCI children, performance was also clinically lower than average compared to the Flemish norm data of the respective tests, especially with regard to morphosyntactic skills and expressive vocabulary, which corroborates the findings of our first study in school-aged children with unaided SSD. Equally important to the test data is that the toddlers appeared to wear their CI and did not seem hindered by acoustic input on the one side and electrical input on the other. The data are not supported by statistical analyses and therefore do not allow us to draw solid conclusions, but this first experience is encouraging. Long term observation will be of key importance in order to draw conclusions with regard to CI benefit. The present thesis provides the first step towards our goal of forming a well-founded advice to the Belgian national health insurance concerning reimbursement of a CI for young children with SSD.

Korte inhoud

Voor kinderen met eenzijdige doofheid (single sided deafness, SSD), een congenitaal, (zeer) ernstig sensorineuraal eenzijdig gehoorverlies ≥ 80 dB HL, bestaat er geen standaard behandeling. Het wordt echter algemeen erkend dat deze kinderen directe en indirecte gevolgen ondervinden van het eenzijdige sensorische gemis. Bij normaal gehoor (NH) wordt informatie van geluid dat de twee verschillende oren bereikt geïntegreerd: interaurale tijd- en level verschillen worden gebruikt om geluidsbronnen te identificeren en van elkaar te onderscheiden. Bij kinderen met SSD is dit binauraal horen afwezig en daarmee wordt het localiseren van geluid en het verstaan van spraak in lawaarige luistersituaties zeer moeilijk. Bovendien hebben verschillende onderzoeken aangetoond dat SSD bij kinderen een negatieve invloed kan hebben op de talige en cognitieve ontwikkeling. Daarnaast worden grotere luistermoeite en moeilijkheden in het verkeer, bij het sporten en in sociale settings vaak gerapporteerd. Deze zaken kunnen een grote invloed hebben op het dagelijks leven.

Het doel van het eerste gedeelte van het huidige doctoraatsonderzoek was bij te dragen aan de kennis over de moeilijkheden die kinderen met onbehandelde SSD ervaren met betrekking tot neurocognitieve vaardigheden en gehoorcapaciteiten in het dagelijks leven. In onze eerste studie hebben we daarom de klinische groep 5-15 jarige Nederlands sprekende kinderen met SSD van het universitair ziekenhuis in Leuven (n=21) vergeleken met NH kinderen gekoppeld op basis van leeftijd en geslacht (n=42). We hebben ons specifiek gericht op een gedetailleerd inzicht van ervaren taalmoeilijkheden, wat nog niet bekend was in de literatuur. We onderzochten morfologie, syntaxis en vocabulaire en analyseerden niet alleen de testscores maar ook de fouten die de kinderen maakten. We onderzochten ook het korte termijn geheugen en het werkgeheugen door middel van cijferreeksen en documenteerden de impact van SSD op het dagelijks leven van de kinderen met behulp van een vragenlijst. Onze resultaten toonden aan dat de kinderen met onbehandelde SSD op groepsniveau significant lager presteerden dan de NH controle groep op de testen van morfologie, syntax en vocabulaire. Vooral het correcte gebruik van voltooid deelwoorden en voornaamwoorden bleek moeilijker te zijn, het formuleren van zinnen ging vaker mis door grammaticale of semantische fouten en plaatjes werden vaker benoemd met een woord dat te algemeen was of dat enkel klonk als het doelwoord. De korte termijn geheugen en werkgeheugen resultaten van beide groepen waren vergelijkbaar. Resultaten toonden verder aan dat

de kinderen met SSD in het dagelijks leven moelijkheden ervoeren met spatieel horen en spraakverstaan in lawaaiige situaties en dat de moeite die ze moesten steken in het luisteren en spraakverstaan beduidend groter was dan voor NH kinderen. Kortom, de resultaten van onze eerste studie suggereren dat er een verschil is in alledaagse situaties en taalontwikkeling met één versus twee goede oren. Vandaar dat er een behoefte is aan interventie om de auditieve waarneming te optimaliseren.

Onbehandelde SSD leidt tot corticale reorganizatie die zich voortzet met toenemende duur van SSD. Het wordt daarom geadviseerd behandeling toe te passen binnen een vroege kritische periode in het leven. Dit om overrepresentatie in het auditieve systeem van het horende oor alsook vertekende input naar hogere corticale gebieden te voorkomen. Het doel van het tweede gedeelte van dit doctoraatsonderzoek was het opzetten van een longitudinale studie naar de effectiviteit van cochleaire implantatie als een mogelijke behandeling voor zeer jonge kinderen met SSD. Dit is de enige behandeloptie die, indien op jonge leeftijd gestart, mogelijk het binauraal horen gedeeltelijk zou kunnen herstellen, omdat het cochleaire implantaat (CI) geluid opvangt aan de aangedane zijde en overbrengt naar de hersenen door middel van electrische stimulatie van de gehoorzenuw. Onderzoek is nodig te bepalen of dit daadwerkelijk mogelijk is, zodat in de toekomst passende revalidatie geboden kan worden aan kinderen met SSD.

Gedurende het PhD project hebben 14 kinderen met SSD een CI gekregen (aangeboden door Cochlear, Ltd). Belangrijk is dat deze kinderen allemaal zeer jong waren ten tijde van implantatie (8-26 maanden oud, gemiddeld 14 maanden SD 4.8). De kinderen worden tweemaal per jaar opgevolgd gedurende de eerste 4 tot 5 jaar met hun CI, en mogelijk langer. Waar vorige studies enkel auditieve resultaten en subjectieve baat beschreven, onderzoeken wij ook de voordelen van het CI met betrekking tot de ontwikkeling van taal en cognitie. We ontwikkelden een protocol bestaande uit gestandaardizeerde gedragsmatige testen en oudervragenlijsten, toegespitst op de specifieke leeftijd van het kind. Daarnaast is de studie vernieuwend omdat prestatie van de geïmplanteerde kinderen vergeleken wordt met die van twee controlegroepen van kinderen met SSD maar zonder CI of met bilateraal normaal gehoor.

In onze tweede studie richtten we ons op de maten voor receptieve en expressieve communicatie in kinderen beneden de leeftijd van 2 jaar. In de eerste twee jaar van het leven is het relatief lastig om zulke vaardigheden te onderzoeken omdat de taal van het jonge kind nog beperkt is. We selecteerden een gedragsmatige test, de Bayley-III-NL, een oudervragenlijst, de N-CDI, en gebruikten het LENA systeem om de kwantiteit van de spraak van het kind alsook die van de volwassenen in zijn of haar omgeving te onderzoeken. We onderzochten of deze drie verschillende typen methodes samen een goede beschrijving konden geven van de communicatieve ontwikkeling van het jonge kind. Data van 27 kinderen met NH of met SSD met of zonder CI kon worden geanalyseerd. We observeerden positieve relaties tussen de Bayley-III-NL gedragsmatige test, de N-CDI vragenlijst en de resultaten van het LENA systeem. Daarnaast leken de Bayley-III-NL taalbegrip en taalproductie scores en de LENA schattingen van kwantiteit van spraak door volwassenen in de buurt van het kind en interacties tussen kind en volwassenen voorspellend te zijn voor latere taalresultaten (tussen 24 en 36 maanden). Dit ondersteunt de construct validiteit van de Bayley-III-NL taalschalen en benadrukt het belang van interactie met en taalinput voor het kind voor zijn/haar taalontwikkeling. We concludeerden dat de gekozen methoden relevante maten zijn voor zeer jonge kinderen in het onderzoeken van communicatieve vaardigheden en taalomgeving, en dat ze complementair zijn.

In onze derde studie presenteerden we de data van de 6 eerst geïmplanteerde kinderen van de CICADE studie die op het moment van schrijven 2 jaar of ouder waren (~5;6 jaar (1 kind), 3;6 (1 kind), 2;6 (3 kinderen) en 2;0 (1 kind)). Resultaten op gebied van taalbegrip, expressieve vocabulaire, morphosyntactische vaardigheden, cognitieve informatieverwerking en gehoorcapaciteiten in het dagelijks leven werden vergeleken met die van 12 kinderen van de SSD_noCI groep en 19 van de NH kinderen. We verwachten over het algemeen genomen dat verbeteringen met het CI veel subtieler zullen zijn voor onze deelnemers met SSD dan voor bilateraal dove kinderen. Bovendien, aangezien onze kinderen geïmplanteerd dienden te worden op een zeer jonge leeftijd zullen potentiële voordelen wellicht pas aan het licht komen na verloop van tijd. Maar, ondanks de jonge leeftijd en de nog beperkte taal op deze leeftijd, lieten de tot nu toe verzamelde data zien dat de SSD_CI groep grotendeels in de lijn van de NH controle groep presteerde op de taaltesten, terwijl de resultaten van de SSD_noCI groep diverser waren. Vergeleken met de SSD_CI groep waren de scores van een groter gedeelte van de SSD_noCI kinderen lager dan die van de NH controle groep. Bij sommige SSD_noCI kinderen was de prestatie ook klinisch lager dan gemiddeld, vergeleken met de Vlaamse normdata van de gebruikte testen, en dan voornamelijk bij de morphosyntactische vaardigheden en expressieve vocabulaire. Dit bevestigt de bevindingen in onze eerste studie met kinderen van 5-15 jaar met onbehandelde SSD. Net zo belangrijk als de testdata is onze bevinding dat de peuters hun CI droegen en niet gehinderd leken te zijn door de akoestische input aan de ene kant en de electrische input aan de andere kant. De data worden niet ondersteund door statistische analyses en maken het daarom niet mogelijk om conclusies te trekken, maar deze eerste ervaring is bemoedigend. Lange termijn observatie zal cruciaal zijn voor het vormen van conclusies met betrekking tot de voordelen van het CI. De huidige thesis is de eerste stap naar ons doel om een gegrond advies te kunnen geven aan de Belgische nationale zorgverzekering met betrekking tot terugbetaling van een CI voor jonge kinderen met SSD.

Acronyms and abbreviations

Bayley	Bayley scales of infant and toddler development
Bayley-C	Bayley subscale cognition
Bayley-LC	Bayley subscale language comprehension
Bayley-LP	Bayley subscale language expression
BCD	bone conduction device
BHL	bilateral hearing loss
BMLD	binaural masking level difference
c	congenital
CELF	clinical evaluation of language fundamentals
CELF-FS / FS	CELF subtest formulating sentences
CELF-NR / NR	CELF subtest number repetition
CELF-WS / WS	CELF subtest word structure
CHILD	children's home inventory for listening difficulties
CI	cochlear implant
CICADE	cochlear implantation for children and one deaf ear
CMV	cytomegalovirus infection
CND	cochlear nerve deficiency
CROS	contralateral routing of signal
d	days
dB	decibel
dB HL	decibel hearing level
dB SL	decibel sensation level
dB SPL	decibel sound pressure level
dBnHL	decibel normal hearing level
DLP	digital language processor (LENA system)
DMN	default mode network
DTI	diffusion tensor imaging
e.g.	exempli gratia: for example
EIORL	European institute for otorhinolaryngology, Antwerp
EOWPVT	expressive one word picture vocabulary test
et al.	et alia: and others
FM	frequency modulated
HA	hearing aid
HEAR-QL	hearing environments and reflection of quality of life questionnaire
HL	hearing loss
HSE	head shadow effect
i.e.	id est: in other words / in essence
IEM	inner ear malformation
IEP	individualized education plan

ILD	interaural level difference
IQ	Intelligence Quotient score
ITD	interaural time difference
IT-MAIS	the infant-toddler meaningful auditory integration scale questionnaire
JND	just noticeable difference
LENA	Language environment analysis system
LENA-AWC / AWC	adult word count (LENA system)
LENA-CTC / CTC	conversational turn count (LENA system)
LENA-CVC / CVC	child vocalization count (LENA system)
littleLINT	limited-set Leuven intelligibility number test
m	meter
M	mean
MAE	mean absolute error
MLU	mean length utterance
mo	months
MRI	magnetic resonance imaging
n	number
N-CDI	MacArthur Bates Communicative Development Inventory, Dutch version
N-CDI-EV	N-CDI subscale expressive vocabulary
N-CDI-RV	N-CDI subscale receptive vocabulary
NH	normal hearing
NHS	newborn hearing screening
PEACH+	parents' evaluation of aural/oral performance of children
PedsQL	pediatric quality of life inventory
PIQ	performance intelligence quotient score
PRISE	the production of infants scale evaluation
PTA	pure tone average
QOL	quality of life
RIZIV/INAMI	rijksinstituut voor ziekte- en invaliditeitsverzekering / institut national d'assurance maladie-invalidité
RMS	root mean square error
SD	standard deviation
SE	standard error
SELT	Schlichting expressive language test
SELT-EV / EV	SELT subtest expressive vocabulary
SELT-MS / MS	SELT subtest morphosyntax
SNR	signal-to-noise ratio
SPIN	speech in noise understanding
SPSS	statistical package for the social sciences
SRLT	Schlichting receptive language test
SRM	spatial release of masking

SRT	speech reception threshold
SSD/ cSSD	congenital single sided deafness
SSQ	the speech, spatial and qualities of hearing questionnaire
TIQ	total intelligence quotient score
UHL	unilateral hearing loss
UZA	university hospital Antwerp
UZG	university hospital Ghent
UZL	university hospital Leuven
VIQ	verbal intelligence quotient score
yr	years

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Motivation

Each year in Flanders about 39% of all newborns with a hearing impairment are diagnosed with congenital sensorineural hearing loss on one side and a normal hearing (NH) ear on the other side. In about one third of this group (~20-25 babies) the unilateral hearing loss (UHL) is profound (> 90 dB HL), also termed congenital single sided deafness (SSD). There is no standard care for children with SSD in Flanders, as in many other places, although it is widely acknowledged that these children experience direct and indirect consequences of the one-sided sensory deprivation (Kuppler et al., 2013; Lieu, 2018; van Wieringen et al., 2019; Vila & Lieu, 2015).

The current PhD research contributes to the knowledge about 1) the difficulties children with unaided SSD experience and 2) the effectiveness of cochlear implantation in very young children with SSD.

In a first study, we compared language, cognitive and auditory outcomes in the clinical population of school-aged children with unaided SSD of the UZ Leuven, to those of typically developing NH peers matched on age and gender. We specially focused on a detailed insight of the language difficulties experienced, which was lacking in the literature. We hypothesized that morphological and syntactical linguistic tasks would be more challenging for children with SSD than for normal hearing (NH) children because of suboptimal perception of important morphemes in daily life.

The second part of the PhD research focused on cochlear implantation. A cochlear implant (CI) is the only rehabilitative option that offers the potential to (partially) restore binaural hearing in individuals with SSD, as it captures sound on the impaired side and transmits it to the brain via electrical stimulation of the auditory nerve. A CI is, however, not reimbursed for children or adults with SSD in Flanders (and most other countries). We have set up a multicenter collaboration (Leuven, Antwerp, Ghent) in which 16 very young children with SSD have received a CI, provided by Cochlear Ltd. These children are followed up longitudinally with regard to development of language, cognition, and spatial hearing.

This CI research is very innovative because we implant only *very young* children with SSD. Early implantation is essential to prevent the cortical reorganization which would otherwise lead to biased input to higher-order auditory and non auditory cortical areas. In addition, the current research compares performance of implanted children to that of control groups of age-matched children with normal hearing and with SSD but no CI. Furthermore, whereas previous studies only describe auditory outcomes and subjective benefit, we also assess the benefit of a CI with regard to the development of language and cognition. We hypothesize that provision of the CI at a very young age will partially restore binaural processing in the following years and hence yield the best conditions for the development of near-normal spatial hearing and speech understanding skills, cognition, language and learning in general.

The overall aim of the longitudinal research is to form a well-founded advice to the Belgian National Health Insurance (RIZIV/INAMI) concerning reimbursement of a CI for young children with SSD. The present thesis provides the first step towards this goal. Furthermore it contributes to the field because of our efforts in developing a protocol to follow the development of such young children.

General Introduction

1 General introduction

In this first chapter, we provide a general introduction on pediatric single sided deafness. We give a definition of SSD and describe the etiology in section 1.1. The neural consequences to untreated SSD are discussed in section 1.2. Section 1.3 describes the hearing difficulties the children experience and the impact SSD has on their daily lives and is concluded with an introduction to the consequences of SSD for language and neurocognition. In section 1.4 the thesis outline is explicated.

1.1 Definition and Etiology of SSD

Hearing loss can be classified from three different perspectives: type, degree and onset. The type of hearing loss describes the part of the auditory system that is compromised (see figure 1.1). When the hearing impairment is due to a deficit in the outer and/or middle ear, it is referred to as a *conductive hearing loss*. In this type of hearing loss, there is a problem in the transmission of the movement of the eardrum to the movement of the oval window which is normally realized by the three ossicles, in the middle ear. *Sensorineural hearing loss* is a result of malfunctioning of the cochlea (inner ear) and/or cochlear nerve. In this type of hearing loss, the problem lies in the transmission of signals from the ear to the brain. A combination of conductive and sensorineural hearing loss is referred to as *mixed hearing loss*.

The degree of hearing loss describes the severity of it, usually quantified as the pure-tone average (PTA) in dB HL which is the threshold for sinusoids averaged over the frequencies 0.5, 1 and 2 kHz. Sometimes other frequencies are included in the calculation of the PTA as well. The commonly used classification of degree of hearing loss is shown in table 1.1.

The onset of the hearing loss can be congenital (i.e. present at birth) or acquired later in life. Another categorization that is often used is prelingual (i.e. hearing loss developed before important aspects of spoken language skills are acquired) or postlingual (i.e. after the development of these skills) (Dijkhuizen et al., 2011). All congenital hearing losses are prelingual but not all prelingual hearing losses are congenital (Musiek et al, 2012).

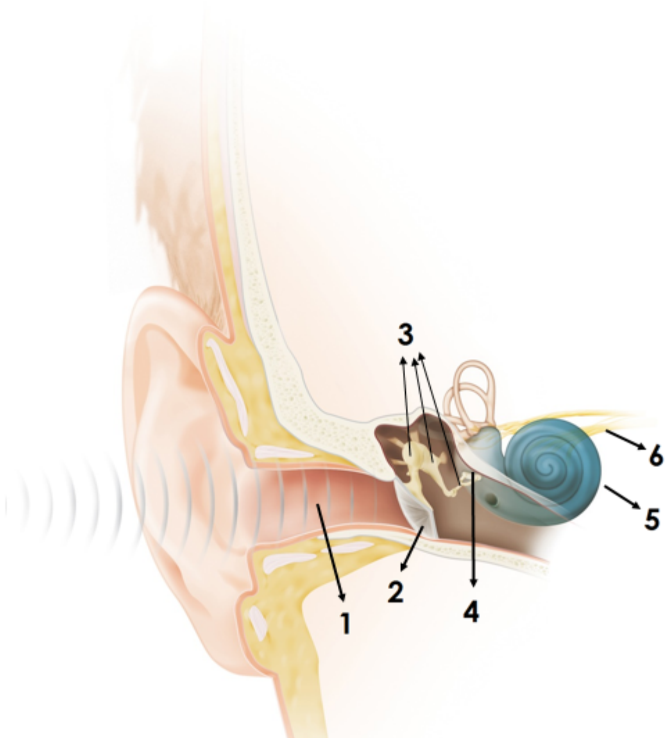

Figure 1.1 Schematic presentation of the anatomy of the ear. Outer ear including 1: the auditory canal. Middle ear including 2: tympanic membrane, 3: the ossicles (malleus, incus, stapes) and 4: the oval window. Inner ear with 5: the cochlea and 6: the cochlear nerve. Modified from an image courtesy of Cochlear.

Table 1.1 Classification of degree of hearing loss (Clark, 1981; Goodman, 1965).

PTA (dB HL)	Degree of hearing loss
-10-15	Normal hearing
16-25	Slight hearing loss
26-40	Mild hearing loss
41-55	Moderate hearing loss
56-70	Moderately severe hearing loss
71-90	Severe hearing loss
> 90	Profound hearing loss

A unilateral hearing loss (UHL) is defined as a permanent hearing loss in one ear with PTA ≥ 20 dB HL or pure tone air conduction thresholds ≥ 25 dB HL at 2 or more frequencies above 2 kHz, with no significant air-bone gap, and PTA ≤ 15 dB HL in the normal hearing (NH) ear (Bess et al., 1998; CDC, 2005). The estimated incidence of sensorineural hearing impairment > 40 dB HL is 1.86 per 1000 newborns in developed countries, of whom 30-40% are unilateral (Fitzpatrick et al., 2017; Giardina, et al., 2014; Morton & Nance, 2006; Van Kerschaver & Stappaerts, 2011). Specifically in Flanders in the last decade, each year approximately 39% of all children diagnosed with a hearing impairment had UHL, which comes down to about 60 (out of ~68000) newborns per year. Approximately one-third of the newborns with UHL in Flanders was diagnosed with a profound UHL (> 90 dB HL), and another 20% had severe UHL (71-90 dB HL) (Van Kerschaver & Stappaerts, 2011). The prevalence of UHL increases with age because of children who develop acquired UHL or delayed congenital UHL (Fitzpatrick et al., 2017). Prevalence in the USA for children 6-19 years of age is estimated at 3 to 6.3% (depending on the definition of UHL used) (Ross et al., 2010).

The present doctoral research focuses on children with a *congenital severe to profound sensorineural unilateral hearing loss ≥ 80 dB HL*, which is also termed single-sided deafness (SSD). Due to the practically full coverage of all newborns by the newborn hearing screening (NHS) program, SSD is now diagnosed shortly after birth, as opposed to remaining undetected until a later age because of the subtlety of symptoms in the first year(s) of life.

Most common underlying etiologies for SSD are cochlear nerve deficiency (CNV) and congenital (c) cytomegalovirus (CMV) infection. In CNV, the cochlear nerve is absent (cochlear nerve aplasia) or smaller than the facial nerve (cochlear nerve hypoplasia). Related to this is stenosis of the bony cochlear nerve canal, the canal through which the cochlear nerve passes (Clemmens et al., 2013; Laury et al., 2009; Lim et al., 2018). CMV infection is a DNA virus from the Herpesviridae family (Vila & Lieu, 2015) and is the most common intra-uterine infection in most developed countries (Philips et al., 2010). The majority of children with cCMV are asymptomatic at birth (~90%), but 7 to 15% of these children develop impairments later on, which can include damage to hearing, vision, cognition or motor function with wide variation in the severity of the impairments (Foulon et al., 2008; Goderis et al., 2014; Pass & Arav-Boger, 2018). Sensorineural hearing loss is by far the most common sequela of cCMV (Goderis et al., 2014). A systematic review by Goderis et al. (2014), reported that 12.6% of newborns with cCMV experience hearing loss and that among asymptomatic children, UHL predominated.

A recent inventory of etiologies of children with UHL in Flanders (university hospitals of Leuven (UZL) and Antwerp (UZA)) shows the distribution of etiologies in function of degree of hearing loss (van Wieringen et al., 2019), see table 1.2. 45% of all 180 children with congenital profound UHL presented with CND and 36% had cCMV. Other observed etiologies of SSD are congenital inner ear malformations (IEM) (e.g. incomplete partition type II, narrow internal auditory canal, enlarged vestibular aqueduct), genetic syndromes (e.g. Goldenhar, Waardenburg, Townes-Brocks, CHARGE, VACTERL), and auditory neuropathy spectrum disorder (a spectrum of pathologies that affect the auditory pathways and cause abnormal or absent auditory brainstem responses). Tumors, bacterial and viral meningitis and ototoxicity from medications such as antibiotics and chemotherapy are strictly no congenital etiologies but can occur in very young children) (Fitzpatrick et al., 2017; Haffey et al., 2013; Laury et al., 2009; van Wieringen et al., 2019; Vila & Lieu, 2015). Often also, no underlying cause of SSD can be identified.

Table 1.2. Distribution of etiology of congenital unilateral sensorineural HI (given in percentage) for university hospital Antwerp (UZA, n=88) and university hospital Leuven (UZL, n=92) separately.

Etiology UZA/UZL (n=88/92)	**Mild**	**Moderate**	**Severe**	**Profound**
	UZA/UZL %/%	UZA/UZL %/%	UZA/UZL %/%	UZA/UZL %/%
Syndromal (4/2)	1.1/1.1	2.3/-	-/-	1.1/1.1
cCMV (21/26)	1.1/-	4.6/1.1	2.3/4.3	15.9/22.6
CND (23/7)	-/-	-/-	-/-	26.1/7.5
Meningitis (1/0)	-/-	-/-	-/-	1.1/-
Neurological (1/7)	-/-	-/4.3	1.1/1.1	-/2.2
IEM (3/7)	-/-	1.1/-	1.1/2.2	1.1/5.4
CMV + CND (1/0)	-/-	-/-	-/-	1.1/-
Unknown (34/43)	9.1/2.2	13.6/9.7	4.6/9.7	11.4/24.7
Total	**11.4/3.2**	**21.6/15.1**	**9.1/17.2**	**57.9/63.4**

Note. The data are presented for different degrees of HI (Mild=41-50 dBHL, moderate=51-70 dBHL, severe = 71-90 dBHL, profound>=91 dBHL). Adapted with permission from van Wieringen et al., (2019).

1.2 Neural consequences of SSD

There are important neural consequences to untreated SSD. Two major (related) factors are cortical reorganization and the aural preference effect.

Cortical reorganization

Hearing loss can be viewed as a connectome disease (Kral et al., 2016). The connectome is the map of effective synaptic connections and neural projections that comprise a nervous system and shape its global communication and integrative functions (Kral et al., 2016, p. 610, 611). It is highly dependent on sensory experience. Therefore, sensory deprivation, such as in SSD, leads to cortical reorganization. Connectivity between primary and secondary auditory areas, but also between auditory and other sensory or higher order cognitive areas, is altered (Kral et al., 2013; Yusuf et al., 2017). Absence of auditory input even seems to have a larger effect beyond than within the auditory system. A recent study with congenitally deaf cats (Yusuf et al., 2017) confirmed that the absence of auditory input affected the higher order (cross-modal) posterior auditory field more than the primary auditory cortex. This is likely indicative of a decreased ability to integrate sensory input into ongoing top-down cortical processing, such as in the generation of error prediction signals – a process required for learning. Recently, results of the first study to look at whole-brain network connectivity patterns in human adults with UHL, also indicated cross-modal reorganization, because functional connectivity strength in the ipsilateral visual cortex was abnormal (Zhang et al., 2018). The reorganization of the brain continues with increasing duration of SSD.

The aural preference effect

In SSD, stimulation of the good ear leads to contra- as well as ipsilateral activity, whereas in a normal hearing person contralateral auditory brain activity is dominant. The abnormal strengthening of ipsilateral pathways is a consequence of the absence of inhibition that would normally come from the other ear (Grothe et al., 2010). This 'aural preference effect' (Gordon et al., 2015) towards the good ear also results in a biased input to higher-order cortical networks, affecting perceptual, language as well as executive functions.

Brain research in children with SSD/UHL

Several neuro-imaging studies have studied brain activity of children with UHL during listening or cognitive tasks. Also in these studies, significant differences between the children with UHL and NH control children have been reported not only in auditory regions but also in higher cortical regions and networks. For example, during listening tasks, children with UHL showed less activation of auditory areas than NH controls but also less activation of auditory association areas and bilateral attention networks (Propst et al., 2010). Results on a cross-modal task of Schmithorst et al. (2014) were indicative of alterations in the connections from auditory into visual areas and of more effort in low level processing of auditory stimuli. Furthermore, a deficiency in the deactivation of the default mode network (DMN) was indicative of insufficient suppression of self-referential activity, such as mind-wandering, during the cognitive task.

In addition, a number of studies have compared interregional functional activity of children with UHL and NH controls in resting (task-free) state (Jung et al., 2017; Tibbetts et al., 2011). Children with UHL showed decreased, as well as aberrant connectivity patterns between and within cingulo-opercular and frontoparietal networks. These networks are related to initiation of tasks and to executive top-down control, involving rapid/adaptive and sustained maintenance control and error-monitoring. As was found during task performance (Schmithorst et al., 2014) also in resting state differences in DMN were detected (linked to introspection and implicit learning) (Jung et al., 2017; Tibbetts et al., 2011). Furthermore, differences in sensorimotor and phonological networks and working memory were observed (Tibbetts et al., 2011). Interestingly, Rachakonda et al. (2014) detected correlations between educational outcomes (the need for an IEP) and microstructural integrity of Heschl's gyrus (an auditory brain region) in children with UHL. In addition to aberrant (network) activity, children with UHL also showed atypical connectivity patterns which likely are indicative of compensatory activity (Jung et al., 2017; Tibbets et al., 2011; Zhang et al., 2018). But, even with compensatory behavior, challenges in hearing and speech and language acquisition remain (Gordon & Papsin, 2019).

1.3 Impact of SSD

By definition, children with SSD do not hear bilaterally (with two ears) but rather they hear monaurally, which means that they only have one good ear for effective communication. Because there still is one good ear, the impact of the hearing loss and experienced difficulties are much more subtle for children with SSD than for bilaterally deaf children. SSD children's situation should, however, not be equated with NH either, and its consequences should not be overlooked.

Good coordination between the two ears normally facilitates binaural hearing, which is of key importance in sound localization and speech in noise understanding. In the following section we discuss the main binaural hearing mechanisms and the impact of having no binaural hearing.

1.3.1 Binaural hearing

1.3.1.1 Concepts

Binaural hearing refers to using the information – detecting and comparing – of differences between sound signals at the two ears (Grothe et al., 2010). Two types of binaural cues are available for sounds that originate from any location in space that is not directly in front or behind a person's head. First, a sound arrives earlier at the ear closest to the location it originates from than at the farther ear. This difference in path length from the sound source to each ear creates an interaural timing difference (ITD). ITDs are dominant for frequencies below ~1700 Hz, because the neural system cannot follow fluctuations faster than this (Moore, 1997).

Second, the sound also reaches the two ears with different intensities because of the shadowing effect of the head, producing an interaural level difference (ILD). ILDs are the dominant cue for frequencies higher than ~1700 Hz, when the wavelength of the sound is less than the distance between the two ears (Kumpik & King, 2019). For larger wavelengths, the head is no obstruction and the sound will just bend around the head.

Humans are very sensitive to these binaural cues of ILD and ITD (Joris & Yin, 2006). Interaural differences are processed in neural circuits at the level of the brainstem and midbrain (the superior olivary complex and the inferior colliculus) (Fitzpatrick &

Batra, 1997) and are used to identify sound sources in space in the horizontal plane. Vertical sound localization rather relies on spectral analysis, which is a monaural cue generated by direction-specific attenuation of particular frequencies by the pinna, the outer ear (Grothe et al., 2010). These spectral cues are also used in the horizontal plane to determine whether sound originates from the front of the listener or from behind (Kumpik & King, 2019).

Hearing with two ears not only enables to localize sound, it also brings several advantages for speech understanding in noisy environments. This can be attributed to three effects. First, the binaural system compares ITDs and ILDs associated with different sources, i.e. speech and noise. The distinct place of speech and noise allows for segregation of the two. The speech signal can then be enhanced, i.a. by suppression of the masking noise, resulting in an internal representation of the speech signal with a higher signal-to-noise ratio (SNR) than the SNR at the level of the single ear. This effect of improvement in internal SNR because of comparison of information at the two ears is termed *binaural unmasking* (Dillon, 2001; Van Deun, 2009).

A second effect involves the head acting as an acoustic barrier causing an ILD between the signals reaching the two different ears. When speech and noise are spatially separated, the head shadow differentially effects speech and noise. The listener can benefit from this by attending to the better ear, i.e. the ear closest to the speech source and thus with the more favorable SNR. In essence this *head shadow effect (HSE)* or *better-ear effect* is a purely physical effect, which requires very little central integration (Guevara et al, 2015). In real life situations often multiple noise sources are present at different spatial locations and therefore the better ear may fluctuate over time and frequency, but the auditory system can 'glimpse' these short-term changes in SNR (Kumpik & King, 2019; Schoenmaker et al., 2017).

A third effect is called the *binaural summation effect* or the *redundancy effect*, which refers to a perceived amplification of sounds when listening with two ears, in the situation where identical combinations of speech and noise are presented to both ears. This is an additive effect facilitated by higher order cortical areas, which produces a 1 to 2 dB improvement in SNR. It can be thought of as the advantage of the brain getting 'two looks' at the same sound (Dillon, 2001; Van Deun, 2009).

Binaural processing thus enables to localize and segregate sound sources and improve the signal-to-noise ratio. This helps with a number of everyday activities, such as alerting the listener about a possibly dangerous approaching source that is not yet in the visual field, and directing attention to a conversation in a noisy environment (Asp et al., 2015; Litovsky et al., 2019).

1.3.1.2 General Development

Brain structures for auditory processing are present at birth but some are not adult-like before puberty (Moore & Linthicum, 2007). Neural changes (e.g. the increase in density of neural fibers and myelination of axons, and the quantity of sound-evoked neural activity), and physical changes (e.g. head size) during development influence perception of interaural cues (Fels, 2008; Moore & Linthicum, 2007).

Regarding spatial hearing skills, results of Van Deun et al. (2009) showed that 5-year old NH children performed at adult level regarding sound localization and binaural masking level differences (i.e. the difference in the signal in noise detection threshold when signal and noise are identical at both ears versus when they are different). This was not yet the case in a just noticeable ITD difference task. Of note, on all three tasks some of the 4 year old children performed as well as the adults, indicating that good spatial hearing skills are possible at the age of 4. Likely, they emerge even earlier in life but are hard to quantify in young children because of task demands.

In studies specifically assessing speech perception in noise, different spatial configurations of speech and noise positions are used to obtain measures that reflect binaural unmasking, binaural summation and head shadow. In addition, two often used measures are *spatial release of masking* (SRM) and *squelch*. SRM is used to refer to the improvement in speech perception obtained as a result of spatial separation of speech and noise and is based on both the head shadow and binaural unmasking. The term *squelch* is used to refer to the improvement in speech perception due to the addition of an ear with a poorer SNR (an ear closer to the noise source) and is based on both binaural unmasking and binaural summation (Van Deun, 2009).

Spatial speech perception benefits have been observed in NH children at a young age (2-8 years) (Garadat & Litovsky, 2007; Hess et al., 2018; Litovsky, 2005), based partly on monaural head shadow cues. Van Deun et al., (2010) in addition showed evidence of true binaural benefits in NH children aged 4-8. Speech reception thresholds are generally found to be poorer for children than for adults (Hall et al., 2002; Litovsky, 2005; Van Deun et al., 2010), which can be attributed to children not being able to extract auditory cues as efficiently as adults yet, but also to still developing linguistic abilities and the ability to fill in the gaps of partially understood words (Litovsky, 2005).

1.3.1.3 Impaired binaural hearing due to SSD

In the previous sections, we explained how listening with two ears facilitates sound localization and speech in noise understanding and that even in very young NH children evidence for binaural hearing could be observed. When having only one good ear, binaural hearing is absent. Also, the monaural head shadow effect will be a disadvantage when sound originates from a source located at the hearing impaired side. In children with SSD therefore, the ability to localize sound sources and to understand speech in noisy situations is hampered.

Speech in noise understanding

A number of clinical studies have demonstrated the difficulties children (aged ~6 to 19 years) with SSD and less severe UHL encounter with speech in noise (SPIN) understanding. Lieu et al., (2013) assessed performance of 107 6-12 year old children with mild to profound UHL. Word recognition in noise was tested in free field at 0 and +5 dB SNR, with stimulus presentation from the front and multitalker babble noise from 30 degrees to both left and right of the participant. The children with UHL had significantly worse scores than the NH controls in both noisy conditions. In addition, word recognition scores in quiet were obtained using CIDW-22 word lists presented monaurally through headphones. Stimuli were presented at 40 dB SL relative to the child's PTA, or at most comfortable loudness for those with more severe UHL. As can be expected, scores of the children with UHL were similar to those of 95 NH (sibling) peers for the good ear, but significantly poorer for the affected ear.

Reeder et al., (2015) compared performance of 20 children with moderately-severe to profound UHL aged 6-17 years and 20 NH peers on three speech understanding tasks. First, *CVC word* recognition was assessed at fixed stimulus presentation levels. Recognition appeared reduced in the children with UHL, not only when presented at average conversational level (60 dB SPL + 8 dB SNR) in multitalker babble noise, but also when presented *in quiet* at a soft conversational level (50 dB SPL). In addition, two adaptive tasks were conducted. In one of these, *sentence* material was presented from a front loudspeaker and restaurant noise (60 dB SPL) from eight loudspeakers encircling the participant. Performance of the children with UHL in this task was again significantly lower than that of the NH controls. In the other task, *single spondees* were presented from a loudspeaker in front of the participant in quiet or noise (single-talker or multi-talker babble at 60 dB SPL) presented 90° to the left or right ear or from the front. In this task, the two groups performed equally well when noise was presented from the front. However, when the noise moved to the right or left, the NH children benefited from spatial unmasking, while the children with UHL only exhibited better word understanding in noise when the noise was moved towards the deaf ear.

Also using an adaptive task, Ruscetta et al. (2005) reported that twenty 6-14 year old children with severe-to-profound UHL required more advantageous listening conditions to perform equally well as 17 NH peers on correctly repeating sentence material and nonsense syllables in continuous multi-talker babble noise from 4 positions around the participant. For nonsense syllables, the average SNR needed for 50% speech recognition (the speech reception threshold, SRT) was significantly higher (and thus worse) for the children with UHL compared to the NH controls for both speech from the front and speech to the affected ear. For sentence material in addition this was also the case for speech to the good ear.

Lastly, Noh and Park (2012) determined the optimal seating position in a noisy classroom for 25 children aged 10-19 years with severe-to-profound UHL compared to 25 NH peers and 25 NH adults. Babble noise was presented from six ceiling speakers at 55 dB A and nonsense syllables from a front loudspeaker at 65 dB A at distance 1m. At distance 6m, stimulus and noise presentation level were equal. The mean recognition score of the UHL group was significantly lower than that of both NH control groups at all measured distances (3, 4, 6, 8 and 10m) (with the exception of NH peers score at 6 m distance). For positions with negative SNR, the difference in mean score of the UHL and NH peers group became larger than for positions with positive SNR. Even in quiet, measured at a distance of 3m, the mean recognition score of the UHL group was significantly lower than that of the NH peers (but no different to the NH adults). With linear interpolation methods, the authors showed that the UHL group needed a seating position of 4.35m and 6.27m distance from the front loudspeaker to achieve equivalent performance as respectively the NH adults and the NH peers seated at 10m.

Sound localization

Sound localization performance was assessed by Reeder et al., (2015) in a 15-speaker set-up spanning 140° with speakers placed 10° apart but only 10 of them active (unbeknownst to the participant). As expected, localization of monosyllabic words was significantly poorer and more varied for the children with moderately-severe to profound UHL (mean RMS 28.1°, SD 13.5°) compared to the age matched NH peers (mean RMS 6.0°, SD 3.7°). Johnstone et al. (2010) assessed the localization abilities of twelve 6-14 year old children with mild-to-severe UHL and NH peers. In an array of 15 loudspeakers placed at 10° intervals between -70° and 70°, the word 'baseball' was presented at 60 dB SPL (roved ± 8 dB). All children with UHL were fitted with a hearing aid and tested with and without the device. Note that a hearing aid is not beneficial for children with SSD, because the degree of HL is too great. This study shows that also with less severe UHL than is the case in SSD, unaided performance was significantly worse for the children with UHL than for the NH children. Further analysis showed that a greater degree of HL was associated with significantly more localization error.

Subjective experience

Finally, subjective experience has been mapped in the study by Reeder et al. (2015) as well. The children with UHL completed the speech, spatial and qualities of hearing questionnaire (SSQ). This questionnaire consists of three parts, focusing on (i) the hearing and understanding of speech in a variety of contexts, (ii) the directional, distance and movement components of spatial hearing, and (iii) other qualities of hearing such as the identifiability of different speakers and sounds and the ease of listening (Galvin & Noble, 2013). Results showed that the UHL group scored significantly lower than the UHL group on all three parts of the SSQ. Within the UHL group, quality ratings were significantly higher than speech ratings, which were significantly higher than spatial ratings. Within the NH group, there were no significant differences between the domains.

Auditory development under age 4

Sound localization and speech in noise understanding are quite difficult to measure in children younger than ~age 4. Several studies have therefore used parent-questionnaires to assess children of younger age. These questionnaires do not specifically target binaural hearing abilities but rather assess general auditory development. Still, differences between children with SSD/UHL and NH peers on these outcome measures have been found. Kishon-Rabin et al. (2015) reported that 21% of 34 infants with UHL demonstrated a delay in auditory behavior (as indicated by a score lower than the norm group mean score -2 SE on the IT-MAIS questionnaire). After adjusting for risk level (i.e. high or low, based on risk factors known to cause developmental delay), delayed auditory behavior was approximately 4 times more common in the infants with UHL compared to a large NH control group of 331 infants. In a study by Fitzpatrick et al. (2015), cross-sectional parent-questionnaire data of an ongoing longitudinal study assessing auditory and linguistic outcomes of children with UHL or mild bilateral hearing loss (BHL) aged 1 to 4 years old are presented. At ages 1, 2, 3 and 4, parents completed the PEACH questionnaire and at ages 3 and 4, in addition, the CHILD questionnaire, both designed to assess the children's abilities in everyday life listening situations. Group scores on the CHILD differed significantly from those of NH peers, but scores on the PEACH were similar between the groups. In their very recent report, cross-sectional data of age 4 was presented separately for the group of children with UHL and the group with mild BHL. Again, the CHILD yielded significantly different scores for both the hearing impaired groups compared to a NH control group. PEACH scores of the UHL group were now also significantly lower than those of the NH group; more specifically, the PEACH scores regarding situations in noise. 72% of the children with UHL obtained scores below – and 44% even more than 1 SD below – the mean of the NH group. Scores of the mild BLH and NH groups were similar, indicating that UHL caused more experienced difficulties than mild BHL for the participants of this study (Fitzpatrick et al., 2019).

Vestibular function

Between 20 to 70% of persons with sensorineural HL also has dysfunction of vestibular end organs (Cushing et al., 2013). Vestibular and cochlear end organs have similar embryological origins and anatomical and physiologic characteristics, so pathology affecting the cochlea could impact on the vestibular system as well (Cushing et al., 2013; Gordon & Papsin, 2019; Wolter et al., 2016). Vestibular abnormalities have been reported for children with SSD, mostly on the side of the deaf ear (Birdane et al., 2016; Sokolov et al., 2019). The risk of cochleovestibular loss likely is dependent on etiology and time course of the HL (Cushing et al., 2013). In children with SSD, Sokolov et al., (2019) observed most vestibular end organ dysfunction in children who had temporal bone trauma or idiopathic sudden sensorineural HL.

Vestibular dysfunction may result in difficulties with maintaining ones position in space. Wolter et al. (2016) and Sokolov et al. (2019) indeed showed that balance deficits occur in children with SSD. In daily life, these children need to expend increased effort to remain upright and stabilize their gaze during difficult motor tasks, which leaves less cognitive resources available for the tasks at hand. For young children, vestibular dysfunction can result in delays in achieving motor milestones.

Importantly, balance impairments in children with HL may not be explained by vestibular dysfunction alone but also by the HL itself. Sensory input is critical in learning balance behavior. The lack of binaural hearing in children with SSD hampers their ability to determine their position in the environment as they move through it (Wolter et al., 2016). Also, mastery of complex motor tasks can be impeded by SPIN understanding difficulties. Wolter et al. (2016) for example explain that for a child with SSD it can be very difficult to listen to an instructor without having to take their eyes from their task. Also, SPIN understanding difficulties may cause a child to avoid the playground/sports field where many of the neuro motor rules needed for complex balance tasks are learned (Wolter et al., 2016).

1.3.2 Daily life

Abovementioned difficulties in sound localization and speech in noise understanding can affect the daily life of children with SSD to a great extent. First of all, incoming information has to be fused into one percept and since in children with SSD that cannot be done based on ITD and ILD cues at the level of the brain stem, a greater demand is placed on processing at cortical level (Hughes et al., 2013; Steel et al., 2015). Importantly, children are exposed to many hours of environmental noise every day, which adds to the high demands in effort needed to listen and understand what others are saying. Busch et al. (2017) reported daily exposure to noisy environments to be about 3.4 hours per day for very young children and even 5.1 hours per day from primary school onwards. Main-stream school settings are often noisy and reverberant. For a child with hearing loss, they represent very difficult environments in which to be involved in the typical classroom activity of listening and simultaneously performing a secondary task (Noh & Park, 2012). In difficult listening situations such as these, the high listening effort and cognitive resources needed for perceptual processing leave decreased cognitive resources available for other functions and other tasks, decreasing performance on those (Howard et al., 2010; Jacobs et al., 2016). Consequently, children's learning and educational outcomes may be compromised and children can experience stress and fatigue (Bess & Hornsby, 2014). In their review, Krishnan and Van Hyfte (2016) summarize that one quarter to one half of children with UHL may have poorer academic performance, and up to a third are likely to have social, behavioral, and emotional problems.

Several studies have investigated quality of life (QOL) in children with UHL by means of the Pediatric Quality of Life Inventory (PedsQL) (Borton et al., 2010; Rachakonda et al., 2014; Umansky et al., 2011). This survey consists of items assessing Physical, Emotional, Social and School functioning, asking for each item how much of a problem it was during the past month. In a systematic review and meta-analysis, Roland et al., (2016) pooled the results of these studies which showed that children with UHL had significantly – and clinically meaningful – lower scores (worse QOL) than those with NH in the school domain and the social domain. Even more tailored to children with hearing loss is the Hearing Environments and Reflection on Quality of Life questionnaire (HEAR-QL) which was designed specifically to determine how a child perceives the social and emotional effects of their hearing loss. Studies using the HEAR-QL have observed significantly decreased but highly variable hearing-related QOL in comparison to children with NH for 7-12 (Umansky et al., 2011) year olds and 13-18 year olds with UHL (Rachakonda et al., 2014).

Interview studies with children with UHL and/or their parents by Grandpierre et al. (2018) (5-8 year olds) and Borton et al. (2010) (12-15 year olds) have shed some light on the impact the hearing loss has on the daily life of the children. In these interviews, the children expressed difficulties in speech understanding at school, where they often are in noisy situations. This required a lot of concentration and caused problems with memory and attention. Many parents also described that their child's speech and academics (i.e. math, reading and writing and learning a second language) were affected and required extra help (Grandpierre et al., 2018). Parents of the teenagers felt that teachers were not educated about UHL and often automatically assumed that their child was not paying attention, rather than understanding that the child didn't hear them (Borton et al., 2010).

Difficulties in social settings were a main worry of the parents, e.g. with regard to interactions with peers and bullying (Grandpierre et al., 2018). The teenagers mainly had one-on-one interactions and did not participate in group activities or parties

(Borton et al., 2010). They described that friends sometimes became annoyed when having to switch sides to the better ear or repeating what they said. Also, they admitted to frequently pretend to understand what friends were saying in noisy situations when they actually did not, and also to stop paying attention in difficult listening situations. Also, sports activities were described to be challenging due to the often noisy, overwhelming environments and difficulties with localizing voices of teammates and understanding instructions of coaches during a game. Despite the barriers, however, the teenagers reported being 'normal' and both they and their parents felt that they learned to adapt to the hearing loss and noticed improvement with time in many aspects of their life (Borton et al., 2010).

A recent study by Lucas et al. (2018) showed that psychological and social consequences to SSD do not disappear as individuals grow older. Adults still reported that speech understanding in background noise and reduced spatial awareness resulted in them limiting activities and participation, worrying about losing hearing in the other ear, embarrassment related to the social stigma attached to hearing loss and reduced confidence (Lucas et al., 2018).

1.3.3 Language and neurocognition

Importantly, the neural consequences of monaural input and the difficulties in speech in noise understanding due to the lack of binaural hearing negatively affect linguistic and neurocognitive development (for a review, see van Wieringen et al., 2019). Key findings are that in infants, delays in preverbal vocalizations were found to be approximately nine times more common compared with NH peers (Kishon-Rabin et al., 2015). Several studies in school-age children reported significantly lower scores on standardized language and IQ tests (Anne et al., 2017; Purcell et al., 2016).

Language and cognitive difficulties are more subtle for children with SSD than for bilaterally deaf children. In order to understand the subtle effects of SSD on linguistic skills, it is important to regard typical development. We refer to the next chapter for an overview of typical language development, as well as an overview of the existing literature concerning language difficulties in children with SSD/UHL.

1.4 Thesis outline

This thesis is divided into two parts.

Part 1 of the thesis is focused on language difficulties in children with SSD and contains two chapters. In **chapter 2**, an overview of typical language development is provided and the literature on language development in children with SSD/UHL is reviewed. **Chapter 3** presents the first study of this research project in which we aim to gain a more detailed insight than has previously been explored in literature of the language difficulties school-aged children with SSD experience.

Part 2 of the thesis focusses on intervention for children with SSD and contains three chapters. In **chapter 4** we discuss the window of opportunity for intervention and introduce our longitudinal study which aims to assess the effectiveness of cochlear implantation as a possible remediation for very young children with SSD. Cochlear implantation is the only rehabilitative option that offers the potential to partially restore binaural hearing when implanted early in life, but it is not reimbursed for children with SSD in Flanders and many other parts of the world. In **chapter 5** we present the results of the second study of this research project concerning methods of assessment of communicative skills in children under age 2. In **chapter 6** we present the first outcomes of the 6 first implanted children in comparison to two control groups.

The thesis is concluded with a general discussion of our findings and suggestions for future research in **chapter 7**.

Part 1

SSD and language development

2 Background: consequences of SSD for linguistic development

In the past, it was believed that speech and language development in children with SSD/UHL would be unaffected because they still have one NH ear. Now, an increasing body of research indicates that SSD is a risk factor for speech-language delay (for an overview, see Anne et al., 2017; van Wieringen et al., 2019). In the following, we will first give an overview of typical language development and address the importance of good hearing for language development. Afterwards, we will review the literature regarding speech and language difficulties in children with SSD and explicate the first research objective of this thesis.

2.1 Typical spoken language development

Language is a complex system with multiple levels or components. An important difference in the acquisition of language is the one between receptive and expressive language skills. Receptive language skills (or language comprehension) refer to the ability to understand (spoken or written) linguistic input, whereas expressive language skills (or language production) refer to the ability to produce words and sentences – in accordance with grammatical and semantical rules. In general, at any moment in a child's language development, receptive language skills are further developed than expressive skills because the understanding of a certain language pattern precedes the ability to actively handle it. Some children are more referential, in that they keep listening and trying to comprehend for a relatively long time before they try to produce, whereas other children are more expressive and quickly start to imitate speech of adults and experiment with production (Gillis & Schaerlaekens, 2000; Zink & Smessaert, 2012).

Then, three components of language can be distinguished: 1) the form of language, 2) its content or meaning and 3) its use. Regarding the form of language, a distinction is made according to the size of the units involved (sounds, words, sentences). First, phonology deals with speech sounds, the smallest units of language. A child has to learn to segment the speech stream into these individual speech sounds, master the technique to articulate the individual sounds and learn how to combine them into syllables. Second, morphology deals with the smallest *meaningful* units of language: morphemes. The child learns how words are formed out of individual sounds and how word form changes due to *inflection* (examples in Dutch from Gillis & Schaerlaekens, 2000; and Zink & Smessaert, 2012): ik kom, jij komt, kom jij? wij komen, ik kwam) and *derivation* (bakken, bakker, bakkerij, gebak, bakmeel). Also, the child learns that new words can be formed by *compounding* shorter words (tafel + poot=tafelpoot). Lastly, syntax comprises the rules, and exceptions, to combining words in order to form phrases and sentences. The term 'grammar' is usually used to refer to syntax and morphology together (Gillis & Schaerlaekens, 2000; Zink & Smessaert, 2012).

The meaning of words and word combinations is also referred to as semantics. The child builds up a vocabulary by learning which combination of sounds belongs to which meaning. In addition, the order of words in a sentence affects the meaning of the sentence, even though the meaning of the single words does not change. Pragmatics is concerned with the use of language, i.e. knowing how to accomplish different things in communication (asking a question, giving an order) (Zink & Smessaert, 2012). In addition, the child also acquires metalinguistic skills, which refers to ability to explicitly reflect on language. This shows when a child corrects his/her own utterances, makes remarks about the language use of adults, asks questions about meaning, gives opinions about grammar or makes philosophical remarks (Gillis & Schaerlaekens, 2000).

The above described components of language influence each other and largely develop parallel to each other. However, the *start* of development of the different components holds a certain order that is usually the same for all children and for all languages, namely: phonology, semantics & vocabulary, syntaxis, morphology and metalinguistics (Gillis & Schaerlaekens, 2000). In general, children go through similar stages in the development of these skills, which will be discussed in the following.

2.1.1 Phonology

Between 0 and 1 year of age, phonological development starts. At the age of merely six weeks, first **vocalizations** emerge. These vowels (eh, uh, euh, aah, eeh) are not language-specific yet but are universal. Already in the first 3 months of life, children can distinguish many different consonants from each other, as well as different vowels, and also words that differ only in one vowel. Between 4 and 7 months of age, children can hear the difference between consonants that are more difficult to distinguish from each other. They become increasingly familiar with sounds from their mother tongue and develop a preference for these sounds over sounds that do not belong to this language. By means of **vocal play**, the child experiments with pitch, intonation, duration and loudness of his/her vowel-sounds (and sometimes an accidental consonant). Around 7 months, the child starts to understand that a certain sequence of sounds corresponds to a certain meaning: the **first words are understood** (in context). The child is then also able to produce consonants and **babbling** commences. The child produces sequences of well-formed syllables consisting of a consonant and vowel, which is referred to as canonical babbling (Lee et al., 2018) and also places identical syllables behind each other, which is referred to as repetitive babbling (Fagan, 2015). Later, usually around 9-10 months of age, babbling becomes more varied. It increasingly sounds like the mother language but does not convey meaning yet (Nathani et al., 2006; Zink & Smessaert, 2012).

Between the age of 1 and 2;6 years, children expand their knowledge of the phonetic system of their mother tongue and learn how to produce words. Different sounds are mastered at different times, because the articulatory motor system is not developed fully yet. Place and manner of articulation determine the difficulty in producing sounds. Furthermore, children's phonological abilities have been linked to the size of their vocabularies, because a speech sound presented in a word likely is easiest to distinguish (Beckman & Edwards, 2019; Pettinato et al., 2017; Yeung & Werker, 2009). When sounds or syllables are too difficult to pronounce, children will show **phonological simplification processes**; they omit a sound or substitute it with one they can produce. Furthermore, in difficult consonant clusters, they include a vowel in between the consonants, swap consonants or place one of them towards the end of the word (Cohen & Anderson, 2011; Kirk & Vigeland, 2015; Zink & Smessaert, 2012).

In the early phase of speaking words children prefer spondees in which the first syllable is stressed (i.e. is audibly most prominent, typically by higher fundamental frequency, higher intensity and longer duration). Word stress is something they can perceive early in development and which can help them to detect words in the continuous speech stream (i.e. in Dutch, the majority of disyllabic words start with a stressed variable) (Curtin et al., 2012; Friederici et al., 2007). Already in their babbling, but with a major increase after appearance of the first words, children show prosodic differentiation (stress, intonation, rhythm) in their words (De Clerck et al., 2017). When producing a word of which the first syllable is not stressed, young children either do stress the first syllable or omit it. In words with three syllables, they omit one or even the two syllables that are unstressed. These simplifying strategies gradually disappear. At the age of 3 to 3;6, a child is generally able to produce all individual speech sounds (Beers, 1995). Only consonant clusters can remain difficult, and are generally mastered between age 5 and 6 (Zink & Smessaert, 2012).

2.1.2 Semantics

Generally, children speak their **first word** around their first birthday, between age 8 and 14 months of age. Use of single words is often referred to as one-word phrases because the words convey the meaning of a sentence in e.g. promoting interaction, expressing feelings and providing information (naming things or events, requesting something, answering questions or asking questions by elevating intonation) (Zink & Smessaert, 2012). In the one-word phase, children often mainly use nouns. Verbs are more difficult and are added later. Gentner (2006) explains that nouns are more transparent, in that they refer to objects or beings that are naturally individuated out of the stream of perception, while verbs refer to changes of state that are transient, and their boundaries are less clearly defined (Gentner & Kurtz, 2005; Gentner, 2006). In the one-word phrase stage, children produce a mix of words and non words (babble and unintelligible word attempts). The ratio of intelligible words to non words increases with time, and is linked to the development of phonological skills and the drive to learn and say new words (Moeller et al., 2007; Robb et al., 1994).

As children's vocabulary increases, their rate of learning new words increases as well. Between 1;6 and 2 years children start to combine words into **2-word phrases**. This happens when they have acquired 50-100 words and enables them to convey more complex messages and express themselves better. It is widely thought that around this time, children display a vocabulary spurt in which the rate at which they add new words to their vocabulary suddenly accelerates to as many as 10-20 new words per week. However, there is evidence that this only happens in a minority of children and that vocabulary growth may be better reflected by a gradual increase than by a spurt (Ganger & Brent, 2004).

Between the ages of 2;6 and 5 years the **vocabulary** of the child expands enormously to about 3000 (production), 5000 (comprehension). In addition to more nouns and verbs, children learn color names and simple prepositions, adjectives and interrogatives. First use of pronouns emerges around the age of 3. Around the age of 4, children understand the concept of (small) numbers and (in Dutch children) the difference between adjectives 'de' and 'een'. At age 4 to 5, children comprehend more abstract concepts of time and more difficult prepositions, conjunctions and interrogatives are acquired. They, however, also often use words incorrectly (e.g. by overextension or underextension) and construct incorrect words (neologisms). Between the ages of 5 to 9 or 10, vocabulary is fine-tuned. Abovementioned categories are expanded with more (difficult) words, mistakes are eliminated and in addition the child learns to use abstract language and figurative speech (Zink & Smessaert, 2012).

2.1.3 Syntax

At the age of 2;6 children can form **sentences** with 4 or 5 words. Usually these consists only of content words (nouns, verbs, adjectives, adverbs) rather than function words (articles, prepositions, interrogatives, conjunctions, pronouns) which are acquired at a later age, as described above. Early sentences can be produced via 1) direct activation or 2) grammatical encoding (Hadley et al., 2018). In direct activation, sentences are composed from memorized chunks that the child heard frequently, which may make the abilities of the child appear more advanced than they actually are. In grammatical encoding, the child desires to translate a message into language, and in order to do so retrieves words from his/her lexicon and assembles a sentence with these words. Such sentences can consist of lower-frequency subjects and verbs and reflect stronger expressive abilities (Hadley et al., 2018). Children start to produce sentences through grammatical encoding between the ages of 27 and 33 months (Rispoli, 2008, 2018). With age, children's sentences become longer, but the **order** of words in the sentence may remain difficult. Children tend to place the most important information at the beginning of the sentence and the inflected verb at the end of the sentence and put articles in the wrong place. Also more important than the length of the sentence is the **diversity in lexical items** used. Using diverse combinations of subjects and verbs provides richer opportunities for the child to encode grammatical information and provides a foundation for learning morphological and syntactical rules. The onset of diverse sentences can be expected by 30 months (see Hadley et al. (2018) for the development of sentence diversity).

Around the age of 3 children have mastered simple **questions** with interrogatives wie/wat/waar and around 3;6 also with waarom/hoe/wanneer. Children start to use **compound sentences** by adding a conjunction between two equivalent sentences, usually 'en (dan)…'. In compound sentences consisting of a main clause and a subordinate clause, children often still forget the conjunction or place the verb of the subordinate clause in the wrong place. The child will fully master syntactic skills between 5 and 9 years of age by virtue of acquiring more difficult conjunctions, adverbs, adjectives, pronouns and other function words (Zink & Smessaert, 2012).

2.1.4 Morphology

Between 2 and 2;6 years of age, **morphological development** starts with the inflection of nouns and adjectives. At first, children merely imitate word forms that most frequently occur in the language output of adults. In this way they learn the regularities, for the Dutch language e.g. that many plurals end with –en, many diminutives are formed by adding the affix –je and that the comparative and superlative adjectives are often formed by –er and –st. In a next stage, the child applies the learned rule to all cases (overgeneralizing). This shows a new insight into the existence of rules of a language and allows the child to start testing hypotheses and in that way master morphological rules. Around age 4, most children have mastered the rules regarding regular plurals and diminutives. It takes more time, however, to know in which cases not to apply a rule, i.e. the irregular words that require a change of vowel or an extra consonant.

Inflection and conjunction of verbs is most difficult, given that verbs occur in many forms, depending on the subject to which they refer to and the tense in which the word is used. Tense marking commonly starts between 21 months and 27 months of age (Rispoli et al., 2009). By the age of 4 to 5, use of basic grammatical morphemes is fairly stable but correct inflection of irregular word forms may still take several years (Rice et al.,1998; Zink & Smessaert, 2012). Irregular word forms need to be stored in memory (rather than generated via appliance of a rule) and acquisition is therefore more dependent on frequency of occurrence in speech input (Hammer, 2010), which takes time.

The acquisition of morphological rules is tied to phonological development. For example, accuracy of verb tense marking is higher in phonologically simple contexts (words ending with a single consonant) than in complex contexts (words ending with consonant clusters) (Song et al., 2009). Morphological development has also been shown to be strongly related to vocabulary size, more so than is syntactical development which seems rather mediated by age (Braginsky et al., 2015; Jung & Ertmer, 2018; Thal et al., 1996). Interestingly, the perceptual salience of morphemes plays an important role in the acquisition. Salience depends on the number of phonemes in a morpheme (phonetic substance), the presence of a vowel in the morpheme (syllabicity) and the sonority of the phonemes in the morpheme (relative loudness) (Goldschneider & Dekeyser, 2001). In accordance, morphemes that are shorter in duration and have lower fundamental frequency and amplitude are more challenging to hear and attend to (Montgomery & Leonard, 1998, 2006; Szagun, 2000). For the Dutch language, past tense morphemes –de and –te are therefore more salient than the 3rd person singular –t, possessive –s and plural –s (Hammer, 2010). Highly salient morphemes typically emerge earlier in the child's grammar than non-salient ones (Goldschneider & Dekeyser, 2001). Also, young children may make more mistakes regarding non-salient morphemes than highly salient ones. Data of Polišenská (2010) for example showed that Dutch children generally acquired present tense morphology by the age of 3 but before that age they made errors in the non-salient affix –t to plurals and –t in third person singular words.

2.1.5 Pragmatics

Young infants do not yet understand that language can convey meaning, but between 6 and 10 months of age they do start to interact with others, e.g. vocalize alternatively with an adult, play peek-a-boo games and later achieve joint attention with an adult towards an object. Around 8 to 10 months, first **intentional communication** starts by means of gestures, facial expression, and so called proto-linguistic utterances. The child displays communicative intentions by using the adult to obtain an object or a specific goal (proto-imperative behavior) or by using an object – giving, pointing or showing – to obtain the attention from the adult (proto-declarative behavior) (Cohen & Billard, 2018; Lichtert & Loncke, 2006). When the child has learned his/her first words, **symbolic communication** starts. Children direct attention, greet, express their feelings and can now also introduce topics of conversation and request things by means of words. Between ages 2;6 and 5, children learn to tell a story, discuss, answer questions, promise, negotiate, compliment, offend, lie and joke. These abilities will, however, still take years to develop fully. Gradually they also understand the system of **turn taking** in conversation: listen, wait until the conversational partner is done talking, and formulate a reaction relating to the content of the conversation. Abiding these rules remains difficult for quite some time, but between age 5 and 10, the child learns to better control this process of turn taking in conversations and learns how to convey a story. Also, improvements are seen regarding the coherence within the information they convey in their messages, and knowledge of the amount of information and level of detail necessary to communicate their message (Zink & Smessaert, 2012).

2.1.6 Metalinguistics

After age 2;6, more and more children reflect on their own language use. First, **phonological awareness** starts to develop, which is the skill to manipulate the word form independently of its meaning (Wachtlin et al., 2017). The child becomes aware of rhymes and starts to experiment with pronunciation and makes up nonsense words. Also, children show awareness of their articulatory mistakes and show revisions in their sentences. Revisions increase in number with age, reflecting change in the ability to monitor their own language production (Rispoli, 2008). Around the age of 4 children start to **reflect on the meaning of words**. They now understand that the same word can have multiple meanings, that animals do not speak language and that people can speak a different language than they do (Zink & Smessaert, 2012).

2.1.7 The importance of hearing for language development

Children's language development is strongly influenced by their hearing abilities. Infants who are bilaterally deaf do not start babbling when normal hearing children do, and when they do – after a delay of 5 to 19 months – there is little variation in the phonemes used (Koopmans-van Beinum et al., 2001; Oller et al., 1985). When access to sound is made possible via cochlear implantation, these young children start babbling within 1 to 2 months (Colletti et al., 2005; Moeller et al., 2007; Schauwers et al., 2004) and use repetition in their babbles as much as their NH peers within 4 months (Fagan, 2015). Results of parent-questionnaires assessing milestones in vocal and auditory development support this strong relation between prelexical vocalizations and early auditory skills, not only in children with severe-to-profound bilateral hearing loss (Kishon-Rabin et al., 2005) but also in children with UHL (Kishon-Rabin et al., 2015).

The acquisition of language likely is a statistical process in which the infant finds patterns in the speech input he/she is exposed to (Moeller & Tomblin, 2015). Infants can learn the probabilities of phoneme sequences by which they identify phonetic boundaries, word classes and grammatical relations (Farmer et al., 2006; Maye et al., 2002; Smith et al., 2018). Importantly, they need to be able to hear (and take in) linguistic input in order to do this.

In addition, language acquisition partly occurs incidentally (Saffran et al., 1997) via overheard, rather than explicitly directed, verbal information, such as conversations between others. Hearing loss, even mild or unilateral, affects access to this relevant acoustic information from natural listening conditions, hampering incidental learning of language. Incidental learning is not only very important in acquisition of language, but also for higher level linguistic skills such as verbal reasoning (Jacobs et al., 2016), which may therefore also be at risk.

2.2 Language development in children with SSD

Children with SSD are not impacted as severely as bilaterally deaf children. However, the influence of diminished auditory input and lack of binaural hearing on their speech and language and cognitive development should be considered. In the following, we will review the literature regarding language and cognition in children with SSD and less severe UHL.

2.2.1 Language development: infants and toddlers with SSD/UHL

In very young children, research has mainly focused on communicative skills according to the parents via questionnaires. In Kishon-Rabin et al. (2015) preverbal vocalizations of 34 infants with UHL aged 4-17 months (median 9.4 months) were assessed by means of the PRISE parent questionnaire. Results of 41% of the children were indicative of a delay in preverbal vocalizations. Compared to the NH control group of 331 infants, this was approximately 9 times more common. Findings of Kiese-Himmel (2002) showed an average delay of 5 months to produce two-word phrases for 20 children with UHL, compared to NH norms. These results are corroborated by demographic information from parental interviews in the study of (Lieu et al., 2013) with a large group of children with UHL (n=109). Results showed that compared to NH controls (n=95) the first occurrence of use of two-word phrases, but not first single word use, was significantly delayed with on average 3 months. In contrast, in a previous study of Lieu et al. (2010), both single and two-word phrases of children with UHL were not delayed.

Fitzpatrick et al. (2015) assessed 27 children with unilateral or mild bilateral HL at 24 and 36 months with questionnaires regarding mean length of their longest utterances (MLU), language comprehension and expressive language. No significant differences were found compared to NH peers, but a closer look at their data shows some large and thus likely meaningful differences. At the age of 24 months, there was a gap of about one SD of test norms (14 points) between the language comprehension median score of the children with hearing impairment compared to that of 36 NH peers. At the age of 36 months, there was a gap of about one-and-a-half SD (22 points) for language expression and the MLU was 2.4 words lower for the children with hearing loss compared to the NH peers (Fitzpatrick et al., 2015). In a study with 24 preschool children with UHL, 33% showed a delayed MLU despite early age of identification of the hearing loss (< 6 months) (Sedey et al., 2005). For two language questionnaires, respectively 17 and 23% of the children scored well below expectations (>10th percentile). For a subgroup of 15 children, longitudinal data was available from assessments of at least 2 occasions between the ages of 12 months to 5 years. The authors report that 27% of these children showed a consistent pattern of language delay, with an additional 7% showing borderline delay (Sedey et al., 2005). All children showing language delay had severe-to-profound UHL.

From 4 years of age onwards, a variety of behavioral language tasks have been conducted to assess linguistic skills of children with SSD/UHL. Borg et al. (2002) reported delayed preschool language development for children with UHL. The pooled score over 9 subtests of a language battery was significantly lower for the 4- and 5-year old participants with UHL compared to NH peers. For the 6-year old participants with UHL, scores were lower than the NH control group as well, but the difference was not significant. In Borg et al. (2007) difficulties were apparent on an expressive vocabulary test for 4-6 year old children with UHL with a PTA > 41 dB HL but not for children with less severe HL. In this study, difficulties did not improve by 6 years of age. In a study by Kiese-Himmel et al., (2002), children with UHL between 2;6 and 10 years of age did not seem to experience difficulty on standardized linguistic tasks. No control group was tested but scores seemed similar to norms of NH peers. Lowest group performance was seen on a task assessing the processing and completing of incompletely spoken words. The authors speak of a ‘possible subtle’ difficulty because the group average did not seem very deviant from NH norms.

In recent research by Fitzpatrick et al. (2019), all participating children were diagnosed at very young age because of the newborn hearing screening. Behavioral test performance of the group of 38 children with UHL age 4 was significantly worse compared to a NH group regarding receptive language as well as expressive communication test scores, but scores were similar for receptive vocabulary and articulation. For the receptive language test individual scores were examined, showing that 16.7% of the children in the UHL group scored below a standard score of 85 (1 SD below the normative mean of 100; considered clinically to be below average), in contrast to none of the NH children (Fitzpatrick et al., 2019). Also Vohr et al., (2012) evaluated early diagnosed children with UHL or mild BHL. The ten 4 to 5-year old children showed significantly lower communication, motor skills, and adaptive behavior scores compared to 74 NH controls. Also, comprehension and expressive language scores were similar to 19 children with moderate-to-profound BHL.

2.2.2 Language development: school-aged children with SSD/UHL

Over the past few years, research by Lieu and colleagues has demonstrated linguistic difficulties in school-aged children with different degrees of UHL (Lieu, 2018). Effects are more pronounced for children with more severe UHL (Anne et al., 2017). Children aged 6-12 years old showed significantly lower scores on listening comprehension and oral expression tests compared to a group of NH peers, as well as significantly lower oral composite scores (a mean language score) (Lieu et al., 2013, 2010). The children with UHL were also more likely than their NH peers to have academic difficulties and to receive speech-language therapy and need individualized education plans (IEPs) (Lieu et al., 2010). Studies in the 1980s already suggested that many children with UHL experience difficulties at school, with up to 35% repeating a grade compared to 3.5% of NH peers (Bess & Tharpe, 1986).

To our knowledge, only one longitudinal study has been conducted, in which 46 children with UHL aged 6-8 were monitored for 3 years (Lieu et al., 2012). Results showed that oral expression and oral composite scores, but not listening comprehension scores, improved significantly over time. However, parent- or teacher identified problems at school did not change and about half of the children continued to need IEPs throughout the 3 years (Lieu et al., 2012). In a following study by Fischer and Lieu (2014), 20 adolescents (12-17 years old) with UHL again showed significantly lower linguistic scores compared to 13 NH peers. Part of the adolescents in this study also participated in the earlier study by Lieu et al. (2013). A comparison between scores of these two studies indicates that raw scores in the 12-17 year olds (for children with UHL as well as with NH) had improved compared to the raw scores of the 6-12 year olds but, importantly, the gap between the two groups was greater in the 12-17 year olds than in the 6-12 year olds.

2.2.3 Cognitive development: school-aged children with SSD/UHL

In addition to testing language skills, a number of studies have also assessed cognitive skills, mainly by means of IQ tests reporting the verbal IQ (VIQ), performance IQ (PIQ) and the total IQ (TIQ) of the participating group of children with UHL in comparison to those of the control group of NH peers. Results for school-aged children are mixed. A number of studies reported TIQ to be significantly (Martínez-Cruz et al., 2009; Schmithorst et al., 2014) or marginally (Lieu et al., 2013) lower for the children with UHL. Lieu et al. (2013) also reported VIQ to deviate. In Lieu et al. (2010), however, there were no significant differences in IQ scores (TIQ, VIQ or PIQ) compared to the NH group and also Ead et al. (2013) showed similar TIQs. Purcell and colleagues (2016) performed a meta-analysis, showing that when taking four studies together, the children with UHL (n=173) scored 6.3, 3.8 and 4.0 points lower on resp. TIQ, PIQ and VIQ, compared to the NH peers (n=202). The differences between the groups were significant but effect sizes were 0.42 (moderate) for TIQ and 0.25 to 0.27 (small) for PIQ and VIQ, respectively. Only Fischer and Lieu (2014) have assessed the IQ scores of teenagers with UHL (12-17 years). TIQ as well as VIQ and PIQ were significantly lower compared to NH controls, and the differences were larger than they were in the study of Lieu et al., (2013), in which part of the adolescents had previously participated. In sum, IQ may be affected in children with UHL and possibly the impact is greater in adolescence than in childhood, but more research would be needed to draw conclusions.

IQ scores are composite scores averaging the results of different sub tests and therefore do not inform us about more specific cognitive abilities. Executive functions such as sequential processing, sequence learning and concept formation have been shown to be highly dependent on auditory experience and language skills and are therefore at risk in children with hearing loss (Kral et al., 2016). Few studies have zoomed in on specific executive functions in children with UHL. Ead et al. (2013) reported significant deficits in a complex working memory task in 9 to 14 year old children with UHL, indicating impaired executive control function when distracted by irrelevant verbal information. Martínez-Cruz et al. (2009) reported impaired verbal, visual and numerical reasoning and impaired short term memory, compared to NH controls.

2.3 Research Objective

In the previous section, we reviewed the literature on language and cognition in children with SSD/UHL. Several studies have shown that these children show differences in their development in this regard, when compared to NH siblings/peers. The studies that have assessed language in school-aged children reported composite language scores (Fischer & Lieu, 2014; Lieu, 2013; Lieu et al., 2013, 2012, 2010). These do not really inform us about the specific language skills that are difficult for the children. Furthermore, in the only longitudinal study that has been conducted in children with SSD/UHL, results indicated that oral language scores improved significantly over time but parent- or teacher-identified problems with school performance did not change (Lieu et al., 2012). Regarding this, it would be interesting to have a look at more specific deficiencies that may not be visible in composite scores.

Children with SSD are prone to suboptimal perception of low salient speech sounds, certainly in noisy environments. Therefore they may sometimes hear, but sometimes miss fine details in linguistic input. We hypothesize that this may impede their phonological development, because for segmenting the speech stream into individual speech sounds, learning how to articulate these and when to use them, it is crucial to be able to hear and distinguish all speech sounds. In turn, phonological difficulties may affect morphological and syntactical rule formation and vocabulary. Indeed, is known that the development of grammatical skills (morphosyntax) is particularly sensitive to good audibility of speech information (Hammer, 2010; Moeller & Tomblin, 2015; Szagun, 2000; Tomblin et al., 2015). For example, the perceptual salience of morphemes, which is (partly) dependent on its phonetic substance and sonority, plays an important role in the acquisition of the morphemes (Goldschneider & Dekeyser, 2001), see section 2.1.4. Morphemes important in learning morphosyntactical rules and exceptions often are not perceptually salient (Tomblin et al., 2015).

In children with mild-to-moderate BHL, a number of studies have investigated these specific linguistic domains and reported delays or difficulties in phonological and morphosyntactical skill*s*. For example, McGuckian and Henry (2007) assessed production of a number of different morphemes in 7-year old children with mild to moderate bilateral hearing loss, in comparison to a 3-4 years younger NH control group matched on MLU. Results indicated that the children with the hearing loss less often correctly produced possessive -s and plural -s than the NH controls. The two groups showed similar performance for other tested morphemes (progressive -ing, articles and irregular past tenses). Because there was a 3-4 year age gap between the two groups, this latter finding does not indicate normal grammatical morpheme use, but it does suggest that the phonemes involved in realizing the morpheme influence the use of it (Koehlinger et al., 2015). Koehlinger et al. (2013) assessed finite verb morphology in a large group of 3- and 6-year old children with mild to severe BHL. The children produced significantly fewer of these morphemes compared to age-matched NH peers. Some children appeared to catch-up, but at group level performance at age 6 was not different from performance at age 3, and more than half of the children scored below the 25th percentile.

Koehlinger et al. (2015) found that correct production of s-related morphemes in 3 year olds with mild-to-moderate BHL was related to better hearing skills (i.e. better audibility in the high frequencies) and better articulation skills (word final production of s/z). Results of Tomblin et al. (2015a) also showed that morphology performance of 4-year olds with mild-to-severe BHL was specifically related to hearing abilities, and that this performance in morphology was poorer than performance on a vocabulary test.

Also in teenagers with mild-to-moderate BHL, evidence of persistent grammatical difficulties have been reported. More than half of the adolescents (11-15 years) in the study by Delage and Tuller (2007) demonstrated deficits in phonology and morphosyntax.

Only a few studies have formally assessed the abilities of children with SSD/UHL in these domains. Ead et al., (2013) conducted a pilot study in 7 children with UHL aged 7-12 years old. Compared to 7 NH peers, the children showed reduced accuracy and efficiency in a number of phonological processing tasks, which was especially pronounced when working with non words (i.e. non word repetition, blending and segmenting), but significantly lower performance also occurred when working with words (blending words and phonological awareness). Anecdotal, in the interview-study of Grandpierre et al., (2018), parents of children with UHL (or mild BHL) reported their child's pronunciation of words to be less accurate than that of (younger) siblings, dropping consonants at the ends of words or 's' or 'sh' sounds within words. Fitzpatrick et al. (2019), however, recently reported no significant differences between 4 year old children with UHL and NH peers on a sound-in-word test.

To our knowledge no other study has zoomed in on specific linguistic domains in children with UHL/SSD. The main objective of **study 1** *(chapter 2)* of this dissertation therefore was to gain a more detailed insight of the language difficulties in school aged children with SSD. We compared task performance of the clinical sample of Dutch-speaking school-aged children with SSD of the university hospital in Leuven to that of age- and gender matched NH peers, with regard to morphology, syntax and vocabulary. We hypothesized that morphological and syntactical linguistic tasks would be more challenging for children with SSD than for NH children because of their dependence on good mastery of the phonology of language. Importantly, in our analysis, we not only looked at test scores but also analyzed the error patterns of the children. We also assessed short term memory and working memory by means of digit span tasks. Given that executive functions are dependent on auditory experience and language skills (Kral et al., 2016), we hypothesized that working memory performance of the children with SSD would differ from that of NH peers. An additional aim of the study was to document the impact of SSD on the children's daily life by means of a questionnaire focused on aspects of hearing abilities.

3 Linguistic and auditory outcomes of the clinical population of school-aged children with SSD in Leuven

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Abstract

Objectives: To examine auditory, linguistic and cognitive outcomes of children with single sided deafness (SSD). An increasing body of research suggests that children with SSD lag behind with respect to their normal hearing (NH) peers. In the present study we tap into certain developmental skills.

Design: Case–control study.

Participants: 21 children with SSD between 5 and 15 years of age participated. Per child with SSD two NH control children were matched on age and gender.

Outcome measures: Morphology, syntax and vocabulary were examined and performance was assessed in depth by focusing on sub skills and type of errors made. Furthermore, tests of short term and working memory were conducted and aspects of hearing disability were assessed by means of the speech spatial and qualities of hearing questionnaire (SSQ).

Main results: The children with SSD lagged behind in their scores on the three language tests and showed some differences to the NH group concerning type of errors and difficulty of the several subskills. Furthermore, scores on the SSQ indicated that in daily life, the children with SSD experience problems in spatial hearing and in understanding speech in noisy situations, and that the effort they have to put into listening and in understanding speech is considerably greater than in NH children.

Conclusions: The present study showed differences between children with SSD and NH children on several language skills and on auditory behavior. Possibly, early intervention could prevent such language difficulties and minimize problems with spatial hearing and speech understanding.

3.1 Introduction

Since the introduction of the newborn hearing screening (NHS) program, unilateral hearing loss (UHL) is detected at infancy. In Flanders in the last decade, each year approximately 39% of all children diagnosed with hearing impairment (HI) had a UHL; ~60 newborns per year. Approximately one third of this group of children has a profound UHL (pure tone average (PTA) > 90 dB HL), also called single sided deafness (SSD). Currently, there is no multidisciplinary audiological rehabilitation for these children and they are not systematically followed up in their (academic) development. Until recently, many professionals believed that children born with SSD would not experience much handicap because they have one normal hearing (NH) ear. The contrary is true: an increasing body of research suggests that SSD is a risk factor for speech-language delay, and that problems with behavior and school performance persist throughout the years (Kuppler et al., 2013; Lieu, 2004).

The mechanisms through which SSD affects language skills and academic performance are considered to be related to impaired binaural hearing. As a consequence of the difficulties with localization of sound and segregation of speech from noise, children with SSD likely miss out on things that are said to them or said in their presence. They may therefore have limited chances of incidental learning of language but might also not pay enough attention anymore when hearing situations are difficult, or put too much effort into trying to localize sound and segregate sound from noise rather than to process it (Lieu et al., 2013; Vila & Lieu, 2015). These factors could affect the language development of a young child as both access and quality of input are crucial (Moeller & Tomblin, 2015).

Several studies have indeed shown that children with SSD or a less severe unilateral hearing loss (UHL) show differences in their language development when compared to NH peers. Kishon-Rabin et al. (2015) report that delays in auditory behavior and preverbal vocalizations are approximately four and nine times more common in infants with UHL compared to the NH children. Other studies have reported delayed use of two-word phrases (Kiese-Himmel, 2002; Lieu et al., 2013) and delays in preschool language development (Borg et al., 2002). When the children reach the school-age, differences in language skills are still present. The children are more likely than their NH peers to receive speech-language therapy and to need individualized education plans (Lieu et al., 2010). Furthermore, research has assessed performance of these children on different standardized language tests (Lieu, 2013; Lieu et al., 2012, 2010) and aspects of phonological processing (Ead et al., 2013) and consistently reported significantly lower scores compared to NH siblings or peers. However, it remains difficult to grasp on which particular language skills the children lag behind. Not only language, but also other cognitive skills seem to be affected, as shown by significantly lower IQ test scores(Lieu et al., 2013, 2012; Martínez-Cruz et al., 2009; Schmithorst et al., 2014) and lower performance on a complex working memory test (Ead et al., 2013). These skills are intrinsically involved in language functions.

The goal of the present study is to investigate language, short term and working memory and auditory outcomes of a clinical sample of Dutch speaking children with SSD. A case-controlled study was conducted in which the children with SSD were compared to age- and gender-matched NH children on outcomes of tests of language and short term and working memory and on a questionnaire of auditory abilities. A second aim is to gain a more detailed insight of the language abilities of the children. To that end, performance on a number of language sub skills was assessed. As has been found in children who are hard of hearing, morphology may be especially vulnerable given its high demands on processing of fine details in linguistic input (Tomblin et al., 2015). Besides a broader look at different language subskills our study also allowed us to analyze the type of errors the children make. Error patterns may be different for children with SSD than for their NH peers. To our knowledge, both sub skill and error analyses of language test performance have not been performed before in children with SSD or UHL. A third aim of the current research is to document the impact of SSD on the children's daily life.

3.2 Methods

Participants

Twenty-one children with SSD, aged 5 to 15 years, participated in the current study. These eleven boys and ten girls were recruited from the ENT group of the university hospital in Leuven. They suffered from congenital sensorineural UHL (4 children: PTA > 70 dB HL, 17 children PTA > 90 dB HL). Ten of the children were HI on the left side and eleven on the right side. All children were enrolled in normal education. Participant characteristics are listed in table 3.1.

Each child with SSD was matched with two typically developing NH children (PTA not exceeding 20 dB HL). The control children had the same gender as the child with

SSD, with the exception of two children where only one of the matched NH children had the same gender. They also had the same chronological age with a maximum deviation of three months, with the exception of 2 children where the deviation was 5 or 6 months. Fisher's exact test indicated no significant association between group (SSD or NH) and maternal education level (p=.609).

Ethical Considerations

The study was approved by the KU Leuven Medical Ethical Committee and all parents signed written informed consent before the start of the testing. The study has been performed according to the Declaration of Helsinki.

Table 3.1. Participant Characteristics

Pair	**Age (years;months)**			**Gender**			**Side of HI**	**Degree of HI**	**PTA (dB HL)**
	SSD	NH	NH	SSD	NH	NH	SSD	SSD	SSD
1	5;00	5;01	5;02	f	f	f	right	Profound	95
2	5;01	5;00	5;00	m	m	m	left	Severe	79
3	5;06	5;02	5;04	m	m	m	left	Profound	NR
4	6;01	6;02	5;11	f	f	f	left	Profound	93
5	6;01	6;01	6;03	m	m	m	right	Profound	103
6	6;02	6;05	6;02	f	f	f	right	Profound	NR
7	6;04	6;07	6;04	f	f	f	right	Profound	116
8	7;03	7;03	7;05	f	f	f	left	Profound	NR
9	7;03	7;03	7;03	f	m	f	left	Profound	>110
10	7;10	7;09	8;00	m	m	m	right	Profound	>115
11	8;04	8;01	8;03	m	m	m	left	Severe	>85
12	8;10	8;09	8;08	f	f	f	left	Severe	>83
13	10;04	10;04	10;01	m	m	m	right	Profound	103
14	10;06	10;04	10;05	f	f	f	right	Profound	>105
15	10;09	10;08	10;07	f	f	f	right	Profound	>95
16	10;10	10;09	10;09	m	m	m	left	Profound	95
17	11;09	11;10	11;07	m	m	m	left	Profound	NR
18	12;03	12;02	12;06	m	m	m	right	Profound	NR
19	12;04	12;04	12;05	m	f	m	right	Profound	NR
20	13;05	13;10	13;08	f	f	f	right	Severe	80
21	15;10	15;04	15;11	m	m	m	left	Profound	>90

Note: Pure Tone Average over 500, 1000, 2000 and 4000 Hz. The > sign indicates no response at one or more of the tested frequencies. NR indicates no response at highest level tested (120 or 130 dB HL), for none of the tested frequencies.

Outcome measures

Every child was tested in a quiet room at home, at school, or at the university hospital. Duration of testing was, on average, 90 minutes and breaks were given if needed.

Language skills were assessed with two subtests of the Clinical Evaluation of Language Fundamentals (CELF-4-NL), a standardized general language test battery consisting of receptive and expressive subtests (Kort et al., 2010). The subtest Word Structure (WS) of the CELF-4-NL was implemented in the current study to assess expressive morphological abilities. In this subtest, children were asked to complete a sentence after seeing a color illustration, using a targeted word structure. The subtest is only intended for children between five and nine years of age. In the subtest Formulating Sentences (FS), which assesses expressive syntactic skills, the children were asked to formulate a sentence about a color illustration using a targeted word or phrase. In addition, the children's expressive vocabulary was tested by means of the Expressive One Word Picture Vocabulary Test (EOWPVT) (Martin & Brownell, 2011), in which the children were asked to name in one word, objects, actions and concepts presented with color illustrations. Lastly, the Number Repetition subtest of the CELF-4-NL was included. Here, the experimenter read sequences of digits out loud and the children were asked to repeat them in the same order (NR forwards) for a measure of their short term memory, and in a backward order (NR backwards) for a measure of working memory.

Besides above-mentioned behavioral measures, the Speech, Spatial and Qualities of Hearing Scale (SSQ) version for children (Galvin & Noble, 2013) was filled out to assess aspects of hearing disability in daily life. This questionnaire consists of three parts, focusing on 1) the hearing and understanding of speech in a variety of contexts, 2) the directional, distance and movement components of spatial hearing, and 3) other qualities of hearing such as the identifiability of different speakers and sounds and the ease of listening (Galvin & Noble, 2013). Each item was to be rated on a scale of 0 to 10, where higher scores indicate greater ability on the hearing aspect posed in the item.

Statistical Analysis

To evaluate the performance of the children on CELF-4-NL subtests and the EOWPVT, raw scores were converted into z-scores (M=0, SD=1) using age-appropriate population distributions. For the SSQ questionnaire, mean scores, on a range of 0 to 10, were calculated for each of the three subscales.

For the three language tests, besides the general scoring of performance, the errors the children made were assessed in depth. First, it was assessed on which sub skills of the test the errors were made (for an overview see table 3.2). Note, the items of the tests become progressively more difficult and a discontinue rule, designed to minimize testing time, is used to determine when to stop test administration. In our sub skill analysis, the percentage incorrectly answered items of a sub skill was calculated over *all* items of the sub skill per child, whether administered to the child or not. Second, the answers the children gave when responding incorrectly to an item were analyzed in more detail. These answers were divided into categories (adapted from (Boons et al., 2013); CELF-WS and EOWPVT, or based on the manual of the test; CELF-FS). An overview of the error categories is provided in table 3.3. In some instances, an answer was wrong for multiple reasons and would then fit into more than one category. The category was then chosen that indicated the most severe mistake. After categorizing the erroneous answers (for examples, see appendix I), for each child we calculated for every category the percentage of the child's total amount of errors that was attributed to the category. With regard to the EOWPVT error type analysis of the NH children, only part of the data for categories 5,6,7,8 was available. Therefore data of 18 of the NH children were not taken into account for these categories.

Parametric assumptions were not met for part of the groups' outcome measures. It was therefore decided to apply non parametric Mann Whitney U tests for all comparisons, with p-value calculation based on the exact distribution of the test statistics. Statistical analysis was performed using SPSS version 23. A two-tailed p-value of 0.01 was considered statistically significant. Effect sizes were calculated using the formula $r = Z/\sqrt{n}$ (Field, 2009).

3.3 Results

Test scores

Mann Whitney U tests showed that the children with SSD had a significantly lower z-score than the NH children on the WS test ($Z=-2.572$, $p=0.009$, $r=0.42$), the FS test ($Z=-2.546$, $p=.010$, $r=0.32$) and on the EOWPVT ($Z=-3.481$, $p<.001$, $r=0.44$), see figure

3.1. In figure 3.2 the individual z-scores on these three language skills of the children with SSD are presented in comparison to the average of the z-scores of the two matched NH children. The two groups performed similarly with regard to short term and working memory (NRf and NRb).

Table 3.2. Sub skill classification of the language tests

CELF- WS (Morphology) 30 items		CELF-FS (Syntax) 20 items		EOWPVT (Vocabulary) 70 items	
Sub skill	Nr. of items	Sub skill	Nr. of items	Subskill	Nr. of items
plural regular form	4	noun	2	concrete noun	137
plural irregular form	4	verb	2	verb	6
diminutive	5	adjective	1	relational noun	27
demonstrative pronoun	2	adverb	4		
separable verb	2	conjunction	10		
past participle regular form	2	prepositional expression	1		
past participle irregular form	2				
comparative & superlative adjectives	5				
pronoun	4				

Table 3.3. Error categories of the language tests

CELF-WS (Morphology)	
1: only–lexeme	the lexeme of the target word
2: related–neighbour	correct lexeme, but an incorrect word form
3: related–overgeneralization	correct lexeme, but the child uses a general, not appropriate rule to create the word form
4: related–other	correct lexeme, but an incorrect word form which cannot be categorized as a neighbor or overgeneralization
5: incorrect gender/number	incorrect gender/number of the target word
6: incorrect lexical category	incorrect lexical category
7: not related	an existing word that is not related to the target word
8: neologism	a non-existing word
9: no answer	the child is not able to respond with an existing or non-existing word
CELF-FS (Syntax)	
Mild Errors	1: a complete sentence with correct structure and only 1 or 2 deviations in grammar or semantics
	2: a complete sentence that holds few information
	3: a complete sentence that is obliquely related to the context of the picture
	4: a complete sentence, but the target word is used as an exclamation
Severe Errors	5: an in complete sentence
	6: a complete sentence with more than 2 deviations in grammar or semantics
	7: a complete sentence that does not make sense
	8: a complete sentence that does not contain the target word/phrase
	9: a complete sentence that is not related to the context of the picture
	10: no answer

Table 3.3 (continued). Error categories of the language tests

EOWPVT (Vocabulary)	
1: related meaning general	a more general term from the correct semantic field
2: related meaning neighbour	a term from the correct semantic field at a similar specificity level
3: related meaning specific	a more specific term from the correct semantic field
4: related sound	a word that sounds like the target word
5: circumlocution	a description of the target word
6: not related	an existing word which is not related to the target word by meaning or sound
7: neologism	a non-existing word
8: no answer	the child is not able to respond with an existing or a non-existing word

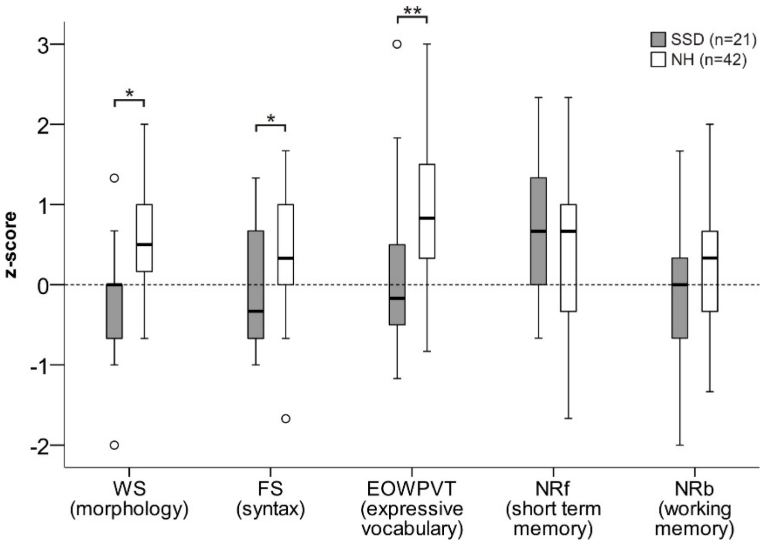


Figure 3.1. Results of the children with SSD (in grey) and the NH control group (white) on the tests of language and memory. Y-axis: z-scores. Boxplots represent the distribution of the z-scores on the tests: the box represents the interquartile range, with a line at the median value. Whiskers extend to the highest and lowest values no greater than 1.5 times the interquartile range, outlying values are depicted with a circle. Asterisks mark a significant difference between the groups (* p<.05, ** p<.01, *** p<.001). The dotted line represents the norm group mean of zero. For the WS test, n was 12 (SSD) and 24 (NH).

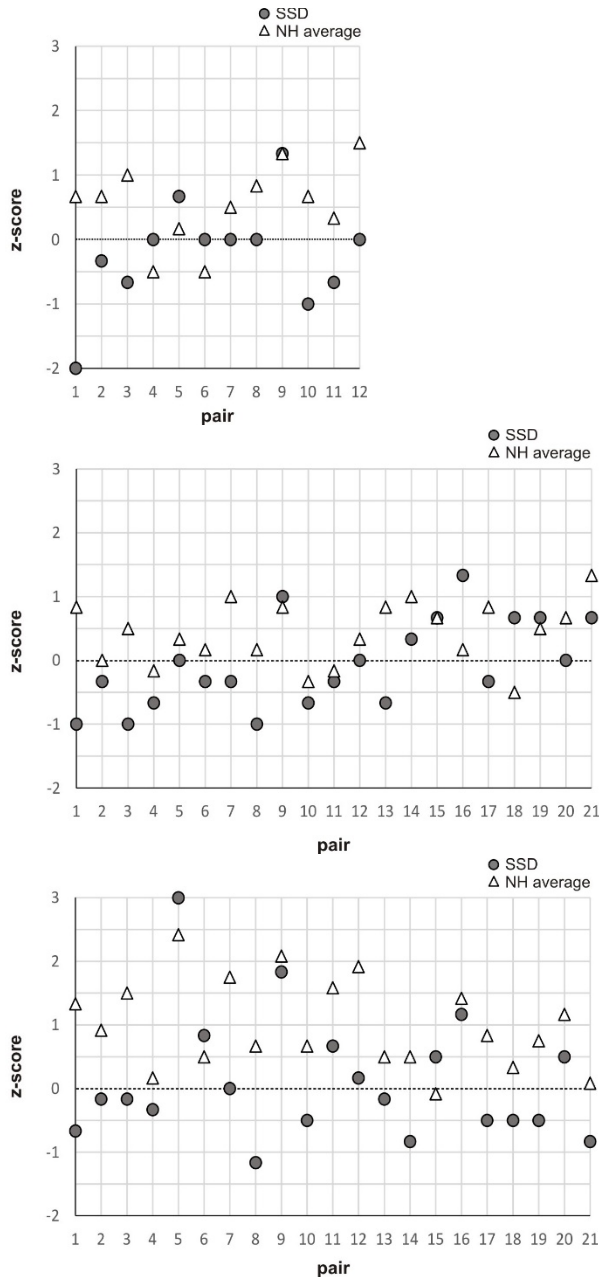


Figure 3.2. Individual data of the children with SSD (dark grey circles) and the control children with NH (light grey triangles) on the language tests of 2a) morphology (only children up to 9 years of age), 2b) syntax and 2c) vocabulary. The child with SSD and the average score of the two matched control children of this particular child are depicted on one vertical line. The dotted line represents the norm group mean of zero.

Questionnaire scores

Analysis of the group's average scores on the three subscales of the SSQ showed a significantly lower average score for the children with SSD in comparison to their NH peers on all three subscales (speech: Z=3.286, p=.001, r=0.42; spatial: Z=5.261, p<.001, r=0.67; qualities: Z=-3.123, p=.001, r=0.40), see figure 3.3. A detailed analysis of the speech subscale on item-level (see Galvin, 2013) for the items) showed that the children with SSD scored significantly lower than their peers on items of speech in noise, speech in speech contexts and on multiple speech stream processing and switching in a group conversation. Concerning the spatial subscale, scores were significantly lower on all items, concerning direction as well as distance and movement of sound. Item analysis of the subscale of other qualities showed significantly lower scores for the children with SSD on items of segregation of sounds and listening effort.

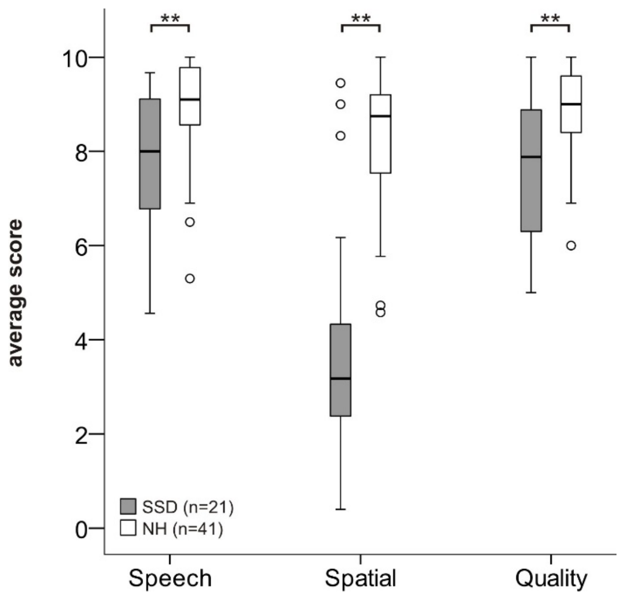


Figure 3.3. SSQ results of the children with SSD (in grey) and the NH control group (white). Y-axis: average score on the SSQ subscale, on a range of 0 to 10. Boxplots represent the distribution of the average scores on the subscales: the box represents the interquartile range, with a line at the median value. Whiskers extend to the highest and lowest values no greater than 1.5 times the interquartile range, outlying values are depicted with a circle. Asterisks mark a significant difference between the groups (** p<.01, *** p<.001)

Error analyses of language test performance

Sub skill analysis of the children's performance on the WS test showed a clear tendency for the children with SSD towards answering incorrectly in a larger percentage of the items on the past participle irregular form (Z=-2.472, p=.016, r=0.41) and on pronouns (Z=-2.374, p=.018, z=.40) in comparison to the NH group. The incorrect answers of the children with SSD were not significantly different in nature from those of the NH group. That is, the distribution of both groups' incorrect answers over the 9 possible error type categories was similar. Our data showed that a larger percentage of the SSD group's errors consisted of an answer that was of an incorrect lexical category, compared to the NH group, but this difference was not significant (Z=-1.963, p=.050, r=.33).

Concerning the FS test, sub skill analysis showed no significant differences in percentage incorrectly answered items between the SSD group and the NH group. The distribution mild versus severe errors was similar between the groups. Analysis of the distribution of the children's incorrect answers over the 10 possible mild and severe error type categories showed two effects of borderline significance. A larger percentage of the SSD children's errors contained sentences with 1 or 2 deviations in grammar or semantics compared to the NH peers (Z=-2.475, p=.013, r=0.31), whereas a larger percentage of the NH children's errors contained sentences that were only mildly informative (Z=-2.237, p=.025, r=0.28). For the other error categories, both groups showed similar error percentages.

Sub-skill analyses of the EOWPVT showed no significant differences in percentage incorrectly answered items between the SSD group and the NH group, though there was a trend towards the children with SSD exhibiting a larger percentage of incorrectly named verb items compared to the NH children (Z=-2.091, p=.036, r=0.26). Analysis of the type of errors showed that a significantly larger percentage of the SSD children's errors contained a more general term from the correct semantic field compared to the NH children (Z=-2.844, p=.004, r=0.36). Furthermore the data showed two trend effects. A larger percentage of the errors of the SSD group consisted of a word that sounded like the target word, compared to the NH peers (Z=-1.898, p=.059, r=0.24), whereas a larger percentage of the NH children's errors consisted of a description of the target word, compared to the children with SSD (Z=-2.231, p=.025, r=0.33).

3.4 Discussion

Key findings and comparisons with other studies

Our study demonstrates significantly lower performance on morphology, syntax and vocabulary for children with SSD compared to their NH peers, but similar performance for short term and working memory. Ead and colleagues (2013) did report differences for their more complex working memory task. In fact, results of recent brain research investigating the impact of SSD beyond low-level auditory processing confirm effects of SSD on working memory (Tibbetts et al., 2011).

Our detailed morphology sub skill analysis showed that the children with SSD experienced more difficulties with the correct use of the past participle irregular form and with pronouns than the NH controls (trend effects). Given that children who are hard of hearing clearly perform poorly on morphology (Tomblin et al., 2015) we would have expected to see more prominent differences between the children with SSD and NH controls on some other sub skills of this test too. Our syntax subskill analysis furthermore showed no significant differences in percentage incorrectly answered items between the two groups, on none of the subskills. We think there must still be, possibly subtle, effects since the z-scores of the children with SSD, that describe in one value the performance of the child on the whole test, were significantly lower than those of the NH control children. Lack of more significant effects on the syntax as well as the morphology test may be due to limited power of the limited sample size and the relatively small number of test items per child. Lastly, in the vocabulary test, children with SSD made more mistakes on the verb items than their NH controls (trend effect), whereas the percentage incorrectly answered items of both concrete and relational nouns was similar. It is known that verbs are more difficult and later learned than concrete nouns. Gentner (2006) explains that concrete nouns are more transparent, in that they refer to objects or beings that are naturally individuated out of the stream of perception. Verbs on the other hand refer to changes of state that are transient, and their boundaries are less clearly defined (Gentner, 2006). Relational nouns, the third type of word we tested, are also less transparent than concrete nouns, since like verbs they have meanings that are centered on relations with other concepts (Gentner & Kurtz, 2005). Although not significant in the sub skill analysis, the significant difference in z-scores of the SSD and NH group on the test seems indicative of vocabulary difficulties on nouns too, as they comprise the majority of test items.

Error type analysis first showed that, when formulating sentences, children with SSD more often than NH peers formulated sentences with one or two errors in grammar/semantics whereas NH children significantly more often than children with SSD formulated sentences that were only mildly informative but not wrong (borderline significant effects). In the vocabulary test, children with SSD significantly more often than NH children answered with a word that was too general. Generalizing is a strategy that is common in language development, certainly amongst younger children (Zink & Smessaert, 2012). Besides that, children with SSD also answered with a word that sounded like the target word more often than the NH children (trend effect). On the one hand, it could be that in these instances, the target word has been incorrectly stored in memory because of suboptimal perception of part of the phonemes, but the stored word form could be correctly retrieved from memory. On the other hand, these mistakes could be due to problems with retrieving the correctly stored target word, leading the child to fill out the blanks in a creative manner and then getting it almost right. NH children, more often than children with SSD, gave a description of the target word instead of replying with the requested single word, not risking it to give a wrong answer. It seems therefore that children with SSD have learned to take on more strategies to still answer with a single word than their NH peers. Type of errors in the morphology test were similar for the two groups.

In the current study the children with SSD gave significantly lower ratings than the NH controls on all three sub scales of the SSQ questionnaire, as was the case in the recent study of Reeder, Cadieux & Firszt (2015) with children of 6 to 17 years. Data of our children with SSD were indicative of more difficulties than NH children in spatial hearing, segregating sounds, understanding speech in speech contexts or other noise and with following a group conversation. Furthermore their ratings pointed to higher listening effort than was the case for the NH controls.

Conclusions and impact of the findings

Our results indicate that children with SSD do not perform at the same level as their NH peers on tests of language and report on difficulties in a number of auditory skills. Due to their impaired binaural hearing children with SSD are more prone than NH children to miss out on fine details in linguistic input or miss out on things that are said to them or in their presence in total, which can affect their language development. In our language tests of morphology, syntax and vocabulary, we indeed found lower performance for the children with SSD compared to a matched NH peer control group. Subskill and error analyses showed that in comparison to the

NH controls mostly the correct use of the past participle and pronouns appeared more difficult, formulating sentences more often went wrong by making mistakes in grammar and semantics, and more often pictures were named with a word that is too general or that only sounds like the target word.

The majority of the children with SSD performed above the -1 standard deviation limit of normal performance on the language tests. Indeed, we expected potential differences between the two groups to be rather subtle, as the children with SSD do have acoustical input on one side. The aim of our study was to investigate whether loss of sensory input on only one side affects language development of the children with SSD as tested with standardized behavioral tests. Our results indicate that at a group level, it does (medium effect sizes between 0.32 and 0.44). Socioeconomic factors such as maternal education level have been reported to be predictors of language and IQ scores and school problems in children with UHL / SSD (Fischer & Lieu, 2014; Lieu et al., 2010). Our study does not yield a significant association between maternal education level and group (SSD or NH), presumably because the group of participating children was rather homogeneous with regard to level of maternal education. We believe that the differences between the groups on the outcome measures, that were found in spite of high maternal education levels, are true effects of the difference in hearing between the two groups and the consequential differences in certain higher order brain functions (Schmithorst et al., 2014; Tibbetts et al., 2011), beyond the effects of maternal education level.

Visual inspection of the individual data points demonstrates variation in development for both the SSD and the NH groups. In three “pairs” the child with SSD even performs better than its NH controls on one or two of the tests. It is important to follow up the children longitudinally to investigate the robustness of the effects in course of time. There are a few studies that have tested the same children with SSD / UHL more than once. These longitudinal data of Lieu et al. (2012) and Fischer & Lieu (2014) show that, at least part of, the difficulties the children face do not dissolve over time. Furthermore, the number of children needing individualized education plans remained high over time, and parents and teachers still reported problems in school performance and behavior (Lieu et al., 2012).

In addition to the abovementioned, persons with SSD experience other difficulties in daily life, such as the listening effort it takes to e.g. follow a group conversation and/or other activities in social and work life. In our SSQ results, scores of three of the oldest children were indicative of no problems in daily life (fig. 3.3 outliers in the spatial scale). In a localization task, however, these children did demonstrate clear difficulties (not shown here). In conversation after the test, the children and their parents mentioned that the children know how to handle difficult situations in daily life, although listening remains challenging in situations that they cannot control well. Similar results have been reported in a questionnaire and interview study by Borton, Mauze and Lieu (2010), in which parents of older children with SSD were still concerned about their children misunderstanding conversations and having difficulties in school, sports and social interactions, even though the children had learned to cope with difficulties throughout the years.

We argue for early intervention for children with SSD to prevent language and educational delays and difficulties and limit auditory challenges in daily life. Research has started to investigate the use of a cochlear implant (CI) on the deaf side in these children, as it offers the potential to restore binaural hearing, whereas other rehabilitative options such as the CROS and the BAHA do not. Recent studies of Távora-Vieira & Rajan (2015, 2016) and Arndt & Prosse et al. (2015) showed binaural benefits for children with post lingual onset SSD and for two very young children with congenital SSD, but not for children with congenital SSD implanted after age four. Likely, there is a critical period for binaural auditory development.

More research is needed to investigate whether differences in the auditory, language and cognitive development of children with SSD and children with NH are large enough to justify cochlear implantation in children with SSD and if yes, what age of implantation would be optimal and what would the long term effects on the development of these children be?

Part 2

SSD and cochlear implantation

4 Background: early intervention via cochlear implantation

Results of our first study (chapter 3) corroborate the recent literature in suggesting that one good hearing ear likely is not sufficient for hearing in everyday life situations and for normal language development. Hence, there is a need for intervention to optimize auditory exposure. In this chapter, we discuss the window of opportunity for intervention in SSD (congenital). Next we introduce the method of intervention we chose to investigate, the cochlear implant (CI). A CI is the only rehabilitative option that offers the potential to partially restore binaural hearing in individuals with SSD. Lastly, we give an overview of the literature on early cochlear implantation in children with SSD.

4.1 The window of opportunity for intervention

Brain plasticity, the ability to develop neural connections with repeated stimulation, is greatest early in life (Sharma & Nash, 2009). The shaping of cortical circuits in this period is attuned by experience, so the juvenile brain adapts rapidly to the environment and is highly sensitive to loss of sensory input (Flexer, 2011; Kral et al., 2016). Hearing impairment during early development increases synaptic elimination, impeding the shaping of cortical circuits, which causes cortical reorganizations that ultimately affect not only primary auditory but also higher cortical functions (Kral et al., 2016), see section 1.2. Treatment should be provided within this early sensitive period to prevent further cortical reorganization and possibly restore cortical organization. Late intervention is only helpful if the hearing loss had a late onset and the auditory system matured in the period of NH before onset of the hearing loss. For children with SSD, intervention thus should be provided early in life (Kral & Sharma, 2012).

Support for early intervention in SSD can also be found in research addressing unilateral cochlear implantation in children with bilateral deafness, leading to a unilateral hearing situation. Gordon et al., (2013) showed that within a period of only ~1.5 years of unilateral hearing, reorganization occurred (i.e. abnormal strengthening of auditory pathways from the stimulated ear), which was not reversed by implanting the second ear (Gordon et al., 2013). In contrast, children with bilateral CIs with short (or no) implant delay showed normal contralateral dominance (Gordon et al., 2013). For children with bilateral deafness it is also widely acknowledged that early implantation yields the best outcomes regarding speech-language development and spatial hearing, that children with two CIs outperform those with only one CI and that duration of inter-implant delay is negatively associated with outcomes (Boons et al., 2012a,b; Litovsky & Gordon, 2016; Sparreboom et al., 2015; Van Deun et al., 2010).

4.2 Cochlear implantation

A number of intervention options are available for children with UHL, but not all are suitable for children with SSD and not all restore bilateral auditory input to the brain. For example, conventional hearing aids (HA) amplify the acoustic signal, which then passes through the outer and middle ear to the cochlea, where hair cells transform sound vibrations into action potentials that travel up the auditory nerve. HA are a good option for children with UHL who have residual hearing, but in children with SSD, too many hair cells are damaged and therefore sound will not be converted to electrical signals. Contralateral routing of signal (CROS) HAs have a microphone on the impaired ear which delivers signal to a receiver in the NH ear. This can benefit the wearer when sound signals originate from the side of the impaired ear. However, it is detrimental when noise is picked up by the device, in which case the SNR will be reduced (McKay et al., 2008). Children might not be aware of this and not capable of manipulating their location or environment to improve outcomes (Winiger, Alexander, & Diefendorf, 2016).

A bone conduction device (BCD) is an intervention option that, like the CROS HA, transfers sound from the impaired side to the good side. The BCD does this (transcutaneously or percutaneously) via bone conduction to the cochlea. This method bypasses the outer and middle ear and stimulates the cochlea and is therefore used in individuals with conductive and mixed (rather than sensorineural) hearing loss (Krishnan & Van Hyfte, 2016). A BCD can, however, also be used in SSD because the bone vibrations on the side of the impaired ear reach not only the cochlea on the impaired side, but also the cochlea on the good hearing side.

Both the CROS HA and BCD can overcome the HSE but, because sound is delivered to the hearing ear's cochlea, bilateral hearing is not achieved. Consequently, binaural hearing cannot be restored with these devices. Generally, BCDs and CROS HAs do not improve localization and speech in noise for patients with sensorineural SSD (for a review, see Peters et al., 2015).

A cochlear implant is the only rehabilitative option that offers the potential to facilitate binaural hearing, because it enables sound transmission via direct electrical stimulation of the auditory nerve, bypassing the hair cells in the cochlea, on the *impaired side*. Cochlear implantation has been standard of care for bilaterally deaf children and adults, but this intervention is not reimbursed for children or adults with SSD in Belgium and most other countries. To our knowledge, only in Germany reimbursement by health insurance companies is becoming more common (Beck et al., 2017).

4.2.1 Technology and candidacy

A CI consists of external and internal parts, see figure 4.1. The external part consists of a microphone that picks up sounds from the environment and sends them to the speech processor. The speech processor translates the acoustic signals into an electrical signal which is sent to the transmitter coil through a cable, although recently also off-the-ear sound processors came available in which the processor and the transmitting coil are combined into a single unit worn on the head over the implant site (Mauger et al., 2017). The transmitter sends the signal through a frequency modulated carrier wave to the surgically implanted internal receiver coil. The transmitter coil and internal receiver coil are connected through a transcutaneous wireless connection positioned by small magnets in both coils. The internal part of the CI furthermore consists of a receiver-stimulator, an electrode array (of up to 22 electrodes) placed inside the cochlea's scala tympani, and 2 ground electrodes placed outside the cochlea. The receiver-stimulator decodes the signal and controls the current on each of the electrodes in the electrode array. The electrodes stimulate the auditory nerve fibers, sending signals to the brain (Nikolopoulos & Vlastarakos, 2010). The electrode design, but even more frequently the external sound processors, are refined, improving listening performance e.g. by new directional microphone options, digital noise reduction, automatic scene analysis and connectivity to external devices (Todorov & Galvin, 2018; Warren et al., 2019).

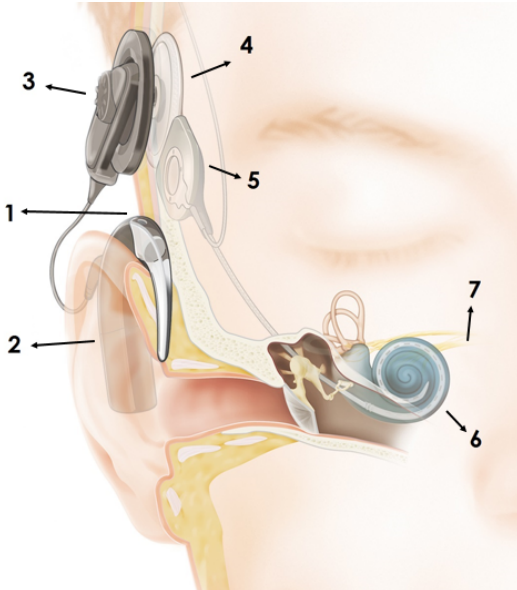


Figure 4.1. Schematic presentation of a cochlear implant. 1: microphone, 2: sound processor, 3: transmitter coil, 4: receiver coil, 5: receiver-stimulator, 6: electrode array, 7: cochlear nerve. Modified from an image courtesy of Cochlear.

Depending on their etiology, children with SSD can qualify for a CI. An intact cochlear nerve is of paramount importance for cochlear implantation because the CI works by direct stimulation of the auditory nerve, bypassing the damaged hair cells in the cochlea. Generally, children with SSD due to CND are therefore not considered to be candidates for implantation. Children with cCMV do qualify for implantation, so this intervention should be considered. Children with congenital IEM are candidates for CI as well, but the implantation may be technically challenging. For children with SSD due to meningitis, there is no contraindication to provide a CI, given good performance outcomes in bilaterally deaf children with this etiology (Boons et al., 2012) but in some cases there is ossification of the cochlea which may require a specially designed double array implant and an adapted surgical procedure (Lenarz et al., 2001).

Based on their etiological work-up for children with SSD in Antwerp and Leuven (Flanders) and the incidence of SSD in Flanders (see section 1.1), van Wieringen et al. (2019) estimate that about 5 to 10 newborns with SSD qualify for a CI each year in Flanders.

4.2.2 Performance of children with SSD and a CI

Since 2012, benefits of cochlear implantation have been reported for children with acquired profound UHL (i.a. Arndt et al., 2015; Hassepass et al., 2012; Plontke et al., 2013; Rahne and Plontke, 2016; Távora-Vieira and Rajan, 2015). These children had acoustic bilateral input before onset of their hearing loss, and thus have normally developed auditory pathways and had binaural hearing experience. For children with SSD (congenital) results are mixed, likely dependent on the age of implantation. As explained above, timing of treatment for children with SSD is essential. It is advised that treatment is provided within the early sensitive period to prevent further preference for the stronger ear and to possibly restore cortical organization.

In the literature so far, children with SSD (congenital) have been implanted as young as 12 months of age (Polonenko et al, 2017), up to 13;10 years of age (Beck et al., 2017). As of yet, the optimal timeframe for implantation is unclear. In bilaterally deaf children, implantation of the first CI before age 2 and an inter implant delay (unilaterally deaf period) of maximum 1.5 years is regarded optimal (Boons et al., 2012a; Boons et al., 2012b; Gordon et al., 2013; Litovsky & Gordon, 2016; Sparreboom et al., 2015; Van Deun et al., 2010), see section 4.1. Based on this knowledge we consider the age of 1,5 to 2 years to be the maximum age at implantation for optimal results after CI in children with SSD. Other research groups extend this hypothetical boundary to 4 years of age (Beck et al., 2017) or even into (early) adolescence (Manrique et al., 2019; Thomas et al., 2017). There is no solid data at this moment to provide evidence for an optimal time window. The results in the current literature on CI in SSD do show that children implanted at an older age did not or only marginally improve with regard to localization and speech understanding in noise (Arndt et al., 2015; Rahne & Plontke, 2016; Távora-Vieira & Rajan, 2015). In contrast, in early implanted children, first results of sound lateralization and (speech) discrimination ability with CI alone or with NH ear masked, as well as subjectively experienced benefit, are promising (for a review, see Peters et al., 2015a). In the following, we will discuss in more detail the results of these children implanted at a young age.

Arndt et al. (2015) and Távora-Vieira and Rajan, (2015) were the first to both include a very young child with congenital SSD (implanted at 21 and 17 months resp.) into their study. Although they were too young for formal testing, the authors reported that the children did exhibit clinical evidence of binaural integration through behavioral responses to sounds and willingness to wear the CI all the time. Távora-

Vieira and Rajan (2016) later reported 36 month follow up data; the child had a maximum score on a free field speech perception test with the normal hearing ear masked with speech noise and could correctly lateralize sounds presented at -90 and 90 degrees. Spatial acquity could not yet be tested.

Beck et al. (2017) reported on ten children with cSSD and a CI. The children implanted at a younger age (between 1;9 and 3;2 years) showed measureable speech discrimination benefits in a free field task with masking or plugging of the NH ear, whereas the older children (implanted between 4 and 13;10 years of age), among which were two children that tended towards non-use, had lower discrimination scores. One child could not be tested due to developmental issues. CAP-scores (categories of auditory performance) based on extensive reports of the children's speech and language therapist, were used to describe the discrimination ability of the implanted ear alone, of eight of the children (two did not show enough language development to allow reliable classification). All but one showed a relatively high level of auditory discrimination: understanding common phrases without lip-reading. In addition, (retrospective) pre-op to post-op SSQ results, as well as anecdotal information, show the benefit of CI in children with SSD.

A recent study by Thomas et al. (2017) shows moderate but significant audiological and subjective benefits in 14 children with congenital SSD implanted between the ages of 3;6 and 11 years. Speech understanding in noise 12 months post implantation was significantly better with CI than without, with most improvement in the head shadow effect (2.11 dB). Squelch (0.95 dB) and summation (0.98 dB) effects were also significant but may not be audiologically relevant, as the authors regard an improvement of 1.5 dB SNR, or more, to be (Thomas et al., 2017). At individual level, improvement ≥ 1.5 dB SNR was observed in 7 children (50%) in the HSE set-up, in 5 (36%) in the squelch set-up and in 3 (21%) in the summation set-up. Signals from the deaf side and from the NH side could be correctly localized in a greater percent of the trials after compared to before implantation, but this was not the case for signals from the front (0°). More precise localization error was not measured. Parent satisfaction with the CI was high, and 84% would decide in favor of the CI again. SSQ scores, completed by the parents, were significantly higher postoperatively compared to preoperatively for all three subscales of speech, spatial and qualities of hearing. However, four children were limited users or nonusers. The authors report no significant differences in any of the abovementioned outcomes between the 7 children implanted under the age of 6 yrs and the 7 older children and thus argue for a prolonged sensitive period of binaural hearing development (beyond ~1.5 years;

Gordon et al., 2015). However, 7 more children were implanted before age 2 but could not be formally tested yet. Possibly, their outcomes will be best.

Interestingly, Polonenko and colleagues (2017) recently reported restoration of bilateral auditory input with normal contralateral cortex activation in five early implanted children with SSD, after only six months of CI use. They investigated cortical evoked activity to trains of acoustic clicks (NH ear) and electric biphasic pulses (to the CI). Peak amplitude activity changed from an atypical distribution from the implanted ear after a few days of implant use (indicated by abnormal lateralization of activity to the ipsilateral left auditory cortex and recruitment of extra-temporal areas) to expected contralateral lateralization from each ear and reduction in extra-temporal activity after only six months of implant use. The early implantation in these children thus rapidly restored bilateral auditory input to the cortex, which is a promising precursor for the (partial) restoring of binaural hearing.

4.3 Research Objective

A second objective of the current PhD project was to contribute to the knowledge about the effectiveness of cochlear implantation in very young children with SSD. We have therefore set up a very innovative project, entitled 'Cochlear Implantation for Children And one Deaf Ear', abbreviated 'CICADE'. The aim of this multicenter collaboration (Leuven, Antwerp, and Ghent) is to investigate the development of language, cognition, and binaural hearing longitudinally in a group of 16 young children with one profound, sensorineural, congenital deaf ear who receive a CI (Cochlear Ltd). Children are followed up twice a year with regard to hearing, cognition and language, during their first 4 to 5 years with a CI, and possibly beyond. Performance is compared to age-matched children with SSD who do not receive a CI (either because they do not qualify or because their parents do not want it), and age-matched NH peers.

Whereas previous studies only describe auditory outcomes and subjective benefit (see 4.2.2), we also assess the benefit of a CI with regard to the development of language and cognition. This is very important given the reported significant differences to NH peers in these domains (see 2.2 and chapter 3). Furthermore, we only included very young children. As the first years of life are the most sensitive period for brain plasticity, treatment should be provided within this early critical period to prevent the cortical reorganization which would otherwise lead to biased input to higher-order auditory and non-auditory cognitive areas (see 1.2). Third, the study is novel because performance of the implanted children is compared to that of two control groups of age-matched children with SSD but no CI or with bilateral normal hearing.

We hypothesize that provision of the CI at a very young age will partially restore binaural processing in the following years and hence yield the best conditions for the development of near-normal spatial hearing and speech understanding skills, cognition, language and learning in general.

Over the course of the current PhD project, 14 children with SSD have been implanted (group SSD_CI). In addition, 14 children with SSD without a CI were included (group SSD_noCI), as well as a group of 23 NH control children (group NH). Characteristics of the children with SSD are presented in table 2. Their auditory brainstem thresholds (air conduction) were ≥ 80 dBnHL on the affected side and ≤ 35 dBnHL on the contralateral side. For some children, auditory brainstem thresholds were not determined for the good hearing side at inclusion in the study. Pure tone audiometry confirmed NH on the good side in these children ($PTA_{0.5,\ 1,\ 2\ kHz}$ ≤ 35 dB HL). In both SSD groups, some of the children receive(d) auditory or linguistic rehabilitation or early home based guidance. None of the SSD_noCI children wears a hearing assistive device.

Care was taken to develop a protocol that consists of standardized behavioral tests and parent questionnaires and is tailored to the specific age of the child, see figure 4.2.

Study 2 *(chapter 5)* of this dissertation focused on the outcome measures for the assessment of receptive and expressive communication in infants under the age of 2. In the first two years of life, assessment is rather challenging because language is still limited. We aimed to investigate whether three different types of outcomes together would provide a good description of a child's communicative development. Specifically, we investigated whether the outcomes as measured by the three different methods related to each other. The methods measure different aspects of communicative development (i.e. comprehension, quantity and quality of production and quantity of language input and interaction), but we still expected relationships between them as a result of well-known links between the constructs that they pose to measure. Second, we investigated whether the outcomes related to those of the same children after the age of 2 with other, age-appropriate linguistic test materials. Finally, we investigated whether they reflected differences in performance between NH children and children with SSD, with and without a CI. We hypothesized that at the young age of these participants (7 months to 2 years), linguistic deficiencies of children with SSD are subtle because children do not yet produce much language. We therefore did not expect the three methods to differentiate at this young age. Data of the 27 children who were included in the CICADE study before the age of 2 years was analyzed.

In **study 3** *(chapter 6)* we present data of the first 6 implanted children who at the moment of writing, close to the end of the PhD project, were 2 years of age or older. Children were asked to 1) identify and carry out tasks with objects and match pictures to auditory presented sentences (language comprehension), 2) name pictures (expressive vocabulary) and 3) imitate or finish sentences with increasing grammatical difficulty during structured play (morphosyntactic skills). In addition, cognitive information processing was assessed and parents were asked to complete a questionnaire regarding hearing abilities in daily life. Their outcomes were compared to those of 12 children of the SSD_noCI group and 19 of the NH peers.

In general, we expect that improvements with CI will be much more subtle for our participants with SSD than for bilaterally deaf children. Moreover, while our children were implanted at a very young age due to the narrow window of opportunity, potential benefits may only become prevalent after some time.

Specifically regarding linguistic skills, we expect deviation from normal (for the SSD_noCI group) and benefit of CI (for the SSD_CI group) to be limited in the first years of life because complex spoken language is still limited. We expect morphological skills (inflection, derivation and compounding of words) to be impeded most by unaided SSD and in that sense aided most by cochlear implantation, because these skills depend heavily on perception of subtle sounds in the speech stream. Morphological difficulties have been shown before in a number of studies with children with mild-to-moderate bilateral hearing impairment (Koehlinger et al., 2013, 2015; McGuckian & Henry, 2007; Tomblin et al., 2015) *and* also in our study with school-aged children (5-9 years) with unaided cSSD (chapter 3). We hypothesize that differences in the CICADE study may emerge around the age of 4 to 5 when typically most children have mastered rules regarding regular inflection of words and are in the process of learning the correct inflection of irregular words.

In Flanders, typically all children start to go to school at age 2;6. They will likely then find themselves in noisy environments more often than before and hearing difficulties due to SSD might become more prominent. We therefore expect that parent-questionnaire outcomes of hearing abilities in daily life will differ between the NH group and the SSD groups. The children with a CI may experience less difficulties than children with SSD without CI. But, the questionnaire used is not specifically focused on binaural hearing, so it might not be sensitive enough to measure subtle differences in this regard.

Lastly, we expect cognitive milestones to be similar for the three groups at this age phase. Complex executive functions such as sequential processing, sequence learning and concept formation are thought to be at risk in children with SSD. At the current age, such skills are typically not well developed yet. Effects are therefore not expected until later in childhood.

Participant	Time of diagnosis	Gen-der	Age † (yr.mo(;d))	Side of HL	Etiology	ABR threshold, (dB nHL) affected ear ‡	Centre
SSD_CI_1	10 months	m	02.02;21	Left	Fracture of left petrous bone	>90	UZL
SSD_CI_2	NHS	m	00.08;21	Left	cCMV	>80	UZL
SSD_CI_3 ¶	NHS	m	01.09;18	Right	cCMV	95	UZA
SSD_CI_4	NHS	f	01.00;26	Left	cCMV	>80	UZL
SSD_CI_5	NHS	m	01.02;24	Right	IEM (incomplete partition type II)	>80	UZL
SSD_CI_6	NHS	f	01.02;15	Right	cCMV	>80	UZL
SSD_CI_7	NHS	f	00.11;12	Right	cCMV	90	UZL
SSD_CI_8	NHS	m	01.02;22	Left	cCMV	100	EIORLA
SSD_CI_9	Perinatal	f	00.10;09	Left	cCMV	>90	UZG
SSD_CI_10	NHS	f	01.00;13	Left	cCMV	>100	EIORLA
SSD_CI_11	NHS	m	01.00;04	Left	unclear	>100	EIORLA
SSD_CI_12	NHS	m	00.10;10	Right	unclear	>100	EIORLA
SSD_CI_13	NHS	m	01.02;27	Right	cCMV	80	UZL
SSD_CI_14	Perinatal	f	00.10;07	Left	cCMV	>95	UZA
SSD_noCI_1	NHS	f	01;03	Left	CND	>85	UZL
SSD_noCI_2	NHS	f	01;02	Right	cCMV	>100	UZL
SSD_noCI_3	NHS	f	03;00	Right	unclear	>80	UZL
SSD_noCI_4	NHS	m	01;06	Right	cCMV	>70	UZL
SSD_noCI_5	NHS	m	02;11	Left	CND	>85	UZL
SSD_noCI_6 ¶	NHS	f	03;01	Left	CND	>90	UZA
SSD_noCI_7 ¶	Perinatal	m	01;11	Left	CND	>95	UZA
SSD_noCI_8	NHS	f	02;02	Right	CND	>90	UZA
SSD_noCI_9	NHS	m	02;06	Left	CND	>90	UZA
SSD_noCI_11	NHS	m	02;00	Right	cCMV	>90	UZG
SSD_noCI_12	NHS	m	01;06	Left	CND	>85	UZL
SSD_noCI_13	NHS	m	02;00	Left	unclear	>90	UZG
SSD_noCI_14	NHS	f	00;09	Right	cCMV	>90	UZA
SSD_noCI_15	NHS	m	00;10	Left	CND	>95	UZA

Table 4.2. Participant characteristics.
Note. † Age at implantation (SSD_CI) / Age at inclusion (SSD_noCI) (yr.mo(;d)). ‡ The > sign indicates no response at the highest level tested. SSD_noCI_4 was not tested beyond 70 dBnHL but additional pure tone audiometry showed no responses at 90 dB HL (250-500-1000-2000 Hz). ¶ SSD_CI_3 was diagnosed with cognitive and motoric comborbidities due to cCMV; SSD_noCI_6 has a pinna deformity on the good side; SSD_noCI_7 was diagnosed with OAV syndrome and hemifacial microsomia.

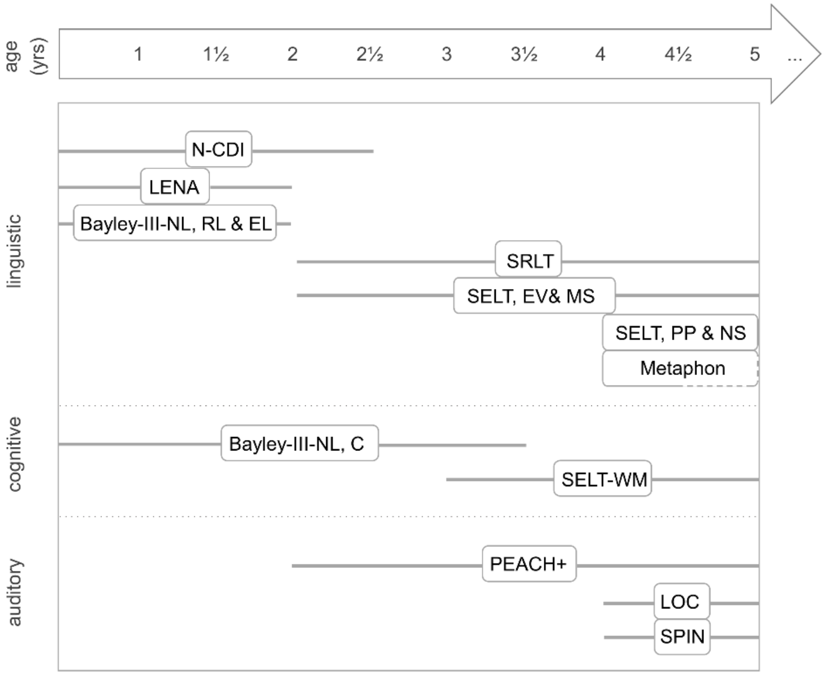


Figure 4.2. Time-line of the protocol for the CICADE study assessing linguistic (upper part), cognitive (middle part) and auditory skills (lower part).
Abbreviations: N-CDI: Dutch Version of the MacArthur-Bates Communicative Development Inventory (Fenson et al., 1993; Zink & Lejaegere, 2002); LENA: Language Environment Analysis system, LENA Foundation, Boulder CO; Bayley-III-NL: Bayley Scales of Infant and Toddler Development (Baar, Steenis, Verhoeven, & Hessen, 2014; Bayley, 2006), subtests receptive language (RL), expressive language (EL) and cognition (C); SRLT: Schlichting Receptive Language Test (Schlichting & Spelberg, 2010a); SELT: Schlichting Expressive Language Test-II (Schlichting & Spelberg, 2010b) with subtests EV (expressive vocabulary), MS (morpho-syntactic knowledge), PP (phonological processing of words and non-words), NS (narrative skills) and WM (phonological working memory capacity); Metaphon: phonological simplifying processes (Dean, Howell, Hill, & Waters, 2002); PEACH+: Parents' evaluation of aural/oral performance of children (Ching & Hill, 2007); LOC: sound source localization test (Van Deun et al., 2009); SPIN: speech in noise understanding by means of the limited-set Leuven Intelligibility Number Test (LittleLINT (Van Deun, van Wieringen, et al., 2010), a subset of the LINT (van Wieringen & Wouters, 2008)).

5 Outcome measures of communicative skills and language environment under age 2

The content of this chapter is under review for publication in *Journal of Child Language* as: Sangen, A., Boudewyns, A., Van Hoecke, H., Offeciers, E., Wouters, J., Desloovere, C., van Wieringen, A. (2019). Relationship between outcome measures of communicative skills and language environment in infants under age 2.

Abstract

Purpose: The purpose of the current study was to investigate whether outcome measures for early communicative behavior (< 2 years) relate to each other, and to what extent they are predictive of later linguistic outcomes (between 2 - 3 years).
Methods: Communicative/linguistic skills were assessed twice a year in 27 children: 19 with congenital single sided deafness, of whom 13 received a cochlear implant, and 8 with normal hearing. Under two years of age, performance was measured using 1) the Bayley-III-NL test to assess language comprehension and production, 2) the N-CDI parent-questionnaire to document receptive and expressive vocabulary and 3) the LENA system to estimate the quantity of child vocalizations, adult words and conversational turns during an audio recorded day. From 2 years onwards, the Schlichting receptive and expressive language tests were conducted.
Results: Positive relationships were observed between the Bayley-III-NL behavioral test and N-CDI questionnaire outcomes under the age of 2. The amount of child vocalization and engagement in interaction as measured by the LENA system corresponded to (part of) the Bayley-III-NL and N-CDI scores. Furthermore, Bayley-III-NL scores and LENA language environment factors – but not N-CDI scores – were significantly related to later Schlichting language outcomes.
Conclusions: The Bayley-III-NL, N-CDI and LENA system are relevant outcome measures for very young children and are complementary to each other. Bayley-III-NL and part of the LENA scores seem predictive of later Schlichting outcomes, which supports construct validity of the Bayley-III-NL language tests and corroborates the importance of both language input and interaction with the child for its linguistic development.

5.1 Introduction

Assessment of communicative behavior in very young children has become more prevalent, for example in children with hearing loss. Due to early detection of congenital hearing loss through the general neonatal hearing screening, hearing intervention (e.g. hearing aid or cochlear implant) can be provided at a very young age. The assessment following this early intervention, however, brings along several challenges. The minimal age for standardized receptive and expressive language testing is two years. Between 0 and 2 years of age, behavioral testing materials often contain only a limited number of items, and consequently a few incorrect or absent answers can significantly affect the final score. Furthermore, assessment itself is tedious due to the limited attention span of a young child, which is influenced by motivation, energy, wellbeing, shyness, etc. Most importantly, spoken language is limited at this age. Communicative skills of children under 2 are marked by preverbal behavior and 1- and 2-word sentences. Children generally do not conjugate words yet and their vocabulary is still relatively limited (Zink & Smessaert, 2012).

A limited number of outcome measures exists for assessing performance of children under 2 years of age. In general, we differentiate between behavioral tests, surveys, and objective measures. Standardized behavioral testing materials such as, for instance, the Mullen Scales of Early Learning (Mullen, 1995), Test of Early Communication and Emerging Language (Huer & Miller, 2011), Bayley Scales of Infant and Toddler Development (Bayley, 2006), the Preschool Language Scale (I. L. Zimmerman, Steiner, & Pond, 2011) and the Receptive-Expressive Emergent Language Test (Bzoch, League, & Brown, 2003) provide important data, but these are dependent on the cooperation of the child. Questionnaires (e.g. MacArthur Bates Communicative Development Inventory, Fenson et al., 1993; The LittlEARS® Early Speech Production Questionnaire, Wachtlin et al., 2017; and the Production of Infants Scale Evaluation, Kishon-Rabin et al., 2004) are also standardized and informative, but the data could be biased, as questionnaires are filled out by the child's caregiver's. Lastly, it is also possible to observe and transcribe natural communicative behavior (e.g. Tait analysis; Tait et al., 2007), which is very time consuming, and/or document behavior with, for example, the automated Language ENvironment Analysis System (LENA Foundation, Boulder, CO). While the different outcome measures are valuable, performance scores are very variable at a young age and, as a result, difficult to interpret. Given the limited testing time in young children it is important to know which performance scores are most relevant and can potentially indicate differences in communicative behavior. The focus of the current paper is to investigate whether different types of outcome are complementary, i.e. can be used together to provide a good description of a child's communicative development.

In an ongoing study we are assessing the linguistic, cognitive and auditory performance of infants, twice per year. The present paper focuses on the linguistic data of the participants aged 7 to 23 months. For children of this age, we chose to administer a) a behavioral test and b) a parent-questionnaire to both document receptive and expressive communicative skills, and c) a measure documenting spontaneous behavior (quantity of child vocalizations, adult words in the vicinity of the child and conversational turns during a normal day). The main aim of the current study is to investigate whether the outcomes as measured by these three different methods relate to each other. Even though the methods measure different aspects of communicative development, we expect relationships between the measures as a result of well-known links between the constructs that they aim to measure. For example, language input (amount, diversity, richness) has been reported to be positively associated with linguistic outcomes (Hoff & Naigles, 2002; Hurtado et al., 2008; Huttenlocher et al., 1991, 2010). Moreover, interaction is thought to provide the best opportunities for a child to take in linguistic input because of the joint attention between child and adult and because linguistic input in interaction is child-directed rather than overheard. Furthermore, in interaction with an adult, children practice their expressive linguistic skills and receive feedback about their language use (Ambrose, Vandam, & Moeller, 2014; Kuhl, 2010; VanDam, Ambrose, & Moeller, 2012; Weisleder & Fernald, 2013; Zimmerman et al., 2009). Given the abovementioned, we expect to find positive associations between linguistic input and amount of conversational turns in daily life, and the performance scores on behavioral test and parent questionnaire in the present study. Possibly, positive relations exist between the quantity of child vocalizations in daily life and the quality of expressive communication skills assuming that more vocalizing gives more opportunity for the development of expressive skills. Furthermore, we expect positive relations between the behavioral test scores and the questionnaire results, because they assess similar linguistic skills (predominantly focusing on the vocabulary of the child).

A second aim is to investigate whether the outcomes of the three methods for children under 2 years of age relate to those of the same children after the age of 2 (with the Schlichting tests; language comprehension, expressive vocabulary and morphosyntactic knowledge) (Schlichting & Spelberg, 2010a, 2010b). It is possible to investigate this for a subset of the participants of the present study who are currently

2 years of age or older. We hypothesize that there will be positive relationships between the test-and questionnaire outcomes regarding receptive communication as measured before the age of 2 and receptive language test scores after the age of 2; and the same for the expressive counterparts. Furthermore, we expect the amount of linguistic input received in daily life before the age of two to be positively related to receptive outcomes after the age of two. We hypothesize child vocalization quantity before the age of 2 to be positively related to language production skills (expressive vocabulary and morphosyntax) after the age of 2. And, we expect amount of interaction to be positively related to both receptive and expressive skills.

The participating children in the current study either have bilateral normal hearing or are diagnosed with a congenital severe to profound sensorineural unilateral hearing loss, also termed single sided deafness (SSD). Children with one deaf ear suffer from limited spatial hearing. In addition, at a group level, school-aged children with SSD (~5-17 years of age) have been reported to lag behind in spoken language (Anne, Lieu, & Cohen, 2017; van Wieringen et al., 2019), especially with regard to complex language skills (Sangen et al., 2017). To date, only a few studies have assessed the communicative skills of very young children with SSD and less severe unilateral hearing loss (UHL) in comparison to NH peers. Using parent questionnaires, Kishon-Rabin et al. (2015) reported that delays in auditory behavior and preverbal vocalizations were approximately four and nine times more common in 34 infants with UHL compared with 331 NH peers. Based on demographic information from parental interviews, Lieu et al. (2013) and Kiese-Himmel (2002) showed that the first occurrence of use of two-word phrases, but not first single word use, was significantly delayed in their participants with UHL (resp. 109 and 20 children) compared to NH peers/NH norms. Some other studies show mixed results, possibly because of the limited speech production at this age or possibly because the outcome measures were not sensitive enough (Fitzpatrick et al., 2015; Lieu et al., 2010).

In our ongoing longitudinal study, part of the children with SSD have received (or will receive) a cochlear implant (CI). A CI offers the potential to (partially) restore binaural hearing as it captures sound on the impaired side and transmits it to the brain via electrical stimulation of the auditory nerve. Over the past few years, an increasing number of children with SSD have received a CI (Távora-Vieira & Rajan, 2015, 2016; Thomas et al., 2017; Arndt et al., 2015; Beck et al., 2017; Sangen et al., 2019) but it is no standard treatment option and more research is needed into the effectiveness. Importantly, timing of the CI intervention is essential. Behavioral and cortical findings indicate that there are important neural consequences to untreated SSD which worsen with increasing duration of the SSD and result in biased input to higher-order auditory and non auditory cortical areas (Kral et al., 2013; Yusuf et al., 2017; Gordon, Henkin & Kral, 2015). The CI should be provided early in life to prevent these neural consequences (Kral & Sharma, 2012).

A final aim of the current study is to investigate whether the three methods reflect differences in performance between normal hearing children and children with SSD, with and without CI. We hypothesize that at the young age of our participants (7 months to 2 years), linguistic deficiencies of children with SSD, as well as possible CI benefit, are subtle because children do not yet produce much language and difficulties often emerge later in childhood. We therefore do not expect the methods to differentiate at this young age.

5.2 Methods

Participants

The participants in the present study are a subset of the participants in an ongoing longitudinal study aimed at investigating the potential benefit of a CI in children with SSD. Nineteen of the 27 participants are diagnosed with severe to profound unilateral hearing loss as indicated by auditory brain stem thresholds (air conduction) ≥ 80 dBnHL on the affected side and ≤ 35 dBnHL on the contralateral side. 13 of these children with SSD received a CI (group SSD_CI), on average at 14 months of age (SD 4.8). Every six months their communicative behavior is assessed, starting one to two months pre implantation (average age 12.3 months (SD 5.0)). Performance of the infants with SSD and a CI (SSD_CI) is compared to that of two control groups of children with SSD without a CI or any other hearing assistance device (SSD_noCI, n=6) and normal hearing children (NH, n=8).

The longitudinal multicenter study was approved by the medical ethical committee of every participating center (B322201523727). All parents gave written informed consent at inclusion in the study.

Outcome Measures for children under 2 years of age

Bayley-III-NL

The Bayley-III Scales of Infant and Toddler development is an internationally renowned behavioral test battery that assesses the developmental abilities of children from 16 days up to 3 years and 6 months of age (Baar et al., 2014; Bayley, 2006). In the present study, the subtests of language comprehension (Bayley-LC) and language production (Bayley-LP) were administered. These tests have good internal consistency (Lambda-2 of .82 LC and .84 for LP, for age at testing between 6;16 and 22;15m) and test–retest reliability (partial correlation of .61 for LC and .67 for LP for age at testing 4;16-10;30m; .61 for LC and .77 for LP for age at testing 11-22;15m). For the current age group (<24 months), items of the language comprehension subscale mainly assess preverbal behavior (e.g. the reaction to different sounds, the child's name, or a request to do a familiar game or social action), receptive vocabulary (e.g. identifying objects and pictures) and emerging vocabulary related to morphology (e.g. by asking for certain actions with objects). Language production items in this age group assess the vocalizations of the child, gestures, ability to imitate sounds and words, expressive vocabulary (naming objects and pictures and spontaneous language use) and emerging morphosyntactical skills (e.g the use of two-word sentences and plurals).

N-CDI

The word lists of the Dutch version of the MacArthur-Bates Communicative Development Inventory (Fenson et al., 1993; Zink & Lejaegere, 2002) were used to obtain a parent-report of the children's emerging receptive (N-CDI-RV) and expressive vocabulary (N-CDI-EV). These lists consist of 434 (8-16 months) or 702 words (16+ months). Parents were asked to report which of these words their child understood and which ones he/she (understood and) produced. N-CDI-EV was only used once children were 12 months old, because this is the age at which a child generally produces its first word (Zink & Smessaert, 2012).

LENA

Audio recordings were made and analyzed by means of the LENA system (Language ENvironment Analysis, LENA Foundation, Boulder CO). The LENA system consists of the digital language processor (DLP), a light and small recorder, and accompanying software. Parents were asked to use the DLP to make a recording of a whole day (or at least for 10 hours). The DLP is inserted into the chest pocket of a specially designed T-shirt. After switch-on, it records continuous audio for up to 16 hours, or until turned off. The t-shirt with inserted device is only taken off for bathing- or nap times and is then placed in close proximity to the child. Parents were free to choose a 'normal day' (the child is not ill, no unusual circumstances such as crowed parties/events and (if applicable) both parents are not longer absent than usual). Parents of children who made a second (or third recording) were asked to choose a comparable recording day to the previous one (with regard to either weekdays or weekend), this request was not met for 2 of the 27 participating children.

After transferring the recording from the DLP to the computer, speech recognition software segments the recording and assigns each segment to a sound class: male adult, female adult, key child (wearing the recorder), other child, overlapping speech, TV/electronic media and noise, which are labeled clear or unclear, or silence or fuzzy/uncertain. Subsequently, the sound segments of the (key) child are categorized as speech (all preverbal communicative sounds/ babbling/ words) or as other vocalizations (crying, or vegetative sounds such as breathing and burping). Speech segments are marked as single vocalizations if they yield a pause of at least 300ms. Single vocalizations are summed up in order to estimate the child vocalization count (CVC). The number of adult words is estimated (adult word count; AWC) on the basis of clear adult segments. Conversational turns are counted when there is a key child vocalization followed by an adult vocalization (or the other way around) within 5 seconds without any intervening speech by another child or adult (non speech such as noise or silence, if shorter than 5 sec, may occur) (conversational turn count; CTC).

Busch et al. (2018) assessed LENA's reliability for the Dutch language and demonstrated good correlations and good average agreement between the number of adult words, child vocalizations and conversational turns as determined by LENA on the one hand and by human transcribers on the other hand.

Language assessment of children older than 2 years

From 2 years of age onwards, linguistic skills were assessed with the Schlichting tests. Comprehension skills were assessed with the Schlichting Receptive Language Test (SRLT), which is validated for children between 2 and 7 years. In seven sections of increasing difficulty, children are asked to identify objects, carry out tasks with objects and match pictures to sentences presented auditorily. This test has a very good internal consistency (Lambda-2 = 0.94) and test–retest reliability (partial correlation between 0.82 and 0.90 depending on time interval between test and retest). The Schlichting Expressive Language Test-II (SELT) consists of 5 subtests of which 2 are validated for children of 2 years and older (up to 7 years). They measure expressive vocabulary (SELT-EV) by asking the child to name pictures or finish sentences, and morphosyntactic knowledge (SELT-MS) by means of elicitation techniques based on imitation or completing sentences during structured play. These SELT subtests have good internal consistency (Lambda-2= 0.90 for both EV and MS) and test–retest reliability (partial correlations between 0.85 and 0.88).

Statistical analysis

Dependent variables

The Bayley-III-NL, N-CDI, SRLT and SELT provide Flemish norm-referenced results obtained for normally developing children. For the Bayley LC and LP these are scores between 0-19 with a population mean of 10 and standard deviation of 3. For the SRLT and SELT test between 55 and 145 with a population mean of 100 and standard deviation of 15. The N-CDI provides percentile scores, separately for boys and girls. Possible percentile scores are 1, 3, 5, 10, 15, 20, 25 and so on up to 95, 97 or 99, rather than continuous on a scale of 0-100. Often, the raw score (sum of the ticked words) did not correspond to one exact percentile score but was rather situated in between two percentile scores. The average of those two percentile scores was then taken as the final percentile score.

For the LENA we focused on CVC, AWC and CTC. Per recording, and separately for CVC, AWC and CTC, the six 5-minute segments with the highest activity were selected. We decided to disregard the first hour of a recording because of potential biased behavior of parent(s) being very aware of the recording being made (e.g. speaking more than they normally would). All selected 5-min segments' counts were checked for obvious classifying errors that would influence the counts, such as confusion of a woman's voice with a child's voice (possibly occurring e.g. in case of motherese), confusion of key child voice with voice of another child, or confusion of electronic sound (TV/radio) and human speech (VanDam & Silbert, 2016). If necessary, these segments were discarded and replaced by the next segment highest in activity. This occurred in nearly 40% of the initial 288 CTC segments but far less for the AWC and CVC segments (resp. 2 and 12%) than for CTC. Overestimation of CTC was mainly due to adults interacting with a child other than the key child, or due to adults talking to each other while the key child was vocalizing as well but not in interaction with them. The statistical analysis is based on the sum of the six final counts.

Spearman's rho correlation coefficients between age at recording and the CVC, AWC and CTC sum counts were not significant, indicating that it was not necessary to control for age at recording in further analyses. In the LENA foundation Natural Language Study with American children aged 0-48 months (NLS, Gilkerson & Richards, 2008), CTC and CVC did increase significantly with age until about ~24 months. AWC was not significantly correlated with age either in the NLS study. The the lack of correlations between the LENA variables and age in our study could be partly explained by our choice of dependent variable, which describes highest activity of the day rather than activity during the total day.

Analysis

Seventeen of the 27 participants were tested multiple times before the age of 2, leading to 48 test sessions in total (see table 5.1). For each test session, 7 dependent variables were documented: Bayley-LC, Bayley-LP, N-CDI-RV, N-CDI-EV, LENA-AWC, LENA-CVC and LENA-CTC (see table 5.2 for descriptive statistics). For some of these variables outcomes were not normally distributed and therefore non parametric tests were conducted for all analyses. To address the first research question, i.e. whether the outcomes as measured by the Bayley-III-NL, N-CDI and LENA relate to each other, Spearman's rho correlation coefficients between the seven dependent variables were determined. For an overall analysis relating one variable to another, all 48 scores were taken into account, regardless of hearing status and the data collection session (i.e. part of the children contributed more than once to this dataset). For more detailed analyses Spearman's rho correlations were also determined separately for data collected from children between 7-11 months of age (n=11), 12-17 months of age (n=23) and 18-23 months of age (n=14). Every score within these data sets according to age class belongs to a different child, with the exception of age class 12-17 months where 3 children contribute twice (SSD_CI_4, 6 and 7).

To address the second research question, i.e. whether communicative performance under two years of age (Bayley-LC, Bayley-LP, N-CDI-RV, N-CDI-EV, LENA-AWC, LENA-CVC and LENA-CTC) is related to linguistic performance above two years of age (SRLT, SELT-EV and SELT-MS), Pearson correlation coefficients were determined for a subset of 13 participants (data of this subset of participants was normally distributed). For children who were tested multiple times in one (or both) of the age categories 0-2 years and 2+ years, for each dependent variable performance scores of all testing sessions within that age category were averaged. In addition, correlation coefficients were calculated separately for data collected at ages 12-17 months (n=12) and 18-23 months (n=9) (children SSD_CI_4 and 6 had two data collection

Table 5.1. Participants.

participant	age at implan-tation (in months)	age at LENA recordings * (in months)			number of data collection sessions	age at Schlichting test sessions (in months)			number of data collection sessions
SSD_CI_2	8,7	8,1	13,1	19,3	3	24,8	30,7	37,6	3
SSD_CI_3**	21,6	21,0			1				
SSD_CI_4	12,9	12,3	17,2		2	24,3	30,3		2
SSD_CI_5	14,8	13,4	18,9		2	25,1	30,8		2
SSD_CI_6	14,5	12,9	17,6		2	24,2			1
SSD_CI_7	11,4	12,6	16,0	22,0	3				
SSD_CI_8	14,7	14,2	19,5		2	25,7			1
SSD_CI_9	10,3	10,2	14,0		2				
SSD_CI_10	12,4	10,8	16,5		2				
SSD_CI_11	12,1	11,1	16,3		2				
SSD_CI_12	10,3	8,7			1				
SSD_CI_13	14,9	13,6			1				
SSD_CI_14	10,2	8,6			1				
SSD_noCI_1		15,9	18,9		2	24,6	30,3	36,6	3
SSD_noCI_2		14,9	22,5		2	25,8	33,7		2
SSD_noCI_4		20,6			1	25,1	32,2	36,3	3
SSD_noCI_12		19,5			1				
SSD_noCI_14		8,9			1				
SSD_noCI_15		10,2			1				
NH_15		9,0	17,7		2	26,7	29,8	35,7	3
NH_16		14,4			1				
NH_18		15,8	19,4		2	26,4	31,2		2
NH_19		8,6	15,1	20,7	3	26,2			1
NH_20		12,7	18,3		2	24,8			1
NH_21		17,8			1	24,0	30,6		2
NH_22		7,4	14,1	20,5	3				
NH_24		12,7	18,2		2				
					Total of 48				

* Age at testing (Bayley-III-NL) and parent-questionnaire (N-CDI) was always close to age at LENA recording.

** child SSD_CI_3 suffers from quadriplegia and developmental delay

Table 5.2. Descriptive Statistics of the seven dependent variables measured in the participants between 7-11 months of age, 12-17 months of age and 18-23 months of age, and for the total data set.

	n	Min	Max	Mean	Std.Dev.
Total					
LENA-CVC	48	124	549	269,7	91,8
LENA-AWC	48	1040	4458	2409,4	881,4
LENA-CTC	48	32	128	74,0	24,9
Bayley-LC	48	1	18	9,6	3,1
Bayley-LP	47	4	19	11,8	2,7
N-CDI-RV	46	0	92,5	37,8	28,0
N-CDI-EV	37	1	82,5	30,5	26,8
7-11 months					
LENA-CVC	11	164	425	256,2	76,9
LENA-AWC	11	1406	4458	2905,0	929,4
LENA-CTC	11	46	102	72,3	23,6
Bayley-LC	11	9	13	10,6	1,4
Bayley-LP	11	8	15	11,6	2,0
N-CDI-RV	9	10	82,5	43,9	23,0
N-CDI-EV	0				
12-17 months					
LENA-CVC	23	156	370	249,9	64,6
LENA-AWC	23	1230	4201	2430,4	821,6
LENA-CTC	23	32	120	70,3	23,2
Bayley-LC	23	5	18	9,4	3,0
Bayley-LP	23	9	17	12,3	2,2
N-CDI-RV	23	0	92,5	36,1	30,1
N-CDI-EV	23	1	80	27,5	27,5
18-23 months					
LENA-CVC	14	124	549	312,9	126,5
LENA-AWC	14	1040	3321	1985,4	774,2
LENA-CTC	14	38	128	81,4	28,4
Bayley-LC	14	1	15	9,2	4,0
Bayley-LP	13	4	19	11,0	3,9
N-CDI-RV	14	0	80	36,5	28,5
N-CDI-EV	14	1	82,5	35,4	26,0

sessions within the 12-17 months' time window; for each dependent variable the two performance scores per child were averaged). Kendall's τ correlation coefficients were calculated because of the small sample sizes. For the data collected between 7-11 months of age, correlations could not be reliably calculated because of the sample size being too limited (n=3).

For all correlational analyses, a two-tailed P-value <0.0125 was considered statistically significant and a P-value <.025 was considered borderline significant.

Kruskall-Wallis tests with post hoc Mann Whitney U tests were conducted, on all seven dependent variables, to investigate whether the Bayley-III-NL, N-CDI and LENA system can differentiate between children of the different hearing statuses SSD_CI, SSD_noCI and NH. For each dependent variable the performance scores of the different test sessions were averaged for children tested multiple times.

Within the CI group, 3 out of 12 children were only tested pre-implantation. They were therefore unaided at the time of measurement and in that regard no different yet from the children of the SSD_noCI group. The remaining 9 SSD_CI children were tested both pre- and post-implantation. As within-child averaging of their (pre- and post-implantation) scores may not be justified, two alternative group comparisons were therefore conducted.

First, the dependent variables were compared between the groups (SSD_CI, SSD_noCI and NH) separately for data collected at ages 7-11 months, 12-17 months and 18-23 months. In the time window 7-11 months, all data points were obtained pre-implantation and in the 18-23 month time window, all scores were obtained post-implantation. Only within the 12-17 month time window scores were mixed with 3 children tested pre-implantation, 4 post-implantation and 3 tested before as well as after implantation (for whom per dependent variable, the two performance scores were averaged). Second, the dependent variables were compared between 3 alternative groups: SSD_aided, SSD_unaided and NH. The SSD_aided group included the post-implantation scores of the SSD_CI children. The SSD_unaided group comprised the pre-implantation scores of the SSD_CI children and the scores of the SSD_noCI group. Again, for a SSD_CI child with multiple post implantation measurements, or a SSD_noCI child with multiple measurements, the scores of the child's different sessions were averaged.

In all group comparisons, Bonferroni correction was applied, indicating that a two-tailed P-value< 0.017 was considered statistically significant. Effect sizes were calculated using the formula $r = Z/\sqrt{n}$ (Field, 2009). Data of child SSD_CI_3 was excluded from all group comparisons. This child's developmental delay negatively influences its linguistic outcomes which would bias the SSD_CI group's performance.

Statistical analysis was performed using SPSS version 25.

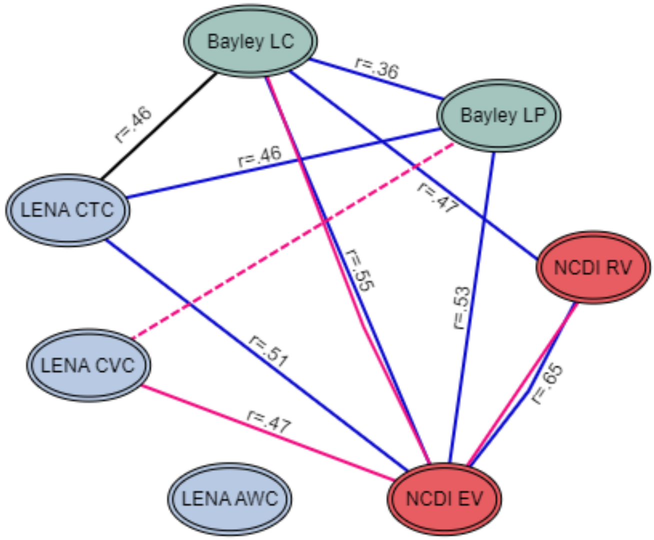
5.3 Results

Do the outcomes as measured by the Bayley-III-NL, N-CDI and LENA relate to each other?

First, figure 5.1 shows significant positive relationships between LENA CVC & CTC and test- and questionnaire outcomes, indicating that children who vocalized more in daily life (LENA-CVC) showed largest expressive vocabulary as documented by their parents (N-CDI-EV; rs=.47, p=.004). Children who were engaged in most conversational turns (LENA-CTC) showed the best language comprehension and production test results (rs=.46, p=.001 for both Bayley-LC and LP) and also scored highest on the parent questionnaire of expressive vocabulary (N-CDI-EV; rs=.51, p=.001). Linguistic input from adults (LENA-AWC) was not significantly related to the test- and questionnaire outcomes. Second, the test- and questionnaire outcomes also yielded significant positive relations showing that children with the largest, parent-reported, expressive vocabulary (N-CDI-EV) scored highest on both the language comprehension test (rs=.55, p<.001) and production test (rs=.53, p=.001). Receptive vocabulary as documented by the parents was positively associated with the language comprehension test results (rs=.47, p=.001) but not with the production data. Finally, for the Bayley test, a positive association was observed between comprehension and production score (rs=.36, p=.012). A similar, but stronger, positive association was detected between the parent questionnaire scores of receptive and expressive vocabulary (rs=.65, p<.001).

The observed associations between LENA, Bayley-III-NL and N-CDI data are driven by outcomes of the children when they were 12-23 months old but not 7-11 months old, see color coding of the correlation coefficients in figure 5.1 (for the corresponding p-values, see appendix II). The relations between the N-CDI-EV and N-CDI-RV and between N-CDI-EV and Bayley-LC were present for both the 12-17 and 18-23 month old children. The relation between LENA-CVC and N-CDI-EV was observed only for the 12-17 month old children. Outcomes of this group yielded an additional relationship between LENA-CVC and Bayley-LP that was not present for the total group. The relations between LENA-CTC and Bayley-LP, LENA-CTC and N-CDI-EV, Bayley-LC and N-CDI-RV, Bayley-LP and N-CDI-EV, and between Bayley-LC and Bayley-LP were observed specifically for the 18-24 month old children. No relation was observed between LENA-CTC and Bayley-LC anymore, for none of the different age categories.

Figure 5.1. Spearman's rho correlation coefficients between Bayley, N-CDI and LENA data (total group, n=48).



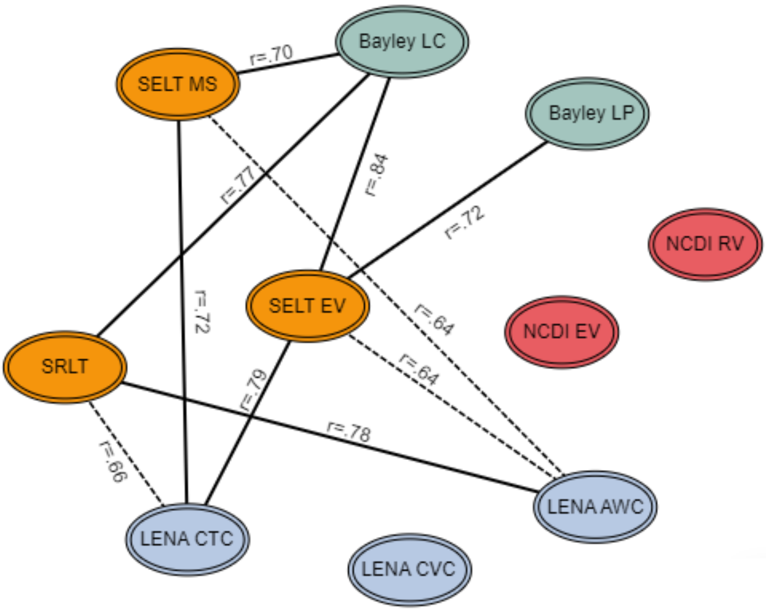
Red colored lines indicate that the relationship was significant as well when only taking into account data collected from the children at 12-17 months of age (n=23). Red dotted line: an additional relationship for the 12-17 month olds that was not present for the total group. Blue colored lines indicate that the relationship was significant as well when only taking into account data collected from the children at 18-23 months of age (n=14). Black line: the relationship was not significant for any of the different age categories.

Are linguistic outcomes before the age of 2 years related to linguistic outcomes after the age of 2 years?

LENA variables and Bayley behavioral test outcomes, but not N-CDI parent questionnaire outcomes, were positively associated with the later assessed linguistic skills (figure 5.2). More linguistic input (LENA-AWC) before the age of 2 was related to better language comprehension test outcomes (SRLT) beyond 2 years of age (r=.78, p=.002). More interaction before the age of 2 (LENA-CTC) was related to better language production results after the age of 2, for expressive vocabulary (SELT-EV; r=.79, p=.001) as well as for morphosyntactic skills (SELT-MS; r=.72, p=.005) The quantity of child speech (LENA-CVC) before the age of 2 did not show a significant relationship with the linguistic skills beyond the age of 2. Furthermore, children with higher language production test outcomes before age 2 (Bayley-LP) showed better expressive vocabulary results after the age of 2 (SELT-EV; r=.72, p=.005). Language comprehension test scores before the age of 2 (Bayley-LC) were positively associated with receptive (SRLT: r=.77, p=.002) as well as expressive linguistic skills after the age of 2 (SELT-EV: r=.84, p<.001; SELT-MS: r=.70, p=.008).

The relation between AWC and SELT-EV and MS performance scores (trend effects) was driven by the 18-23 month old children (Kendall's τ=.78, p=.004; Kendall's τ=.61, p=.022, respectively for EV and MS). The other, and thus most of the, relationships that were observed for the total group (between AWC and SRLT, CTC and SELT-EV & MS, Bayley LC and SRLT & SELT-EV & MS, Bayley LP and SELT-EV) were not present in any of the separate age groups, possibly due to the small sample size. For these specific effects, we explored whether they would still hold and be similar in effect size for the total group when data of the 7-11 month old children would be discarded. Without exception, they all did (data not shown).

Figure 5.2. Pearson correlation coefficients between the linguistic data collected before the age of 24 months (LENA, Bayley-III-NL, N-CDI) and after the age of 24 months (Schlichting) (total group, n=13).

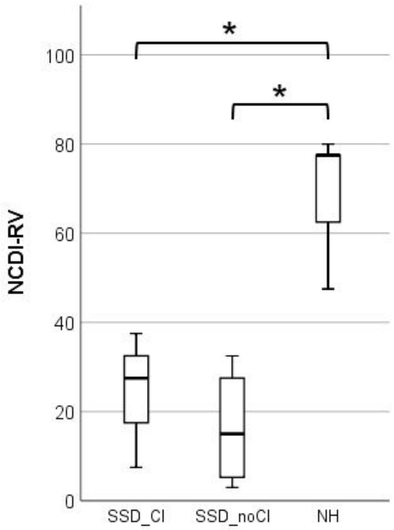


Solid lines indicate significant relations (p<0.0125), dotted lines indicate trend effects (p<.025).

Can Bayley-III-NL, N-CDI and LENA differentiate between children of the different hearing statuses SSD_CI, SSD_noCI and NH?

None of the seven outcome measures differentiated between the hearing statuses, neither in the analysis comparing group SSD_CI to group SSD_noCI and group NH, nor in the analysis comparing group SSD_aided to group SSD_unaided and group NH. A significant difference between the groups was only detected for the N-CDI-RV scores (H(2)=9.05, exact p=.001) when assessed separately for the three different age categories, within the 18-23 month old age category. Post hoc Mann Whitney U tests showed lower performance for both SSD groups compared to the NH group (U=.00, exact p=.016, r=.82 for both comparisons), see figure 5.3.

Figure 5.3. NCDI-RV data of the 18-23 month old children.



Left: group SSD_CI (n=4); middle: group SSD_noCI (n=4); right: group NH (n=5). Boxplots represent the distribution of the percentile scores: the box represents the interquartile range, with a line at the median value. Whiskers extend to the highest and lowest values no greater than 1.5 times the interquartile range. Asterisks mark a significant difference between the groups according to Mann-Whitney U-test (*p ≤ .017).

5.4 Discussion

Assessment of linguistic development for children under 2 years of age is challenging, mainly because linguistic behavior is still limited at this young age. The present study examined whether early communicative behavior outcomes of the Bayley-III-NL behavioral test, the N-CDI parent-questionnaire and the LENA system of 27 children under the age of two related to each other, and to what extent they were predictive of later linguistic outcomes. Correlational analyses showed relationships between outcomes according to the three different methods. Furthermore, Bayley-III-NL scores and LENA language environment factors – but not N-CDI scores – as assessed before 2 years of age were significantly related to behavioral language outcomes assessed between 2 and 3 years of age.

Bayley-III-NL, N-CDI and LENA: correspondence between the outcomes

Positive associations were observed between the comprehension counterparts of the Bayley-III-NL test and the N-CDI questionnaire, as well as between the expressive parts of both. Both the behavioral test and the questionnaire predominantly focus on the vocabulary of the child, which likely explains the good correspondence, even though the Bayley-III-NL does this from a behavioral test perspective and the N-CDI from a parent perspective. Netten and colleagues (2015) report similar correlations between N-CDI-EV (short form) performance scores and behavioral language outcomes in bilaterally deaf and hard of hearing Dutch children of 30-66 months of age (Netten et al., 2015).

Also, within behavioral test and, more strongly, within questionnaire, we found positive associations between comprehension and production outcomes. In general, language comprehension precedes language production (Zink & Smessaert, 2012) and therefore a child with good language production skills likely has good language comprehension skills as well. This likely contributes to the detected associations. The relations are not per se mutual, because a child with good language comprehension skills does not necessarily possess good language production skills. Ribot, Hoff, & Burridge (2018) propose that children who do not talk much will show a greater discrepancy between receptive and expressive skills than children who do. During word learning, lexical representations of words are formed based on input but also based on output, i.a. representations regarding articulatory movements. The act of producing a word benefits the creation of output-based lexical representations of that word. These output-based representations are, in turn, necessary in order to produce the word, whereas for recognition of the word representations based on input alone are sufficient (Ribot et al., 2018). Talkative children will therefore build up more and/or better lexical representations which boosts their expressive vocabulary development.

The correspondence between comprehension and production performance scores was weaker within the Bayley-III-NL behavioral test data than it was for the N-CDI questionnaire data. This may be attributable to a difference between the two Bayley scales intrinsic to the skills they assess. In both the Bayley comprehension and production scale, children are awarded points when they appropriately respond to requests (e.g. identifying (LC) or naming (LP) an object or a picture). On top of that, in the production scale children are awarded points when they spontaneously produce certain vocalizations (e.g. when displaying conversation-like prosodic babble or when using 2 correct words). In the comprehension scale, in contrast, more compliance is needed because the child only demonstrates understanding a request or question by (appropriately) responding to it. Consequently, a high Bayley production score does not necessarily indicate a high Bayley comprehension score. A second possible explanation for the stronger association within the N-CDI data could be that the N-CDI-EV was only used from child age 12 months onwards. Therefore, data of 7-11 month old children was not taken into account in the relationship between N-CDI-RV and EV, whereas it was for Bayley-LC and LP. If comprehensive and/or expressive communicative skills of the 7-11 month olds are difficult to map with the current methods, this could have possibly weakened the Bayley correlation for the total group aged 7-23 months.

The used subscales of the Bayley behavioral test and the N-CDI questionnaire assess qualitative aspects of the child’s communicative skills. The LENA system, on the other hand, documents quantity thereof (LENA-CTC), as well as quantity of linguistic environmental factors of speech input to the child (LENA-AWC) and interaction (LENA-CTC). In the current study, correspondence was found between part of the LENA outcomes and the behavioral test and questionnaire scores. Amount of child vocalizations, LENA-CVC, was positively associated with the expressive vocabulary parent questionnaire results, and specifically for the 12-17m old children also with expressive language behavioral test scores. Amount of engagement in interactions, LENA-CTC, was positively associated with both receptive and expressive linguistic behavioral test outcomes as well as with expressive vocabulary as documented by the parents. We observed no significant associations between LENA-AWC and the other linguistic outcomes.

Talkativeness, as measured with LENA-CVC, thus was specifically related to language production but not language comprehension skills. These findings fit with those reported by Ribot, Hoff, & Burridge (2018), who also show an effect of a child's (parent reported) amount of linguistic output on expressive – but not receptive – language growth in NH bilingual children of 30 to 42 months. Ribot and colleagues (2018) propose possible mechanisms underlying the important role of output for a child's language acquisition. First, producing speech confronts the child with what it cannot produce yet, which, in turn, likely triggers the child to figure out what it needs to know in order to do so. Also, when a child speaks it often receives feedback from adults or older children about its language input. In this process of talking and receiving feedback the child can test linguistic hypotheses (Ribot et al., 2018). Furthermore, output could promote language learning in general because producing output requires retrieval from memory and the retrieval process itself facilitates learning (Ribot et al., 2018; Roediger & Butler, 2011). As mentioned above, children who talk a lot build up most output-based lexical representations which facilitates their expressive vocabulary growth (Ribot et al., 2018). Perhaps in the period from 12-17 months, a period in which children start to use words and build up their expressive vocabulary, the gap between talkative and less talkative children's expressive vocabulary is most pronounced. This could have contributed to the observed relationship between talkativeness and expressive behavioral test result for the 12-17 month olds but not the younger and older participant groups in the present study.

Regarding the LENA language environment factors, CTC but not AWC was significantly associated with the linguistic outcomes collected during the same time span. A similar relation between CTC – but not AWC – and receptive as well as expressive linguistic results has been reported for twenty-eight 2 year-old hard of hearing toddlers in a study by Ambrose and colleagues (2014). In the study of Zimmerman et al. (2009), effects of AWC on linguistic test outcomes of a large group of 275 NH children aged 2-48 months were significant but were partially mediated by CTC.

The amount of linguistic input that is taken in by the child may explain the different results regarding AWCs and CTCs relation to communicative outcomes. Sheer amount of linguistic input is important, because it is related to the frequency with which words are presented to the child (Hoff & Naigles, 2002). Frequency facilitates word learning because different presentations of a word often vary in accompanying (non)linguistic context and therefore each occurrence provides somewhat new information about the meaning of the word (Hoff and Naigles, 2002). LENA-AWC represents the amount of clear adult speech, so all linguistic input a child could take in. However, part of this linguistic input is not child-directed but rather consists of conversations between others, which increases the chance that the child will either not attend to it or, especially for children with a hearing impairment, cannot hear it well enough. In those cases, input will not be taken in by the child. In interaction situations, in contrast, there often is joint attention between child and adult and all input is child-directed. Furthermore, as Ambrose and colleagues (2014) proposed, in interaction situations the conversational partner is physically close to the child and thus likely more audible. Also, the conversational partner can perceive whether their input is accessed by the child and change their volume or the environmental noise level if it is not (Ambrose et al., 2014). This is especially important for children who suffer from hearing loss, which is the case for 70% of the present participant group. Given abovementioned factors, linguistic input in CTC is more likely to be taken in fully than linguistic input in AWC, resulting in a greater contribution of CTC to the child's linguistic development compared to AWC.

Additionally, CTC contributes to linguistic development because it provides an opportunity for the child to produce linguistic output and thus practice linguistic skills, receive corrections and feedback by the adult and consolidate newly acquired language (Ambrose et al., 2014; Kuhl, 2010; Ribot et al., 2018; VanDam et al., 2012; Weisleder & Fernald, 2013; Zimmerman et al., 2009). In addition, Zimmerman et al., (2009) propose that exposure to the child's output in interaction situations helps the adult in keeping a good sense of the child's changing linguistic abilities. This is necessary for the adult in order to be able to adjust their own speech so that it is not too simple and not too complicated. Adults promote the child's language best by providing input that is just challenging enough (Wood & Middleton, 1975; Zimmerman et al., 2009). The relationship between CTC and linguistic outcomes likely is bidirectional. Not only does CTC support linguistic development, children with more advanced language skills could also be more skilled in initiating and prolonging conversations (Ambrose et al., 2014; Zimmerman et al., 2009) which would lead to more CTC in a LENA recording.

It should be kept in mind that our LENA results do not describe the activity of the child or its environment during the total recording day. LENA has a very conservative approach towards counting overlapping, faint and noisy speech (Busch et al., 2018). Factors such as type of recording day (week or weekend) and following, the environment in which the child spent the largest part of day time (e.g. at day care or with parent(s)/other care giver) could influence amount of speech in noisy (speech) situations and thus the LENA counts. Many studies using LENA methodology analyze the full recording either by using the total count of the variable(s) of interest (e.g. Zimmerman et al., 2009), by using an average count per hour (e.g. Ambrose et al., 2014) or by using LENA percentile scores based on the LENA foundation Natural Language Study with American children (Gilkerson & Richards, 2008). Alternatively, one can choose to limit the amount of recording analyzed (e.g. Burgess et al., 2013; Gilkerson et al., 2015; Jackson & Callender, 2014; Ramírz-Espara et al., 2014). In the present study we opted for analysis of highest activity of the day rather than analysis of the total day, in an attempt to decrease the influence of type of recording day on the LENA counts of CVC, AWC and CTC. Studies using a similar approach vary in number and length of the interval(s) of analysis (for a review, see Ganek & Eriks-Brophy, 2018). We decided to select thirty minutes per LENA outcome CVC, AWC and CTC for each recording, consisting of six separate 5 minute segments rather than one 30-minute block, in order to increase the variation regarding time-of-day the peak activity originated from. For each outcome CVC, AWC and CTC, the 288 (48 recordings * 6 top segments) segments were distributed over the total day. For CVC this distribution was evenly and for AWC and CTC a somewhat larger part of the segments originated from the late afternoon and early evening. Within a single recording, the selected 6 segments (or clusters of 2 or 3 out of the 6) could be concentrated within a shorter time window (i.e. a few hours or in some cases within one hour).

Possible predictive value of the three methods

The abovementioned correlational analyses do not allow to draw conclusions regarding causality within the detected relationships. In exploring possible predictive value of the methods, we detected associations between Bayley-III-NL and LENA outcomes, but not N-CDI outcomes, and linguistic skills as measured later on (age 2-3 years) with SRLT/SELT tests. Bayley-LP scores were positively related to the SELT expressive vocabulary results, and Bayley-LC scores were positively related to the SRLT language comprehension scores. Assuming that the SRLT and SELT performance scores describe the children’s actual linguistic abilities well, these relationships support construct validity of the Bayley-III-NL language test results before the age of 2. Surprisingly, Bayley-LC scores were also significantly related to the SELT scores of expressive vocabulary and morphosyntax. We expected that good infant expressive (LP) rather than receptive (LC) communication skills would be a precursor for morphosyntactical outcome. However, as described above, at young age a high Bayley comprehension score is likely more difficult to achieve than a high Bayley production score because of more compliance needed and less spontaneous behavior scored. Possibly, Bayley-LC performance scores may therefore be linked stronger to more advanced later expressive linguistic outcomes than Bayley-LP scores. It is also possible that we did not observe correspondence between Bayley-LP and SELT-MS, and between N-CDI and SRLT/SELT data, because of the limited sample size of participants with data both before and after age 2.

LENA AWC and CTC outcomes were also positively related to later collected SRLT language comprehension and SELT language production scores emphasizing the importance of language input to and interaction with a young child for its linguistic development. In the research by Ambrose et al. (2014), CTC at 24 months corresponded to linguistic outcomes at 36 months in hard-of-hearing toddlers. Very recent results of Gilkerson et al. (2018) showed that CTC at very young age even predicted language outcomes of teenage children 9 to 13 years old, also after adjustments for socio-economic status and child language skills at the time of LENA recording (N-CDI vocabulary size, LENA-CVC and the average score of two language tests). More specifically, this was the case for CTC of their participants between 18 and 24 months of age, but not between 2 and 17 months of age and between 25 and 47 months of age. The authors argue that perhaps in this period of 18-24m, "children increasingly engage in especially impactful, referentially meaningful exchanges and that this may prepare the child's cognitive and linguistic capacities for enhanced growth" (Gilkerson et al., 2018, p. 8). In these studies AWC was, however, described to be a weaker predictor of later linguistic outcomes than CTC (Gilkerson et al., 2018) or to not have predictive value at all (Ambrose et al., 2014). Possibly, the presence of an association in the present study could be attributed to the parents of our group of participants using a lot of child directed speech. Parents of children with a hearing impairment may be concerned with doing this, and reminded of the importance (e.g. in early intervention settings) even more than parents of NH children. But, one would expect a similar association between AWC and Bayley-III-NL and N-CDI outcomes then, which was not present. Alternatively, the relationship could be explained by CTC or by a mediating factor not measured, such as specifically child directed speech around the age of SRLT/SELT testing. In these analyses for a small sub group of our participants, we did not investigate how much of the variance in SRLT and SELT outcomes was accounted for by the Bayley and LENA outcomes and i.e. whether one of them mediates relationships of the other, so further research is warranted. Our results did not yield any significant relations between LENA-CVC and later Schlichting scores. We are not aware of other studies using the LENA methodology that investigate associations between CVC and later linguistic outcomes.

Group comparisons for communicative outcomes under 2 years of age

In the present study the LENA outcomes, CVC, AWC and CTC, were similar for the different groups of participants with SSD (with and without CI) and with NH. This is in line with the literature regarding children with bilateral hearing loss (Aragon & Yoshinaga-itano, 2012; VanDam et al., 2015, 2012) and indicates that our participants with SSD (with and without CI), in their communicatively most active parts of the day, vocalize as much as their NH peers, are exposed to similar amounts of adult words and participate in similar amounts of conversational turns. Also the Bayley-III-NL test scores and the N-CDI results did not differ between the groups, suggesting similar receptive and expressive communicative skills for the three groups. These results implicate that the methods may not be sensitive enough to reflect differences in linguistic skills between the participants, or, more likely, that potential linguistic differences are not present yet at this young age in which language development is often confined to 2-word phrases or less complicated vocalizations. Regardless of this, most of the implanted children only had their CI for approximately 4 months at the time of their last testing session. This relatively short period with CI may not be long enough for a measurable benefit. Lastly, it is also possible that sample sizes of the groups were too limited to detect differences.

Group comparisons were conducted separately for age categories 7-11m, 12-17m and 18-23m in order to explore whether differences would be dependent on age, as was the case in Gilkerson et al., (2018). Cut-offs at 12 and 18 months were chosen because these ages generally represent new stages in a child’s linguistic development; namely first use of one-and two-word phrases resp. for age 12 and 18 months. In these analyses, only for the N-CDI-RV a significant difference was detected, indicative of larger receptive vocabulary for the NH group compared to both the SSD_CI and SSD_noCI groups between 18-23 months of age. The N-CDI-RV thus seems to be able to differentiate children with and without SSD after all, but only from a certain age/ within a certain age window. We need to be cautious, however, given the possibility that the results of this small sample reflect a biased parent perspective of the parents of children with SSD. The awareness of the child’s hearing impairment and knowledge about the importance of good hearing for language development could result in a more conservative response strategy compared to parents of NH children.

Conclusions and future directions

Positive relationships were observed between the Bayley-III-NL behavioral test, N-CDI questionnaire and LENA system outcomes of children under the age of 2 with NH or with SSD with or without a CI. The three methods are relevant outcome measures for very young children and are complementary to each other. Furthermore, Bayley-III-NL LC and LP scores and LENA-AWC and CTC seem predictive of later linguistic outcomes (between 24 and 36 months). This supports construct validity of the Bayley-III-NL language tests and stresses the importance of interaction with and language input to the child for its linguistic development. Due to the limited sample sizes of the groups with different hearing statuses (NH, SSD_CI, SSD_noCI) it was not possible to examine these relationships separately per hearing status group. Even though in the current cohort we did not observe significant differences between the NH, SSD_CI and SSD_noCI groups regarding the seven outcome variables, further analyses with a larger sample would be appropriate.

In the future, when more participants will have reached the age of 2 years, we will be able to investigate whether the detected predictive relationships differ for children with SSD who received hearing rehabilitation through cochlear implantation and those who did not. It is expected that a CI is beneficial to the linguistic development of a child with SSD (van Wieringen et al., 2019). Under the age of 2, communicative abilities of children with SSD may not differ much from those of NH peers. Indeed in the present study, no differences were detected between the SSD groups and the NH group regarding Bayley-III-NL, N-CDI and LENA results (with the exception of N-CDI-RV scores for 18-23 month old children, which could be the result of a biased parent perspective). However, at group level, linguistic difficulties do emerge later in childhood for children with untreated SSD (Anne et al., 2017; Sangen et al., 2017). The CI is expected to (partly) compensate for these difficulties. If so, predictive relationships between data collected before and after 2 years of age may not be different for children with SSD and a CI and NH children, but they may be for children with SSD without a CI when linguistic outcomes start to deviate.

In clinical practice and clinical research, it is important to limit the efforts and time asked from a child and family. In the present study, the detected correspondence among the Bayley-III-NL, N-CDI and LENA data appeared to be driven by outcomes of the children when they were 12-23 months old, but not 7-11 months old. Furthermore, the significant relations between the outcomes before 2 years of age (Bayley-III-NL, N-CDI and LENA) and the SRLT/SELT outcomes after 2 years of age remained significant and similar in effect size when data of the 7-11 month old children was discarded. Taken together, the data of the 7-11 month old children did not seem to contribute substantially to the detected relationships in the present study, suggesting that it may not be meaningful to test before the age of 12 months. Therefore in future, research with this or similar populations (children with normal hearing or a unilateral/mild bilateral hearing loss) and the current methods, we would recommend starting assessment at 12 months of age instead of earlier.

6 First outcomes of the CICADE study

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Key Points:

1. This longitudinal study is the first to assess linguistic and cognitive outcomes of children with cSSD implanted at a very young age.
2. Despite the young age, these developing skills could be assessed by means of standardized test material and comparison to control groups.
3. The toddlers of the SSD_CI group wear their device and perform largely in line with the NH control group.
4. Linguistic and cognitive results of the SSD_noCI control group appear more diverse.
5. Longitudinal observation is of key importance to draw conclusions regarding CI benefit.

6.1 Introduction

Each year in Flanders about 20-25 newborns are diagnosed with profound (> 90 dB HL) sensorineural hearing loss on one side and normal hearing contralaterally (Van Kerschaver & Stappaerts, 2011) also termed congenital single sided deafness (cSSD). In Flanders, as in many other parts of the world, there is no standard care for these children. It is, however, widely acknowledged that their ability to localize sound sources and to understand speech in noisy situations is hampered (Ruscetta et al., 2005; Reeder et al., 2015) due to absent binaural hearing. Moreover, at group level SSD has been shown to negatively affect language and cognitive development and to increase listening effort (Kishon-Rabin et al, 2015; Fitzpatrick et al., 2019; Lieu et al., 2013; Fischer & Lieu, 2014; Ead et al., 2013; Grandpierre et al., 2018). These results indicate that intervention should be considered.

Untreated cSSD leads to cortical reorganization that continues with increasing duration of SSD (Kral et al., 2013). As duration of SSD is negatively associated with outcomes after intervention (Cohen & Svirsky, 2019), it is advised that treatment is provided within this early critical period. This is to prevent overrepresentation of the hearing ear in the auditory system and biased input to higher order cortical areas, and to possibly restore cortical organization.

A cochlear implant (CI) is the only rehabilitative option that offers the potential to facilitate binaural hearing, as it enables sound transmission via electrical stimulation of the auditory nerve on the impaired side. In Flanders, the number of newborns with cSSD that qualify for a CI, depending on etiology, is estimated to be 5 to 10 each year (van Wieringen et al., 2019). Currently, it is unknown if early CI in cSSD will yield similar results as CI in a maturated auditory system (Arndt et al., 2017). First results of early implanted children with cSSD are promising (Arndt et al., 2015; Beck et al., 2017; Távora-Vieira & Rajan, 2016; Thomas et al., 2017).

To date, the benefit of a CI for children with SSD has only been reported for auditory skills and subjective experience. It is equally important, however, to document the benefit of CI for these children with regard to the development of language and complex cognition, given the reported significant differences to NH peers in this regard. The aim of our multicenter longitudinal study is to investigate the potential benefit of a CI in 16 children with cSSD, implanted between 8-26 months of age, with regard to language, cognition and auditory performance. It is hypothesized that provision of the CI at a very young age will partially restore binaural processing in the following years and hence yield the best conditions for near-normal auditory, linguistic and cognitive development. Although the CI is provided at a very young age, potential improvements are expected to be much more subtle than for bilateral deaf children.

Here, we present data of the first 6 implanted children who currently are 2 years of age or older (group SSD_CI). Performance is compared to that of two age-matched control groups: toddlers with SSD who did not receive a CI (group SSD_noCI, n=12) and normal hearing peers (group NH, n=19).

6.2 Methods

Ethical Considerations

The study was approved by the medical ethical committee of every participating center (B322201523727).

Participants

Characteristics of the toddlers with SSD are presented in table 6.1. Their auditory brain stem thresholds (air conduction) are ≥ 80 dBnHL on the affected side and ≤ 35 dBnHL on the contralateral side. With the exception of one child, none of the children suffer from comorbidities. Parents were thoroughly informed and given the current scientific knowledge about outcomes and possible risks and benefits. About a third of the initially counseled parents declined implantation.

Outcome Variables

CI use is monitored through the data logging software of the device of the SSD_CI children at their mappings sessions.

Language and cognitive performance are assessed twice a year with respectively the Schlichting Receptive test (Schlichting & Spelberg, 2010a) and Expressive Language (Schlichting & Spelberg, 2010b) sub tests expressive vocabulary and morphosyntactic knowledge, and the Bayley-III-NL Scales of Infant and Toddler Development (Baar et

Participant	Time of diagnosis	Age at implantation † (SSD_CI) / Age at inclusion (SSD_noCI) (yr.mo(;d))	Side of HL	Etiology	ABR threshold, (dB nHL) affected ear ‡	CI experience (mo)	CI use (average hours per day±SD)
SSD_CI_1	10 months	02.02;21	Left	Fracture of left petrous bone due to fall	>90	42,1	3,0±1,3 §
SSD_CI_2	NHS	00.08;21	Left	cCMV	>80	31,8	7,0±3,7
SSD_CI_4	NHS	01.00;26	Left	cCMV	>80	18,8	4,7±1,2
SSD_CI_5	NHS	01.02;24	Right	IEM (incomplete partition type II)	>80	17,2	8,1±1,1
SSD_CI_6	NHS	01.02;15	Right	cCMV	>80	14,4	7,0±1,6
SSD_CI_8	NHS	01.02;22	Left	cCMV	100	11,5	6,8±1,3
SSD_noCI_1	NHS	01;03	Left	CND	>85		
SSD_noCI_2	NHS	01;02	Right	cCMV	>100		
SSD_noCI_3	NHS	03;00	Right	unclear	>80		
SSD_noCI_4	NHS	01;06	Right	cCMV	>70		
SSD_noCI_5	NHS	02;11	Left	CND	>85		
SSD_noCI_6	NHS	03;01	Left	CND	>90		
SSD_noCI_7 ¶	Perinatal	01;11	Left	CND	>95		
SSD_noCI_8	NHS	02;02	Right	CND	>90		
SSD_noCI_9	NHS	02;06	Left	CND	>90		
SSD_noCI_11	NHS	02;00	Right	cCMV	>90		
SSD_noCI_12	NHS	01;06	Left	CND	>85		
SSD_noCI_13	NHS	02;00	Left	unclear	>90		

Table 6.1. Participant Characteristics.
Note: †Age at implantation was generally 1 to 2 months after first test moment at inclusion. ‡ The > sign indicates no response at the highest level tested. SSD_noCI_4 was not tested beyond 70 dBnHL but additional pure tone audiometry showed no responses at 90 dB HL (250-500-1000-2000 Hz). § Hours of use relatively low because of family related issues. ¶ SSD_noCI_7 was diagnosed with OAV syndrome. In both SSD groups, some of the children receive(d) auditory or linguistic rehabilitation or early home based guidance. None of the SSD_noCI children wears a hearing assistive device.

al., 2014) sub scale cognition (up to age 42 months). Testing is done at the children's home, divided over multiple sessions. All tests provide Flemish norm-referenced test scores. For interpretation and comparison purposes, the norm-referenced scores are converted into z-scores (M=0, SD=1).

Parents are asked to complete the Parents' Evaluation of Aural/Oral Performance of Children (PEACH, Dutch version) (Ching & Hill, 2007).This questionnaire assesses communicative behavior and listening effort in daily life, using a five-point scale. Percentage scores are calculated separately for quiet and noisy situations.

Analysis

Outcomes of all children with SSD are visually and descriptively compared to average performance of the NH children ± 1 SD. Per test or questionnaire scale, the proportion of the group performing lower than the NH control group is presented separately for the SSD_CI and the SSD_noCI children. In addition, per test it is investigated how many children show a z-score ≤ -1, indicating that performance is clinically lower than average with respect to the Flemish norm data of the test itself. Both calculations are based on the child's performance at last measurement moment.

6.3 Results

Data logging shows that the SSD_CI children wore their CI for on average 6,1 ± 1,9 hours per day (across data logs), with individual CI use varying from 3,0± 1,3 to 8,1±1,1 hours per day, see table 6.1.

With regard to language development, the toddlers of the SSD_CI group seem to perform largely in line with the NH control group, whereas results of the SSD_noCI group appear to be more diverse, see figure 6.1 and table 6.2. For instance, while only 1 out of 6 SSD_CI children performs lower than the NH control group on language comprehension (z < NH group mean - 1SD), 6 out of 12 SSD_noCI children deviate from this mean. For one SSD_noCI child, yet none of the SSD_CI children, the score is also clinically deviant (i.e. outside the clinically considered normal performance range of z > 1). Expressive vocabulary performance deviates from the NH control group for 2 out of 6 SSD_CI children compared to 7 out of 12 SSD_noCI children, and is clinically deviant for 3 out of 12 SSD_noCI children as opposed to 0 out of 6 SSD_CI children. All of the SSD_CI children score in line with the NH group and within clinically normal performance concerning morphosyntactic knowledge. In the SSD_noCI group, however, performance of 5 out of 11 children deviates from the NH control group and out of this group for 2 out of 11 children it is below clinically normal performance.

Cognitive performance deviates from the NH control group for 1 out of 6 SSD_CI children, yet 6 out of 12 SSD_noCI children. For 3 of the 12 SSD_noCI children, compared to 1 of 6 SSD_CI children, the score is also below the clinically considered normal performance range.

Proportion of children showing lower PEACH questionnaire scores than the NH group was quite similar for the SSD_CI and SSD_noCI children, see figure 6.2.

Table 6.2. Performance of the SSD groups in comparison to the NH control group and test norm data.

Test/Questionnaire		Lower than performance NH control group		Lower than clinically considered average performance	
		SSD_CI group	SSD_noCI group	SSD_CI group	SSD_noCI group
Language comprehension (SRLT)		1/6	6/12	0/6	1/12
Expressive vocabulary (SELT-EV)		2/6	7/12	0/6	3/12
Morphosyntactic knowledge (SELT-MS)†		0/6	5/11	0/6	2/11
Cognitive skills (Bayley-III-NL,C)		1/6	6/12	1/6	3/12
PEACH+ ‡	Auditory functioning in quiet	2/6	3/9	-	-
	Auditory functioning in noise	3/6	7/9	-	-
	Ease of listening in quiet	2/6	4/9	-	-
	Ease of listening in noise	5/6	7/9	-	-

Left: number of children per SSD group with, at last measurement, a score lower than performance of the NH control group (as indicated by the NH group's average score ± 1 SD); right: number of children with at last measurement a z-score below clinically considered average performance with respect to Flemish norm data (z-score ≤ -1) (only for test outcomes).
Note. †data of SSD_noCI_6 not taken into account because cooperation was insufficient due to severe shyness and it is therefore unclear if the scores represent true abilities.
‡data of SSD_noCI_7 and SSD_noCI_12 missing.

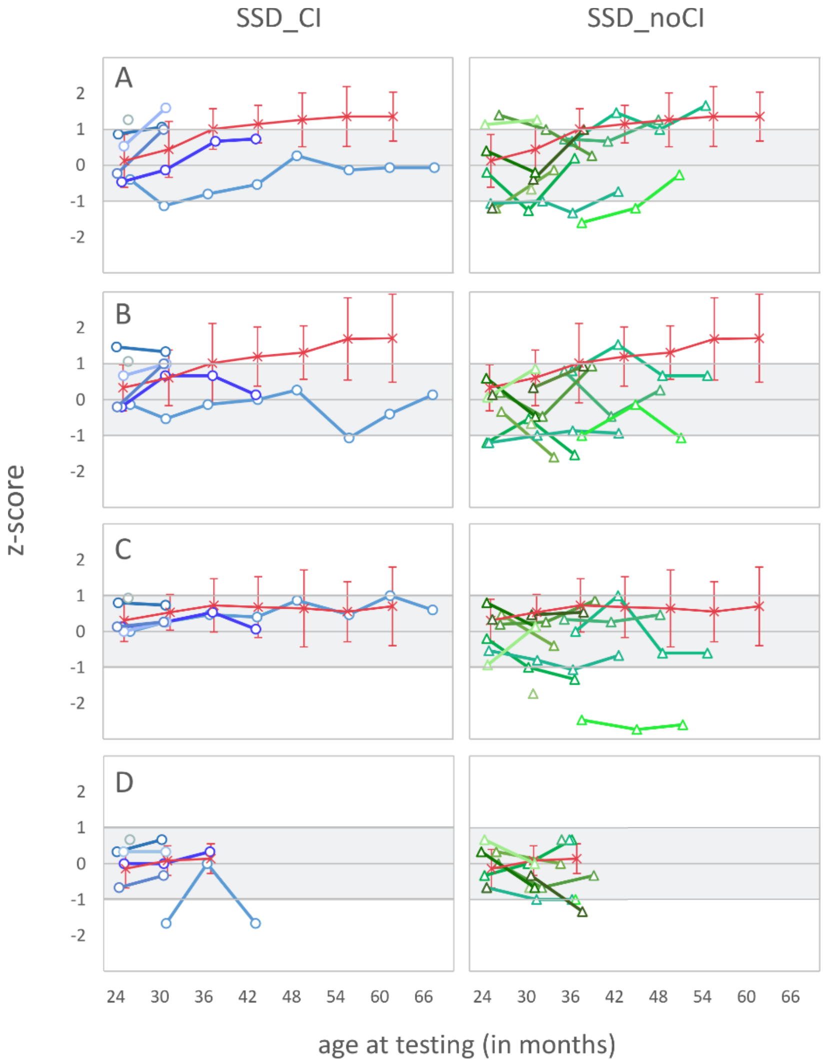

Figure 6.1. Individual test outcomes. 1a: language comprehension; 1b: expressive vocabulary; 1c: morphosyntactic knowledge †; 1d: mastery of mile stone skills in cognitive development. Left picture, in blue dots: group SSD_CI, n=6; right picture, in green triangles, group SSD_noCI, n=12. Y-axis: z-score. X-axis: age at testing, in months. Each data point represents the score of one child, data points of the same child are connected. In red: average score of the NH control group ± 1 standard deviation, based on n=19, 16, 12, 11, 9, 8 and 6 resp. for measurements around 25, 31, 37, 43, 49, 55 and 61 months of age. The grey box represents the normative mean of 0 plus/minus 1 SD, scores below this box are considered clinically to be below average.

Note. † In fig. 2C (relatively very low) scores of 1 child of the SSD_noCI group were not included in interpretation/analysis because cooperation was insufficient due to severe shyness and it is therefore unclear if the scores represent true abilities.

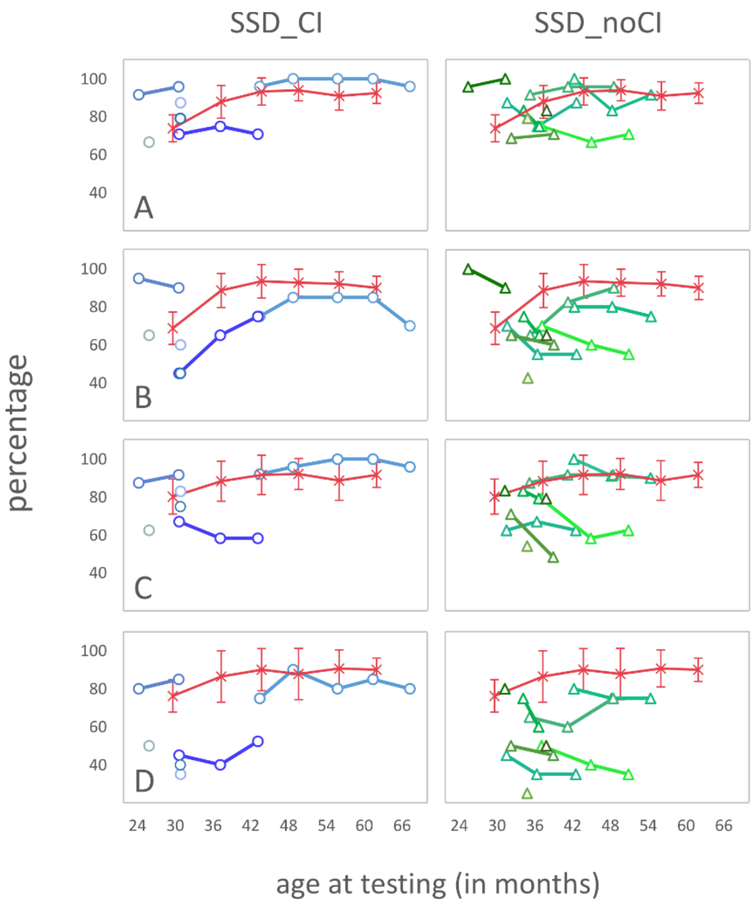

Figure 6.2. Individual outcomes on the PEACH+.
2a: auditory functioning quiet; 2b: auditory functioning noise; 2c: ease of listening quiet; 2d: ease of listening noise. Left: SSD_CI group, n=6; right: SSD_noCI group; n=9. Y-axis: percentage scores. X-axis: age at testing, in months. Each data point represents the score of one child, data points of the same child are connected. In red: average score of the NH control group ± 1 standard deviation, based on n=4,11,10,9,7 and 5 resp. for measurements around 30, 37, 43, 49, 56 and 61 months of age.

6.4 Discussion

The current research presents the first data of our longitudinal study on the potential benefit of a CI in children with congenital SSD. To our knowledge, we are the first to assess linguistic and cognitive skills in children implanted at a very young age. Preliminary data are encouraging, as five out of six SSD_CI children appear to perform largely in line with NH children on tests of expressive and receptive language. In the SSD_noCI group scores of a larger part of the children are lower than those of the NH controls. For some of the SSD_noCI children, performance is also clinically lower than average with respect to the Flemish norm data of the respective tests, especially with regard to morphosyntactic skills and expressive vocabulary. Difficulties in these branches of linguistics have recently been reported for school-aged children with unaided SSD as well (Sangen et al., 2017).

Also test scores concerning cognition show lower performance compared to the NH control group for relatively more SSD_noCI children than SSD_CI children. Time will show whether differences in cognitive abilities persist and if so, whether these are caused by deprived auditory input or by other factors, such as etiology.

Equally important to the test data, the toddlers wear their device and do not seem to be hindered by acoustic input on one side and electrical input on the other. The average number of hours of CI use per day, as well as the range of individual hours of CI use, are quite similar to those reported by Polonenko et al. (2017). Both their and our study have a relatively short follow up time as of yet, so it remains to be seen how CI use will be in the years to come. Nonuse (or limited use) is reported for some children with cSSD (Beck et al., 2017; Thomas et al., 2017), but these particular children were not implanted in the first years of life.

Our parent questionnaire data indicate that listening and communicating in noisy situations is still challenging for the SSD_CI children and requires high listening effort, as is the case for the SSD_noCI group. Hearing handicap presumably persists at this stage despite a CI.

An important strength of the current study is its longitudinal between-subject design which allows for careful comparison of performance of cSSD children with a CI to those without a CI and to NH children from the same population.

Our protocol is extended when the children are older to include evaluation of auditory performance, phonological processing, executive functioning and subjective CI benefit. Speech in noise understanding results of a first tested child, SSD_CI_1, show encouraging audiologically relevant (>1.5 dB; Thomas et al., 2017) differences with CI switched on compared to CI switched off in different spatial conditions.

Conclusions

Preliminary results for children with cSSD implanted at a very young age, show that the children wear their device and appear to perform largely in line with the NH children with regard to linguistic skills and cognitive milestones, whereas results of the SSD_noCI group are more diverse.

The current sample of data of the longitudinal project does not allow yet for drawing solid conclusions on the benefit of a CI in children with cSSD but is important to make evidence-based decisions regarding intervention. Long term observation of the linguistic and neurocognitive development of the children as well as their hearing abilities are of key importance to draw conclusions on CI benefit in this population.

General Discussion

7 General Discussion

Children with SSD, a congenital severe to profound sensorineural unilateral hearing loss ≥ 80 dB HL, constitute a patient group for which there is no standard care. It is widely acknowledged, however, that these children experience direct and indirect consequences of the one-sided sensory deprivation. The general aim of the present doctoral research was twofold:
1) To contribute to the knowledge about the difficulties children with unaided SSD experience with regard to language skills and hearing abilities in daily life.
2) To set up a longitudinal study focused on the effectiveness of cochlear implantation as a possible remediation for very young children with SSD. This is the only rehabilitative option that offers the potential to partially restore binaural hearing when implanted early in life, but research is required to determine the evidence for this in order to provide appropriate rehabilitation.

7.1 Core findings

Three studies were designed and worked out. In the following we will summarize and interpret the main findings.

7.1.1 Part 1: Language and hearing difficulties in school-aged children with unaided SSD

In **study 1 (chapter 3)**, we investigated language, cognitive and auditory outcomes in the clinical population of school-aged children with unaided SSD of the UZ Leuven, in comparison to those of age- and gender matched NH peers. Several behavioral studies have shown that children with SSD and less severe UHL show differences in their language and cognitive development when compared to NH siblings/peers. The studies reported composite language scores, but these do not really inform us about the specific language skills that are difficult for children with hearing impairment. The main aim of our study was to gain a more detailed insight of the language difficulties the school-aged children with SSD experience. Importantly, in our analysis, we not only looked at test scores but also analyzed the error patterns of the children.

The outcomes of study 1 suggest that at group level, our school-aged participants with SSD do not perform at the same level as their NH peers on tests of language and report on difficulties in a number of auditory skills. Morphological, syntactic and vocabulary skills deviated from those of the control group, but performance of both groups was similar for short term memory and working memory. Possibly, differences only exist in more complex cognitive functions. Language test error analysis pointed towards specific difficulties and answering strategies that can e.g. be targeted in rehabilitation (see also appendix I). The children with SSD experienced more difficulties with the correct use of the past participle irregular form and with pronouns than the NH controls. In the vocabulary test, they more often named verb items incorrectly, and more often answered with a word that was too general or only sounded like the target word. When formulating sentences, children with SSD more often than NH peers formulated sentences with errors in grammar/semantics whereas NH children lost more points because of sentences that were only mildly informative (rather than incorrect).

An additional aim of the study was to document the impact of SSD on the children's daily life by means of the SSQ questionnaire focused on aspects of hearing abilities. Results showed higher listening effort for the children with SSD compared to the NH children and more difficulties in spatial hearing, segregating sounds, understanding speech in speech contexts or other noise and with following a group conversation. Four of the children with unaided SSD rated their spatial hearing abilities to be sufficient. Three of them, amongst our oldest tested children, even gave very high ratings (see the outliers in figure 3.3). These children were invited for a formal localization test at the research group ExpORL, where they indicated the direction of the sound presented from an array of loudspeakers (data not shown). RMS errors ranged between 53 and 75°, whereas the RMS error of (young) children with NH has been reported to be as small as 4° (Van Deun et al., 2009). In conversation with the children afterwards they reported that they had learned to handle daily life situations as to make speech understanding problems as minimal as possible, e.g. by always standing on the "good side" of other people in conversation. Strategies like this decrease their difficulties in daily life and likely are the reason behind their good ratings on the SSQ. However, not everyone learns these strategies, and it remains questionable whether they can be applied well in difficult listening situations, e.g. in traffic situations.

7.1.2 Part 2: Early intervention by means of cochlear implantation for young children with SSD

In the second part of our research, we have set up a longitudinal study named CICADE: Cochlear Implantation for Children And one Deaf Ear, in which very young children with SSD have received a CI and a protocol was developed to follow the children up longitudinally with regard to auditory, linguistic and cognitive outcomes.

Outcome measures of communicative skills and language environment under age2

As explained in section 4.1 of this thesis, treatment for children with SSD should be provided within the early sensitive period in life to prevent further cortical reorganization and possibly restore cortical organization. The children participating in the CICADE study are very young at follow-up, as a consequence of providing the CI *early* in life. In **study 2 (chapter 5)**, we focused on the outcome measures for the challenging assessment of early communicative behavior of children under age 2. We selected three internationally used methods: the Bayley-III behavioral test (language comprehension and language production), the N-CDI parent questionnaire (receptive vocabulary and expressive vocabulary) and the automatic LENA system (quantity of child vocalizations, adult speech and interaction). Data were analyzed of 27 children.

Results indicate that the communicative skills of children under age 2 can be assessed by means of the Bayley-III-NL, the N-CDI and the LENA system. The methods are complementary to each other and describe similar but also distinct aspects of the children's communicative development. Positive associations were observed between the comprehension counterparts of the Bayley-III-NL test and the N-CDI questionnaire, as well as between the expressive parts of both. Within test and, more strongly, within questionnaire, positive associations were detected between comprehension and production outcomes. Interestingly, amount of engagement in interactions in daily life, as measured with LENA-CTC, was positively associated with linguistic behavioral test outcomes and expressive vocabulary questionnaire results. Amount of child vocalizations, LENA-CVC, was also positively associated with the expressive vocabulary results.

The abovementioned correlational analyses do not allow to draw conclusions regarding causality within the detected relationships. In exploring possible predictive value of the methods, we detected associations between Bayley-III-NL & LENA outcomes and linguistic skills as measured later on (age 2-3 years) with SRLT/SELT tests. Assuming that the SRLT and SELT performance scores describe the children's actual linguistic abilities well, these relationships support construct validity of the Bayley-III-NL language test results before the age of 2 and emphasize the importance of language input to and interaction with a young child for its linguistic development. In these analyses for a small sub group of our participants, we did not investigate how much of the variance in SRLT and SELT outcomes was accounted for by the Bayley and LENA outcomes and i.e. whether one of them mediates relationships of the other, so further research is warranted.

No differences were detected between the outcomes of the SSD groups and the NH group, with the exception of N-CDI-RV scores for 18-23 month old children which could be the result of a biased parent perspective. These results implicate that the methods may not be sensitive enough to reflect differences in linguistic skills between the participants, or, more likely, that potential linguistic differences are not present yet at this young age in which language development is often confined to 2-word phrases or less complicated vocalizations. It is also possible that sample sizes of the groups were too limited to detect differences.

Informative to professionals in clinical practice or clinical research working with similar populations to ours, is that data of our 7-11 month old participants did not seem to contribute substantially to the detected relationships. We therefore suggest that it may not be meaningful to test before the age of 12 months.

The 6 first implanted children of the CICADE study

The goal of **study 3 (chapter 6)** was to present data of the first 6 implanted children of the CICADE study who, at the moment of writing, close to the end of the PhD project, were 2 years of age or older (~5;6 years (1 child), 3;6 (1 child), 2;6 (3 children) and 2;0 (1 child)). Outcomes of language comprehension, expressive vocabulary, morphosyntactic skills, cognitive information processing and hearing abilities in daily life were compared to those of 12 children of the SSD_noCI group and 19 of the NH peers.

In general, we expect that improvements with CI could be much more subtle for our participants with SSD than for bilaterally deaf children. Moreover, while our children had to be implanted at a very young age due to the narrow window of opportunity, potential benefits may only become prevalent after some time. Despite the young age and limited language, the current data acquired around the age of 2;6 years show that the CI group seems to perform largely in line with the NH controls on tests of expressive and receptive language, whereas performance of the SSD_noCI group is more varied. Compared to the SSD_CI group, scores of a larger part of the SSD_noCI children are lower than those of the NH controls. For some of the SSD_noCI children, performance is also clinically lower than average compared to the Flemish norm data of the respective tests, especially with regard to morphosyntactic skills and expressive vocabulary, which corroborates the findings of our first study (chapter 3) in school-aged children with unaided SSD. The data are not supported by statistical analyses and therefore do not allow us to draw solid conclusions, but this first experience is quite promising.

Interestingly, performance of the SSD_CI children is virtually indistinguishable from performance of the NH group with regard to morphosyntactic skills, see figure 6.1c. As explained in section 4.3, we expect morphological skills to be impeded most by unaided SSD and in that sense aided most by cochlear implantation. We hypothesized that differences in morphological test performance between our groups would be significant around the age of 4 to 5 when typically most children have mastered rules regarding regular inflection of words and are in the process of learning the correct inflection of irregular words. The currently good performance of the SSD_CI group regarding this skill is encouraging.

Our first test data concerning cognition show lower performance compared to the NH control group for relatively more SSD_noCI children than SSD_CI children. But note that at this age the task is very basic. It assesses cognitive aspects such as object exploration and manipulation, understanding of relations between objects, concept forming, ability to count and memory. There is a limited number of items per cognitive aspect and the method presents a composite score. We should therefore be cautious drawing conclusions. Time will show whether the current seeming differences in cognitive abilities persist and if so, whether these are caused by deprived auditory input or by other factors, such as etiology.

Equally important to the test data, the toddlers wear their device and do not seem to be hindered by acoustic input on one side and electrical input on the other. The average number of hours of CI use per day, as well as the range of individual hours of CI use, are quite similar to those reported by Polonenko et al. (2017).
In Flanders, typically all children start to go to school at age 2;6. They then find themselves in noisy environments more often than before and hearing difficulties

due to SSD might become more prominent. As expected, the parent questionnaire data indicate that listening and communicating in noisy situations is challenging for the SSD_CI children and requires high listening effort, as is the case for the SSD_noCI group. The current results of the children with SSD with and without CI seem very similar, so hearing handicap presumably persists at this stage despite a CI.

The sample size of children in the CICADE study is limited. In addition, the follow up time of the children as of yet is relatively short. Consequently, the current data set (study 3) does not allow for statistical analyses. We acknowledge that the results are preliminary and do not allow us to draw solid conclusions regarding CI benefit. Long-term observation is of key importance in this matter. At the end of the longitudinal study we will statistically evaluate, by means of growth analysis, the effect of having a CI – compared to not having a CI or having bilateral normal hearing – on within-person change over time on the different outcome measures.

In about half of the total group of participants with SSD in the CICADE study (14 out of 31), hearing loss was caused by cCMV. Children with cCMV are at risk for comorbidities. These comorbidities could limit CI outcome (Yoshida et al., 2017). For one of our participants with cCMV (SSD_CI_3), motor and developmental delay has become prevalent. Data collection for this child is tailored to his abilities. Note that he was not included in study 3. Our other participants with cCMV have not been diagnosed with any comorbidities. These may, however, still develop in time. In order to investigate the benefit of the CI in children with a cCMV diagnosis, it is important to compare performance with children without CI who were also diagnosed with cCMV.

7.2 Considerations

In the following paragraphs we describe two factors which are important to consider in general in this and similar research.

7.2.1 Cochlear implant use

It is of utmost importance that the children wear their device throughout the day. A great deal of auditory stimulation is needed to develop and maintain effective neural connections (Flexer, 2011). CI use of our participants is quite satisfying so far (see appendix III), and similar to the hours of the subgroup of children implanted at max 3;6 years in the study by Polonenko et al. (2017b). In some circumstances, such as illness or sea side visits, the infants did not wear their device. It is important to council parents concerning the use of the CI despite the normal ear as much as possible. Both Polonenko's (2017) and our study have a relatively short follow up time as of yet, so it remains to be seen how CI use will be in the years to come.

Nonuse (or limited use) is reported for some children with SSD in the literature (Beck et al., 2017; Thomas et al., 2017), but these particular children were not implanted in the first years of life. In pediatric CI users with bilateral deafness, decline of regular use of the CI over time has been reported to be mainly caused by poor hearing benefit (Contrera et al., 2014). A negative relation exists between duration of unilateral auditory deprivation and speech perception outcomes with the CI (Cohen & Svirsky, 2019). We have high hopes that due to *early* implantation of the children with SSD, hearing benefits will be significant and nonuse can be prevented. CI use can, however, also be negatively influenced by a feeling of stigmatization, which sometimes occurs in older children (Contrera et al., 2014; Thomas et al., 2017). Stigmatization is the result of a negative social reaction by others, which is normally based on lack of sensibility, awareness, and education in the understanding of the health issue (Távora-Vieira & Rajan, 2015, p. 1457, in response to Probst, 2015). We need to be aware of possible feelings of stigmatization in our CICADE participants in the future.

7.2.2 Hearing rehabilitation

The data presented in this thesis are the first data obtained of children with SSD and a CI. Our first data shows that children with SSD and a CI are doing well. However, we do not know whether and to what extent the child with the CI is using the CI, as formal testing with only the CI is not possible yet. The children of the CICADE study do not receive rehabilitation from the implant centers. However, we do encourage the CI children to actively listen with their CI by looking and listening to children's stories (e.g. YouTube) via a tablet and a mini mic provided by the study (Cochlear ltd). It is known that input from the deaf ear is at disadvantage compared to input from the hearing ear because of the cortical aural preference for the hearing ear (Kral et al., 2013; Tillein et al., 2016). Also after cochlear implantation, the NH ear likely plays a dominant role in listening in daily life. It is therefore important to actively stimulate the brain hemisphere contralateral to the CI ear to process input from the

CI. In that way the residual cortical responsiveness to the deaf ear is exploited and normal contralateral cortex activation in reaction to input from both ears can be restored (Polonenko et al., 2017).

Although children with SSD are not entitled to speech therapy, 3 out of the 18 children with SSD (2 with and 1 without CI) reported on in study 3 (chapter 6) do receive therapy (speech/language/hearing) following individual efforts of the parents. To our knowledge, currently 7 children (6 with and 1 without CI) receive therapy of the total group of 31 children with SSD in the CICADE study. We expect that speech therapy promotes a child's speech- and language abilities and thus can positively influence language development. We always encourage parents to promote language growth by interacting with and reading with their child a lot.

All children with hearing impairment, including the ones with SSD, are entitled to home guidance in Flanders (Lichtert et al., 2016). Most of the SSD_CI children and a few SSD_noCI children also receive home based guidance. This is – for children of this young age – predominantly focused on the questions of the parents (and indirectly other family members and teachers) regarding the hearing loss. A home based guidance counselor keeps track of possible emerging difficulties in the (speech/language) development or daily experiences of the child that require additional help or resource and provides solutions to difficult hearing situations and assistance with the CI (battery, programs, connection to other devices/software).

7.3 Future research directions

The longitudinal CICADE study is ongoing at the moment. The protocol will be adjusted with time according to the respective ages of the participants.

In the linguistic domain, two tests assessing **phonological skills** are added to the comprehension, vocabulary and syntax tests when the children turn 4 years of age. In our opinion, phonological outcomes are very important to measure. We hypothesize that segmenting the speech stream into individual speech sounds, learning how to articulate these and when to use them is particularly difficult in children with (unaided) SSD because of suboptimal perception of soft speech sounds, as we stated on page 34. Deviating performance of the unaided SSD groups on the morphological tasks in study 1 and study 3 – which depend heavily on phonological skills – support this idea, as does the finding in the vocabulary test in study 1 showing that children with unaided SSD more often than NH controls answered with an incorrect word that *sounded* like the target word. The first phonological test we add to the CICADE protocol is the Metaphon test (Dean et al., 2002), in which presence of phonological simplifying processes is assessed. We expect children of the SSD_noCI group to show more use and longer duration of use of simplifying processes, compared to NH children. The children with SSD and a CI are expected to show less difficulties in this regard, because of the CI improving their perception of sounds and thereby promoting mastery of phonological skills. Second, in a sub test of the Schlichting battery (Schlichting & Spelberg, 2010b) exact repetition of words and non-words of increasing difficulty is assessed, which draws on receptive phonological skills. This test is expected to differentiate as well, because of the importance of perceiving every sound of the word in this task. It would be very interesting to also add an expressive task assessing phonological awareness (i.e. the skill to manipulate word form independently of its meaning), e.g. with sub tests of the comprehensive test of phonological processing (blending non-words and segmenting non-words) as used by Ead et al. (2013) in teenagers with UHL (currently not translated and validated for the Dutch language).

When the children are old enough, **executive functions** such as sequential processing, sequence learning, concept formation and complex working memory will be assessed. These skills have been shown to be highly dependent on auditory experience and language skills and are therefore at risk in children with hearing loss (Kral et al., 2016), but have not – with the exception of complex working memory (Ead et al., 2013) – been assessed in children with SSD or UHL before.

We have currently started with assessment of **speech in noise understanding (SPIN) and localization abilities** in the first implanted child, two children of the SSD_noCI control group and a small group of NH controls (n=7 to 10). Our efforts (will) add to the existing literature because we not only compare to CI off performance but also to performance of the children of the two control groups. SPIN skills are assessed with the limited-set Leuven Intelligibility Number Test, (LittleLINT, a subset of the LINT; van Wieringen & Wouters, 2008), an adaptive task with single digits in continuous speech weighted noise. Sound localization abilities are assessed with a telephone game in which a 1 sec broadband bell-ring is presented from one of nine loudspeakers between -60° to 60° azimuth. For a description of the methods, see Van Deun et al., 2010, 2009. A graphical presentation of our first SPIN results can be found in figure 7.1.

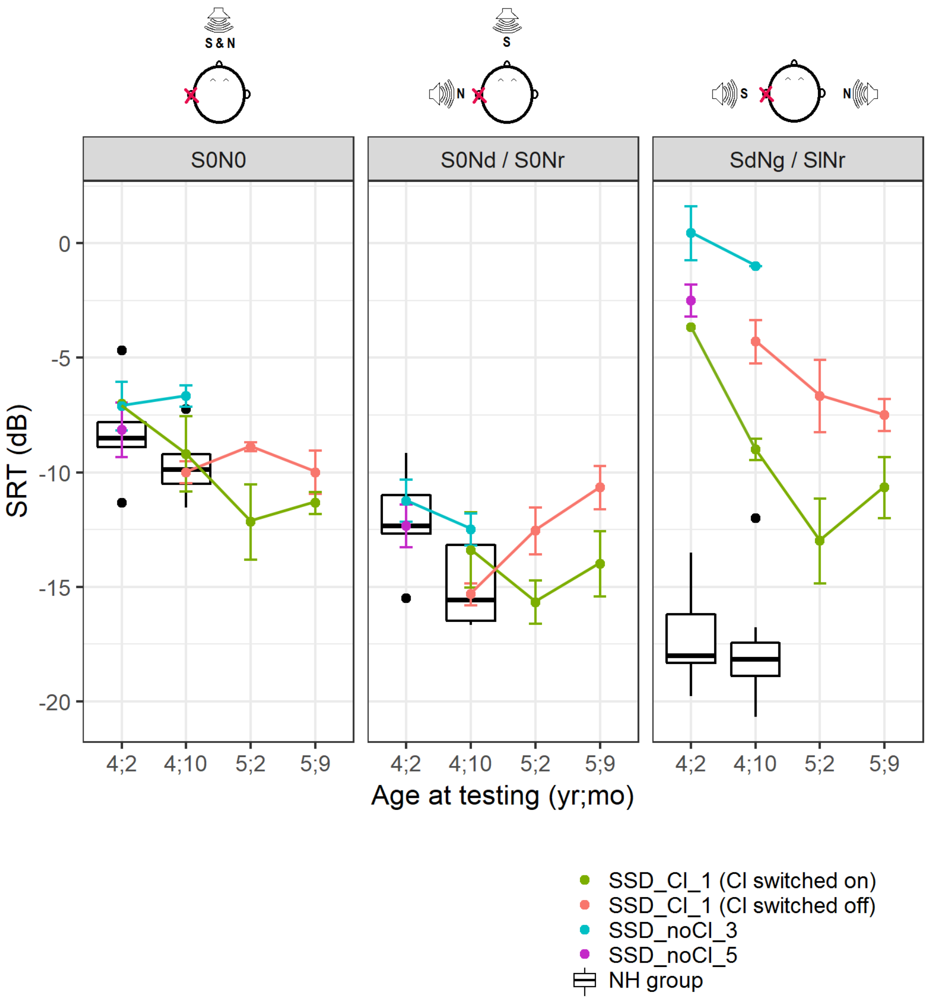

Figure 7.1. SRTs in dB on the LittleLINT for the three different spatial configurations. Colored dots: performance of the 3 SSD children. Error bars: ± 1 SD. Connected data points belong to the same child. Boxplots: distribution of the NH control children's SRTs (interquartile range with a thick line at the median value, whiskers extending to the highest and lowest values no greater than 1.5 times the interquartile range, outliers depicted with a black dot), resp. n=9 and n=8 for age 4;2 and 4;10.

In short, results of a first tested child, SSD_CI_1, show encouraging audiologically relevant (>1.5 dB (Thomas et al., 2017)) differences in performance with CI switched on compared to CI switched off in different spatial conditions. When the speech signal was presented to the deaf side and noise to the good ear (one of the most complicated daily life situations for persons with SSD), performance of child SSD_CI_1 deviated substantially from performance of the NH control group at his first testing at age 50 months, but seemed to improve a lot from age 50 to age 69 months (and much more so than with CI turned off). This result is not indicative of binaural hearing but might indicate that the child can make use of the better-ear-effect. As of yet, neither SSD_CI_1 nor SSD_noCI_3 and 5 showed evidence for localization abilities. We emphasize, however, that the speech in noise understanding and localization data present single-case descriptions and therefore no conclusions can be drawn. Our future measurements in all CICADE participants and corresponding statistical analyses will be very important with regard to drawing conclusions about CI benefit and binaural hearing skills.

An important outcome of our research is the children's **subjective benefit** of the CI, because this eventually determines whether the CI is an asset to their general wellbeing. Also, subjective benefit will likely determine how much the children wear their device in daily life. We feel it is important to asses 1) hearing abilities and difficulties in daily life and 2) perceived QOL. Currently, hearing abilities in daily life are measured in the CICADE study by parent proxy, by means of the PEACH+ and for the children under 2 (data not shown) by the Littlears questionnaire. The PEACH+ and Littlears questionnaire are not specifically focused on binaural hearing and may therefore not be able to pick up CI benefit. Research in the field utilizes the SSQ, as we did in study 1 (chapter 3), in which domains relevant to SSD are assessed (spatial hearing, speech understanding, listening effort). For adults, the Bern Benefit in Single-Sided Deafness Questionnaire is available, which was originally developed to measure benefit of a BAHA in this patient population and could possibly also be translated and adjusted for use with children. Regarding QOL, surveys such as the HEAR-QL questionnaire are generally used from age 7 onwards. We will need to decide which surveys to implement into the CICADE protocol, in which form and at which age, in order to effectively assess (spatial/speech) hearing quality in daily life and perceived quality of life after implantation.

Participants are encouraged to wear their CI as much as possible and to actively listen with their CI, via stimulation of the CI separately from the normal ear. **Training** procedures may further facilitate (at least some) binaural hearing development (Tillein et al., 2016). At ExpORL, a game was developed to train binaural abilities of hearing impaired adults based on ITDs and ILDs. In the game, a moving sound is presented while, on the screen of the tablet, a helicopter passes by from left to right (or vice versa) carrying a log. When the sound is perceived in the middle of the head the participant activates a button to drop the log. After a set of successful responses the paradigm is continued without visual cues (the helicopter disappears). In the near future, this tool will be validated for acoustical-electrical stimulation and adapted to the interests and attention span of young children.

Potential other research could investigate how the CI influences music appreciation in children with SSD, which can affect well-being (Meehan et al., 2017) and could be a possible domain in transferable training (White et al., 2013). Interestingly, Peters et al. (2018) asked adults with acquired SSD and a CI to listen with their non implanted ear to simulations of CI sound (speech and music) and rate the similarity of that sound to the sound of their CI ear. Patients with SSD and a CI indeed form a unique population, being able to compare these two sounds. It would be interesting to see whether results of early implanted children with congenital SSD differ from those of Peters et al. (2018).

7.4 General conclusions

Our research showed that the language and hearing difficulties in school-aged children with unaided SSD are significant and should not be overlooked but rather warrant intervention. We have set up a longitudinal study to assess possible CI benefit in children with SSD implanted at a very young age. We developed a protocol to follow the development of these young children and focus not only on spatial hearing skills but also on linguistic and cognitive development. An important strength of the study is its between-subject design in which performance of the children with CI is compared to those of children with SSD but no CI and to NH peers. Data of the first implanted children as of yet are very encouraging, but long term observation is of key importance in order to draw conclusions with regard to CI benefit. The present thesis provides the first step towards our goal of forming a well-founded advice to the Belgian National Health Insurance (RIZIV/INAMI) concerning reimbursement of a CI for young children with SSD.

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Appendices

Appendix I - Examples of incorrect responses in study 1

WS: Error Category	Assignment	Target response	Erroneous response
1: only–lexeme	Dit is een boom en dit is een klein…	boompje	boom
2: related–neighbour	Een kuiken, twee…	kuikens	kuikentjes
3: related–overgeneralization	Een ei, twee…	eieren	eien
4: related–other	Dit meisje is het…	snelst	heel sneller
5: incorrect gender/number	Zij zeggen, de hond is van…	ons	mij
6: incorrect lexical category	De jongen heeft een bal. De bal is van…	hem	hij
7: not related	Het meisje bouw een raket. Dit is de raket die ze heeft…	gebouwd	gemaakt
8: neologism			
9: no answer			

Error Category EOWPVT	Target word	Erroneous Response
1: related meaning general	wortel	groente
2: related meaning neighbour	rechthoek	vierkant
3: related meaning specific	post	brief
4: related sound	statief	statiek
5: circumlocution	acquarium	voor de visjes
6: not related	pincet	naald
7: neologism	telescoop	skylofoon
8: no answer		

Appendix II - Additional statistics to study 2, p. 78-79

Spearman's rho correlation coefficients between LENA and Bayley & N-CDI data.

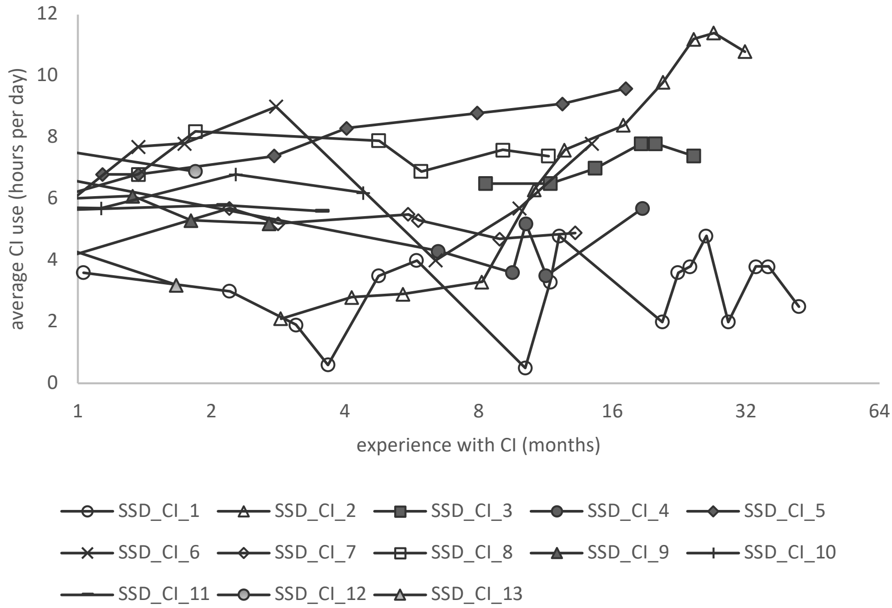
	LENA-CVC			LENA-AWC			LENA-CTC		
	7-11m n=11	12-17m n=23	18-23m n=14	7-11m n=11	12-17m n=23	18-23m n=14	7-11m n=11	12-17m n=23	18-23m n=14
Bayley-LC									
Bayley-LP		.52 p=.011							.70 p=.008
N-CDI-RV									
N-CDI-EV*		.54 p=.008							.69 p=.007

Spearman's rho correlation coefficients between Bayley and N-CDI data and, within both, between receptive and expressive data.

	Bayley-LC			Bayley-LP			N-CDI-RV		
	7-11m n=11	12-17m n=23	18-23m n=14	7-11m n=11	12-17m n=23	18-23m n=14	7-11m n=11	12-17m n=23	18-23m n=14
Bayley-LC									
Bayley-LP			(.63) p=.021						
N-CDI-RV			.77 p=.001						
N-CDI-EV*		(.48) p=.021	.65 p=.012			.80 p=.001		.69 p<.001	(.61) p=.022

Note. Correlation coefficients are presented separately for data collected from the children at 7-11 months, 12-17 months and 18-23 months of age. Trend effects are presented in brackets.

Appendix III - Average CI use CICADE participants



Average CI use (hours per day). Every data point represents the average use since the last data point. Data points of a single child are connected.

Participant	CI experience (months)	Average hours per day ± SD
SSD_CI_1	42,1	3,0±1,3 *
SSD_CI_2	31,8	7,0±3,7
SSD_CI_3	24,5	7,2±0,6
SSD_CI_4	18,8	4,7±1,2
SSD_CI_5	17,2	8,1±1,1
SSD_CI_6	14,4	7,0±1,6
SSD_CI_7	13,2	4,5±1,6
SSD_CI_8	11,5	6,8±1,3
SSD_CI_9	2,7	6,1±0,8
SSD_CI_10	4,4	6,2±0,4
SSD_CI_11	3,6	5,6±0,2
SSD_CI_12	1,8	6,9±0,7
SSD_CI_13	1,7	5,1±1,2

* Hours of use relatively low because of family related issues.

Addendum

During the PhD training, the author had the privilege to be involved in, or contribute to, different other projects. This work was outside the scope of the main project and is therefore mentioned in addendum.

The LENA system – validation for the Dutch language

Published as: Busch T., **Sangen A.**, Vanpoucke F., van Wieringen A. (2018). Correlation and agreement between Language ENvironment Analysis (LENA™) and manual transcription for Dutch natural language recordings. *Behavior Research Methods*, 50(5), 1921-1932.

The author contributed to the design of the experiment and collection of the data.

Abstract

The Language ENvironment Analysis system (LENA™) automatically analyzes the natural sound environments of children. Among other things, it estimates the amounts of adult words (AWC), child vocalizations (CV), conversational turns (CT), and electronic media (TV) that a child is exposed to. To assess LENA's reliability, we compared it to manual transcription. Specifically, we calculated the correlation and agreement between the LENA estimates and manual counts for 48 five-min audio samples. These samples were selected from eight day-long recordings of six Dutch-speaking children (ages 2–5). The correlations were strong for AWC, r =. 87, and CV, r =.77, and comparatively low for CT, r =. 52, and TV, r =. 50. However, the agreement analysis revealed a constant bias in AWC counts, and proportional biases for CV and CT (i.e., the bias varied with the values for CV and CT). Agreement for detecting electronic media was poor. Moreover, the limits of agreement were wide for all four metrics. That is, the differences between LENA and the manual transcriptions for individual audio samples varied widely around the mean difference. This variation could indicate that LENA was affected by differences between the samples that did not equally affect the human transcribers. The disagreements and biases cast doubt on the comparability of LENA measurements across families and time, which is crucial for using LENA in research. Our sample is too small to conclude within which limits LENA's measurements are comparable, but it seems advisable to be cautious of factors that could systematically bias LENA's performance and thereby create confounds.

Congenital UHL - review of the most recent evidence on the consequences for auditory and neurocognitive factors

Published as: van Wieringen, A., Boudewyns, A., **Sangen, A.**, Wouters, J., & Desloovere, C. (2019). Unilateral congenital hearing loss in children: Challenges and potentials. *Hearing Research*, 372, 29–41.

The author contributed to the writing of this paper.

Abstract

The estimated incidence of sensorineural hearing impairment (>40 dB HL) at birth is 1.86 per 1000 newborns in developed countries and 30-40% of these are unilateral. Profound sensorineural unilateral hearing impairment or single sided deafness (SSD) can be treated with a cochlear implant. However, this treatment is costly and invasive and unnecessary in the eyes of many. Very young children with SSD often do not exhibit language and cognitive delays and it is hard to imagine that neurocognitive skills will present difficulties with one good ear. In the current paper we review the most recent evidence on the consequences of unilateral hearing impairment for auditory and neurocognitive factors. While data of both adults and children are discussed, we focus on developmental factors, congenital deafness and a window of opportunity for intervention. We discuss which etiologies qualify for a cochlear implant and present our multi-center prospective study on cochlear implants in infants with one deaf ear. The large, state-of-the art body of research allows for evidence-based decisions regarding management of unilateral hearing loss in children.

Monaural sound localization

Under review as: Snapp, H., **Sangen, A.**, Snels, C., Wesarg, T., Kuntz, I., Zarowski, A., Theunen, T., van Wieringen, A., Agterberg, M. (2019). Sound localization for the monaural hearing condition: the limitations of a single stimulus level. *Clinical Otolaryngology*.

The author contributed to the design of the experiment, collection of the data and analysis of the data.

Abstract

Objectives: Sound localization is a key outcome measure in the evaluation and management of individuals with unilateral hearing impairment. In monaural listeners, spatial hearing is poor. Still, it has been well documented that monaural spectral and head-shadow cues provide information for sound localization in monaural listening situations, especially in familiar environments. An increasing number of studies provide evidence that sound localization performance can be enhanced through training. The aim of the present study is to demonstrate how information and feedback about the participant's localization ability, rather than training per se, can bias localization outcomes in acute monaural listeners.
Design: Normal hearing participants (n=39) were tested. Instant adaptation to stimulus level cues is demonstrated by a short duration (<25 min) experiment consisting of four listening conditions investigating effects of sound level and prior knowledge on monaural sound localization in azimuth.
Results: Results demonstrate that monaural sound localization improved when stimuli were presented at one level and deteriorated immediately after roving the stimulus level.
Conclusions: The present study demonstrates that the monaural sound level cue can be used instantly to improve the sound localization accuracy, especially in an unrealistic listening situation were sounds are presented at one single sound level.

List of publications

Research articles in internationally reviewed academic journals

Published

- **Sangen, A.**, Dierckx, A., Boudewyns, A., Dhooge, I., Offeciers, E., Wouters, J., Desloovere, C., van Wieringen, A. (2019). Longitudinal linguistic outcomes of toddlers with congenital single sided deafness – six with and twelve without cochlear implant and nineteen normal hearing peers, *Clinical Otolaryngology*, 00, 1-6. doi:10.1111/coa.13347
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Submitted

- **Sangen, A.**, Boudewyns, A., Van Hoecke, H., Offeciers, E., Wouters, J., Desloovere, C., van Wieringen, A. (2019). Relationship between outcome measures of communicative skills and language environment in normal hearing and hearing impaired infants under age 2. *Journal of Child Language*.
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Contributions to conferences

- **Sangen, A.**, Dierckx, A., Boudewyns, A., Dhooge, I., Offeciers, E., Wouters, J., Desloovere, C., van Wieringen, A (2018). How do we assess communicative skills in children under the age of 2, following early cochlear implantation for congenital single sided deafness? B-audio meeting 2018, Antwerp (Belgium), 23-11-2018.
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Personal Contribution

Anouk Sangen has contributed to the design, data acquisition, data analysis, and data interpretation of the studies included in this doctoral thesis, and to the drafting of the articles.

Conflict of Interest Statement

The author and co-authors of this doctoral thesis declare that the studies were conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Tine (Arras), nu is het aan jou ☺ Je hebt (mijn gedeelte van) het CICADE project nu al een tijdje van me overgenomen en je bent supergoed bezig!! Veel plezier en succes met het opvolgen van onze kindjes. Ik kan niet wachten om te zien wat de resultaten zijn die jij gaat vinden tijdens jouw doctoraatstijd. Keep me posted ;-)

Anouk, 1 juni 2019

About the author

Anouk Sangen was born on April 30, 1989, and grew up in Maastricht (the Netherlands). She graduated from secondary school (VWO) in June 2008. In the same year she started her Bachelor studies in Psychology at Maastricht University, followed by the Research Master in Cognitive and Clinical Neuroscience. She obtained her Master's degree, with a specialization in Neuropsychology, in October 2013. During her studies, she completed a research internship at the Behavioral Science Institute of the Radboud University Nijmegen, focused on motor imagery ability in children with unilateral cerebral palsy (an ERP approach), as well as a clinical internship at the medical Psychology department of Maastricht University Medical Centre (MUMC+), where she mainly worked with people with acquired brain injury. After her studies, Anouk worked as an assistant psychologist at the Medical Psychology department and the Memory Clinic of MUMC+, until April 2014. She then worked as a research assistant at Maastricht University, research group Developmental Cognitive Neuroscience, until September 2014. In October 2014 she started her PhD at KU Leuven, Research Group Experimental Otorhinolaryngology. Her studies focused on children with single sided deafness, aiming to contribute to the knowledge about the difficulties they experience and to start the longitudinal research into the benefit of cochlear implantation as a possible remediation. During her time as a PhD student she was an Early Stage Researcher in the ITN Marie Curie European project 'Improving Children's Auditory Rehabilitation' (iCARE), from October 2014 to December 2017.