Plasticity of the auditory modality

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Martina Feierabend

aus München, Bayern

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Dekan der Math.-Nat. Fakultät: Prof. Dr. Thilo Stehle

Dekan der Medizinischen Fakultät: Prof. Dr. Bernd Pichler

1. Berichterstatter: Prof. Dr. Dr. Hans-Otto Karnath

2. Berichterstatter: Prof. Dr. Stephan Huber

3. Berichterstatter: Prof. Felix Wichmann Dphil

Prüfungskommission:
Prof. Dr. Cornelius Schwarz

Prof. Dr. Stephan Huber

Prof. Felix Wichmann Dphil

Prof. Dr. Dr. Hans-Otto Karnath

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Abbreviations

- ANOVA: analysis of variance
- CI: cochlear implant
- Ci: confidence interval
- CPP: cocktail party problem
- SD: standard deviation
- LMM: linear mixed-effects model
- SOA: stimulus onset asynchrony
- SSD: single-sided deafness

List of contributions

I am the sole author of the here presented monography. In the process of developing the ideas for the different studies, their execution and subsequent analysis, further people were involved. Their contributions are mentioned for each of the individual studies of this thesis.

Horizontal sound localization in acoustically complex situations in blinds

Martina Feierabend, Hans-Otto Karnath, Jörg Lewald, Ida Zündorf, Peter Dillmann

HOK and JL designed the study; PD prepared the software and parts of the electronic equipment; IZ recruited and measured the controls; MF recruited and measured the blind subjects; MF, HOK and JL analyzed the data. MF wrote the corresponding part of this monography. This work is published under: Auditory Space Perception in the Blind: Horizontal Sound Localization in Acoustically Simple and Complex Situations, Perception (2019): 0301006619872062.

Effects of training on the visual processing speed in deafs

Martina Feierabend, Katherine E. Lawrence, Julius Gervelmeyer, Hans-Otto Karnath

HOK designed the study; during an internship at the Center of Neurology, Division of Neuropsychology, University of Tübingen funded by the DAAD, KL created the software which included the stimuli for the experiments; JG recruited and measured the controls as part of his bachelor's thesis for a Bachelor of Science; MF recruited and measured the deaf subjects, MF analyzed the data, MF wrote the corresponding part of this monography.

Long-term impact of implantation of a unilateral cochlear implant in single-sided deafness on target sound localization in multiple-sounds environments

Martina Feierabend, Hans-Otto Karnath, Ida Zündorf, Anke Tropitzsch, Lina Maria Serna Higuita, Peter Dillmann

HOK designed the study, PD prepared the software and parts of the electronic equipment, IZ recruited and measured the controls, MF recruited and measured the SSD-patients, LH helped to setup and interpret the linear mixed-effects models, MF and HOK analyzed the data, MF wrote the corresponding part of this monography.

Summary

The human brain shows remarkable abilities to adapt to change. This faculty, called neuroplasticity is the driving factor enabling an organism to respond to development, experience and physiological changes. It is a lifelong property of the brain that takes place on various macro- and microscopic levels. Neuroplasticity can occur within a local neural network but it can also take place cross-connecting different brain regions responsible for different functions. Two highly interconnected neural systems are the visual and auditory system. The behavioral relevance of their interconnection becomes especially prominent in the ability for spatial orientation. A loss or a reduced function in one of these two systems has repeatedly been reported to affect the functionality of the remaining intact system. This thesis investigated qualitative and quantitative effects of neuroplasticity of the auditory system for three defined deficitary situations: blindness, deafness, and single-sided deafness as a unilateral loss of a paired sensory organ. The first study tested the ability of horizontal sound localization in blinds when compared to sighted controls using simple and complex acoustic sound scenes. Behaviorally relevant auditory abilities have been shown to be enhanced in blinds, such as auditory motion processing. The localization of a sound-source among multiple distractor sounds is such a frequent and behaviorally relevant task for blinds. It was thus hypothesized that blinds outperform sighted controls in horizontal sound-localization in acoustically complex situations. Unexpectedly, the performance of blind subjects was not better than the one of sighted controls but it was found to be on a comparable level. This finding might, however, be explained by the fact that blinds do not possess the ability to calibrate their auditory space by visual feedback. They, therefore, have to rely on other compensatory mechanisms to counteract the effects of the lost visual modality. To perform on a comparable level as sighted controls can thus be interpreted as compensatory neuroplasticity. The second study investigated in congenital deafs and hearing controls the trainability of processing fast-presented visual stimuli in three experimental conditions: As visual stimuli masked squares, everyday objects, and fast-forwarded videos were trained for several days. Testing was performed before and after the training phase. It had already been demonstrated that blinds can learn faster to understand highly accelerated speech when compared to sighted controls. This observation was attributed to cross-modal reorganization of the brain as a result of blindness. For the present study, it was thus hypothesized that with training the performance of deaf subjects on such tasks would increase

faster than in hearing controls. After training, deaf subjects indeed showed a significantly better performance than hearing controls for the most difficult task, the fast-forwarded videos. The performance in the easier tasks was comparable between both groups. It thus appears that it is especially in complex visual situations that a supposed cross-modal reorganization of the brain enables deafs to quicker adapt to new visual conditions when compared to hearing controls.

Locating the spatial origin of a target sound among various distracting sounds represents an enormous challenge for the auditory system. Normal-hearing individuals can localize horizontal sound by processing various physical auditory cues largely depending on binaural input. Since many of these cues are not possible with monaural hearing, single-sided deaf subjects show great localization errors when trying to pinpoint a target sound. A unilateral cochlear implant helps these patients to reestablish a certain degree of binaural hearing. The final study examined the development over time of spatial localization ability in postlingually single-sided deaf adults who received a cochlear implant. Testing took place in a single- and in a multiple-sound sources condition before implantation and in the postoperative course. It was hypothesized that the cochlear implant would enable single-sided deaf subjects to localize sounds again. Before implantation sound localization was indeed only possible with respect to sounds originating on the side of the healthy ear, while identifying the horizontal source of a sound originating on the affected side was merely guesswork. After surgery, the unilateral cochlear implant enabled patients in their postoperative rehabilitation to regain access to the full horizontal auditory space. It can thus be concluded that a unilateral cochlear implant helps to reestablish binaural sound localization. Since the signal coming from the implant is highly different in its auditory quality from normal sound input, this relearned ability strongly suggests that it is neuroplasticity which allows subjects with an initially properly developed sensory modality to relearn its functionality after loss in adulthood.

Compensatory neuroplasticity can thus occur within a single modality but also cross-modally. It appears, that it is especially in demanding situations that cross-modal reorganization can be measured. Interestingly, in all three studies neuroplasticity could be experimentally demonstrated in behaviorally relevant situations. Since, by definition, these behaviorally relevant situations are also those that strongly affect people in their everyday life, future investigations might try to further delineate their underlying neural interplay.

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1 Introduction

The human brain shows remarkable abilities to adapt to change. This intrinsic feature is commonly referred to as neuroplasticity and represents a lifelong property of the brain. Neuroplasticity can be seen as evolution's response of the nervous system to the restraints of its own genome: It enables the organism to respond to development, experience and physiological changes and is, therefore, a way to cope with environmental pressure (Pascual-Leone et al., 2005). Neuroplasticity encompasses dynamic alterations on different organizational levels, on morphological and physiological scales as well as changes in both strength and connectivity between different cortical and subcortical structures.

Several factors can induce neuroplasticity, for example experience, aging of the brain with its decaying sensory systems, damage or injury to the brain (for example the aftereffects of strokes or lesions) or reduced (for example sensorineural hearing loss) or even lacking or lost functionality (for example blindness, deafness) of sensory systems. Neuroplasticity represents the coping strategy of the brain to induce cortical reorganization that eventually leads to adaptive compensatory functionality. Many studies on cortical reorganization focus on behaviorally beneficial aspects of neuroplasticity. Nevertheless, neuroplastic changes can also result in no behaviorally measurable effects or they can be maladaptive. This thesis will focus on the plasticity of the auditory modality in defined deficitary situations.

1.1 Neuroplasticity

The umbrella term neuroplasticity describes the ability of the central nervous system to adapt to changes in the environment and the internal milieu (Zilles, 1992; Pascual-Leone et al., 2005; May, 2011; Nudo and McNeal, 2013; Sharma et al., 2013). This intrinsic and lifelong property (Elias and Wagster, 2007; Moore and Linthicum Jr, 2007; Merzenich et al., 1996) of the synaptic organization of the nervous system encompasses a broad multitude of different aspects and functions ranging from the molecular level and genetics to changes at the cellular level up to cognitive strategies on a macroscopic level (for example addiction: Badiani and

Robinson, 2004 or stress: Davidson and McEwen, 2012). Additionally, these neuroplastic changes influence each other and are interdependent (Shaw and McEachern, 2013). On the molecular and cellular level neurotrophic factors represent important mediators of adult neuroplasticity (Kowiański et al., 2018; Leal et al., 2017). Neurotrophic factors are involved in dynamic alterations of the anatomy of axons and dendrites, the formation of synapses (Parkhurst et al., 2013; Poo, 2001) or neurotransmitter release (Leal et al., 2017; Fritzsch et al., 2016). Neuroplasticity also occurs on the level of membranes (Forsyth et al., 2015) and synapses (Marrone and Petit, 2002; Collingridge et al., 1983). The changing nature of afferent nerval input and efferent demand can lead to recruitment of previously not recruited neural networks (Sadato et al., 1998, 1996) and altered functional connectivity between neural connections and networks (Paraskevopoulos et al., 2015). Furthermore, neuroplasticity has altering effects on the sensory systems and their cortical map representation (for example auditory: Pantev et al., 1998, visual: Rauschecker, 2001, somatosensory: Mogilner et al., 1993, motor: Sanes and Donoghue, 2000). Additionally, neuroplasticity can also affect and alter behavioral strategies (Kolb and Gibb, 2008) that allow for a better adaptation to environmental demands. Neuroplasticity occurs in many different shapes, but the driving force behind it is related to synaptic changes (Kolb and Gibb, 2014, Caroni et al., 2012).

Three general types of plasticity have been categorized in the normal brain (Kolb and Gibb, 2014): experience-expectant, experience-dependent and experience-independent plasticity. The first two types mainly delineate developmental neuroplasticity. Experience-expectant neuroplasticity describes those sensory experiences that are required for a system to develop, for example the ocular dominance of the visual system (Wiesel and Hubel, 1963; Kolb and Gibb, 2014). Experience-independent plasticity mainly encompasses developmental processes which are independent of sensory input, for example the development of the lateral geniculate nucleus (Campbell and Shatz, 1992; Kolb and Gibb, 2014). The final form of plasticity, experience-dependent plasticity, describes a subtype which enables the neural system to adapt to its environment by incorporating changes in an already existent neural ensemble (Kolb and Gibb, 2014). An example of this type of plasticity is learning. Experience-dependent plasticity leads to increases or decreases in the number of synapses which in turn can result in behavioral changes (Kolb and Gibb, 2014). This thesis will mainly focus on the experience-dependent type of neuroplasticity.

For the purpose of functional classification of neuroplasticity, Grafman and colleagues (Grafman and Litvan, 1999; Grafman, 2000) additionally proposed the following four subtypes of neuroplasticity: 1. Homologous area adaptation, where the homologous region in the opposite hemisphere overtakes a certain process. 2. Cross-modal reassignment which involves the introduction of new inputs into a representational brain region that has been deprived of its main inputs. 3. Map expansion which delineates the functional expansion of a brain region. 4. Compensatory masquerade that describes the novel allocation of specific processes to perform a task which had been done before by a now no longer functional system. Röder and Rösler (2004) also suggest an additional type of neuroplasticity which differentiates between intramodal and cross-modal neuroplasticity. This thesis will work with the suggested classification of Grafman and colleagues since its classificatory scheme is best applicable to the neuroplastic matters discussed in this thesis.

Neuroplastic changes are interdependent (Shaw and McEachern, 2013). Therefore changes is one system are most likely to affect the remaining systems as well. A large body of research investigated the subsequent effects of reduced, lost, or lacking function of sensory modalities and their associated sensory maps (Buonomano and Merzenich, 1998; Cruikshank and Weinberger, 1996; Pons et al., 1991; Renier et al., 2014; Kaas, 1991). In particular, the cortical reorganization induced by blindness or deafness as well as the continuing success of neuroprosthetic devices such as the cochlear implant (CI) or the retina implant show that the formerly held belief of the brain as a rigid and stiff organ, once finished with maturation (for example y Cajal, 1959), does not withstand. The work of Wiesel and Hubel (Wiesel and Hubel, 1963; Hubel and Wiesel, 1963), the discovery of long-term potentiation (Bliss and Lømo, 1973) or the discovery of neurogenesis in the adult brain (Eriksson et al., 1998; Gage, 2002; Alvarez-Buylla and Garcıa-Verdugo, 2002) have shifted the understanding of the brain and help to establish a picture of the brain as a lifelong dynamic organ. To better understand the mechanisms of neuroplasticity, it is essential to highlight its necessity. To this end, it is helpful to take a look at the broader picture and consider the brain as the result of a long evolutionary biological process (Shettleworth, 2010). Shettleworth (2010) describes the role of the brain as the essential unit to create behavior in order to enable an organism to interact with its environment. To ensure survival of an organism and compensate for potential genetic shortcomings, the organism needs to have a certain degree of flexibility. This is where neuroplasticity comes in (see also Kolb and Gibb, 2014). Neuroplasticity enables the brain to adapt to internal and external changes and therefore enables the organism to survive. It thus makes sense from an evolutionary point of view that first, neuroplasticity is a lifelong process and second, that it occurs on multiple levels to ensure the highest degree of flexibility.

1.2 Audio-visual integration as an example of multisensory interaction

Humans stand in continuous interaction with their immediate environment. Of special importance is a continued update of environmental signals that enable the organism to detect changes in sensory inputs and adapt its resulting behavioral goals (Stein and Meredith, 1993; King and Palmer, 1985; Shettleworth, 2010; Whitmire and Stanley, 2016). In order to do this, humans have multiple sensory channels where each sense provides a unique qualitative sensory input. The transformation of sound waves into an auditory signal in the auditory modality or the transformation of discrete photons reaching the retina into a meaningful visual perception are just two examples. There is no counterpart for the perception of a sound wave in the visual system nor does the auditory system react to photons (Kandel et al., 2012, p. 456). Many natural objects often stimulate more than one sensory modality and are perceived by multiple senses and allow the brain to extract multiple facets of a specific object. Gibson (1966) therefore called perception as being multisensory. Multisensory integration (or also cross-modal integration) is essential to recognize that different types of sensory input belong to the same object. Multisensory integration is here defined as activity which is elevated by one stimulus and that can be modulated by a stimulus from another modality (Macaluso, 2006). Multisensory integration is also found on the level of neurons where it describes their response behavior: Neurons are said to be multisensory if neural activity elicited by one stimulus can be modulated by a stimulus from another modality (Macaluso, 2006). This way, multisensory integration helps to increase the saliency and perceptual reliability of an object (for example Talsma et al., 2010; Sumby and Pollack, 1954; Summerfield, 1992). Multisensory integration does not only complement each other, it also offers overlapping yet distinct information on a perceptual object.

Multisensory integration has been well studied for the auditory and visual system. Audio-visual integration has been reported to facilitate behavior by speeding up reaction times or changing the perceptual quality of a stimulus such as in the McGurk illusion (McGurk and MacDonald, 1976) or the ventriloquism effect (Alais et al., 2010). The McGurk illusion describes a non-coherent percept between an auditory and a visual signal, where the perceived sound does not match the seen lip movement. The viewer assumes to "have heard" the observed sound instead of the actually heard sound. The ventriloquism effect describes the misinterpretation in case of a spatial discrepancy between the auditory and the visual cue. These auditory cues are spatially perceived as coming from that position where the visual cue is seen. Bertelson and Radeau (1981) showed that when auditory and visual stimuli are presented synchronously but the visual stimulus is slightly displaced relative to the auditory stimulus, then the perceived location of the sound source is thought be found at the position of the visual stimulus. In case of ambiguity or discrepancies between sensory input, the system prevails which is known to obtain more reliable information for the given situation (Dahmen and King, 2007). In the reported cases, vision, as the modality with the highest spatial acuity, prevails in the interpretation of the spatial ambiguity between visual and auditory information. When comparing the visual and the auditory system, the auditory modality is considered to be the modality with the higher temporal accuracy (Dahmen and King, 2007). When a single visual flash is accompanied by a sequence of auditory beeps, the single visual flash is perceived as multiple flashes (Shams et al., 2000). Audio-visual integration also plays an essential role in the understanding of speech (see Cherry, 1953) or the localization of a sound source (Blauert, 1997; reviewed by

Middlebrooks and Green, 1991).

These examples demonstrate that multisensory integration alters the perceptual information of formerly unimodal sensory input. The sensory information of the auditory modality is influenced by the information of the visual modality and vice versa. Their mutual influence has also been shown on subcortical and cortical levels. A higher firing rate of neurons in the polymodal areas of the superior colliculus and the anterior ectosylvian area in cats was discovered when both the auditory and the visual part of an object fall within the overlapping part of a neuron's receptive field (Kadunce et al., 2001). The firing rate of the multisensory neurons was higher than what would have been expected by the maximum response to either single modality. A comparable finding has been reported for humans (Driver and Spence, 1998). The response properties of multisensory neurons in the superior colliculus in guinea pig in response to audio-visual stimulation had been investigated by King and Palmer (1985). Their response behaviors were significantly altered when both auditory and visual stimulation where simultaneously presented. On a cortical level, Bizley and King (2009) demonstrated that visual input to visually-sensitive neurons in the auditory cortex of ferrets increases the spatial accuracy of perceived objects. Given the polymodal nature of the sensory input and the unimodal and polymodal subsequent processing, the question arises of how and where the sensory integration happens in the brain. Early studies (for example Stein and Meredith, 1993; Felleman and Van, 1991; Jones and Powell, 1970) supported the idea of a hierarchical processing with sensory information converging only in higher association areas and specialized subcortical structures. However, accumulating examples over the last years (e.g Hertrich et al., 2009; Lomber et al., 2015; Ostry and Gribble, 2016; Sadato et al., 1996) have pointed to the fact that formerly perceived unimodal sensory cortices can be modulated by the other modalities and that the hierarchical processing view does not hold true. Since these close connections appear to exist between these different modalities, it is clear that sensory deprivation of one of these systems will also have consequences on the other functional modalities and their subcortical and cortical processing (see also 1.5).

1.3 Sound localization

Sound describes the perceptual result of mechanical vibration that travels through a medium (usually air or water). The compressed medium reaches the recipient organ/system. In humans, the vibration of the medium is channeled through the exterior ear into the ear canal. There, the sound waves set the tympanic membrane into vibration causing the three bones of the middle ear to transmit this vibration through the oval window to the cochlea. In the cochlea, the mechanical energy is changed into a chemical signal by hair cells in the organ of corti, which synapses onto spiral ganglion fibers that travel through the cochlear nerve into the brain (Middlebrooks and Green, 1991). The input from each ear is processed in both the ipsilateral and the contralateral auditory cortices, with the contralateral projection pathway dominating on both a functional and an anatomical level (Møller, 2012). It is the circumstance that humans have two ears with each of them on a different side of the head that enables sound localization (Schnupp et al., 2011, Bronkhorst, 2015). The integration of spatial information about a target sound is computed by the brain. Due to differences in the distance and position of the two ears with respect to the sound source, it can use a set of very subtle differences in intensity and spectral composition as well as timing of when the sound reaches each ear. With this information, the spatial origin of a sound can be calculated. These very subtle spectral differences occur because of the geometry of the head and the external ears (Schnupp et al., 2011). They encompass the interaural time difference, the interaural level difference for sounds from the left or right and also spectral cues. Horizontal sound localization is based on the difference of arrival times between the two ears, on the relative amplitude of high-frequency sounds and on asymmetrical spectral reflections from various body parts (Blauert, 1997). Vertical sound localization relies on the location of specific spectral cues (Middlebrooks and Green, 1991). The equal height of both human ears relative to the head presents the anatomical reason why humans perform better at horizontal sound localization than at vertical (Møller, 2012) (for a review of the other spatial dimensions of sound localization: vertical sound localization, distance and velocity see Middlebrooks and Green, 1991).

The qualitative information obtained through these auditory cues varies within a lifetime of an individual due, for example to the maturation and growth of head and ears. The usability of the different auditory cues depends on the transmitted frequencies (reviewed by Middlebrooks and Green, 1991). Unlike the visual system which can only integrate sensory information that falls into the corridor of the retina, the auditory system can integrate information from any spatial direction relative to the head (Schnupp et al., 2011). In addition to its greater spatial usability, the auditory system is a paired sensory organ, implying that it works best with access to binaural hearing (Møller, 2012). Binaural hearing is not only essential for the localization of sounds, but it also helps in the detection of target sounds against an interfering background (Blauert, 1997; Cherry, 1953). Although sound localization is possible with monaural hearing, spatial accuracy improves with access to binaural information (Schnupp et al., 2011). Hearing loss or auditory deprivation in one or both ears usually results in an qualitatively altered integration of these cues (Dahmen and King, 2007). In these cases, the brain has to adapt to how to weigh these different spatial cues in terms of their reliability (Dahmen and King, 2007).

1.3.1 The cocktail party problem

Under realistic environmental conditions, the localization of a sound source seldom occurs in isolation. In most situations, the target sound source has to be detected among an auditory cacophony. The challenges associated with the detection and localization of a sound source of interest (in humans most often speech) in an auditory setting with multiple distractors is commonly referred to as the cocktail party-problem (CPP, Cherry, 1953. For a review on the role of selective auditory attention, see Bronkhorst, 2015). The CPP is comprised of two subproblems, that are closely interconnected: the first one is the problem of sound segregation. Sound entering the ear comprises the sound sums of all current sound sources in the environment. This sound sum, the mixture of all different sounds, does not yet make much sense to the organism. The first task in the CPP is to derive the properties of the individual sound sources from this sound mix. The second part of the CPP is to now selectively give attention to the sound source of interest while the remaining sound sources in this mix remain unattended (McDermott, 2009).

A neural solution to the CPP comes from the use of different perceptual mechanisms. One of these is a bottom-up segregation mechanism (McDermott, 2009). From a physical point of view a sound is the composition of energy waves at different frequencies. If a mixture of sounds contains energy of various frequencies that start and stop at the same time, it is very likely that these different frequencies belong to one specific sound source. These different energetic frequencies with their statistical regularities are then grouped together and interpreted by the brain as belonging to the same sound (bottom-up integration of auditory spatial information see also: King and Carlile, 1995). There are, however, numerous situations where a mere bottom-up segregation and following integration are not sufficient to identify the sound. In many situations listeners must rely on their prior knowledge about specific sounds (McDermott, 2009). This becomes most visible when trying to understand speech in the CPP. Listeners can better follow coherent sentences in a CPP than the presentation of isolated words (McDermott, 2009). Listeners are also better able to listen to speech when it is given in a familiar accent (McDermott, 2009). In other words, prior knowledge helps to deduce meaning into the sound cacophony. Attentional influences on sensory processing, like in the CPP, are important modulators. The CPP is strongly associated with the top-down mechanism (Bronkhorst, 2015; Woods and McDermott, 2015; Kaya and Elhilali, 2017) with spatial selective attention representing the most important cognitive influence on the processing of sensory information (Gaese and Wagner, 2002). Spatial selective attention is closely connected to sound localization (Gaese and Wagner, 2002; Fritz et al., 2007; Kaya and Elhilali, 2017; Woods and McDermott, 2015). The brain has limited processing capacities and cannot analyze and resolve a complex visual or auditory scene with all of its sensory inputs in all of its details (Gaese and Wagner, 2002). Spatial selective attention helps to resolve this issue. Processing resources are directed towards a sound of interest (for example in a cocktail party setting the opposing speaker, Gaese and Wagner, 2002). This, in turn, results in “attending” the sound source of interest which allows the target sound to receive processing resources. On the other hand, it implies that other temporarily irrelevant sounds are faded out (for example the piano music at the cocktail party setting) (Gaese and Wagner, 2002; Fritz et al., 2007; Woods and McDermott, 2015; Colby and Goldberg, 1999). Even though the CPP appears to occur with such ease in normal-hearing individuals, it represents an enormous challenge to the auditory system (Schnupp et al., 2011). This becomes evident in subjects with single-sided deafness (SSD). These individuals do no longer have access to binaural information. This will massively hamper their ability to localize sound or understand speech (Tokita et al., 2014).

1.4 Neuroplasticity of the auditory modality

The sensory experience of an individual strongly influences structure and function of the underlying neural system. The effects of sensory experience on the neural system are most prominent during infancy with the formation and refinement of the neural architecture. These effects continue over various timescales throughout the life of the individual. Auditory neuroplasticity continues well into adulthood with the neural function and structure adapting to perceptual learning or altered inputs (Dahmen and King, 2007). Auditory plasticity can encompass both subcortical and cortical adaptations. The focus of this thesis will be on the plasticity of the central auditory system.

1.4.1 Plasticity of the developing auditory system

Even though the auditory structures of the brain stem already possess a mature appearance at the end of the perinatal period, the auditory cortex of young infants still looks very different from that of an adult. Its final step in structural axonal maturation will occur by the age of twelve (Moore and Linthicum Jr, 2007). Only at this age is the density of mature axons comparable to that of an adult auditory cortex (Moore and Guan, 2001).The plasticity during this developmental period helps to optimize brain circuits to an individual's sensory environment (Schnupp et al., 2011). Generally, the maturation of the auditory cortex occurs over a longer timescale, especially when compared with other primary sensory cortices (Moore and Linthicum Jr, 2007). This prolonged period could be explained by the anatomical complexity (Moore and Linthicum Jr, 2007) of the auditory system with a continuous need for reevaluation for the the auditory cues due to the growing head. Additionally, the prolonged process of language acquisition also affects the developing auditory system (Moore and Linthicum Jr, 2007).

The maturation of the auditory system is not only a time-intensive process, but in addition it also requires an adequate auditory environment during the critical period (see also Dahmen and King, 2007). This, on the other hand, implies that when an adequate auditory environment is not present during the developmental phase, dramatic consequences for the auditory system of the investigated individual can occur (Kral and Eggermont, 2007; Kral et al., 2001, 2012; Meredith and Lomber, 2011). Rearing rat pups in a continuously moderate-level noise environment leads to a delay in the emergence of the topographic representation order of the primary auditory cortex long beyond the normal developmental period (Chang and Merzenich, 2003). Increases in the cortical area of representation of a restricted frequency range in the primary auditory cortex of adult owl monkeys could be also demonstrated (Recanzone et al., 1993). Recanzone et al. (1993) showed that behaviorally relevant sounds for the monkeys resulted in an altered cortical representation and that attended natural stimulation can modify the tonotopic organization of the primary auditory cortex.

The development of the auditory modality does not occur in isolation but it happens parallel with the other modalities. It takes children up to eleven years to be able to optimally integrate multimodal sensory information (Nardini et al., 2008; Gori et al., 2008; Petrini et al., 2014). The various modalities are co-dependent and require feedback and fine-tuning from the other modalities (Petrini et al., 2014). The consequences of a modality loss are further elaborated in 1.5.1 and 1.5.2.

1.4.2 Plasticity of the auditory system in later life

Especially auditory neuroplasticity is not strictly restricted to the developmental phase. Moore (2002) reports the auditory system to be able to adapt to its input on a lifelong time scale. However, the initializing circumstances, the triggers and the magnitude of neuroplasticity in later life differ. These initializing circumstances and triggers are for example altered perceptual thresholds, hearing impairment or hearing loss, injury to the hearing system, or generally a decaying hearing system (Howarth and Shone, 2006). As pointed out in 1.1, mainly experience-dependent neuroplasticity is the driving force of neuroplasticity in the adult brain. The magnitude of adult neuroplasticity is less in comparison to developmental plasticity (Dahmen and King, 2007). The synaptic turnover in adults is reduced which leads to a reduced general capability for neuroplasticity (Grutzendler et al., 2002; Holtmaat et al., 2005). The reduced synaptic turnover becomes problematic since the formation of new synapses and elimination of old ones is likely to be essential for producing a persistent physical remodeling of neural circuits in the face of changes in the sensory environment (Dahmen and King, 2007). This implies that it is more difficult for a matured auditory system to adapt to different sensory situations. However, when a sufficiently altered sensory experience with a sufficiently large behavioral relevance occurs, then this can lead to considerable neuroplastic changes in the adult brain (Dahmen and King, 2007). One also has to take into account that a more stable system is desirable since it might be a necessity in order to achieve the efficiency and reliability of a mature neural system (Holtmaat et al., 2006).

The most characteristic central auditory plasticity in adults can be observed for the response characteristics of single neurons and the functional organization of groups of neurons (Irvine et al., 2006). The most dramatic examples of this plasticity are provided by changes in frequency selectivity and organization as a consequence of either partial hearing loss or procedures that alter the significance of particular frequencies for the organism (Irvine et al., 2006). Changes in temporal resolution are also seen as a consequence of altered experience. These forms of plasticity are likely to contribute to the improvements exhibited by CI users in the post-implantation period (Irvine et al., 2006). Auditory plasticity has also been suggested to occur without any behavioral training by passive exposure to acoustically altered environments (for example Pienkowski and Eggermont, 2009, 2010; de Villers-Sidani and Merzenich, 2011). Studying neuroplasticity in adult individuals often is performed by investigating the effects of plasticity caused by lesions (Dahmen and King, 2007). In case of the auditory modalities, these effects can be studied by inducing acoustic traumata (Dahmen and King, 2007) such as exposure to high intensity sounds (Dahmen and King, 2007) or by damaging hair cells in the cochlea (Dahmen and King, 2007). The effects of acoustic traumata will usually result in altered sensory inputs. As a response to these lesions, the lesioned frequency ranges in the primary auditory cortex have been reported to become occupied by an expanded representation of the neighboring sound frequencies (Robertson and Irvine, 1989).

1.4.3 Auditory plasticity induced by training

So far, neuroplasticity has been discussed in the developmental phase and in terms of the adult individual. Another mechanism that is applicable to probably most individuals in their everyday life is learning and training (for a review on auditory learning, see Wright and Zhang, 2008). In this thesis, training is defined as repeated performance of a specific task within a controlled time-frame.

Neurophysiogical studies have shown that the exposure of an animal to a specific sound environment can result in altered auditory response behavior (for example Recanzone et al., 1993; Rutkowski and Weinberger, 2005; Polley et al., 2006). Cortical reorganization is then most pronounced when a behavioral relevance is present and if the task is actually trained (for example Recanzone et al., 1993; Kacelnik et al., 2006; Ohl and Scheich, 2005). The effects of training have been extensively investigated in the field of musical training. Studying the effects of musical training has the advantage that music is multimodal and that it has a higher degree of complexity than most other daily activities (Herholz and Zatorre, 2012). Learning to play a musical instrument is a complex task that requires a fine-grated interaction of the sensorimotor system and which also involves higher-order cognitive functions. The auditory system naturally plays an essential role for musical training. Of note, it has been reported to be also the most altered by musical training (Herholz and Zatorre, 2012). Structural and functional auditory neuroplasticity induced through musical training has been documented for various stations of the auditory pathway from the subcortical brain stem (for example Wong et al., 2007) to higher-order auditory cognition (for example Lappe et al., 2008). Musical training has been reported to induce metaplasticity (Herholz and Zatorre, 2012). Metaplasticity describes a concept that trained skills or aspects not only lead to better results in the specifically trained for domain. Additionally, it eases the way for new short-term learning and plasticity (Herholz and Zatorre, 2012). This concept originates from cellular and molecular phenomena such as long-term potentiation (for example Huang et al., 1992). It has also been applied to explain features of experience-dependent plasticity in the visual cortex (Bienenstock et al., 1982), and it can explain enhanced short-term plastic effects due to modulation of the involved networks by previous sensory experience or learning (Hofer et al., 2006, Zelcer et al., 2006). It can thus be underlined that training of perceptual and higher-order cognitive tasks can induce neuroplasticity.

1.4.4 Maladaptive effects of auditory neuroplasticity - tinnitus

There is abundant literature on beneficial aspects of neuroplasticity. However, also maladaptive aspects of neuroplasticity exist. In the field of auditory neuroscience, tinnitus is a prominent example for such maladaptive neuroplasticity. For a long time tinnitus had been considered to be an otological disorder. Only recently it could be shown that tinnitus also has a central nervous system component that contributes to its development (further elaborated below). Tinnitus is common in nearly all age groups (Mühlnickel et al., 1998; Axelsson and Ringdahl, 1989), however, with a higher prevalence among elderly people (Boenninghaus and Lenarz, 2007). Tinnitus appears in various forms: Objective tinnitus is by far the less common form of tinnitus affecting only about 1% of all patients. It is caused by an internal sound source such as abnormal blood flow or muscle spasms in the ear (Langguth et al., 2017) and triggers an actual hearable sound for the patient. In contrast, subjective tinnitus which affects about 99% of patients suffering from tinnitus, describes the perception of a sound with no corresponding external sound equivalent (Lockwood et al., 2002). Subjective tinnitus is very heterogeneous. Its percept has been characterized by for example ringing, buzzing, hissing or a combination of these (Boenninghaus and Lenarz, 2007). Tinnitus can appear as a continuous or intermittent percept and tinnitus can occur as an acute or chronic form. Its comorbidities often include hearing loss (Hoffman and Reed, 2004) or hyperacusis (Schecklmann et al., 2014). In animal models several factors tightly connected to the tinnitus percept could be identified. Tinnitus can start as a consequence of damage to the inner ear cell population. This damage can be induced by noise exposure (Roberts et al., 2010) or for example ototoxic substances (Evans and Borerwe, 1982). The damage leads to a decreased activity of the auditory nerve which now in turn triggers a shift in the central balance between excitation and inhibition (Kaltenbach, 2011). It is this imbalance that causes central hyperactivity, increased bursting activity and increased synchrony, which are typically perceived as the maladaptive neuroplasticity of tinnitus. Accompanying consequences include altered synaptogenesis or changes in the neurotransmitter system (see Kaltenbach, 2011). These effects have also been found in the limbic system (Mahlke and Wallhäusser-Franke, 2004) or the somatosensory system (Levine, 2004). Tinnitus is therefore a system-wide neuroplastic maladaptation with essential contributions from the auditory system and non-auditory systems (Kaltenbach, 2011).

1.4.5 Adaptation to altered auditory inputs

The auditory system also has to be able to adapt to altered auditory inputs. This property is essential in the developmental phase of the brain (see Recanzone et al., 1993 and 1.4.1) and continues throughout life (1.4.2). Also in the adult and mature healthy auditory system adaptation to altered auditory inputs is possible: When adult human subjects were equipped for example with molds in the concha of either the left or the right pinna resulting in altered auditory spectral cues, after a behavioral training subjects were again able to localize sound despite the altered auditory spectral cues (Van Wanrooij and Van Opstal, 2005). Altered auditory spectral cues are, however, not just an experimental artificial condition, but also occur due to natural phenomena, such as aging. In case of the aging auditory system, this can result in a hearing impairment, be it by middle or inner ear causes. Hearing impairment, no matter how profound it is, leads to an altered perception of auditory cues (Schnupp et al., 2011), meaning that the brain has to adapt to these new cues. This hearing impairment may nowadays be treated with a CI, the most effective neural prostheses ever developed (Moore and Shannon, 2009). Although highly successful, CIs provide a completely different auditory hearing experience thus requiring central auditory adaptation: By direct electrical stimulation of the auditory nerve, the central auditory system receives peripheral input that greatly differs from the input of a healthy cochlear. The transmitted signals are degraded with respect to their natural sound and appear initially highly unnatural (Moore and Shannon, 2009). Subjects who receive their CI postlingually are nevertheless able to complete complex auditory tasks such as to converse on the phone (Moore and Shannon, 2009). Cerebral lesions in brain regions involved in hearing can show the limits of adaptation to altered auditory inputs. When the auditory cortex of adult ferrets with unilateral earplugs had been bilaterally lesioned, despite training these animals were no longer able to localize horizontal sound accurately. The lesioned auditory cortex hampered the process of adapting to the altered auditory cues provided by the unilateral earplugs (Nodal et al., 2009). While adult ferrets without lesions can adapt to altered auditory cues (Kacelnik et al., 2006), the effects of the lesioned auditory cortex were so strong that the auditory system could not relearn the new monaural auditory spectral cues. Even though the adult auditory system can adapt to altered auditory input, this example shows that there are limits to the compensatory abilities of the brain.

1.5 Auditory plasticity in defined deficitary situations

Neuroplasticity can cause major cortical reorganization. The following section will discuss the effects of auditory neuroplasticity for three defined deficitary situations. These are blindness, deafness and SSD.

1.5.1 Blindness

1.5.1.1 Etiology of blindness

Bourne et al. (2017) report a prevalence of blindness in 2015 of 36 million people. Blindness is defined as a visual impairment with a visual acuity in the better eye of <3/60 (WHO, 2019a). The most common causes for blindness are age-related macular degeneration, glaucoma, diabetic retinopathy, injuries, or uveitis (Grehn, 2012). Blindness, especially in the developmental phase, strongly influences cortical development (Lazzouni and Lepore, 2014). In order to compensate for the visual deprivation, the neural system has to undergo vast neuroplastic changes affecting its structure, function, connectivity as well as neural interactions (Lazzouni and Lepore, 2014; Rauschecker, 1995; Merabet et al., 2005; Pascual-Leone et al., 2005; Merabet et al., 2005; Lessard et al., 1998). The degree of compensatory reorganization strongly depends on the age at onset of blindness, duration by blindness, and residual vision (see also Collignon et al., 2013). The following section focuses on congenital blind adults unless mentioned otherwise.

1.5.1.2 Structural reorganization in blindness

From a structural point of view, early blindness is found to be associated with an atrophy of the gray matter as well as with an increased cortical thickness in the occipital cortex (Bridge et al., 2009; Park et al., 2009; Voss and Zatorre, 2011). In a voxel-based morphometric analysis experiment, Noppeney et al. (2005) found changes in white and gray matter density for the visual, somatosensory, and motor system in early blind subjects in comparison to sighted controls. While early onset of blindness led to decreased white matter density in the optic tracts, the density in those tracts that were associated with the motor and somatosensory cortices, increased. Also reduced volume in gray matter for the visual areas BA 17 and 18 were found. Noppeney et al. (2005) suggested that these changes in density are the result of changes in synaptic density, the number of dendritic spines or axonal arborizations. Additionally, blindness seems to cause atrophy of the geniculocortical tracts while cortico-cortical connections to the frontal and temporal cortices are not affected (Shimony et al., 2005). Blindness also affects the shape and the volume of the corpus callosum (Tomaiuolo et al., 2014), the hippocampus (Leporé et al., 2009), and subregions of the thalamus which are involved in visual processing (Cecchetti et al., 2016).

1.5.1.3 Functional reorganization in blindness

The structural reorganization of the visually deprived brain is accompanied by a functional reorganization. The central visual system has repeatedly been reported to be involved in non-visual tasks. These include perceptual tasks as well as higher-order cognitive tasks. Blinds have been shown to possess altered thresholds for the following perceptual tasks: tactile (Alary et al., 2009; Norman and Bartholomew, 2011, Goldreich and Kanics, 2003, 2006; Van Boven et al., 2000; Ricciardi et al., 2007), taste (Cuevas et al., 2009; Manescu et al., 2018; Kupers et al., 2011), pain (Slimani et al., 2013, 2014), odor (Beaulieu-Lefebvre et al., 2011), and temperature discrimination (Slimani et al., 2015).

Changes regarding higher-order cognitive tasks have been reported in blinds: Amedi et al. (2003) tested the occipital activation in early blind subjects during a verbal-memory task as well as during a verb-generation task and a Braille-reading task in a fMRI-study. They reported a reorganization and specialization of the occipital cortex along an anterior-posterior axis for both tasks which were not present in sighted controls. In their study, blinds also showed a superior performance in a verbal-memory task which they interpreted as superior verbal-memory abilities. Their study is interesting for two reasons: First, they were able to demonstrate selective cognitive functions that are enhanced in blind subjects but not in controls. Secondly, the visual cortex was activated by a non-visual stimulus in blinds. In their follow-up study (Raz et al., 2005), the same blind subjects were tested on an episodic-memory task, in which subjects had to recognize words that had originally been presented in the first study (Amedi et al., 2003). Interestingly, the magnitude of the primary visual activation during the recognition task could be correlated with memory performance. Across the blinds, the better-remembered set of words elicited greater primary visual cortex activation than words from the poorly-remembered set. Enhanced higher-order cognitive functions in blinds have also been reported elsewhere (Pasqualotto et al., 2013; Amedi et al., 2004; Röder and Rösler, 2003. Sadato et al., 1996). Sadato et al. (1998) investigated the question of activation of the primary visual cortex in early blinds while reading Braille using positron-emission tomography imaging - a technique which visualizes metabolic processes in the investigated area. Passive sweeping of the finger over a homogeneous pattern of Braille dots (so meaningless Braille) did not result in an activation of the visual cortex. However, the primary visual cortex was active in non-Braille tactile discrimination tasks. These studies show the compensatory neuroplastic recruitment of the visual cortex by non-visual processes. This recruitment is either not or not as strongly present in sighted controls. Sadato et al. (1996, 1998) repeats the importance of behavioral relevant and meaningful stimuli. If behavioral relevance is present, the visually-deprived brain appears to compensate the deficit of visual input by a more efficient usage of the remaining functional modalities.

1.5.1.4 Effects of blindness on the auditory modality

Röder and Rösler (2004) describe three different qualities of compensatory neuroplasticity: it can either lead to a behavioral benevolent, a maladaptive, or no measurable behavioral effect. In terms of the effect of blindness on the auditory modality, this can be interpreted as blindness causing enhanced, worse, or comparable performance when contrasted with sighted controls (Röder and Rösler, 2004). Enhanced functional performance of blind subjects were reported for the following auditory domains: auditory motion processing (Jiang et al., 2014; Vercillo et al., 2015), orienting in auditory far space (Voss et al., 2004), horizontal sound localization at eccentric positions (Röder et al., 1999; Lessard et al., 1998), monaural sound localization (Voss et al., 2015; Lessard et al., 1998), pitch discrimination (Gougoux et al., 2004; Hamilton et al., 2004), temporal discrimination (Muchnik et al., 1991), spectral discrimination (Stevens and Weaver, 2005), and a better memory for auditory stimuli (Bull et al., 1983). Neuroimaging studies could also show activation of the occipital cortex in blinds when performing sound localization tasks (Gougoux et al., 2005; Weeks et al., 2000; Leclerc et al., 2000) which again emphasizes the observation that non-visual processing occurs in the visual cortex of blind subjects.

No difference in performance between blind subjects and sighted controls was found for the following auditory domains: auditory sensory thresholds (Bross and Borenstein, 1982; Niemeyer and Starlinger, 1981; Starlinger and Niemeyer, 1981; Collignon et al., 2006b), audio-spatial performance under normal binaural hearing conditions (for example Voss et al., 2015; Zwiers et al., 2001a,b), and horizontal sound localization in the sagittal plane (Röder et al., 1999; Voss et al., 2004, 2015; Zwiers et al., 2001a,b).

A worse performance in the auditory domain in blind subjects when compared to sighted controls was described for distance judgment (Wanet and Veraart, 1985; Vercillo et al., 2016), audio-spatial complex tasks (Finocchietti et al., 2015; Gori et al., 2013), or movement judgment (Vercillo et al., 2018). The exact underlying reasons why certain abilities improve while others do not are still a matter of debate. It appears clear, however, that behavioral relevance is a driving force in the auditory neuroplasticity in visually-deprived subjects and includes both perceptual and higher cognitive functions (Lazzouni and Lepore, 2014; King, 2014).

1.5.2 Deafness

1.5.2.1 Etiology of deafness

Hearing loss represents the most prevalent sensory impairment and is considered to be one of the most common neuropathological disorders (WHO, 2019b). The World Health Organization estimates that worldwide currently 466 million people are affected by disabling hearing loss (WHO, 2019b). Disabling hearing loss is defined by a hearing threshold of more than 40Db in the better hearing ear in adults (WHO, 2019b). The degree of hearing loss can vary on a scale from mild to moderate, severe, and profound (WHO, 2019b; Kral and O'Donoghue, 2010). Profound deafness is described by a hearing loss of more than 81dB in both ears (WHO, 2019b). With respect to its etiology, deafness can be congenital or acquired with about 50% of cases of congenital deafness being caused by genetic factors (Resendes et al., 2001, Gorlin et al., 1995). More than 400 different genetic conditions have been identified as potential causes for congenital deafness (Toriello and Smith, 2013) of which roughly one third has been identified as resulting in syndromes (Petit, 1996). Congenital deaf subjects are more likely to be without pathological neurological or psychiatric medical histories (Dye et al., 2008). Acquired deafness can result from prenatal, perinatal or postnatal infections, trauma, or as the result of ototoxic drugs (WHO, 2019b). Additionally, many of these previously mentioned causes for deafness are associated with neurological sequelae (Hauser et al., 2006). With respect to deficits and compensatory mechanisms used by patients affected by hearing loss, a crucial landmark is language acquisition. While blind subjects often have acquired Braille reading skills in addition to the spoken mother tongue, not all deafs have gone through language acquisition and not all have undergone language acquisition as a child. Subsequent development without access to any language model comes at a developmental price. In their imaging study, Mayberry et al. (2011) found an "age of acquisition" effect in deaf adults who had been exposed to sign language at different ages (birth to 3 years, 4-7 years, 8-14 years) and who had been using sign language for more than 30 years for communication, but who could not communicate in a spoken language. Subjects were asked to watch sign language sentences on a computer screen. Those who had been exposed to sign language at an early age, showed more activation in anterior language regions and less in posterior visual regions. In contrast, the later exposed subjects showed more activation in posterior visual brain regions and less in anterior language brain regions. This implies that those deafs late(r) exposed to sign language process the stimuli as visual stimuli and not as language. Visual processing of language is far less efficient than processing spoken language as language (Lederberg et al., 2013).

1.5.2.2 Structural reorganization in deafness

Comparable to visual deprivation, also the auditory-deprived brain undergoes structural reorganization. This includes an increase in total volume of the visual cortex in deafs when compared to that of hearing subjects (Allen et al., 2013). An increase in the gray-white matter ratio of the auditory cortex relative to hearing subjects has been reported. This difference is likely to be the result of reduced myelination and/or fewer fibers that project to and from the auditory cortex (Good et al., 2014). The deafened auditory pathway appears to result in dystrophic changes which affect cells and synapses resulting in smaller soma size and a restructured synaptic morphology (Berger et al., 2017; O'Neil et al., 2010). Deaf animals have been found to expose extensive functional deficits in the primary auditory cortex which demonstrates a difference between neuronal function and preserved fiber tracts to the primary auditory cortex (Berger et al., 2017). This in turn could be caused by a dysfunction at a synaptic or cellular level (Kral et al., 2017). In congenitally deaf cats, congenital deafness leads to a dysfunctional intrinsic cortical micro circuitry with delay in the activation of supra granular layers and reduced activity in infra granular layers (Kral et al., 2006). These deficits show that the primary auditory cortex cannot properly process thalamic input or incorporate top-down modulations from the higher order auditory cortex into the processing within the primary auditory cortex (Kral et al., 2006). The authors suggest that this might be a consequence of postnatal development. Detailed changes in neural connectivity to various auditory cortical regions have been shown to exhibit varying degrees of structural reorganization (reviewed by Alencar et al., 2019).

1.5.2.3 Functional reorganization in deafness

Comparable to the visually-deprived brain (see 1.5.1.3), sensory thresholds and higher-order cognitive functions have been reported to be altered for the auditory-deprived brain. These changes include altered haptic (van Dijk et al., 2013; Cattaneo et al., 2018; Sharp et al., 2018) and somatosensory thresholds (Meredith and Lomber, 2011; Karns et al., 2012) and altered visual abilities (see 1.5.2.4).

1.5.2.4 Effects of deafness on the visual modality

Unlike the visual system, the auditory system can obtain auditory information from any direction of a sound source relative to the head. Therefore, one would expect that vision as the other spatial modality, shows compensatory mechanisms to favor visual events outside the fovea in auditory-deprived subjects (Pavani and Bottari, 2012). Such a selective attentional peripheral modulation had indeed been reported (reviewed by Bavelier et al., 2006). Recent studies, however, spelled out that enhanced visual abilities are also present without selective peripheral attention (Megreya and Bindemann, 2017; Smittenaar et al., 2016; Shiell et al., 2014). Comparable to the visually-deprived brain, in deafness the auditory cortex has been reported to become involved in non-auditory processes such as vision (Lomber et al., 2010). Sign language for example as a highly visual mode of communication is “heard” in the auditory cortex (Nishimura et al., 1999; Twomey et al., 2017) if acquired early in life (Mayberry et al., 2011).

While deafness does neither appear to cause a global deterioration nor a general enhancement of visual abilities, very specific alterations have been described in the literature. For the following visual tasks deaf subjects have been reported to show better visual skills: motion detection (Shiell et al., 2014), face discrimination (Megreya and Bindemann, 2017), lip-reading (Mohammed et al., 2005), object discrimination (Megreya and Bindemann, 2017), visual localization (Codina et al., 2011; Lomber et al., 2011), visuo-motor synchronization (Iversen et al., 2015), and visual-spatial memory (Hall and Bavelier, 2010). Deafs have also been reported to benefit from valid cueing of spatial selective attention (Pavani and Bottari, 2012) while they are also less susceptible to invalid cues (Colmenero et al., 2004).

Equal performance between deafs and controls was found with respect to the eccentricity of the object (Brozinsky and Bavelier, 2004), temporal thresholds (Nava et al., 2008), contrast sensitivity (Finney and Dobkins, 2001), nature of the stimuli with respect to movement in space (static: Bross, 1979, moving stimuli: Finney and Dobkins, 2001; Brozinsky and Bavelier, 2004), and motion thresholds (Bosworth and Dobkins, 2002, Brozinsky and Bavelier, 2004).

A worse visual performance for deaf subjects has been described to be especially prominent in tasks where irrelevant information is presented in the visual periphery (Dye et al., 2007; Sladen et al., 2005). The altered network of visual attention in deafs with for example greater susceptibility to peripheral distractors appears to play an essential role here (Dye et al., 2007). Compensatory enhanced visual processing is thus present in deafs for certain subtasks. However, it might be more conducive to interpret these "enhanced visual processes" as enhanced reactivity to visual events (Pavani and Bottari, 2012): Normally, the auditory system plays an essential role in the detection of auditory oddities, which is crucial for survival of the individual in the environment (for example the roaring of a predator in the acoustic scene). Deafs do not have access to this informational input. To still allow an adequate and fast behavioral response in deafs, faster reactivity to visual events might be the equivalent neural reaction (Pavani and Bottari, 2012).

1.5.3 Single-sided deafness

Until this point, the loss of the sensory input of one modality has been mainly described as a complete congenital or early loss. The last defined deficitary auditory situation presented here will focus on adult subjects affected with sensorineural SSD acquired postlingually.

1.5.3.1 Etiology of single-sided deafness

Deafness or hearing loss can affect both ears or only one ear. SSD describes an asymmetric hearing loss condition in which only one ear is affected. SSD is defined as a hearing threshold of over 81Db in one ear and can occur as a result of idiopathic sensorineural hearing loss, head trauma, lateral skull neoplasms or Menière's disease (Pross et al., 2015). Based on the anatomic location of the origin of deafness, hearing loss can broadly be classified into two different types: conductive hearing loss and sensorineural hearing loss. Conductive hearing loss usually results in only a reduced degree of acoustic input of the affected ear (Moore et al., 1989; Kumpik et al., 2010; Lupo et al., 2011) and is often reversible (Keating and King, 2013). Sensorineural hearing loss, on the other hand, is usually irreversible (Keating and King, 2013) and often leads to complete lack of transduction of sound at the affected ear (Tucci et al., 1987; Keating and King, 2013).

SSD is estimated to affect 1 in 30.000 individuals per year (Pross et al., 2015). Patients suffering from SSD report difficulties in sound localization (Dorman et al., 2016; Arndt et al., 2011b; Jacob et al., 2011), reduced word discrimination abilities (Arndt et al., 2011b; Tokita et al., 2014), and especially a reduced understanding of speech (Tokita et al., 2014; Arndt et al., 2011b). SSD may also cause an accelerated decline of the poorer ear (Cheung et al., 2017): Moore and Alcántara (2001) showed the emergence of spectrally dead regions where no functioning inner hair cells and/or neurons are present. These spectrally dead regions can lead to decreased audibility and frequency selectivity which in turn potentially causes certain speech sounds to become difficult to understand (Shannon et al., 2002). Typical rehabilitative means for SSD are CIs, contralateral routing hearing aids, or bone conductive devices (Pross et al., 2015; Tokita et al., 2014; Peters et al., 2015). The following section focuses on sensorineural SSD in postlingual adult subjects unless mentioned otherwise. In this thesis, postlingual SSD is defined as the normal development of the brain with SSD occurring after the acquisition of language.

1.5.3.2 Effects of single-sided deafness on the auditory modality

When an asymmetric sensory impairment occurs in a modality with paired sensory organs such as the ear, the fine-tuned connection between convergent sensory information all the way to higher auditory central processing is disrupted (Schnupp et al., 2011). Thus, asymmetric sensory impairment strongly reduces the functionality of the modality and its associated functions such as sound localization as these greatly depend on binaural sensory information (Cheung et al., 2009).

1.5.3.3 Structural changes in single-sided deafness

When monaural stimuli were presented to the healthy ear, SSD-subjects had no difference in cortical response in terms of size and location when compared to normal-hearing controls in a fMRI-study of Scheffler et al. (1998). However, after monaural acoustic stimulation of the SSD-affected ear, a significantly different cortical response pattern was present: Healthy subjects showed a strong contralaterality of cortical response patterns (lateralization ratio between response of the left and right hemisphere: 3.4-5.2) while SSD subjects showed an almost balanced cortical response pattern. Their lateralization ratio after acoustic stimulation was 1.3 towards the contralateral hemisphere of the healthy ear and, therefore, corresponds to the lateralization ratio of the cortical response pattern of binaural stimulation of normal-hearing subjects (Scheffler et al., 1998). This study demonstrates that SSD leads to a neuroplastic change of the interhemispheric response patterns. While the normal interhemispheric pattern in normal-hearing subjects is both asynchronous (contralaterally earlier than ipsilaterally) and asymmetrical (contralateral amplitude greater than ipsilateral amplitude), this pattern shifts in SSD subjects towards a more synchronous and symmetrical activation pattern.

This reorganization towards a more balanced activity of the central auditory system has also been reported for measured auditory evoked potentials in subjects with postlingual SSD (Ponton et al., 2001). These auditory evoked potentials represent an objective measure of activity of the auditory central nervous system and primarily reflect the synchronous neural activation of structures in the thalamic-cortical segment of the central auditory system (Ponton et al., 2001). In SSD subjects, these potentials were recorded from central electrode sites which were located over auditory cortical areas. Potentials showed substantial changes from the normal pattern of asymmetrical and asynchronous central auditory system activation. Comparable to Scheffler et al. (1998), the normally found cortical response patterns of healthy subjects were replaced by a stronger symmetrical and synchronous activation in SSD subjects. Also, these changes in cortical activity appear gradually and continue for a period of at least two years after the onset of hearing loss (Ponton et al., 2001). A stronger symmetrical and synchronous activation in SSD-subjects was further confirmed by Maslin et al. (2013).

Interestingly, the side of the hearing loss also appears to affect the degree of central auditory plasticity: While SSD on the left side caused the already described symmetrical and synchronous auditory evoked potentials when presented with non-speech stimulation, these were not present with SSD on the right side (Hanss et al., 2009). Hanss and colleagues describe an interesting example of the effects of SSD on hemispheric laterality in auditory processing. This across-hemispheres different cortical reorganization also extends to other functions: The auditory cortex contralateral to the hearing ear has been reported to dominantly take over auditory central processing, while the auditory cortex in the hemisphere ipsilateral to the ear with hearing shows reduced activation (Pross et al., 2015). In addition to the altered central auditory processing, topographical reorganization of tonotopic maps (Cheung et al., 2009; Schreiner and Winer, 2007), reorganization of the frequency map in the contralateral primary auditory cortex (Syka, 2002), and elevated neuronal thresholds (Robertson and Irvine, 1989; Rajan et al., 1993; Schwaber et al., 1993; Cheung et al., 2009) have been reported as a structural consequence of SSD.

1.5.3.4 Functional changes in single-sided deafness

These above mentioned structural consequences must manifest themselves in functional changes, especially when considering that hearing as one of two spatial modalities is greatly impaired in its functionality. The most obvious functional change in SSD is the poorer hearing when compared to healthy controls and, interestingly, also subjects with symmetric hearing impairment (Silverman et al., 2006). The consequences of poorer hearing are also found in the recognition of words, where SSD subjects without a hearing aid have a worse recognition of words than SSD subjects with a monaural hearing aid (Silverman et al., 2006). The authors also conclude that the lack of amplification causes a decline in word-recognition performance over time in the worse ear. The foundation of hearing, may this be speech or sounds, depends strongly on the access to auditory spectral cues such as interaural time differences or interaural level differences (Schnupp et al., 2011).

SSD deafness results in an altered usability of auditory spectral cues (Keating and King, 2013) and has therefore profound effects on the usefulness of these (Moore et al., 1989; Kumpik et al., 2010; Lupo et al., 2011) with only the intact ear still having access to information contained in the spatial auditory cues. Even though sound localization is still possible with monaural spectral cues (Dahmen and King, 2007) it comes at the cost of decreased spatial accuracy. The exact mechanisms of how this sound localization is still achieved are yet unknown. It has been suggested, that either an auditory cue remapping takes place or alternatively a cue reweighing (Keating and King, 2013). The first mechanism, cue remapping, implies that the auditory system has to learn to reinterpret the spatial meanings of the cues. A sound originating directly in front of a person with intact hearing has an interaural level difference of 0. If a person has asymmetric hearing abilities, a level difference is perceived with the sound being louder on the side with intact hearing. This would result in a perceived spatial shift towards the healthy ear. The auditory modality with an asymmetric hearing now has to reinterpret the frontally presented auditory cues and give them a new spatial meaning. In the second proposed mechanism, cue reweighing, the auditory systems relies more on those available auditory spatial cues that are not (as much) affected by the asymmetric hearing. In terms of unilateral hearing, this would mean that binaural cues are ignored, while monaural spatial cues become more important for spatial localization (now done with the intact ear) (Van Wanrooij and Van Opstal, 2004, 2007; Kumpik et al., 2010; Agterberg et al., 2012). It is, however, not yet known if cue reweighing represents the only strategy in humans with unilateral hearing loss. Keating and King (2013) also propose that different factors such as age at onset may lead to different spatial strategies to compensate the hearing loss.

1.5.4 Cross-modal plasticity induced through modality loss

While the brain is able to partly compensate the loss of a modality, the question remains why certain abilities change while others seem to be unaffected. Why is the performance of deaf subjects on low-visual tasks comparable to that of controls while deaf subjects outperform controls for tasks testing peripheral visual attention? Lomber et al. (2010) propose an interesting hypothesis that could explain this gap in understanding. Certain object features such as color or tone represent unimodal sensory qualities and address only the visual or only the auditory modality. Many objects in the environment are, however, multimodal and stimulate more than one modality. For example, localizing an object uses the complementary information provided by the visual and auditory modality. The localization of a passing train is more accurate when both the auditory and visual information is integrated. Lomber et al. (2010) argue that to compensate the absence of one input modality, these abilities that use polymodal information develop superior performance with respect to those informational cues that can still be registered by the remaining modalities. These supramodal functions may thus be more likely to engage cross-modal plasticity as a result of their functional reallocation in homologous areas of the brain. It can also be assumed, that behavioral relevance plays an important role. In blinds, this includes various aspects of the auditory domain such as enhanced accuracy in sound localization or enhanced pitch discrimination. In deafs, this would include enhanced facial discrimination or faster visual reaction times.

1.5.5 Cross-modal plasticity through reduced modality functionality

The case of postlingual SSD represents an interesting situation since initially, a fully functional modality had been developed. Later in adulthood, this modality partially lost its functionality due to peripheral sensory impairment. Collignon et al. (2015) showed that already a brief period of visual deprivation resulted in enhanced auditory activation of the visual cortex in adults. In the case of subjects with SSD who then receive a CI, the modality would have to re-learn how to interpret the electric signal from the CI and remap (and probably also recue) spatial auditory cues. It can be hypothesized that a modality which had been exposed to adequate stimuli during the developmental phase and therefore had developed accordingly, would be able to relearn these new auditory signals (see 1.4.3). Interestingly, again supramodal behavioral relevance is a strong driving factor in the observed cross-modal plasticity of subjects with a reduced functionality of a modality. Subjects equipped with a CI have been reported to show enhanced performance in lip-reading (Stropahl et al., 2015) and face recognition (Stropahl et al., 2015). These represent two highly behaviorally relevant mechanisms when full access to hearing is not possible. Not all changes and not all of the observed reorganizations are necessarily due to neuroplasticity. Especially in case of the auditory modality, alterations can also occur due to passive adaptation to altered input. A most prominent example in the auditory modality is the frequency tuning of the fibers of the auditory nerve that occurs following the destruction of outer hair cells (Dallos and Harris, 1978).

1.6 Aims of this thesis

Neuroplasticity and its effects have long been established and confirmed. The loss of one modality leads to compensatory reorganizational mechanisms in the remaining functional modalities. A functional interplay between the visual and auditory modality is of high relevance in daily life. To better understand these cross-modal changes, it is of high importance to define those conditions where such adaptations can be observed and to quantify their specific changes. The aim of this thesis was to further delineate such specific adaptations under well-defined experimental conditions to also allow a quantitative read-out of the observed effects. To this end three different studies were conducted:

The first study tested the ability of horizontal sound localization in blinds when compared to sighted controls using simple and complex acoustic sound scenes. Based on previous studies (Röder et al., 1999; Lessard et al., 1998) it was hypothesized that blinds outperform sighted controls in horizontal sound localization in an acoustically complex situation, thus demonstrating compensatory neuroplasticity.

The second study examined behavioral measures of visual processing speed in deaf participants. Different stimuli (masked squares, everyday objects, and fast-forwarded videos) were briefly presented to the participants who then were asked to answer recognition-based questions related to the stimuli. This experimental setup was repeatedly performed on consecutive days as training. It was hypothesized that already before training deaf individuals complete these tasks more accurately than hearing controls, thereby indicating enhanced processing speed. Furthermore, it was hypothesized that with training the performance of deaf subjects on such tasks would increase at a faster rate than in the hearing control subjects, thus demonstrating that neuroplasticity exists in the mature and adult brain. Additionally, it would show that neuroplasticity can be induced by explicit training in adults.

The third study investigated the development of horizontal sound localization in single-sided deaf adults before CI implantation and in the postoperative rehabilitation phase using the same setup as in the first study with simple and complex acoustic settings. It was hypothesized, that before CI implantation single-sided deaf subjets would not be able to localize a sound in the horizontal plane. It was moreover hypothesized, that with implantation of the CI, subjects would re-learn to localize sounds. Being able again to localize sound in the horizontal plane would thus demonstrate that neuroplasticity allows subjects with an initially properly developed sensory modality, to relearn its functionality after loss in adulthood.

2 Material and methods

Material and equipment which were employed to conduct the three studies of this thesis are depicted in Table 1. The first and third study both used the same experimental setup and subsequent software for analysis. Materials that were used in both studies are only listed once under the section of the third study. Material that was exclusively used in one of the two studies is mentioned under the corresponding section of Table 1.

Table 1: Material used in the three studies. Individual material is listed under each study.

Horizontal sound localization of blind subjects in acoustically complex situations	
Audiometric testing	DA 324 Audiometer by Hortmann Neuro-Otometrie, Neckartenzlingen, Germany
Effects of training on the visual processing speed in deafs	
Computer for experimental presentation	IBM ThinkPad R61i with Windows XP (screen width 14.1 inch, refresh rate: 20.007ms)
Light works for Windows XP (version 11.5)	EditShare EMEA, Basingstoke, UK, www.lwks.com
Matlab (version 2009a)	Mathworks, Natick/Massachusetts, USA, www.mathworks.com/download
Psychotoolbox (version 3.0.10)	Brainard (1997), www.psychtoolbox.org/download
Software for experiment	custom-made+
VLC player (version 2.0.1)	free and open source software, VideoLan non-profit organization, Paris, France, www.videolan.org/vlc
Python (version 3.7)	free and open source software, Python Software Foundation, Beaverton/Oregon, USA, www.python.org/downloads/release/python-370
Long-term impact of implantation of a unilateral cochlear implant in single-sided deafness on target sound localization in multiple-sounds environments	
IBM SPSS (version 25)	IBM Deutschland GmbH, Ehningen, https://www.ibm.com/products/spss-statistics
Latex (version 3.14)	free and open source software, www.latex-project.org/get
Python (version 3.7)	free and open source software, Python Software Foundation, Beaverton/Oregon, USA, www.python.org/downloads/release/python-370
Inkscape (version 0.92.3)	free and open source software, https://inkscape.org/download
Sound proof room (2.0*3.5*2.2m^3)	Industrial Acoustics Company GmbH, Niederkrüchten, Germany, www.iac-gmbh.de
PC*	
Sound PC*	
Software for sound production	Auvi300, custom-made*
Software for pontiometer	custom-made*
Loudspeakers	broadband loudspeakers: SC 5.9, Visaton, Haan, Germany, www.visaton.de
Accoustic fabric for loudspeakers	
Headrest	
Swivel	custom-made*
Clamps to fixate swivel on chair	o+k Werkzeug und Maschinen GmbH, Gutach, Germany www.o-k-werkzeuge.de, article number: 5219006

+ a custom-made software script was written by Katherine E. Lawerence during an internship at the Center of Neurology, Division of Neuropsychology, Hoppe-Seyler-Str.3, 72076 Tübingen

* all custom-made material, hardware and software and the setup of the computers were done by the Leibniz-Institut für Arbeitsforschung, TU Dortmund, Ardeystraße 67, 44139 Dortmund.

2.1 Horizontal sound localization of blind subjects in acoustically complex situations

The goal of this study was to investigate the auditory selective spatial attention of blind subjects in acoustically complex situations. Subjects were asked to localize a target sound which was either presented in isolation (single-source condition) or among multiple distractor sounds (multiple-sources condition).

2.1.1 Participants

Nine blind subjects (mean age: 45.56 years, standard deviation (SD) 13.50 years, range: 24-67 years, 4 women, 5 men) participated in this study (see Table 2). Inclusion criteria for patients were blindness, normal hearing and being of age. Blindness was defined by the World Health Organization standards as having best-corrected visual acuity in the better eye of <0.05 (see WHO 2019a). All blind subjects had a best-corrected visual acuity in the better eye of ≤ 0.02. Detailed information about their etiopathology of blindness is given in Table 2. All subjects received standard audiometric testing prior to inclusion in the study. Based on these results, hearing of all subjects was classified as normal according to the hearing impairment classification of the WHO (see WHO 2019b). Subjects had to have mean hearing thresholds of $\leq$25dB hearing level for both ears across frequencies of 0.25, 0.50, 1.00, 1.50, 2.00, 3.00, 4.00, 6.00, and 8.00 kHz. All blinds who agreed to participate in the study passed the audiometric testing. Exclusion criteria for participants of this study were lack of capacity for informed consent and previous history of neurological deficits or psychiatric disorders. In addition, 18 age- and sex-matched sighted controls (mean age: 45.11 years, SD 14.58 years, range: 24-70 years, 8 women, 10 men) with normal hearing as confirmed by audiometric testing were included. One further blind subject also completed the experiments, but was excluded from the analysis due to erratic responses at the lowest task difficulty level. All participants were right-handed as revealed by the Edinburgh Handedness Inventory (Oldfield, 1971). Copies of the participant information and the agreement form were sent to the blind subjects prior to the experiment. On the day of the experiment, an external person, who was not affiliated with the experiment, read the participant information and the agreement form to the participants. All participants gave their written informed consent to participate in this experiment. All subjects received monetary compensation for their participation in the study. Prior to commencement, the study had been approved by the local Ethics Committee of the University of Tübingen (project number: 723/2012 BO2). The study was conducted in accordance with the ethical guidelines of the Declaration of Helsinki.

Table 2: Etiological characterization of the blind subjects (f: female, m: male).

Subject's ID	Sex	Age [yrs]	Cause of blindness	Age at onset of blindness [yrs]	Residual vision
1	m	29	repeated retinal detachment	8	none
2	f	48	cone dystrophy	28	none
3	m	55	optic nerve avulsion	10	none
4	m	67	corneal opacity, glaucoma	birth	none
5	f	36	damage to the optic nerve as side-effect of antibody-based immunotherapy	34	diffuse light
6	m	52	bilateral retinoblastoma	1	none
7	f	24	Leber's congenital amaurosis	birth	none
8	f	49	choroid coloboma	birth	diffuse light
9	m	50	retinitis pigmentosa	birth	diffuse light

2.1.2 Experimental setup and procedure

The experimental setup, stimuli and pointing procedure used in the present study have been described before (see Zündorf et al., 2011). In short, the experiment was conducted in a non-illuminated sound-proof room of the Department of Neurologoy, Section Neuropsychology at the University of Tübingen. During the experiment, the participant sat on a comfortable chair and wore a blindfold. A semicircle, centered to the subject's head, was mounted in the frontal horizontal plane at ear level (radius 1.5m, see Figure 1). Five broadband loudspeakers were mounted on the semicircle at 45° and 90° to either side of the subject's sagittal plane as well as within the sagittal plane (0°). An acoustically transparent fabric of rectangular shape was put over the semicircle with the loudspeakers. This way the position of the loudspeakers was covered and sighted subjects were not able to obtain knowledge about the position of the loudspeakers. Before performing the task in the sound-proof room, sighted controls were able to see the experimental setup and blind subjects had the opportunity to feel the setup by touch. Both groups were, however, not able to see or touch the loudspeakers which were hidden by the fabric. Five environmental sounds (cuckoo clock; laughing man; crying baby; barking dog; ringing telephone) were taken from a sound library (Marcell et al., 2000). They had already been tested on their recognizability and familiarity (for details on the specific sound stimuli used, see Zündorf et al., 2011). All sound stimuli lasted about 2 seconds and were presented at 65dB(A) sound-pressure level (the unit dB(A) stands for a standardized frequency filter which tries to mimic the hearing abilities of human ears for those frequencies where human hearing is best (1-4kHz) while reducing the effects of frequencies outside this bandwidth (Möser, 2005, p.11)). Sound localization was assessed using a swivel hand pointer, consisting of a 50cm long metal rod that was mounted in front of the subject at the arm rest of the chair. The swivel could be rotated in the horizontal plane. A response key was mounted on the upper side of the rod. When the subject pressed the response key, the position of the pointer was measured by a potentiometer and delivered to a computer with custom-written software, which recorded the position and timing. Data acquisition took place in a single session.

The main experiment consisted of two conditions of auditory stimulation. In the single-source condition, each of the five target sounds was presented at each of the five speaker positions two times in isolation, thus resulting in a total of 50 trials. In the immediately following multiple-sources condition, all five sounds were presented simultaneously, each sound from a different speaker. Of the 120 theoretically possible sound arrangements with this setup, 20 positional combinations were chosen for the experiment. These were presented twice in each block, thus leading to 40 trials per block. In each block, one of the five sounds was the target sound on which participants were instructed to focus. With one block for each sound, the study altogether consisted of six measurement blocks: one block with 50 measurements for the single-source condition and five blocks of 40 measurements comprising a total of 200 measurements for the multiple-sources condition. Stimulus/position combinations were presented following a fixed, pseudo-randomized order, which was identical for all participants. Trials were arranged in such a way that ensuing repetitions of similar or identical auditory scenes were avoided and the distribution of the location of the target sound was balanced within each block. No practice trials were performed before the actual experiment. In both conditions of stimulation, participants were instructed to point with the swivel hand pointer as accurately as possible towards the target location and then to press the response button on top of the swivel. Participants were free in choosing how to operate the swivel pointer (with both hands or with the dominant hand only). If participants failed to respond within 4 seconds after sound offset, the trial was repeated at the end of the block. The next trial began 8 seconds after sound offset.

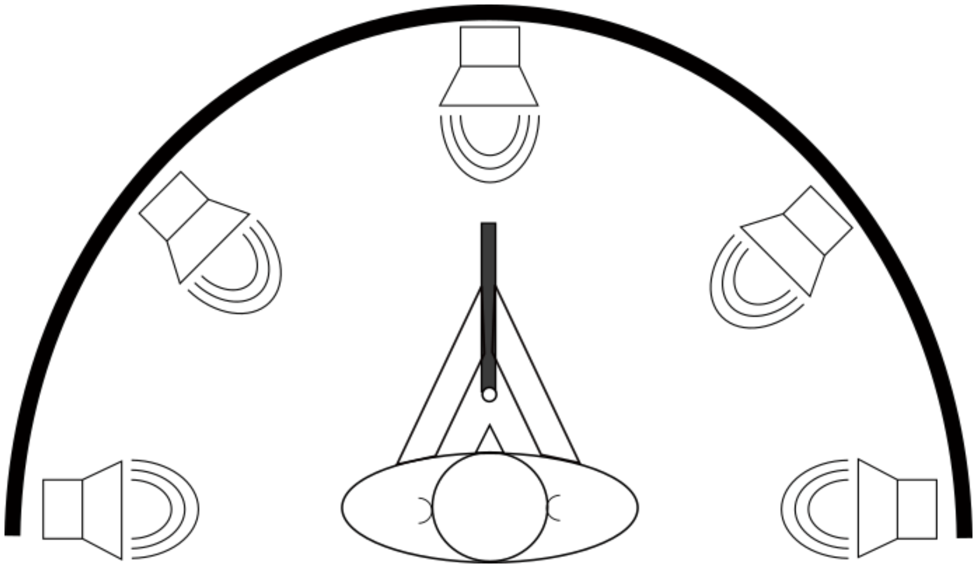

Figure 1: Experimental setup for the sound-localization experiment. Five covered loudspeakers were arranged on a semicircle at a distance of 1.5 m from the center of the subject‘s head. Loudspeakers were positioned at the sagittal plane (0°) and at ±45° and ±90° to either side of the subject. The subject was instructed to indicate the position of a target source by using a swivel-mounted hand pointer that could be rotated in the horizontal plane. The experiment included two auditory stimulation conditions: in the single-source condition, a single target sound from one of the five possible options for this study was presented in isolation. In the multiple-sources condition, the target was presented simultaneously with the four other sounds as distractors emitted from the other four loudspeakers, each from one loudspeaker.

2.1.3 Data analysis

The mean absolute error in pointing (also referred to as target deviation) was used as a measure of localization performance. It was defined as the mean of the unsigned deviations from the actual target positions for each target position and for each condition (*target position* and *target eccentricity* are used synonymously in this and the last study of this thesis). Blinds differ in their sound localization ability for central and peripheral target eccentricities (Röder et al., 1999; Voss et al., 2004). To take this finding into account and to additionally increase statistical power, the mean absolute errors of the left and right hemispaces for each eccentricity were averaged, resulting in three eccentricities (0°, ±45°, ±90°). The average of the mean absolute error was calculated by computing the arithmetic mean for all data points for each of the three eccentricities for each of the sound conditions. Previous studies with the same experimental setup had used a parametric statistical approach (see Zündorf et al., 2011, 2014). For better comparability with these studies, in this and the last study, a parametric analysis was again performed. To allow further statistical analyses with the data presented in this thesis, the median absolute error along with the interquartile range with the 25% and 75% interval are additionally reported here (see Table 7). The choice for these intervals instead of the minimum and the maximum value is based on the assumption that the minimum absolute value should in all cases be 0 and thus only the most outlying absolute error as maximum would provide some information on the data distribution. As inferential statistics, analysis of variance (ANOVA), single-case analysis and Spearman's ρ were used. For analyses of variance, Mauchly's sphericity test was used to assess sphericity, and Greenhouse-Geisser correction was used whenever the assumption of sphericity was violated. Spearman's ρ was used to assess a potential correlation between onset of blindness and performance of blind subjects as well as to evaluate the relationship between the degree of blindness and performance of blind subjects. All reported p-values are one-tailed and were $\alpha-$corrected as reported in section 3.1.

The inferential statistical analysis of single-case studies or studies with small cohorts of patients can usually not be performed with standard statistical tests since these require a known data distribution, which is not possible with a single subject, a small cohort of patients or deviant behavioral or test scores of these groups. In order to compensate for this lack of known data distribution and not to lose statistical power, Crawford and colleagues (Crawford et al., 2010) developed a set of statistical single-case (and small patient cohorts) methods for the field of neuropsychology. This set allows the comparison between the investigated person or group and a set of controls. These methods include testing for a deficit in the investigated group (applied in this thesis using the program singlim).

For the analyses in the present study, the single-case method singlim was used (Crawford and Garthwaite, 2002, updated version: Crawford et al., 2010). This method allows to measure the degree of (potentially) significantly different performance on a given task between an individual subject and a control group. It is a modified t-test that is based on a non-central t-distribution. The program calculates a z-score, z_{cc}, which is basically an effect size for the difference between the investigated individual and a random member of the control group (Crawford et al., 2010). The z-score is calculated by dividing the difference between a patient's score (x) and the control's sample mean ($\bar{x}$) by their standard deviation (s$_x$):

$$z_{cc} = \frac{x-\bar{x}}{s_x}$$

More information on the mathematical background can be obtained at Crawford and Garthwaite (2002) and Crawford et al. (2010).

2.2 Effects of training on the visual processing speed in deafs

This study aimed to investigate the influence of training on the visual processing speed of deaf subjects. Three different tasks (meta-contrast masking task, object recognition task, and video recognition task) were used. Subjects were first tested on the three tasks, then they received a training which was spread over several days. At the end of the training, subjects were tested again.

2.2.1 Participants

Seven profoundly deaf subjects (mean age: 35.00 years, SD 8.59 years, range: 25-51 years, 6 women, 1 men) participated in this study. All deaf subjects were able to communicate in sign language and had acquired it at the latest in early childhood. Inclusion criteria for this study were prelingually acquired profound deafness in adult subjects and normal or corrected-to-normal vision. Profound deafness was defined as by the World Health Organization standards by having a hearing impairment of more than 81dB in both ears (WHO, 2019b). Exclusion criteria for this study were lack of capacity for informed consent, prior history of neurological deficits or psychiatric disorders. Deaf subjects were recruited through personally established contacts outside the clinical setting in self-help groups. All subjects reported to be congenitally deaf. Since no access to clinical data on the causes of deafness was available, etiological characterization of the deaf subjects had to rely on personal information given by the subjects. The reasons for deafness were unknown to all except one subject who reported a genetic factor responsible for deafness (see Table 3). Two of the seven deaf subjects were left-handed as revealed by the Edinburgh Handedness Inventory (Oldfield, 1971). A sex-matched group (mean age: 29.25 years, SD 2.19 years, range: 23–58 years, 6 women, 2 men) of 8 subjects served as control. All controls had normal hearing and normal or corrected-to-normal vision. All participants gave their written informed consent to participate in this experiment. All subjects received monetary compensation for their participation in the study. Prior to commencement, the study had been approved by the local Ethics Committee of the University of Tübingen (project number: 174/2013 BO2) and was conducted in accordance with the ethical guidelines of the Declaration of Helsinki.

Table 3: Etiological characterization of the deaf subjects, f: female, m: male.

Subject's ID	**Sex**	**Age [yrs]**	**Cause of deafness**	**Deaf relatives**	**Onset of deafness**
1	f	51	unknown	yes	birth
2	m	25	unknown	yes	birth
3	f	32	unknown	yes	birth
4	f	38	genetic (Connexin 26-GJB2)	no	birth
5	f	29	unknown	yes	birth
6	f	39	unknown	no	birth
7	f	31	unknown	yes	birth

2.2.2 Experimental stimuli and procedures

One week before the beginning of the experiment, detailed information about the experiment (information sheet of the study, Edinburgh Handedness Inventory, text with all instructions that would appear during the experiment on the screen, consent form) were sent to all subjects via email. The subjects' tasks consisted of three different paradigms (meta-contrast masking, object recognition, and video recognition) which are explained in more detail below. All experimental stimuli were shown on an IBM ThinkPad R61i with a custom-made Matlab script (created by Katherine E. Lawrence). The screen was positioned at a distance of 57cm from the subjects' forefront. A specially marked keyboard was used. This keyboard allowed the hand to rest comfortably during the experiment and it enabled left-handers or right-handers to use their hand of choice for keyboard interaction. Training and testing of the deaf subjects took place in their homes. Training and testing of controls took place in a lab room of the Department of Neurologoy, Division of Neuropsychology at the University of Tübingen. The first and the last measurement of each subject served as the actual testing for the study (see Figure 2). Measurements in between served as training. Before the beginning of the first testing, all subjects were familiarized with the three tasks and took test trials on the same set of stimuli that was later used for testing and training. Subjects did not receive feedback on the correctness of their answers. Thereafter, the first testing was performed. The experimental phase for deaf subjects encompassed four days (mean: 3.57 days, SD 0.53) and for controls five days (mean: 5.00 days, SD 0.00). The difference in training phase between deafs and controls was due to logistic difficulties. Since not all deaf subjects were available on five consecutive days and additionally measurements were performed across Germany, in some cases measurements could only be obtained for four consecutive days. Each experimental session (both testing and training) took place on a new day and all experimental sessions were held on consecutive days. Thus all subjects (except one) only had one experimental session per day. In the case of one deaf subject, the last training session and the final testing session had to be placed on the same day due to logistic reasons.

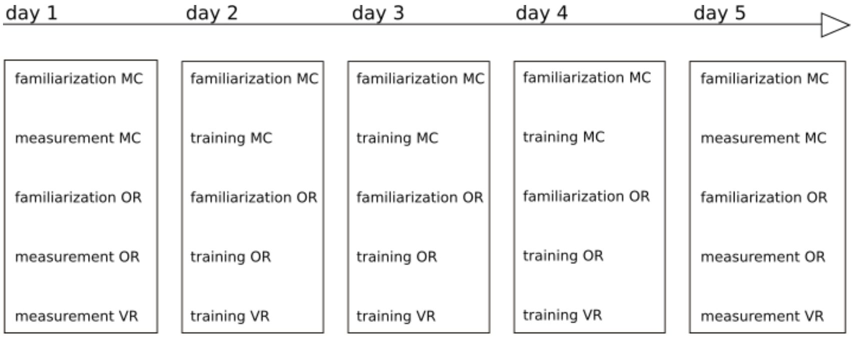

Figure 2: Time-points of measurement for deafs and controls. Subjects were measured on five consective days. While testing was performed at the first and last measurements, the experiments on the other days served as training units. MC: meta-contrast masking, OR: object recognition, VR: video recognition.

2.2.2.1 Meta-contrast masking - stimuli and task

In the meta-contrast experiment, a target and a mask were presented in close temporal proximity. A square with either a gap in the upper horizontal or the lower horizontal line served as target. Subjects had to determine if the gap in the target was in the upper or in the lower horizontal line of the square.

Stimuli for the meta-contrast experiment were taken and adapted from Rassovsky et al. (2004) and Green et al. (2003). The stimulus consisted of an outline square and a mask surrounding it. The square contained either a gap in the upper horizontal line ("gap on top") or the lower horizontal line ("gap on bottom"). The mask was gap-free and encompassed the square without overlapping (see Figure 3). Stimulus and mask were shown at the same position of the screen. Either both were shown at the center of the computer screen or peripherally with a distance of 13cm to the center of the screen at the same vertical height as the center of the screen. Pilot experiments had shown that using the same stimulus in terms of color and size for central and peripheral stimuli did not provide discriminative results. On the one hand using a black stimulus centrally resulted in a very high accuracy rate. On the other hand, using the size of central stimuli for peripheral stimulation again resulted in a very low accuracy rate. In order to increase the discriminative precision of the experimental setup and to balance these extreme experimental outcomes, the size and the color of the central stimuli were designed differently from the peripheral stimuli. For this purpose, the original size as proposed by Rassovsky et al. (2004) and Green et al. (2003) was taken for the central stimulus. The size of the peripheral stimuli was experimentally evaluated and chosen in such a way that when showing the stimulus on the edge of the computer screen an acceptable accuracy rate could be achieved by the participants. Additionally, the central stimulus had to be presented in gray while the peripheral stimulus was shown in black. Central stimuli were presented at a visual angle of 0.88° and peripheral stimuli at a visual angle of 11.61° height. Central stimuli were of 0.32°, and peripheral stimuli of 0.88° width. Before the start of the experiment, subjects were asked to fixate a centrally located fixation cross which was shown for 4 seconds. In order to avoid habituation concerning the beginning of the presentation of the stimulus, a jitter between the disappearing of the fixation cross and the stimulus was used. The jitter appeared for the following different durations: 500ms, 800ms, 1100ms and 1500ms. These different jitter intervals randomly preceeded the stimulus. When presenting the target and mask, the following stimulus onset asychronies (SOAs) between the target and the mask were used: 0ms, 20ms, 60ms and 80ms (a SOA of 0ms implies a simultaneous presentation of target and mask). For each type of stimulus (gap either on top or on bottom), each position (central versus peripheral), and each laterality (left versus right), and each SOA, 12 trials were presented. To counteract the issue of laterality, an equal number of presentations was performed for the left and for the right side. To perform an equal number of presentations for central versus peripheral as a condition, the central position was measured two times with respect to each single lateral position. This resulted in a total of 384 trials in one experimental session.

Subjects were instructed to focus on the center of the screen where the fixation cross was located. The task of the subjects was to determine the gap position of the stimulus irrespective of its position on the screen and with the eyes still focused on the center of the screen (which was controlled by the experimenter). Two answers were possible. Either the gap was located at the top or at the bottom of the square (see Figure 3). The experiment began with the presentation of a centrally located cross that served as a fixation point, followed by the presentation of stimulus and mask. After each presentation of a stimulus and mask, subjects were asked to give the position of the gap. Subjects could enter their response on a keyboard by pressing specially marked keys. No feedback concerning the correctness of their answer was given. Subjects were able to self-determinedly initiate the start of the next stimulus presentation, allowing them to take breaks in between. Before the start of the actual experiment, subjects underwent a training with 33 test trials without receiving feedback on the correctness of their answers. For testing and training, the same set of stimuli was used.

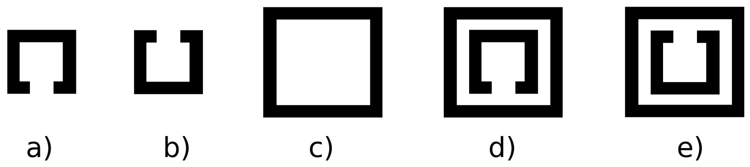

Figure 3: Stimuli and mask of the meta-contrast masking experiment. The stimuli consisted of an outline of a square with either a gap in the upper **(a)** or the lower **(b)** horizontal line. The mask **(c)** consisted of an outline of a square that encompasses the stimulus without overlapping with it. **(d)** and **(e)** show the combination of stimulus and mask. Peripheral stimuli were presented in black, while central stimuli were shown in gray.

2.2.2.2 Object recognition - stimuli and task

In this task, subjects watched streams with objects from different categories at different speeds and they had to determine the number of objects in that stream of a previously specified category.

Colored object stimuli were taken from „The Object Database“, hosted at wiki.cnbc.cmu.edu/Objects and described in more detail in Konkle et al. (2010). Objects were grouped into five distinct non-overlapping categories. The items for these categories were chosen after prior testing on five subjects who were not involved in the actual experiment; any item that was categorized into more than one distinct category was excluded from the experiment. These categories were: kitchen supplies, office supplies, musical instruments, food, and furniture. Streams of objects were created and each stream contained ten different objects (for an exemplary object stream see Figure 4). Of these ten objects, either zero, one, two, three, or four objects belonged to one of the above mentioned five categories, the remaining objects of the stream belonged to the other four categories with non-repeating objects. As in the meta-contrast masking experiment, subjects were seated with their eyes at 57cm distance from the screen. Subjects were asked to fixate a centrally positioned cross which was set at the center of the screen, where the object stream would appear. Before the beginning of a stream, the name of the upcoming category was shown slightly above the position where the objects would later appear. Objects had a vertical size of 8cm in average and a horizontal width of approximately 6cm. They were presented against a white background. The subjects' task was to answer at the end of the stream how many objects between zero to four of the previously named category were present in the just presented stream. They were asked to enter this number on a specially marked keyboard at the end of the stream. No feedback was given concerning the correctness of their answers. After entering the number, a new trial started. A new trial was only started after subjects had entered a number. During the experiment, participants were able to take self-determined breaks at the end of a stream.

Object streams were presented at seven different presentation times per object either 20ms, 40ms, 60ms, 80ms, 100ms, 200ms or 300ms. Within one stream, all objects were shown at the same speed. A total of 10 trial repetitions was performed for each category and presentation time with each of the correct answers regarding how many of the ten streamed objects actually belonged to the desired category (ranging from 0-4) being present two times. For example for the combination of "office supplies" and 0 objects in this category, 2 trials exist at each of the 7 different speeds. This resulted in 70 trials for each category and a total of 350 trials per session which each category being tested once. Before the start of each experiment, a training trial without feedback took place to familiarize the subjects with the stimuli. For testing and training, the same set of stimuli was used.

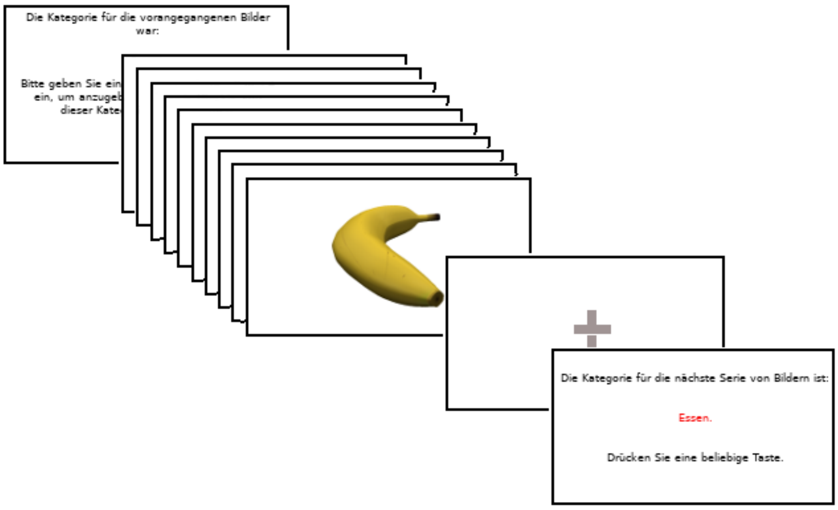

Figure 4: Exemplary trial of an object stream. The object stream started with the presentation of the instruction screen (shown at the right bottom) where the name of the category to be observed was presented. Then a fixation cross was shown for 4 seconds. A stream of ten objects was shown with all objects presented at the same speed. Of these ten objects 0, 1, 2, 3, or 4 belonged to the initially named category. The duration of the object stream depended on the presentation time (described in "Object recognition - stimuli and task"). At the end of the stream, subjects were asked to enter a number between 0 and 4 on the keyboard according to their recollection of how many of these objects had actually been presented. After entering a number, a new trial stream started.

2.2.2.3 Video recognition - stimuli and task

In this task, short films, whose presentation time was 25-times accelerated, were shown. Subjects had to choose the correct synopsis out of a set of 5 different synopses and they had to recognize objects.

Different short films were downloaded from the youtube channel „Virgin Media“ and accelerated to 25 times the usual presentation time with Light works (see Table 1). All short films contained little to no (essential) dialogue and no scenic changes essential for understanding the story of the film. The contents of the short films were independent of each other. All non-task relevant information were cut out (for example film title). The accelerated films had a duration of approximately 20 seconds. All films were presented in a pseudo-randomized manner in full screen mode with the open-source software VLC media player (see Table 1). For each film, a questionnaire was created that comprised two tasks: Choosing one out of five possible synopses, that depicted the film best. All synopses were sufficiently different so that only one choice of synopsis qualified as being correct. In addition, subjects had to determine if objects from a given list appeared in the film (for example a coffee mug). The choice of responses consisted of either „present“ or „not present“ which the subjects could mark with a cross. For the object recognition task of each short film, 40% to 60% of the objects in the questionnaire were actually present in the short film. Subjects were free to choose which of the subtasks they wanted to start with.

During the whole testing and training period, five different short films were shown. For every experimental session, a new short film was presented so that subjects did not see any short film twice. Within one experimental session, this film was then shown ten times in a row. After each single film presentation, subjects were handed out a yet unanswered questionnaire that they were asked to fill out. A single film trial ended when the questionnaire was returned to the experimenter. Subjects were not able to see the previously given responses in their questionnaires. After the questionnaire was handed over, the experimenter started a new trial and the previously already shown film was presented again. This was repeated nine times resulting in ten presentations of the same film in one experimental session. Subjects were not given any feedback on the correctness of their answers.

2.2.2.4 Connection between the three experiments

The meta-contrast masking experiment tested if deafs were able to see "better" a masked square, so a simple visual stimulus which was presented at those SOAs that are known to be difficult to perceive for sighted subjects. This was tested for both centrally and peripherally presented stimuli. The object recognition task already tested a more complex task. Apart from the sole perception of the shape of an object, the objects had to be consciously discriminated and classified according to their semantic category. The video recognition task presented the most complex task. In order to fully master this task, the above mentioned object recognition task had to be done and extended with an actual understanding of the film (synopsis). Objects had to be put into a greater context and the greater theme of the short film had to be found.

2.2.3 Data analysis

For each of the three experiments, the accuracy rate was calculated. In the meta-contrast masking experiment, the accuracy rate was defined as the rate of correctly classified targets. The accuracy rate was subsequently investigated for central and peripheral stimuli for the different SOAs before and after training. In the object recognition experiment, the accuracy rate was defined as the rate of correctly identified objects at a given presentation time. For each of the 7 presentation times, the accuracy rate was calculated from a total of 50 trials with 0 to 4 objects from the 5 different presented categories. In the video recognition experiment, the accuracy rate in the synopsis subtask was defined as the rate of correctly marked synopses of the same video over the 10 presentation repetitions. The accuracy rate in the object recognition subtask of the video recognition experiment was defined as the rate of correctly marked objects out of the ten measurement repetitions. For a more intuitive presentation, the calculated rates were transformed in percent. Additionally, the relative gain was computed for all tasks. The relative gain is defined as the difference of the accuracy rates before and after training in relation to the accuracy rate before training in %. Improvement in accuracy rate is defined as the difference between the accuracy rates before and after training. Distribution of these variables (that is the different accuracy rates) was assessed by plotting histograms. Due to the small sample size, a clear distribution could not be determined. In order to test if deaf subjects already differed from controls before training, Mann-Whitney U tests were conducted for each of the three experiments. To assess if training actually resulted in improved levels of performance, Wilcoxon signed-rank tests were conducted for deafs and controls. To compare the effects of training between both groups, Mann-Whitney U tests were used. Due to the small sample size and the exploratory nature of this study, the $\alpha-$level was not corrected. All reported p-values in this study are one-tailed.

2.3 Long-term impact of implantation of a unilateral cochlear implant in single-sided deafness on target sound localization in multiple-sounds environments

The following study tested whether a unilateral CI at the affected side of patients suffering from SSD helps to improve their ability to localize a target sound among multiple distractor sounds. Testing was done before and 3, 6, and 12 or more months after the implantation.

2.3.1 Participants

Twenty-one patients (mean age: 44.70 years, SD 12.71 years, range: 24–74 years, 9 women, 11 men) participated in this study (see Table 4). Inclusion criteria for this study were: adult subjects with SSD caused through sensorineural hearing loss, SSD acquired postlingually and normal or corrected-to-normal vision. Exclusion criteria were lack of capacity for informed consent and prior history of neurological deficits and psychiatric disorders. Patients who were in the process of getting a unilateral CI due to SSD at the Department of Otolaryngology, Head and Neck Surgery of the University of Tübingen, were informed about the study and were then personally asked if they would be interested in participating. One initially included patient dropped out of the study since only preoperative measurements could be acquired. After obtaining information about another patient suffering from cerebellar ataxia, the data of this patient were also excluded. All except two participants were right-handed as revealed by the Edinburgh Handedness Inventory (Oldfield, 1971). Detailed information about the clinical and demographic background of all patients is given in Table 4. An age- and sex-matched normal hearing group of 21 individuals (mean age: 46.53 years, SD 14.54 years, range: 23–72 years, 9 women, 11 men) with normal or corrected-to-normal vision served as controls. All participants gave their written informed consent to participate in this experiment. The study had been approved by the local Ethics Committee of the University of Tübingen (project number: 576/2014 BO2) and was conducted in accordance with the ethical guidelines of the Declaration of Helsinki.

Table 4: Etiological characterization of the single-sided deafness affected cochlear implant patients, f: female, m: male.

Patient ID	Sex	Cause of deafness	Age at implantation [yrs]	Duration of deafness [yrs] at time-point of implantation
1	f	sensorineural hearing loss	61	10
2	f	acute hearing loss	46	10
3	m	sensorineural hearing loss	37	7
4	m	sensorineural hearing loss	48	10
5	f	acute hearing loss	48	10
6	m	acute hearing loss	46	15
7	f	sensorineural hearing loss	48	since childhood
8	f	acute hearing loss	77	5
9	m	sensorineural hearing loss	70	13
10	f	cholesteatoma with progressive hearing loss	45	since childhood
11	m	sensorineural hearing loss	53	10
12	f	Menière’s disease	45	5
13	f	cerebellar ataxia, sensorineural hearing loss	56	10
14	m	sensorineural hearing loss	25	since childhood
15	f	sensorineural hearing loss	54	since childhood
16	f	sensorineural hearing loss	46	since childhood
17	m	craniocerebral injury	37	3 months
18	m	acute hearing loss	44	1
19	m	sensorineural hearing loss	35	9
20	m	sensorineural hearing loss	49	2
21	m	sensorineural hearing loss	26	3

2.3.2 Experimental setup and procedure

The experimental setup and set of stimuli used for this project was identical to the one described in 2.1.2 (see Figure 1). Data acquisition was performed at several time-points: patients were tested one week before unilateral CI implantation and at three different time-points during the postoperative rehabilitation at the University Department of Otolaryngology, Head and Neck Surgery in Tübingen: 3 months, 6 months, and $\geq$12 months (the latter: mean: 28.23 months, SD 15.82 months) after CI implantation. During each of the postoperative rehabilitation appointments, patients received a medical checkup, a readjustment of the CI was performed, and patients took part in various auditory test batteries and received speech therapy. Results of these tests were not taken into further consideration for this study nor did they influence the outcome of this study. Due to logistic reasons, it was not possible to acquire each patient’s data at each time-point (such as patients did not attend their scheduled rehabilitation program, they did not want to further participate in the study). Data of the control group were only acquired at one single time-point. Table 5 shows the number of patients who participated at each single measurement point.

Table 5: Number of patients and controls participating at each of the four measurement time-points: preoperatively, 3 months, 6 months, and ≥12 months postoperatively (post-op).

Time-points	preoperatively	3 months post-op	6 months post-op	≥12 months post-op
Number of SSD-patients	21	14	12	15
Controls	21	/	/	/

2.3.3 Data analysis

The localization performance in both the single-source and the multiple-sources condition was expressed as the mean absolute error in pointing. As in 2.1.3 the mean absolute error was defined as the mean of the unsigned deviation of the subject's responses (in degrees) from the actual target position. To describe the degree of change before and after CI implantation, this absolute mean error was calculated for the single-source and for the multiple-sources condition (see Tables 19 and 21). In addition to the mean absolute error, the median absolute error with the interquartile range is reported to also allow future further comparison of the data with studies with a non-parametric analysis strategy (see Tables 20 and 22). Similarly as in 2.1.3, the median absolute error provides a more accurate impression of the data distribution since the data of the absolute error are not normally distributed. Patients received their unilateral CI on either the left or the right ear. When registering the data, the loudspeaker positions were labeled with reference to the side of the CI. Ipsilateral describes the most eccentric target position (90°) that is on the same side as the implanted ear. The contralateral position describes the loudspeaker position on the opposite not implanted side. Semi-ipsilateral and semi-contralateral describe the ±45° positions and the central position (0°) describes the position directly in front of the subject. Naturally, controls do not have an ipsilateral side. The target eccentricity (0°, ±45°, and ±90°) was thus used when refering to these target positions. In order to compensate for the unilaterally tilted hearing of CI patients and to still allow a comparison between patients and controls and make the patients' "ipsilateral" and "contralateral" position equal in controls, in every other control the obtained results were swapped with the results from the opposing positions: the mean absolute errors for the 90° and -90°, as well as the 45° and -45° positions. The mean absolute error for the 0° position remained the same. For further analysis of the data, linear mixed-effects models (LMM) (see Verbeke and Molenberghs, 2009, West et al., 2014, Heck et al., 2013) were set up. The setup of the LMMs is described in more detail in the following section. All reported p-values are one-tailed. The α-level is 0.05.

2.3.3.1 Setup of the linear mixed-effects models

Standard linear models such as regression analysis, ANOVAs, or general linear models can not be correctly applied in the longitudinal data set of the present study since the assumption of independence of data or for homogeneity of regression slopes are violated (Field, 2009) and data points are missing. LMMs are an extension of the normal linear model (Heck et al., 2013) and allow to model correlated data with random intercepts and slopes (Field, 2009). LMMs prove especially useful when dealing with longitudinal, dependent, hierarchical and nested, repeated measures with missing data points (Heck et al., 2013). LMMs are mixed models because they contain both fixed and random effects. An effect is said to be a fixed effect when all possible conditions are present in the experiment. When repeating this experiment, these are the effects that one would expect to find again. Random effects describe an effect where only a random sample of the possible conditions is present in the experiment (Field, 2009). More information on LMMs can be found in Bates et al. (2015). The data were analyzed with the MIXED procedure in SPSS. A REML estimation was chosen due to the small sample size and to accommodate the repeated data structure with occasional missing values as recommended by Heck et al. (2013). The best fitting covariance structure was determined by using the restricted log-likelihood.

For the LMMs of this study, the following parameters were used: position (mean absolute error of the contralateral, semi-contralateral, central, semi-ipsilateral and ipsilateral position), time-point of measurement (preoperatively, 3, 6, and $\geq$12 months postoperatively) and group (patients, controls). Since a reference variable for the comparison between the different target positions is required, the position ‘contralateral’ of the equivalent time-point served in all following LMMs as reference. This contralateral position was chosen because it showed the least change for all time-points and all conditions (see Table 19 and 21). In this study, four different LMMs were set up. LMM 1.1 and LMM 1.2 model the mean absolute error in the single-source (LMM 1.1) and the multiple-sources condition (LMM 1.2) for controls and patients at the preoperative time-point. LMM 2.1 and LMM 2.2 model the performance of patients only in the single-source (LMM 2.1) and the multiple-sources condition (LMM 2.2) over time.

The best fitting model for LMM 1.1 and LMM 1.2 included the following factors: mean absolute error of the single-source condition (LMM 1.1) or the multiple-sources condition (LMM 1.2) for all positions (in the future referred to as position) except the contralateral position, with group and by position. As fixed effects group, position, and the interaction between group and position was used. To model the random effects, the factor subjects was used. As covariance structure, the variance components covariance matrix was used. The best fitting model for LMM 2.1 and LMM 2.2 included the following factors: mean absolute error for the single-source condition (LMM 2.1) or the multiple-sources condition (LMM 2.2) for all (except the contralateral) positions, by position with time-point of measurement. Only the data of the patients were used for LMM 2.1 as well as for LMM 2.2. As fixed factors, position, time-point of measurement, and the interaction between position and time-point of measurement significantly improved the model's fit and were therefore included. To model the random effects, the factor subjects was used. As covariance structure, the first-order autoregressive structure AR(1) was used.

3 Results

3.1 Horizontal sound localization of blind subjects in acoustically complex situations

The ability of blind subjects to localize a target sound both in isolation and within a sound setting with multiple distractors was measured (see Figure 1). No significant or relevant connection between onset of blindness and performance of blind subjects could be detected (Spearman's ρ=0.17, p=0.65). The same holds true for the correlation between the degree of blindness and performance of blind subjects (Spearman's ρ=0.09, p=0.83). Therefore, no subsequent distinction between onset of blindness nor degree of blindness was made and the data for all blind subjects were pooled.

3.1.1 Descriptive statistics

Both blinds and controls showed in both conditions an increase in the mean absolute error with increasing target eccentricity (see Table 6 and Figure 5). While the central position (0°) showed in both groups the smallest mean absolute error, this error more than doubled for the 90° positions in both groups and conditions. The greatest relative increase was thereby detected in the single-source condition in the control group where the mean absolute error at 0° was 2.40° (SD 1.46°) and rose to 13.76° (SD 5.97°) when the sound was coming strictly from the lateral side (±90°). The greatest absolute difference was also observed in the control group, where in the multiple-sources condition the mean absolute error increased from 7.55° (SD 6.28°) at 0° to 24.96° (SD 6.28°) at ±90°. Interestingly, in the present data set controls showed a lower mean absolute error in both tested conditions at all target eccentricities with only one exception: in the supposedly most difficult subtask - that is the multiple-sources condition at 90° eccentricity - the mean absolute error of blinds was slightly lower (22.04°, SD 9.55°) than that of the controls (24.96°, SD 6.28°).

Table 6: Mean absolute error (standard deviation) in degrees in the single-source and multiple-sources condition for the target eccentricities 0°, ±45° and ±90° in blinds and controls.

Target eccentricity	Blinds	Controls
Single-source condition		
0°	6.45 (3.60)	2.40 (1.46)
45°	9.55 (3.79)	5.31 (2.77)
90°	15.51 (7.27)	13.76 (5.97)
Multiple-sources condition		
0°	8.64 (3.14)	7.55 (6.28)
45°	9.35 (4.77)	8.19 (3.81)
90°	22.04 (9.55)	24.96 (6.28)

Table 7: Median absolute error (interquartile range) in degrees in the single-source condition and multiple-sources condition for the target eccentricities 0°, ±45° and ±90° in blinds and controls.

Target eccentricity	Blinds	Controls
Single-source condition		
0°	8.12 (2.81 - 11.25)	3.31 (1.46 - 7.33)
45°	10.20 (6.33 - 14.06)	6.00 (2.98 - 10.08)
90°	13.71 (7.03 - 24.61)	12.06 (7.66 - 19.68)
Multiple-sources condition		
0°	6.33 (4.04 - 10.55)	3.95 (3.35 - 12.13)
45°	13.01 (7.73 - 24.08)	10.33 (8.25 - 21.35)
90°	31.64 (14.06 - 48.16)	18.09 (7.25 - 29.91)

3.1.2 Inferential statistics

To further analyze the data, a three-factorial ANOVA was conducted. Group (blinds, controls) served as between-subjects factor and condition type (single-source condition, multiple-sources condition) and target position (0°, ±45°, ±90°) served as within-subjects factors. A significant main effect of condition type ($F(1,25)=25.40$, $p<0.001$) and a significant main effect of target position ($F(2,50)=52.88$, $p<0.001$) was found. These indicate that larger localization errors were made in the multiple-sources condition than in the single-source condition. Moreover, increasing target eccentricity also led to larger localization errors. Other interactions did not reach statistical significance and are reported in Table 8.

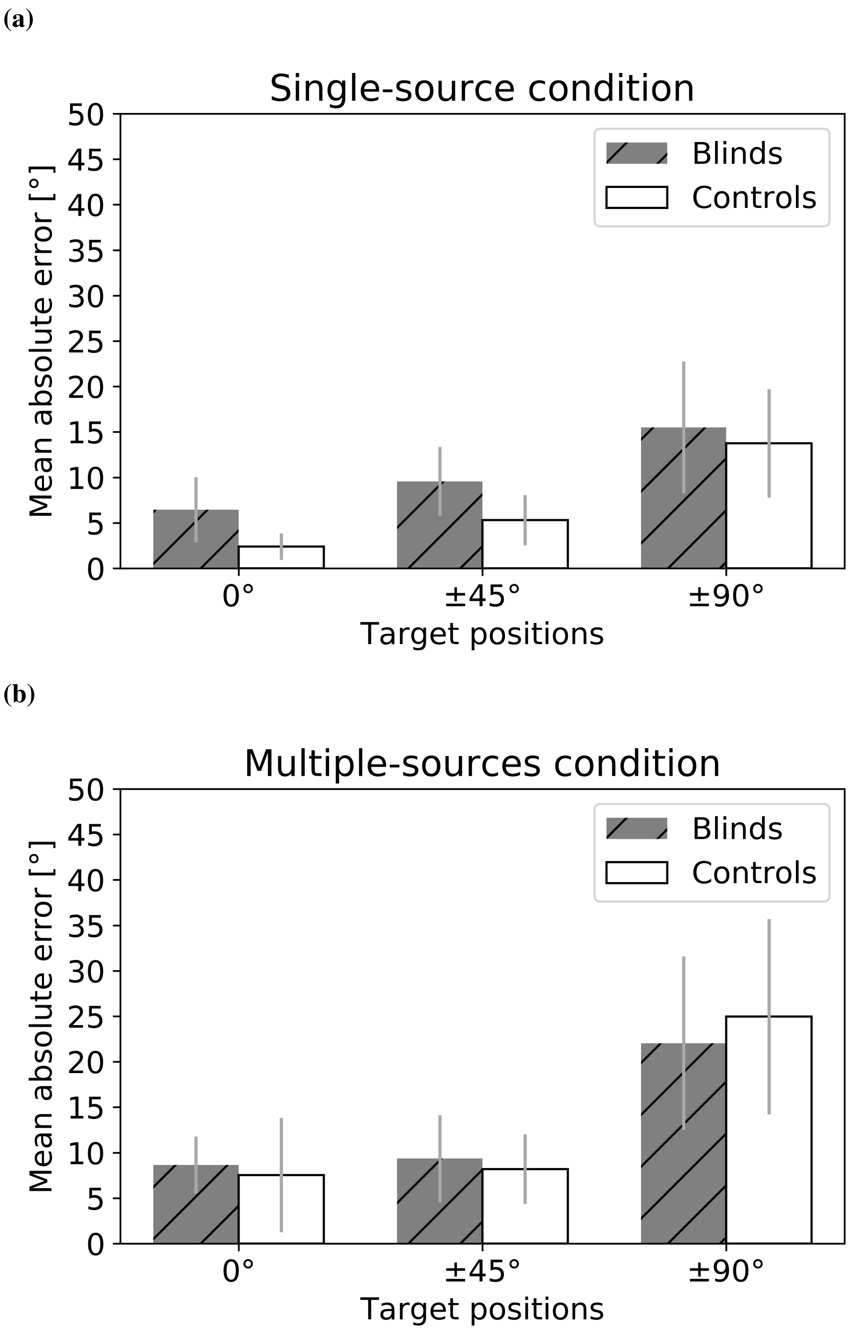

Figure 5: Mean absolute errors in degrees in pointing to the target positions in the single-source condition (a) and the multiple-sources condition (b) for blinds (gray hatched bars) and controls (white bars). Left and right target positions are averaged. Error bars display the standard deviation. Values for the mean absolute error in pointing precision increased with also increasing eccentricity in both experimental conditions and in both groups. Interestingly, the only condition where blinds present with better values than controls was for the supposedly most difficult task: 90° eccentricity in the multiple sources condition.

3.1.2.1 Post-hoc tests

In order to further analyze possible interactions between condition type and group, two post-hoc multivariate ANOVAs were set up. The first one tested the mean absolute error in the

Table 8: Results of the three-factorial ANOVA with group (blinds, controls) as between-factor and condition type (single-source, multiples-sources) and target position (0°, ±45°, ±90°) as within-factors.

Parameter	F-statistic, p-value
Main effect of condition type	F(1,25)=25.40, p<0.001
Main effect of target position	F(2,50)=52.88, p<0.001
Factor between-groups	F(1,25)=1.344, p=0.257
Interaction between condition type, group	F(1,50)=3.76, p=0.064
Interaction between condition type, group, target position	F(2,50)=0.115, p=0.891

single-source condition for both patients and controls with the target positions (0°, ±45°, ±90°) as dependent variables. For the second one, the mean absolute error in the multiple-sources condition was used, while the other parameters stayed the same. To adjust for multiple comparison, Bonferroni-correction was used (Bonferroni-adjusted α=0.025). No difference between groups was found for the multiple-sources condition (F(3,23)=0.42, p=0.74). The performance in the single-source condition showed a significant difference between groups with (F(3,23)=7.48, p=0.001). This significant difference between groups in the single-source condition was subsequently tested in follow-up univariate ANOVAs with group (blinds, controls) as between-subjects factor and target position as within-subjects factor. These ANOVAs resulted in a greater error for the target positions 0° (6.45°, SD 2.49°) and 45° (9.55°, SD 3.27°) in blinds than in controls (0°: 2.40°, SD 2.50°; F(1,25)=15.94, p=0.001, 45°: 5.31°, SD 3.27°; F(1,25)=10.09, p=0.004). For the target position of 90°, no significant difference between groups was found (blinds: 15.51°, SD 6.66°, controls: 13.79°, SD 6.67°; F(1,25)=0.40, p=0.53). The effect of the target position was subject for further post-hoc testing. Pairwise t-tests were used to assess the role of the target positions (0°, 45°, 90°) in the single-source condition for blinds versus controls. Increasing target position (0° to 45° to 90°) led to a greater mean absolute error in the control group (t(26)=4.00, p=0.001; Bonferroni-adjusted α=0.0083). This effect was also present in blinds, however less pronounced: The comparison of the target position 0° with 90° led to the smallest non-significant p-value in blinds (t(8)=3.23, p=0.012; Bonferroni-adjusted α=0.0083).

3.1.2.1.1 Analysis of individual blind subjects

The greatest difference in performance between blinds and controls was observed at the target position 0° in the single-source condition (mean absolute error in blinds: 6.45°, SD 3.60° and in controls: 2.40°, SD 1.46°). Therefore, in another post-hoc analysis step, the performance of individual blind subjects at this position was investigated using the single-case method singlim by Crawford et al. (2010). Table 9 lists the results for all individual blind subjects.

Table 9: Results of the analysis of individual blind subjects with the single-case method singlim for the target position 0° with z-score and p-value. Controls had a mean absolute error of 2.40° (SD 1.46°) at target position 0°.

Subject's ID	Etiology of blindness	Deviation from target position 0° [in °]	z_{cc}-score	t-statistic, p-value
1	blind since childhood, no residual vision	3.52	0.75	t(17)=0.73, p=0.477
2	late blind, no residual vision	6.36	2.65	t(17)=2.58, p=0.020
3	blind since childhood, no residual vision	10.15	5.15	t(17)=5.02, p<0.001
4	congenitally blind, no residual vision	7.95	3.70	t(17)=3.60, p=0.002
5	late blind, residual vision	12.59	6.79	t(17)=6.61, p=0.001
6	blind since childhood, no residual vision	3.80	0.93	t(17)=0.91, p=0.376
7	blind since childhood, no residual vision	4.43	1.35	t(17)=1.32, p=0.205
8	congenitally blind, residual vision	9.70	4.87	t(17)=4.74, p<0.001
9	congenitally blind, residual vision	7.45	3.84	t(17)=3.28, p=0.004

Subject 2, 3, 4, 5, 8 and 9 exposed a significantly greater error for the target position 0° in comparison to controls. Interestingly, no common etiological parameter (onset, duration of blindness, degree of residual vision) could be identified in the analysis of these subjects. They rather present a heterogeneous subset of the whole blind test group. Subject 2 and 5 were the only late blind subjects in the study, while subjects 4, 8 and 9 were the only congenitally blind subjects. Subject 3 was the only subject who turned blind at the age of 10. Subjects 5, 8 and 9 were the only subjects with residual vision, while subjects 2 and 3 had none. The duration of blindness within this subset is also widely spread with a range of 2 to 67 years.

3.2 Effects of training on the visual processing speed in deafs

The effects of training on the visual processing speed in deafs were investigated in a meta-constrast, an object recognition and a video recognition task.

3.2.1 Meta-contrast masking

3.2.1.1 Descriptive statistics

In this task, subjects had to identify the position of the gap of the target stimulus. The target was followed by a mask which was shown at different SOAs. The visual stimuli were either presented centrally or peripherally.

The accuracy rate was defined as the number of correctly classified targets (number of correctly identified gap openings) in percent out of a theoretical maximum of 50 correct answers. When looking at the averaged accuracy rates obtained from the different SOAs for the central and peripheral condition before training (see Table 10 and Figure 6), it can be noted that controls showed a better performance at the central position, while deafs outperformed controls at the peripheral position. Now interestingly, the effect of training in both groups was observed mostly at that presentation position, where they performed worse than their group counterpart: controls improved their accuracy rates at the peripheral position (from 55.79%, SD 10.62% to 61.85%, SD 9.05%), whereas deafs mostly improved at the central position (from 51.22%, SD 19.43% to 57.55%, SD 17.38%).

When looking at the effects of training on the accuracy rates for the individual SOAs (see Table 10 and Figure 7), two observations stick out: First, in both deafs and controls the observed absolute changes in accuracy rate from before training to after training were within a scope of -5% to +11%, with a slight improvement after training in most experimental conditions. Secondly, as already implied by the averaged values, controls showed greater improvement after training for the peripheral position (4% to 11%), while the changes for the central position were between -2% to +2%. Of note, the largest effect of training for controls was found for the SOA of 80ms at the peripheral position with the accuracy rate improving from 50.00%

(SD 10.08%) to 61.01% (SD 8.73%). Complementary to this, deaf subjects mostly improved at their weaker central position ranging from 1% at a SOA of 0ms to 11% at a SOA of 60ms, while accuracy rates for the peripheral position changed only marginally ranging from -5% to 8%.

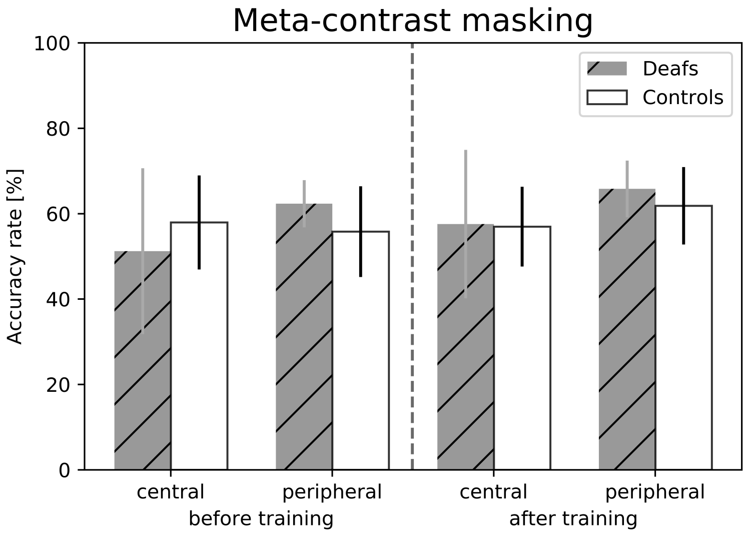

Figure 6: Averaged accuracy rates for the meta-contrast masking experiment. The accuracy rates in percent are averaged across all four stimulus onset asynchronies (SOAs) for central and peripheral meta-contrast stimuli in deafs and in controls before and after training. Error bars represent the standard deviation. Bars on the left side of the dashed vertical line show the performance before training, bars on the right side of the dashed line show the performance after training. While in the present data set, a higher accuracy rate was observed in controls at the central position, deafs achieved a higher accuracy rate at the peripheral positions.

Table 10: Accuracy rate (standard deviation) in percent and relative gain averaged across all four stimulus onset asynchronies (SOAs) and for all four individual SOAs for centrally and peripherally presented meta-contrast stimuli in deafs and in controls before and after training.

SOA	**Position**	**Deafs**			**Controls**		
		before training	after training	relative gain	before training	after training	relative gain
Averaged	central	51.22 (19.43)	57.55 (17.38)	12.36	57.94 (11.01)	56.97 (9.35)	5.75
	peripheral	62.22 (5.53)	65.80 (6.64)	1.67	55.79 (10.62)	61.85 (9.05)	10.86
0ms	central	58.33 (20.62)	59.72 (19.48)	2.38	60.16 (9.99)	58.63 (16.94)	-2.54
	peripheral	74.31 (4.10)	82.29 (11.24)	10.74	66.67 (12.65)	72.32 (18.27)	8.47
20ms	central	45.49 (24.06)	55.90 (21.87)	22.88	55.99 (15.61)	54.76 (9.82)	-2.20
	peripheral	57.99 (12.94)	62.85 (10.66)	8.38	52.86 (16.33)	57.14 (6.68)	8.10
60ms	central	47.57 (24.42)	59.03 (12.41)	24.09	58.85 (11.77)	57.44 (8.06)	-2.40
	peripheral	61.81 (7.05)	56.60 (10.81)	-8.43	53.65 (10.25)	59.82 (19.16)	11.50
80ms	central	45.14 (21.64)	55.56 (19.21)	23.08	56.78 (13.44)	58.63 (9.27)	3.26
	peripheral	55.21 (8.62)	61.46 (5.86)	11.32	50.00 (10.08)	61.01 (8.73)	22.02

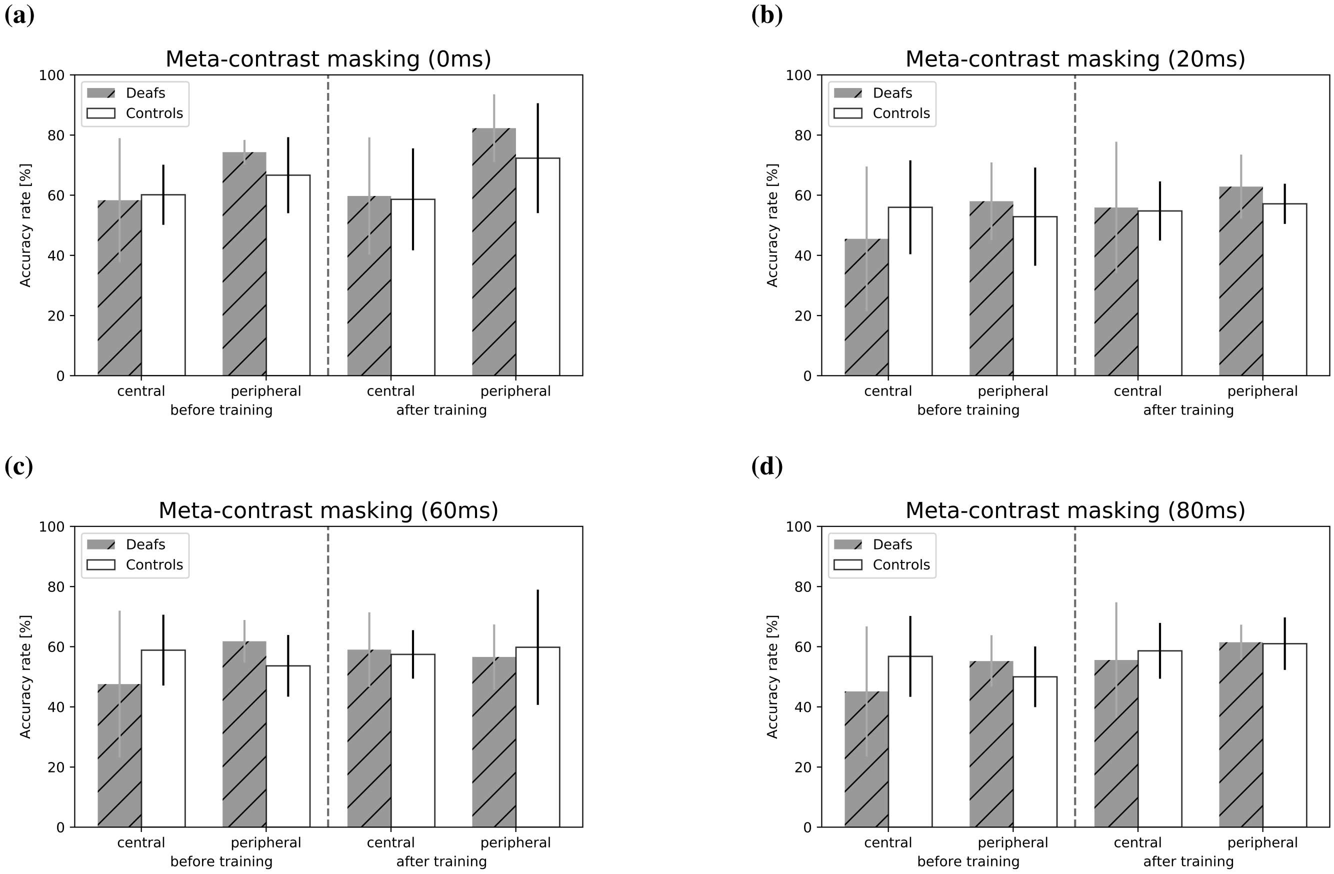

Figure 7: Accuracy rates for the meta-contrast masking experiment reported for the different stimulus onset asynchronies. Accuracy rate in percent for all four stimulus onset asynchronies (SOAs) (**a**) 0ms, (**b**) 20ms, (**c**) 60ms and, (**d**) 80ms) for central and peripheral meta-contrast stimuli in deafs (grey hatched bars) and in controls (white bars) before and after training. Error bars represent the standard deviation. Bars on the left side of the vertical dashed line show the performance before training and on the right side of this line the performance after training. While the overall performance was at comparable levels across all conditions and both groups, deaf subjects outperformed the controls at the peripheral positions whereas higher accuracy rates were observed in the control group at the central position.

3.2.1.2 Inferential statistics

To further analyze if deaf subjects outperformed controls already before training, two Mann-Whitney U tests for deaf subjects and controls on the accuracy rate of centrally and peripherally presented targets averaged over all SOAs before training were setup. No statistically significant difference in performance before training between deaf subjects and controls could be found for centrally presented stimuli (U=316.00, p=0.130). However, the Mann-Whitney U test for peripherally presented stimuli resulted in a significant difference (U=254.50, p=0.016) implying that deaf subjects showed a higher accuracy rate for peripherally presented stimuli before training.

To compare the effects of training between both groups, two Mann-Whitney U tests on the averaged accuracy rates of all SOAs before and after training for centrally and peripherally presented targets were set up. Averaged across all four SOAs, deafs improved in absolute value by approximately 8.42% (controls: -0.6%) for centrally presented targets and by 3.47% (controls: 7%) for peripherally presented targets (see Table 10 and Table 12). These differences were, however, not statistically significant (see Table 12). When analyzing the differences in the SOAs separately, none of the individual SOAs resulted in a significantly better performance in deafs (all p-values>0.05). In general, the p-values for the central presentations were smaller in magnitude than those p-values for peripheral presentations (except for the larger central p-value for the SOA 60ms: U=15.50, p=0.134). To test if training resulted in better performance, two Wilcoxon tests on the averaged difference across the accuracy rates of all SOAs before and after training for centrally and peripherally presented targets for both deafs and controls were set up (see Table 11). Only the level of performance in deafs for centrally presented targets (Z=-2.91, p=0.001) and the level of performance in controls for peripherally presented targets (Z=-1.76, p=0.038) improved significantly with training. Deafs' level of performance for peripherally presented targets and the central presentation position in controls did not improve significantly with training (see Table 11).

Table 11: Wilcoxon test on the effects of training on the accuracy rates in the meta-contrast masking experiment in deafs and controls. Accuracy rates were averaged over all four SOAs. Results are presented for central and peripheral stimuli separately.

Presentation position	group	Wilcoxon test
Central	deafs	Z=-2.91, p=0.001
Central	controls	Z=-1.23, p=0.112
Peripheral	deafs	Z=-0.52, p=0.309
Peripheral	controls	Z=-1.76, p=0.038

Table 12: Comparison of the improvement in accuracy rates in the meta-contrast masking experiment between deafs and controls. Results are presented for central and peripheral stimuli separately and are reported for each stimulus onset asynchrony (SOA).

SOA	Mann-Whitney U	p-value	Mann-Whitney U	p-value
	central		peripheral	
Averaged	10.50	0.111	18.50	0.238
0ms	17.00	0.180	21.50	0.373
20ms	13.00	0.076	23.00	0.448
60ms	15.50	0.134	12.00	0.056
80ms	10.50	0.053	22.00	0.398

3.2.2 Object recognition

In this task, subjects had to identify the number of objects belonging to a certain category in an object stream. Objects streams were shown for different presentation times.

3.2.2.1 Descriptive statistics

The accuracy rate was defined as the rate of correctly identified objects in the streams in percent averaged for all five object categories with each of them being presented 10 times at a specific speed (so a total of 50 streams) (see Table 13). Before and after training, both groups had the lowest accuracy rate for the shortest presentation time of 20ms. With increasing presentation time, the accuracy rates also increased, reaching the highest rates in both groups at the longest presentation time (300ms) with deafs having an accuracy rate of about 80% and controls of about 75% (see Table 13 and Figure 8). Relevant improvements through training were observed in both groups and for almost all presentation times, the greater effects being at shorter presentation times. The absolute increase in accuracy rates ranged from 8% to 16% in both groups signifying a relative increase of up to 35% of the original rate (see Table 13). The presentation times of 20 ms, 40ms and 60ms led to an accuracy rate that was between 8% to 12% higher. For the presentation time of 80ms, the effects of training were stronger in deafs than in controls. While deafs improved their accuracy rate by about 14% (47.71% (SD 4.39%) to 62.00% (SD 3.02%), controls only improved by about 8% (51.25% (SD 9.38%) to 59.50% (SD 14.33%)). The most pronounced absolute increase in the accuracy rate in deafs was observed for the presentation time of 200ms where deaf subjects improved their performance from an initial accuracy rate of 66.57% (SD 3.95%) to 80.57% (SD 1.80%), while the controls increased their rate only from 70.75% (SD 10.53%) to 73.50% (SD 11.05%). While the initial accuracy rates were already very high at the longest presentation time, it was at this presentation time that also the least effects of training were observed with only an absolute increase in accuracy rate of less than 2% in both groups (deafs: 79.43%, SD 6.70% to 80.86%, SD 1.90%, controls: 75.25%, SD 10.36% to 75.50%, SD 9.30%).

Table 13: Accuracy rates (standard deviation) in percent and relative gain (calculated as the percentual change from before to after training taking the value before training as baseline value of correctly identified objects for the streams across all five categories per given presentation time in deafs and controls before and after training.

Presentation time	**Deafs**			**Controls**		
	before training	after training	relative gain	before training	after training	relative gain
Averaged	53.18 (5.79)	62.33 (2.78)	17.21	53.79 (9.83)	61.46 (13.67)	14.26
20ms	34.00 (5.66)	42.57 (3.35)	25.21	35.50 (8.40)	47.75 (18.71)	34.51
40ms	39.71 (4.82)	51.71 (4.12)	30.22	43.00 (9.97)	52.75 (17.85)	22.67
60ms	47.43 (5.97)	55.14 (3.02)	16.26	48.50 (11.25)	58.25 (14.83)	20.10
80ms	47.71 (4.39)	62.00 (3.02)	29.95	51.25 (9.38)	59.50 (14.33)	16.10
100ms	57.43 (9.07)	63.43 (2.23)	10.44	52.25 (8.91)	63.00 (9.62)	20.57
200ms	66.57 (3.95)	80.57 (1.80)	21.03	70.75 (10.53)	73.50 (11.05)	3.89
300ms	79.43 (6.70)	80.86 (1.90)	1.80	75.25 (10.36)	75.50 (9.30)	0.33

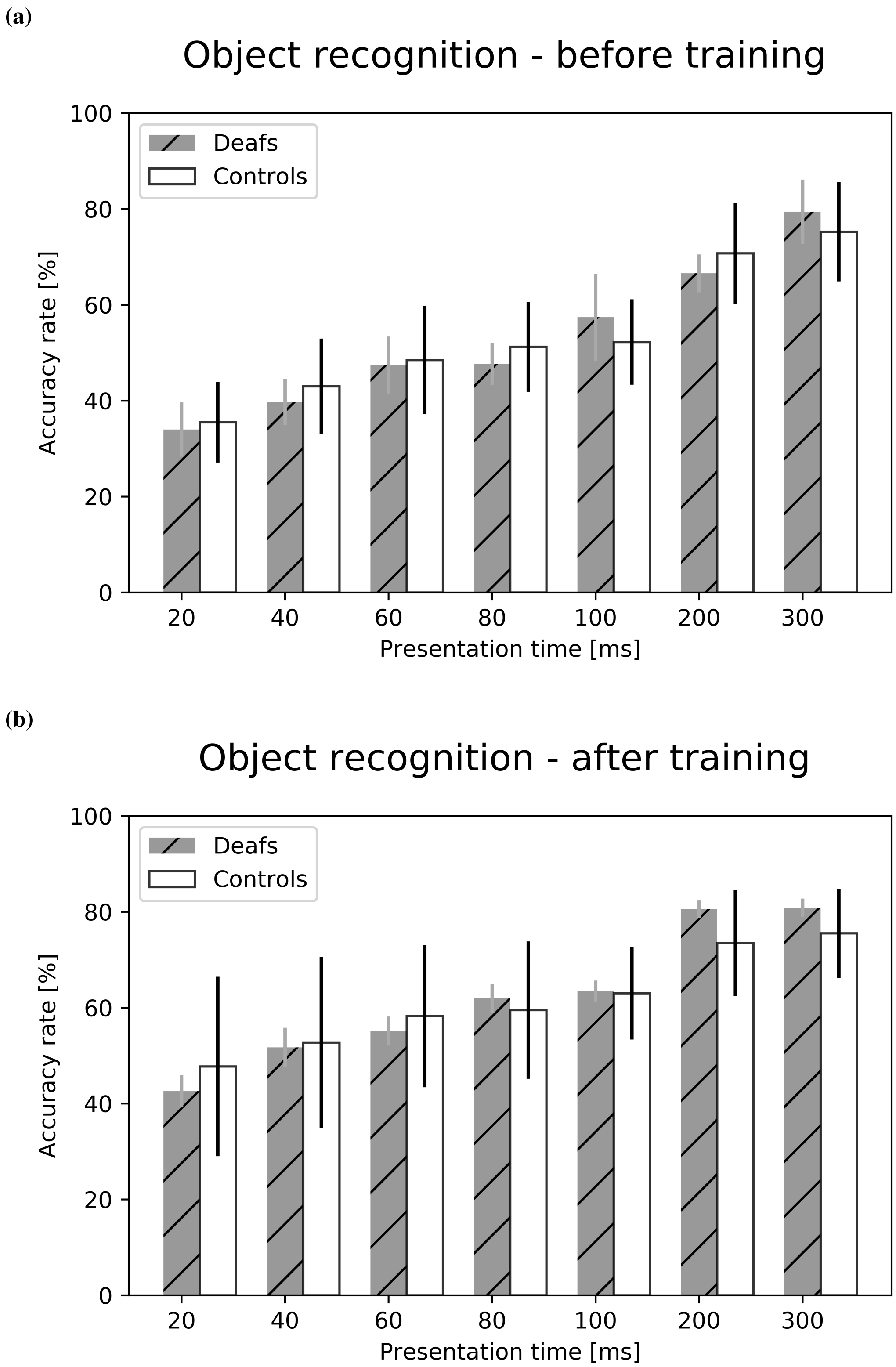

Figure 8: Accuracy rate in percent of correctly identified objects for the object streams at different presentation times for deafs (grey hatched bars) and controls (white bars) before (a) and after (b) training. Error bars display the standard deviation. An increase in accuracy rate can be observed in both deafs and controls with increasing presentation duration.

3.2.2.2 Inferential statistics

To analyze if deaf subjects and controls already differed before training, a Mann-Whitney U test on the accuracy rates of correctly identified objects, including the results of all presentation times between groups was set up. No significant difference was found (U=1330,00, p=0.394). To analyze if training resulted in better performance in both groups, two Wilcoxon tests on the accuracy rates of correctly identified objects averaged over all presentation times for deafs and controls before and after training were set up. Both groups had indeed significantly better performance levels after training (deafs: Z=-4.32, p<0.001, controls: Z=-4.52, p<0.001, see also Table 14). For further analysis, Mann-Whitney U tests were set up on the improvement in accuracy rates of correctly identified objects on given speeds in object streams between deaf subjects and controls after training (Table 15). These tests were first performed across all presentation times and then for each presentation time separately. The trend of the meta-contrast masking experiment could also be found here: Both groups benefited equally from the effects of training. The improvment of deafs was significantly higher than in controls for objects presented for 200ms (U=14.50, p=0.003).

Table 14: Wilcoxon test on the effect of training on the accuracy rates in the object recognition experiment in deafs and controls. Accuracy rates were averaged over all different presentation times

Group	Wilcoxon test
Deafs	Z=-4.32, p<0.001
Controls	Z=-4.52, p<0.001

Table 15: Comparison of the improvement for the different presentation times of the object recognition task between deafs and the control group. Analyses were performed pooled for all tests together and for all different presentation times separately.

Presentation time	Mann-Whitney U	p-value
Averaged	12.49	0.215
20ms	22.50	0.268
40ms	26.00	0.433
60ms	25.50	0.390
80ms	19.00	0.168
100ms	14.50	0.061
200ms	11.00	0.003
300ms	25.00	0.390

3.2.3 Video recognition

In this task, subjects watched accelerated short films. After each film presentation, subjects had to chose the correct synopsis for this film out of five offered possibilities. Additionally, subjects completed a questionnaire about objects depicted in the film.

3.2.3.1 Descriptive statistics

The video sequences were shown ten times in a row during one measurement session. Subjects were asked to complete the questionnaire and to chose the corresponding synopsis after each single video presentation without receiving feedback on the correctness of their answers. The rate of correctly identified synopses before training among deaf subjects was 44.29% (SD 3.82%) and in controls 30.00% (SD 3.87%). Thus, both groups already showed an absolute difference of approximately 14% in reference to the theoretically maximum number of ten correct answers (for the ten measurement repetitions). After training, this difference was even stronger with deafs almost having doubled their accuracy rate, while controls only improved to 42.86% (SD 4.03%)(see Table 16 and Figure 9).

Table 16: Accuracy rates (standard deviation) and relative gain in percent for the video recognition experiment reported for the synopsis task and the object recognition task in deafs and controls before and after training.

Task	**Deafs**			**Controls**		
	before training	after training	relative gain	before training	after training	relative gain
Synopsis	44.29 (3.82)	78.51 (3.67)	77.26	30.00 (3.87)	42.86 (4.03)	42.87
Object recognition	68.88 (7.12)	70.16 (10.57)	1.86	67.38 (13.88)	69.85 (9.23)	0.37

While in the synopsis task a pronounced difference in performance between groups and time-points could be observed, in the object recognition part of the video recognition task no such difference between groups and through the training was present (see Table 16 and Figure 10). Before training, the rate of correctly identified objects in deafs was 68.88% (SD 7.12%) and 67.38% (SD 13.88%) in controls. After training, these values were only marginally increased in deafs to a rate of 70.16% (SD 10.57%) and in controls of 69.85% (SD 9.23%).

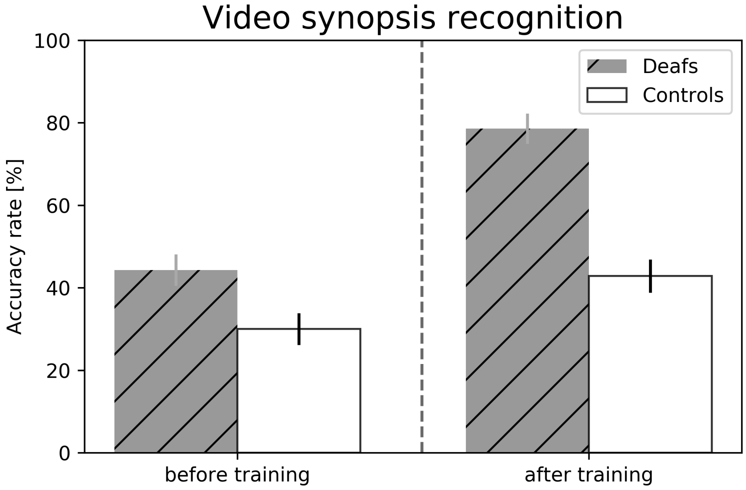

Figure 9: Mean accuracy rates (standard deviation) of correctly identified video synopses in percent for deafs (grey hatched bars) and controls (white bars) before and after training. A higher improvement in the number of correctly identified synopses can be observed in the deaf group while the effects of training on controls are less pronounced.

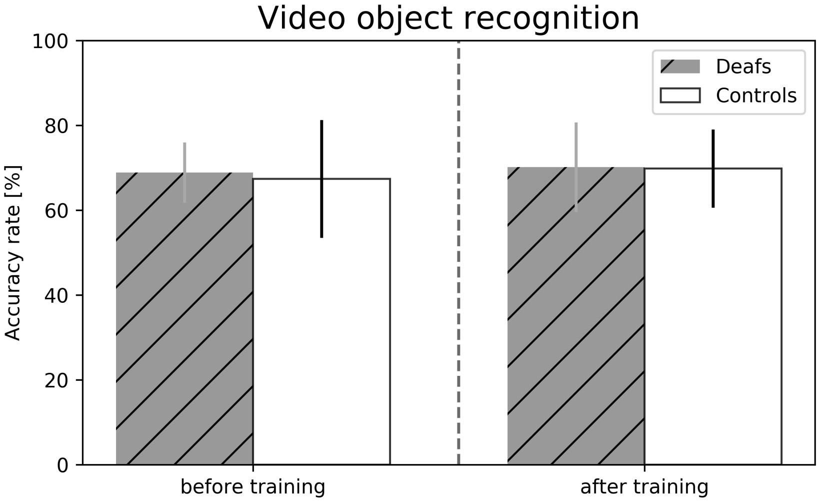

Figure 10: Bar diagrams illustrating the rate of correctly identified objects in the video in percent (standard deviation) for deafs and controls before and after training. No relevant difference could be detected between groups and before and after training.

3.2.3.2 Inferential statistics

To analyze if deaf subjects already outperformed controls before training, two Mann-Whitney U tests were set up on the accuracy rate of correctly identified synopses of the short film and on the accuracy rate of correctly identified objects in the short film between groups before training. Neither test resulted in a significant difference between groups (synopsis: U=21.00, p=0.463; object recognition: U=2164,50, p=0.318). To analyze if deafs and controls improved their performance with training, Wilcoxon tests were set up on the accuracy rates of correctly identified synopses of the short film and on the accuracy rate of correctly identified objects in the short film for each group before and after training. Only the performance of deafs in the video synopsis task was significantly better with training (Z=-4.99, p<0.001) while training did not result in a better performance level for the object recognition task in deafs. Training did not lead to a better performance in controls for any of the subtasks (see Table 17). To further analyze the effects of training, Mann-Whitney U tests were set up on the differences in accuracy rates of correctly identified synopses and on the accuracy rates of correctly identified objects in the films before and after training between groups (see Table 18). When comparing the results of the effects of training on deafs with the effects of training on controls in the synopsis task, a significant difference in the number of correctly identified synopses could be detected (U=396.00, p=0.001). This implies that after training, deafs chose the correct synopsis for the highly accelerated films significantly more often than controls. The effects of training for the object recognition task did not result in a significant difference in accuracy rate between groups after training (U=2280.50, p=0.307) (see Table 18).

Table 17: Wilcoxon test on the effect of training on the accuracy rates in the video recognition experiment in deafs and controls.

Task	group	Wilcoxon test
Object recognition	deafs	Z=-0.85, p=0.200
Object recognition	controls	Z=-1.48, p=0.070
Synopsis	deafs	Z=-4.99, p<0.001
Synopsis	controls	Z=-0.87, p=0.243

Table 18: Comparison of the improvement through training in the accuracy rates between deafs and controls, calculated for both subtasks of the video recognition experiment.

Task	Mann-Whitney U	p-value
Object recognition	2280.50	0.307
Synopsis	396.00	0.001

3.3 Long-term impact of implantation of a unilateral cochlear implant in single-sided deafness on target sound localization in multiple-sounds environments

This study investigated the impact of unilateral CI implantation in patients suffering from SSD on their ability for simple and complex target sound localization. The simple target sound task consisted of a single sound source that had to be localized in a horizontal frontal semicircle. In the multiple-sounds condition the target sound had to be localized while four distractor sounds were additionally emitted from different positions on the frontal semicircle.

3.3.1 Descriptive statistics

3.3.1.1 Single-source condition

In the single-source condition controls showed a mean absolute error at the central position of 4.1° (SD 3.3°). This error increased for the ±45° target eccentricities at a comparable level (6.7°, SD 3.9° and 6.7°, SD 4.2°) and was most pronounced at the ±90° positions (13.9°, SD 5.2° and 12.0°, SD 5.1°) (see Table 19/20 and Figure 11). When looking at the patient cohort, a very distinct pattern could be observed preoperatively: While the mean absolute errors for the central, semi-contralateral and contralateral position were all at a comparable level between 23.4° (SD 11.9°) and 40.2° (SD 15.3°). This error was greatly increased at the semi-ipsilateral position (64.6°, SD 22.9°) and showed its highest value at the ipsilateral position (104.7°, SD 25.2°).

During the postoperative rehabilitation period, interesting changes could be observed: while no relevant improvement could be detected for the central, semi-contralateral and contralateral position, marked changes were present for the semi-ipsilateral and ipsilateral position. For the ipsilateral position (that is the side with the CI), the mean absolute error dropped from the preoperative value of 104.7° (SD 25.2°) to 40.0° (SD 18.3°) at the last measurement ≥12 months after surgery. The magnitude of the preoperative mean absolute error for this ipsilateral target position implies, that for SSD-patients sound localization even in the single-source condition was not possible ipsilaterally and that the location of sounds presented at this target position were merely guessed. This observation also applies to a lesser extent to the semi-ipsilateral position, where also a major improvement was observed in the mean absolute error from preoperatively 64.6° (SD 22.9°) to 20.5° (SD 12.4°) at the 6-months follow-up. It needs to be pointed out, that the greatest improvement was detected between the preoperative assessment and 3-months after surgery.

Table 19: Mean absolute error (standard deviation) in degrees at the five target positions in controls (one measurement time-point) and in single-sided deaf patients (four measurement time-points: preoperatively, 3 months, 6 months, ≥12-months postoperatively (post-op)) in the single-source condition.

Mean absolute error in the single-source condition

Target position	controls	preoperatively	3 months post-op	6 months post-op	≥12 months post-op
Ipsilateral	13.9 (5.2)	104.7 (25.2)	61.5 (21.6)	42.6 (15.7)	40.0 (18.3)
Semi-ipsilateral	6.7 (3.9)	64.6 (22.9)	31.7 (16.0)	20.5 (12.4)	31.7 (14.2)
Central	4.1 (3.3)	39.1 (17.0)	31.1 (17.1)	23.4 (16.5)	32.3 (21.2)
Semi-contralateral	6.7 (4.2)	23.4 (11.9)	19.2 (14.5)	22.0 (12.9)	18.0 (9.8)
Contralateral	12.0 (5.1)	40.2 (15.3)	32.8 (14.3)	38.9 (15.6)	36.4 (13.3)

Table 20: Median absolute error (interquartile range) in degrees of the five target positions in controls (one measurement time-point) and in single-sided deaf patients (four measurement time-points: preoperatively, 3 months, 6 months and ≥12 months postoperatively (post-op)) in the single-source condition.

Median absolute error in the single-source condition

Target position	controls	preoperatively	3 months post-op	6 months post-op	≥12 months post-op
Ipsilateral	11.1 (4.4 - 18.5)	105.3 (72.3 - 134.3)	35.2 (24.9 - 60.1)	40.4 (26.9 - 56.6)	31.6 (14.8 - 54.5)
Semi-ipsilateral	5.3 (2.3 - 11.0)	65.5 (35.5 - 87.2)	17.1 (7.9 - 38.2)	16.5 (8.4 - 29.3)	21.5 (11.1 - 33.9)
Central	3.0 (0.9 - 5.5)	36.6 (21.0 - 57.0)	25.3 (6.7 - 48.2)	21.3 (11.5 - 33.4)	26.0 (14.0 - 43.6)
Semi-contralateral	5.5 (8.3 - 19.5)	23.0 (10.5 - 32.7)	13.8 (5.6 - 27.6)	19.7 (11.3 - 35.1)	15.8 (5.8 - 26.8)
Contralateral	13.8 (8.3 - 19.5)	28.3 (14.8 - 57.7)	33.1 (20.2 - 45.0)	32.4 (17.6 - 46.6)	32.1 (16.9 - 49.7)

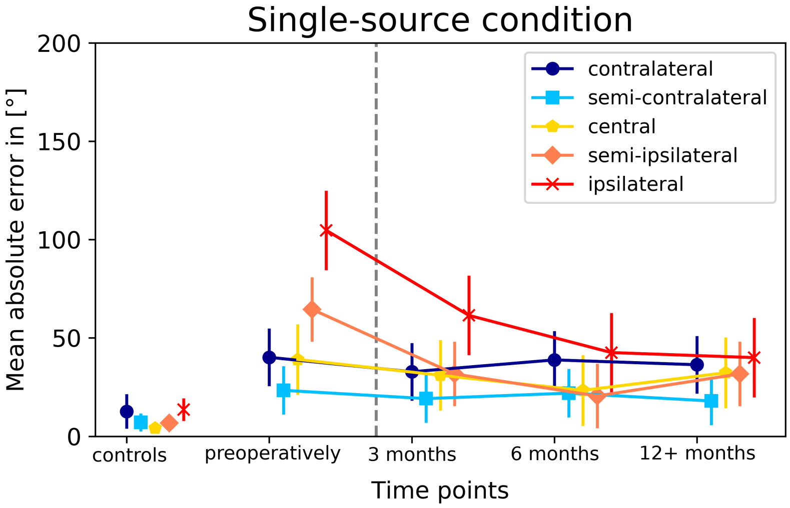

Figure 11: Pointing errors in sound localization in the single-source condition. Line-diagram displaying the mean absolute error in degrees (error bars: standard deviation) in pointing at the different target positions for controls and patients in the single-source condition. Controls are reported as a single time-point measurement on the left side. The dashed vertical line indicates the time-point of surgery, with the follow-up assessments at 3, 6, and ≥12 months postoperatively. Results are reported for each of the five target positions. It can be noted that it is especially at the semi-ipsilateral and even more at the ipsilateral target position that a marked improvement after surgery can be measured, while no relevant change can be observed at the central, the semi-contralateral, and the contralateral sound-position.

3.3.1.2 Multiple-sources condition

In the multiple-sources condition, controls showed comparable results as in the single-source condition with, however, slightly larger mean absolute errors. The smallest mean absolute error was found at 0° with 11.3° (SD 15.9°), while increasing target eccentricity led to larger mean absolute errors which were most pronounced at the ±90° positions (23.9°, SD 20.0° and 14.1°, SD 13.2°). Generally, the mean absolute error in controls in the multiples-sources condition was at all positions similar in size to the error measured in controls in the single-source condition at ±90° (the only exception being the ipsilateral position) with the mean absolute error varying only from 11.3° (SD 15.9°) to 14.1° (SD 13.2°) (see Table 21/22 and Figure 12).

Similar as in the single-source condition, SSD-patients presented the worst performance at the ipsilateral position with a preoperative mean absolute error of 111.7° (SD 25.7°) and at the semi-ipsilateral position with preoperatively 66.6° (SD 22.3°). Again, the ipsilateral position showed the greatest improvement of the mean absolute error over time which dropped down to 61.3° (SD 36.0°) by the final assessment (see Table 21). Also the mean absolute error at the semi-ipsilateral position was reduced by about half of its original value: the preoperatively measured mean absolute error of 66.6° (SD 22.3°) dropped to 33.8° (SD 19.5°) by the end of the study. Comparable to the single-source condition, the changes in the patient group for the central, the semi-contralateral and the contralateral position were of a marginal nature. Changes in these three positions were approximately between 5° to 9° when comparing the preoperative with the last assessment.

Table 21: Mean absolute error (standard deviation) in degrees of the five target positions in controls (one measurement time-point) and in single-sided deaf patients (four measurement time-points: preoperatively, 3-months, 6-months and ≥12-months postoperatively (post-op)) in the multiple-sources condition.

Mean absolute error in the multiple-sources condition

Target position	controls	preoperatively	3 months post-op	6 months post-op	≥12 months post-op
Ipsilateral	23.9 (20.0)	111.7 (25.7)	85.1 (34.0)	59.5 (31.6)	61.3 (36.0)
Semi-ipsilateral	13.0 (13.6)	66.6 (22.3)	47.6 (25.7)	33.3 (22.1)	33.8 (19.5)
Central	11.3 (15.9)	39.2 (19.9)	34.3 (19.8)	33.1 (21.4)	30.3 (27.2)
Semi-contralateral	12.5 (14.4)	25.9 (16.4)	25.7 (21.0)	28.3 (24.5)	24.0 (18.5)
Contralateral	14.1 (13.2)	47.7 (19.4)	48.2 (24.7)	56.4 (30.2)	54.8 (18.5)

Table 22: Median absolute error (interquartile range) in degrees of the five target positions in controls (one measurement time-point) and in single-sided deaf patients (four measurement time-points: preoperatively, 3-months, 6-months and ≥12-months postoperatively (post-op)) in the multiple-sources condition.

Median absolute error in the multiple-sources condition

Target position	controls	preoperatively	3 months post-op	6 months post-op	≥12 months post-op
Ipsilateral	11.2 (5.0 - 20.7)	121.2 (87.8 - 143.0)	61.6 (34.5 - 114.6)	60.5 (37.7 - 96.3)	44.3 (22.8 - 78.4)
Semi-ipsilateral	7.0 (2.9 - 14.0)	71.0 (42.3 - 94.8)	26.0 (11.3 - 69.3)	23.6 (12.7 - 52.7)	24.6 (11.8 - 39.4)
Central	4.2 (1.7 -10.9)	42.3 (18.1 - 58.1)	32.3 (18.2 - 50.4)	33.4 (17.7 - 54.0)	34.6 (16.7 - 55.0)
Semi-contralateral	8.7 (4.2 - 18.3)	20.0 (7.8 - 37.3)	20.4 (9.8 - 39.4)	21.8 (9.9 - 43.6)	22.5 (10.1 - 44.3)
Contralateral	18.7 (11.7 - 30.8)	39.7 (22.5 - 60.4)	47.8 (27.4 - 69.1)	40.1 (25.1 - 67.5)	49.9 (33.1 - 76.6)

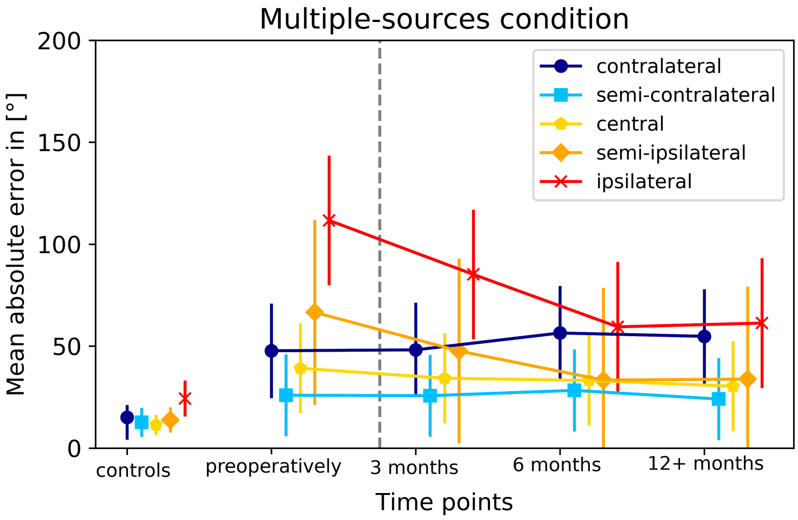

Figure 12: Pointing errors in sound localization in the multiple-sources condition. Line-diagram displaying the mean absolute error in degrees (error bars: standard deviation) in pointing at the different target positions for controls and patients in the multiple-sources condition. Controls are reported as a single time-point measurement on the left side. The dashed vertical line indicates the time-point of surgery, with the follow-up assessments at 3, 6, and ≥12 months postoperatively. Results are reported for each of the five target positions. Similar as in the single-source condition, it can be noted that it is especially the at semi-ipsilateral and even more at the ipsilateral target position that a marked improvement after surgery can be measured, while no relevant change can be observed at the central, the semi-contralateral, and the contralateral sound-position.

3.3.2 Inferential statistics

Four different LMMs were used to assess the performance of CI patients and controls at various measurement time-points. Reportings of the LMMs are based on the guidelines given in Field, 2009, p.775.

3.3.2.1 LMM 1.1 and 1.2

LMM 1.1 and 1.2 modeled the patients' preoperative ability to localize a target sound in a single-source setting (LMM 1.1) and a multiple-sources setting (LMM 1.2) in comparison to controls (see Tables 23 and 24). The contralateral position served as reference position and was therefore not further analyzed.

Preoperatively the factor 'group' already resulted in a significant difference in sound localization performance of 30.6° averaged over all positions (except for the reference position). This implies that preoperatively, patients already showed this significantly worse target deviation of 30.6° in the single-source setting ($p<0.001$) at all positions (except the reference position) when compared to the performance of controls. When analyzing the performance for the individual target positions, the differences were especially pronounced for the interactions of the ipsilateral positions with 'group' ('ipsilateral position' and 'group': 64.0°, p=0.001; 'semi-ipsilateral position' and 'group': 25.8°, p=0.004) and the semi-contralateral position ('semicontralateral position' and 'group': -16.7°, p=0.029) while the interaction of the central position with 'group' was not significant. Absolute mean errors were used for the setup of the LMMs. This means that the direction of the target deviation (either towards the healthy or the implanted ear) - usually indicated by the sign of the slope - cannot be inferred from the results of the LMMs. The variance of intercept differed significantly (p=0.029) implying that the study cohort and controls did not have a common intercept in this LMM.

Table 23: Results of LMM 1.1 for the single-source condition reporting slope, standard error (SE) of the slope, p-value, and lower and upper boundary of 95% confidence interval (Ci).

Parameter	slope	SE	p-value	95% Ci	
Group	30.6	4.5	0.001	20.9	40.3
Ipsilateral position and group	64.0	5.9	0.001	49.7	78.4
Semi-ipsilateral position and group	25.8	5.9	0.004	11.5	40.2
Central position and group	0.3	5.9	0.996	-14.3	14.4
Semi-contralateral position and group	-16.7	5.9	0.029	-31.0	-2.3
Variance of intercept	272.4	125.0	0.029	110.8	669.7

Interestingly, LMM 1.2 shows almost the same tendencies as already seen in LMM 1.1. The factor 'group' resulted preoperatively already in a significant difference implying that patients in general - when averaged for all positions except the reference position showed an impaired sound localization performance by 31.9° in the multiple-sources setting ($p<0.001$) when compared to the performance of controls. Again, the interactions of the ipsilateral positions exhibit a significant difference between patients and controls ('ipsilateral position' and 'group': 59.6°, $p<0.001$; 'semi-ipsilateral position' and 'group': 19.3°, p=0.008) as well as the interaction of the semi-contralateral position and 'group' (-20.5°, p=0.005). The interaction of the central position with 'group' showed no significant difference.

Table 24: Results of LMM 1.2 for the multiple-sources condition reporting slope, standard error (SE) of the slope, p-value, and lower and upper boundary of 95% confidence interval (Ci).

Parameter	slope	SE	p-value	95% Ci	
Group	31.9	4.9	0.001	22.0	42.0
Ipsilateral position and group	59.6	6.8	0.001	45.7	73.5
Semi-ipsilateral position and group	19.3	6.8	0.008	5.4	33.3
Central position and group	-6.8	6.8	0.329	-20.7	7.2
Semi-contralateral position and group	-20.5	6.8	0.005	-34.4	-6.6
Variance of intercept	5.6	20.1	0.779	0.1	60.4

3.3.2.2 LMM 2.1 and 2.2

LMM 2.1 and 2.2 tested, how the sound localization ability in patients changed over the course of time of the assessments. Only patients' data were used in both LMMs. Again, the contralateral position served as reference position. LMM 2.1 tested the single-source condition (see Table 25) and LMM 2.2 tested the multiple-sources condition (see Table 26). The estimate describes the difference to the contralateral reference position.

In LMM 2.1 the estimates of the ipsilateral and the semi-contralateral positions (ipsilateral position: 56.4°, $p<0.001$; semi-ipsilateral position: 18.6°, $p=0.003$; semi-contralateral position: -16.5°, $p=0.009$) showed a significant difference to the reference position which was not the case for the central position. These estimates are to be interpreted as the initial mean absolute errors in the single-source condition for each of the individual locations with respect to the contralateral position. The mean absolute error of the ipsilateral position was across patients on average 56.4° greater than that of the reference position. The mean absolute error of the semi-ipsilateral position was across patients on average 18.6° greater than that of the reference position, et cetera. According to the model, averaging over all measurement time-points and positions, the mean absolute error changed by -2.3° through the postoperative rehabilitation period (as shown by the slope for the parameter 'Time-point', Table 25). However, the individual interactions give a better picture. Only the interaction of the ipsilateral positions with 'time-point' was significant ('ipsilateral position' and 'time-point': -19.3°, $p<0.001$; 'semi-ipsilateral position' and 'time-point': -11.0°, $p=0.002$). These results are to be interpreted in the sense that with each measurement time-point, the mean absolute error for the ipsilateral position became smaller by 19.3° (semi-ipsilateral: 11.0°) in reference to the contralateral position.

Table 25: Results of LMM 2.1 - single-source condition with slope, standard error (SE) of the slope, p-value, and lower and upper boundary of 95% confidence interval (Ci).

Parameter	slope	SE	p-value	95% Ci	
Ipsilateral position	56.4	6.3	0.001	43.9	68.8
Semi-ipsilateral position	18.6	6.3	0.003	6.2	31.0
Central position	-1.9	6.3	0.866	-14.3	10.6
Semi-contralateral position	-16.5	6.3	0.009	-29.0	-4.1
Time-point	-2.3	2.5	0.367	-7.3	2.7
Ipsilateral position and time-point	-19.3	3.6	0.001	-26.3	-12.3
Semi-ipsilateral position and time-point	-11.0	3.6	0.002	-18.0	-4.0
Central position and time-point	-0.9	3.6	0.805	-7.9	6.1
Semi-contralateral position and time-point	2.7	3.6	0.442	-4.3	9.7
Variance of intercept	101.0	59.5	0.090	31.8	320.6
Variance of slope	2.4	9.7	0.805	0.0	118.6
Covariance intercept, slope	-0.7	0.9	0.500	-1.0	1.0

LMM 2.2 tested the multiple-sources condition in patients over time. Interestingly, in this model, all four positions already initially showed a significant difference when compared to the reference position (as depicted in Table 26) with the ipsilateral position (59.3°, $p<0.001$) and the semi-contralateral position (-23.7°, $p<0.001$) sticking out in magnitude. According to the model, averaging over all measurement time-points and positions, the mean absolute error changed by 1.4° through the postoperative rehabilitation period (as shown by the slope for the parameter 'Time-point', Table 26). Here again, the individual interactions give a better picture. When looking at the interaction between individual positions and time-points, again the interaction of both ipsilateral positions and time-points stick out ('ipsilateral position' and 'time-point': -20.1°, $p<0.001$; 'semi-ipsilateral position' and 'time-point': -13.6°, $p<0.001$). The mean absolute error for these two positions decreased with every visit. So, with every measurement time-point, the implanted ear regained a target accuracy of 20.1° and 13.6°, respectively.

Table 26: Results of LMM 2.2 - multiple-sources condition with slope, standard error (SE) of the slope, p-value, and lower and upper boundary of 95% confidence interval (Ci).

Parameter	**slope**	**SE**	**p-value**	**95% Ci**	
Ispilateral position	59.3	5.5	0.001	48.5	70.1
Semi-ipsilateral position	15.1	5.5	0.006	4.3	26.0
Central position	-11.2	5.5	0.042	-22.0	-0.4
Semi-contralateral position	-23.7	5.5	0.001	-34.5	-12.9
Time-point	1.4	22.3	0.544	-3.2	6.0
Ipsilateral position and time-point	-20.1	3.1	0.001	-26.2	-14.0
Semi-ipsilateral position and time-point	-13.6	3.1	0.001	-19.7	-7.5
Central position and time-point	-1.7	3.1	0.581	-7.8	4.4
Semi-contralateral position and time-point	1.4	3.1	0.648	-4.7	7.5
Variance of intercept	418.1	114.4	0.001	244.6	714.8
Variance of slope	35.1	27.3	0.199	7.6	161.6
Covariance intercept, slope	-0.9	0.1	0.001	-1.0	-0.4

4 Discussion

This thesis investigated functional neuroplasticity of the auditory system with three different studies. The first study tested the horizontal localization ability of blind subjects. In a first step, the single-source condition, blind subjects had to localize a target sound presented in isolation. In the more complex multiple-sources setting, they were asked to localize a target sound, now played simultaneously with multiple distractor sounds. Based on the literature (for example Röder et al., 1999; Collignon et al., 2009, 2006a), it was hypothesized that blind subjects would localize target sounds in the complex acoustic setting with a higher accuracy. The second study tested the effects of training on the visual processing speed of deaf subjects. In three different paradigms (meta-contrast masking, object recognition, video recognition) the effects of training were tested. Based on the literature (for example Dietrich et al., 2013a), it was hypothesized that already before training deaf individuals complete these tasks more accurately than hearing controls, thereby indicating enhanced processing speed. Furthermore, it was hypothesized that with training the performance of deaf subjects on such tasks would increase at a faster rate than in the hearing control subjects. The final study investigated the development of horizontal sound localization in single-sided deaf adults before CI implantation and in the postoperative rehabilitation phase. Based on the literature (for example Arndt et al., 2011a; Hansen et al., 2013), it was hypothesized, that before CI implantation single-sided deaf subjects would not be able to localize a sound in the horizontal plane. It was moreover hypothesized, that with implantation of the CI, subjects would re-learn to localize sounds.

4.1 Horizontal sound localization of blind subjects in acoustically complex situations

This study investigated the ability of blind subjects for horizontal localization of a single sound presented in isolation and in a complex acoustic setting with multiple distractors presented simultaneously. Both the study and the control group showed increasing target deviation with increasing eccentricity in both experimental conditions. The localization errors at the 0°

position were smaller than those at the 45° position which in turn were smaller than at the 90° position. This phenomenon of increasing target deviation with increasing eccentricity from the median plane has been described before (see Charbonneau et al., 2013; Wood and Bizley, 2015; Mills, 1958). This observation can largely be attributed to the physical fact that with increasing eccentricity, a given angular change of a sound source induces a lower change in binaural spatial cues (see also Blauert, 1997). The present study was therefore able to replicate and confirm this finding in the study cohort and in controls.

Performance of blinds was at a comparable level as that of controls for most positions, with all mean localization errors being even slightly higher in blinds than in controls. Interestingly, only for the maximum target eccentricity in the more complex multiple-sources condition the mean localization error was smaller by about three degrees in blinds than in controls. When looking at the median for this specific position and experimental condition, even this statement could not be maintained: while blinds showed a median localization error of about 32° at the maximum eccentricity, this error was only 18° in controls. Given the nature of the absolute localization error, the median actually provides a more precise description of the actual data distribution of this non-normally distributed variable. Since in the inferential statistical analyses a significant difference could not be detected, it can be at least safely assumed that in the present data set blinds did not outperform their controls. It thus appears that even though enhanced auditory abilities of the visually-deprived brain have been described (for review, see Röder and Rösler, 2004), the present study design did not detect superior abilities in sound localization in both a single-source and multiple-sources condition. Even more so, the target deviation at the central position (0°) was almost three times as large in size (6.45°, SD 3.60°) in blinds than in controls (2.40°, SD 1.46°). As some blind individuals managed to perform this task at a precision comparable to that of the controls a subsequent analysis of the individual blind subjects and their etiopathological reason for blindness war performed. No common etiopathology of blindness was, however, found for those blinds showing a larger localization error. None of the investigated blind subjects shared a common onset, duration or degree of residual vision in terms of their etiopathology.

Sound localization has its highest precision when the sound source is coming from near the median plane relative to the head. This phenomenon could also be confirmed by the findings presented in this study. Adjusting the sensors' position (that is the ears) in such a way that the sound is originating closely to that median plane thus leads to a higher pointing accuracy (Middlebrooks and Green, 1991). This is of high relevance when interpreting the present findings: Lewald (Lewald, 2002a, 2013) reported that the calibration of auditory space in blind subjects is critically connected to audio-motor feedback, especially in terms of changes in interaural time differences and interaural level differences (the term audio-motor feedback here means motor movements of the head or body aimed at positioning the head and body optimally relative to the sound source). The new and improved sensor positioning with respect to the sound source as a result of audio-motor feedback then leads to subtle changes in auditory spectral cues, when compared to the original position. This improves the accuracy in localizing the sound source (Lewald, 2002a, 2013). Therefore, in general, processing of central sounds is more difficult in humans when no access to audio-motor or visual feedback is possible as in the present study design. This poses a special problem for the blind subjects in the present study since it is a behavioral highly unusual situation to not be able to adjust the head or body relative to the sound source. In the present experimental setup, the head of subjects was fixed in a headrest and could not be moved. Also due to the position of the fixated swivel on the armrest of the chair, movement of the upper body was not possible. Only the hands could rotate freely. Another factor possibly explaining the better performance of sighted subjects in the present study could be the different ways of calibration of auditory space by the two groups: According to Lewald (Lewald, 2002a, 2013, 2002b), in sighted subjects auditory space is constantly calibrated by visuo-motor feedback to maintain a continuous and stable alignment of auditory and visual space. Blinds do not posses the capability of visuo-motor feedback and thus recalibration of auditory space. This could thus explain their higher localization errors, especially at the central position.

It is noteworthy, that despite the lack of the visual modality to calibrate auditory space blinds performed almost as good as sighted controls, even in the multiple-sources condition. The multiple-sources condition is associated with a higher level of complexity in terms of several aspects: Besides the actual localization of the target sound, it also demands a segregation of the target sound from the remaining distractor sounds (Bregman, 1994). The process of segregation of the target sound from the distractor sounds is a process that demands the analysis of spectro-temporal features of the target sound. It has already been demonstrated that blind subjects show enhanced performance in terms of pitch discrimination (Gougoux et al., 2004; Hamilton et al., 2004; Arnaud et al., 2018) as well as spectro-temporal analysis (Voss et al., 2011; Doucet et al., 2005). The superior pitch discrimination and the more efficient analysis of spectro-temporal auditory stimuli may thus be the reason for the relatively good performance of blinds in the multiple-sources condition.

Röder and Rösler (2004) had suggested three dimensions of the effects of neuroplasticity: Either the neuroplastic adaptations result in a beneficial or maladaptive behavioral effect or in no measurable behavioral effect. The here presented study suggests that the neuroplastic adaptations due to visual deprivation enable blinds to perform almost equally as sighted controls. In terms of the classification scheme of Grafman (Grafman and Litvan, 1999; Grafman, 2000) compensatory neuroplasticity thus allows a performance without a measurable behavioral effect. Due to the rareness of the condition the sample size of the blind cohort of this study is small and the underlying etiopathology is heterogeneous, which limits the statistical power of the presented findings.

When Haber et al. (1993) investigated the question of an ideal pointing method for blind subjects, they concluded that own body parts (finger, head, et cetera) represent the best method for pointing towards an object. While for technical reasons the use of a swivel as in the present study seemed necessary, the validity of this pointing method is limited: although in the applied experimental setup the results obtained from the swivel are considered as the direction where the subjects perceived the sound origin, they actually also show how well subjects could imagine the current position of the swivel in space. After pointing towards a sound, subjects returned the swivel to their perceived 0° location. Since the swivel had no integrated (for example haptic) feedback for the central position, subjects did not know if the swivel really was again positioned at 0°. The lack of feedback in terms of location of the swivel might therefore have resulted in a continuous production of additional target deviations since subjects had no access to calibration of auditory space. Also, from a physical point of view, the target positions are not equally reachable. While the 0° and ±45° positions can easily be pointed at, the extreme positions (±90°) could not be comfortably reached without turning of the upper body. Making a larger target deviation at the ±90° positions was thus more likely than at the 0° or the ±45° positions simply because this position could not be reached as easily as the ±45° or the 0° position. This is especially problematic since more eccentric target positions already result in larger target deviations (see above).

Based on the results of this study, it can be concluded that blinds did not outperform sighted controls in the horizontal localization of a sound source in a complex acoustic setting. Nevertheless, despite the fact that no visuo-motor calibration is possible in blind subjects, they reached a performance level that is almost equal to that of sighted controls. Thus, compensatory auditory neuroplasticity enables blinds to perform this task at a comparable level. As suggested by the literature (Röder et al., 1999; Gougoux et al., 2005), these compensatory mechanisms may include enhanced spectro-temporal analysis, pitch discrimination and audio-motor feedback, sound segregation, and spectro-temporal interpretation. A better understanding of the interplay of these mechanisms might be obtained in future studies when looking at the role of interaction between audio-motor feedback and visuo-motor feedback.

4.2 Effects of training on the visual processing speed in deafs

This study compared the visual processing speed of prelingually deaf subjects with that of controls in a meta-contrast masking task, an object recognition task and a video recognition task. Furthermore, the effect of training on the performance of deafs and controls in those tasks was evaluated and compared. Based on the results from studies analyzing the auditory capabilities of visually deprived subjects, it was expected that deaf subjects before training complete these tasks more accurately than hearing controls, thereby indicating enhanced visual processing speed (see also Dietrich et al., 2013a). Due to the cross-modal reorganization induced by deafness it was further expected, that deafs show a greater trainability in those tasks than their sighted controls.

In meta-contrast masking, the mask reduces the visibility of the target stimulus. If the interval between stimulus and mask is either short (for example SOA 0ms) or long (for example SOA 200ms), then the performance has been reported to be good while intermediate intervals result in a worse performance (for example Rassovsky et al., 2004), thus possibly allowing a higher discrimination between the performance of deafs and controls. Therefore, the present study mostly used intermediate SOAs. For peripheral stimuli, deaf subjects did indeed show a better performance than controls before training (p=0.031). Surprisingly, for central stimuli measurement results were with higher accuracy values in controls than in deafs, although this difference was not statistically significant (p=0.259). After training these differences between groups could no longer be detected, with deafs still showing only slightly higher results than controls at the peripheral position and both groups performing equally at the central position. When compared with controls, deafs improved their levels of performance at the central position while controls when compared with deafs, improved at the peripheral position. Again, these differences from pre- to post-training performance were not statistically significant. Interestingly, trainability of the visual processing speed in deafs was most prominent for centrally presented stimuli in all SOAs (except of the SOA 0ms) with a relative gain of about 23%. The relative gain for peripheral stimuli in deafs was only half in size of the one for the central position. It ranged from 8% to 11% (the only exception being at the SOA of 60ms where the relative gain was negative). The magnitude of the peripheral gain in deafs was comparable to the one observed in controls (the only exception being at an SOA of 80ms with 22% relative gain in controls). When calculating the arithmetic mean of the relative gain across all 4 SOAs and the central and the peripheral position, deafs improved by 11.18% and controls by 5.78%. Deafs showed improved levels of performance after training for centrally presented targets ($p<0.001$) while the level of performance in controls was significantly improved for peripherally presented targets after training ($p=0.038$). One could interpret this finding that both groups are able to learn to "see faster" depending on the group and presentation position. It also appears that already a short number of training units is sufficient to induce this effect. This experiment also shows that the simple visual task of a meta-contrast experiment belongs to those tasks with a selective attentional peripheral benefit for deafs which is supported by their better performance before training ($p=0.016$).

When interpreting these results caution is advised. On the one hand, the presented results appear conclusive, since they are consistent across the different experimental conditions. On the other hand, the obtained improvements do not reach statistical significance. Assuming that visual processing speed is trainable, it can be argued that the number of training units used in the present study is too small to result in changes strong enough to be also statistically significant. Moreover, given the rareness of the condition and naturally the small sample size resulting from that obstacle, the statistical analysis might just be underpowered. It is clear however, that although the null-hypothesis could not be rejected with respect to a different trainability of deafs and hearing controls, these results do by far not imply that visual processing speed is not trainable. The problem of the small sample size will be difficult to overcome. Performing a synopsis taking into account also the results obtained in the two other study arms might help to better interpret trainability of visual processing speed in deafs.

In the object recognition task, in both groups the obtained accuracy rates increased with longer presentation times, which is consistent with findings from other studies (for example Turk-Browne and Scholl, 2009; Toro et al., 2005). No significant difference in performance was observed between deafs and controls before training. After training, all mean accuracy rates without exception were higher than those measured before training. When averaging the relative gain in both groups across all presentation times, deafs showed an averaged relative gain of 17.21% while controls showed a relative gain of 14.26%. In the inferential statistical analyses, the level of performance of both deafs and controls indeed improved significantly after training (deafs and controls: $p<0.001$) implying that both groups were significantly better at this task after training. The spread of the relative gain across presentation times was, however, relatively large for this task for both groups, ranging from 0.33% to 34.51%. When looking at a possible difference in trainability between the two groups, it can be noted that only at the object stream presentation time of 200ms a significantly greater improvement was observed in deafs than in controls. For all other presentation times the differences in improvement between the two groups were not significant. Generally, the object recognition task poses a higher level of difficulty than the meta-contrast task. It involves an identification and discrimination component and also requires shifts of spatial attention in order to bind multiple features of the target together. Due to the high spread of the data at the different presentation times and the small sample size, it is not possible to draw robust conclusions on the different trainabilities of the visual processing speed of deafs when compared to controls for the object recognition task. The same considerations apply as for the meta-contrast experiment. It is, however, an interesting observation that a significant improvement - depending on the presentation time, a relative gain of more than 25% was possible - was found in both groups within this rather short training period.

The video recognition task consisted of two subtasks: an object recognition task and a synopsis task. With respect to the object recognition task, no significant difference in accuracy rates was found between deafs and controls both before and after training. Also the observed improvement in both groups was only marginal with 1.86% in deafs and 0.37% in controls. A completely different picture presented itself in the synopsis task: Already before training deafs managed to identify more synopses correctly than did the controls, although this difference was not statistically significant. Despite this higher pretraining benchmark, improvement (expressed as the relative gain) was still significantly higher in deafs (77.26%) than it was in controls (42.87%, p=0.001). Again, only deafs improved their level of performance in the synopsis task with training (p<0.001), while neither deafs' level of performance in the object recognition task or the level of performance in both tasks in controls significantly improved with training. Already the object recognition was more demanding than the previous tasks of this study, since it had to be performed simultaneously with the synopsis task and subjects could not clearly focus on one predefined area of the visual field. Even more difficult and thus the most complex task of all experiments in this study, the video recognition synopsis subtask did not just require the recognition of a shape or an object, but a semantic understanding of the content of the film. Of all three experiments in this study, the video recognition setup also represented the most „realistic“ task since no artificially created stimuli exclusively created for this experiment were used. The significantly better performance of deafs in the synopsis task is therefore an interesting finding. It has already been reported that deafs outperform hearing controls in tasks that require a global perceptual processing (Parasnis, 1983), whereas hearing subjects are considered to be better with specific perceptual processing (Megreya and Bindemann, 2017). A global perception of the film would allow to grasp the content of the film. It would not, however, necessarily result in a better performance of deafs in the object recognition task which requires more specific perceptual processing. The obtained results are thus in line with this proposed separation between global and perceptual processing skills in deaf and hearing people. It, moreover, appears that this global perceptual processing in deafs is highly trainable when watching highly accelerated videos. The specific perceptual processing required in the object recognition task in the videos did not seem to be improved by the training units performed. Since values before and after training were relatively high ranging from 67%-70%, it is conceivable that this experiment did not work in a discriminative window. A more complex object recognition task might potentially have yielded different results. Alternatively, specific perceptual processing might be more difficult to train than global perceptual processing. The additional recruitment of cross-modal networks might just not be as effective for specific tasks that usually only require limited and predefined neural networks, as for such a highly integrative task like forming a synopsis of a video.

This would be consistent with the other results obtained in this study which also mostly tested specific perceptual processing where only marginal improvements could be detected.

Green and Bavelier (2003) tested the effects of visual selective attention in a video games training. Healthy experienced video game players were trained on action games that demanded a fast shift in visual attention. The controls had no to little video gaming experience and played tetris. Training took place for ten days for one hour per day. After the training phase, changes for various different aspects of visual attention such as enhanced visual capacity or enhanced allocation of spatial attention could be measured in the experienced video game player group (Green and Bavelier, 2003). Thus the effects of training on visual tasks are apparently measurable after ten days. In the present study, alterations were already measurable within half this time. As Green and Bavelier (2003) trained healthy hearing subjects, it would be interesting to repeat this experiment also with sensory-deprived brains. The strong trainability of such sensory-deprived brains has already been demonstrated in the context of blindness, where trained blind subjects learned to „hear faster“ (Dietrich et al., 2013a,b). While sighted controls can, on average, without training understand about 8-10 syllables per second, blinds managed to „hear“ up to 25 syllables per second after a 3 months training of one hour per day (Dietrich et al., 2013a). In a real-time strategy video game, elderly subjects were trained on diverse executive control functions and visual-spatial memory tasks as these are observed to decline in elderly adults (Basak et al., 2008). Even with about 24 hours of training in several sessions, the trainees improved significantly in the measures of game performance. They also improved significantly more in executive control functions than the untrained control participants. This study is interesting because it shows that a group associated with declining cognitive abilities can already benefit from training performed within a short time scale. Deafs have repeatedly shown enhanced visual skills in certain tasks such as face discrimination (Megreya and Bindemann, 2017) or motion detection (Shiell et al., 2014). If the training period of deaf subjects for certain visual tasks were to be extended, this might result in very promising results.

Deafness can result from a large variety of etiopathological reasons. Finding an etiopathologically homogeneous sample with a comparable age of acquisition of sign language large enough to allow studies with a high statistical power is challenging. It would be interesting to see how the inferential statistics turn out in the meta-contrast masking experiment or the object recognition experiment when being redone with a larger sample size. Since other comparable studies trained their subjects for at least ten days (Hertrich et al., 2009; Green and Bavelier, 2003), it can not be ruled out that the observed effects might have been stronger when allowing a training period longer than four days.

Based on the results of this study, it can be concluded that the visual processing speed in deaf subjects is trainable. The results of the most difficult task (the synopsis task of the video recognition experiment) also suggest that visual processing speed can indeed be trained faster than in hearing controls. In the simpler visual tasks like the meta-contrast masking or the object recognition tasks, the differences between both groups through training were not strong enough to allow to generalize this conclusion. A possible explanation for this discrepancy between the video synopsis task and the other experiments might lie in the fact, that only the video synopsis task requires global perceptual processing where the interplay of numerous cerebral networks is required. As already shown for blinds (for example Lazzouni and Lepore, 2014), it thus appears that deaf subjects also process complex sensory information in a more efficient manner which then results in compensatory abilities.

4.3 Long-term impact of implantation of a unilateral cochlear implant in single-sided deafness on target sound localization in multiple-sounds environments

Sound localization depends on the ability to process binaural input. This study measured the long-term effects of unilateral CIs on the sound localization ability in the horizontal plane in patients suffering from SSD. Accuracy of sound localization was first tested in a single-source condition where only one target sound in isolation had to be localized. In a subsequent multiple-sources condition, target sounds had to be localized with the simultaneous presentation of multiple distractors. Measurements of patients were performed at four different time points: before implantation, 3 months, 6 months, and $\geq$ 12 months after implantation. It was expected that preoperatively, patients are not able to localize target sounds. It was then hypothesized that in the postoperative course after implantation of a CI, patients learn again to localize sound. Controls were measured at a single time-point.

As expected, controls showed the expected increase in pointing deviation from the target with increasing target eccentricity, which was also observed in the first study of this thesis (3.1.1) and which is in accordance with the present literature (for example Charbonneau et al., 2013; Wood and Bizley, 2015; Mills, 1958).

It has been repeatedly shown that sounds presented in isolation are easier to localize while the localization of a target sound among distractors represents a substantially greater challenge for the auditory system resulting in greater localization errors (Blauert, 1997; Middlebrooks and Green, 1991). This finding could be replicated in the present study. In general, the localization errors in the single-source condition were smaller in magnitude than those in the multiple-sources condition for both groups.

In comparison to the first study analyzing sound localization and where the localization errors of blinds substantially differed between conditions (see 3.1.1), the localization errors of preoperative patients for the multiple-sources condition were only marginally larger than those in the single-source condition. This can be explained by the already extremely high target deviation in the single-source condition in SSD-patients.

In the SSD group, the preoperative sound localization ability differed substantially from controls in both conditions and for all five positions. The order of magnitude of the deviation from the target in these cases was between two (semi-contralateral position and multiple-sources condition) to eight times larger than that of controls with the largest target deviation at the ipsilateral position in both conditions. Patients‘ mean target deviation for the ipsilateral position was in fact greater than 100° (single-source: 104.7°, multiple-sources 111.7°). Assuming that subjects randomly guessed the position of the target at the ipsilateral positions, this would result in a target deviation of 90°. This implies that at this particular position they were not able to localize the target sound at all and merely guessed. With CI implantation, the strongest improvement in target deviation over time could be observed for the ipsilateral position in both conditions. With each visit, the ipsilateral target deviation lessened on average by 19.3° in the single source and by 20.1° in the multiple-sources condition, resulting in a final target deviation of 64.7° in the single source and of 50.4° in the multiple-sources condition by the end of the study. Also strong improvements could be observed for the target deviation at the semi-ipsilateral position, which in the single-source condition decreased by 11.0° (multiple-sources condition: 13.6°) per time point, resulting in a target deviation half the size from the originally measured value (from 64.6° to 31.7°, multiple-sources condition: 66.6° to 33.8°). Several studies have already described deficits in horizontal sound localization in preoperative SSD-patients (for example Jacob et al., 2011; Arndt et al., 2011a; Litovsky et al., 2017). To the knowledge of the author, this study is the first that can provide specific data on the magnitude of this deficit and relate them to defined horizontal spatial positions relative to the implanted ear.

This difficulty in localizing sounds in preoperative SSD-patients is to be expected since sound localization is known to be highly dependent upon binaural input (for example Schnupp et al., 2011; Tokita et al., 2014). In SSD the functionality of the affected ear is dramatically reduced (for example Tokita et al., 2014; Litovsky et al., 2017), thus not allowing proper binaural input. While compensatory mechanisms can partly maintain the ability of sound localization with the intact ear (Schnupp et al., 2011), the auditory spatial cues at the affected ear do not contribute relevantly to sound localization. Even more so, the head can provide an acoustic shadow which can favor one ear, depending on the location of the sound source (Blauert, 1997; Middlebrooks and Green, 1991). Thus, the head shadow effect increases the associated problems with deficient sound localization at the affected ear. It is, therefore, clear that the inability of sound localization in SSD is predominantly at the ipsilateral position and in the present experimental setting also still to a lesser extent at the semi-ipsilateral position. Given the present data, it seems that auditory reorganization after CI implantation also appears to mainly improve sound localization at the ipsilateral positions which thus approximate their values of the localization errors to those of the central and contralateral positions. The central and contralateral positions do not show any relevant further improvement and remain at an elevated level over time when compared to the control group: By the end of this study, when averaging all positions of patients at the last measurement time-point, they still showed a target deviation in the single-source condition that was by 23.0° (multiple-sources condition: 25.9°) larger than that of the initially measured controls. Of note, the localization error at the contralateral position shows the least improvement (that is in the present data set it even slightly increases). On the one hand, this is somewhat expected since it is the side where the subjects already had normal hearing before surgery. On the other hand, it is also unexpected since spatial hearing results from a paired sensory organ. Thus one would assume that all of the auditory space recalibrates when suddenly receiving binaural input again. It can be speculated, that the lacking improvement at the contralateral positions is due to the fact that it is indeed the entire auditory space being recalibrated when receiving a unilateral CI. Thus, instead of also further improving with a CI at the contralateral positions, the affected subject also needs to relearn spatial localization at these positions.

In this study, the greatest improvement in terms of sound localization ability occurs until the 6 months postoperative assessment. Only minor changes still occur after this time. This improvement can be attributed to an underlying auditory cortical reorganization which then successfully translates the incoming signals from the implant and integrates this information with those auditory signals obtained by the normal hearing ear (Litovsky et al., 2017). Several studies have already described a comparable time frame of 6 to 12 months after surgery for postoperative improvement of sound localization: Arndt et al. (2011a) report an improvement 12 months after CI implantation which was, however, the first measurement time-point after surgery. Jacob et al. (2011) describe the greatest improvement within the time frame of 6 to 12 months (their first assessment of implanted patients occurred 6 months after implantation). Firszt et al. (2012) also report a significant improvement in sound localization ability at their first postoperative assessment time-point 6 months after surgery. Hansen et al. (2013) measured 3, 6 and 12 months after implantation and reports the greatest variability in terms of accuracy of localization between the 3rd and the 6th month. Adjustment of the CI and learning to hear with a CI usually takes about 3 weeks (Rauch et al., 2019). This time period also initiates the learning process that encompasses the integration of the new acoustic signals of the CI with the normal hearing ear. It has been shown that these integrative processes of re-learning to comprehend sound with a CI in a quiet setting improved on average by 8% within a monthly assessment conducted over the period of one year postoperatively (here with speech: Drennan et al., 2016).

To reorganize auditory input, the neural circuits and networks need a certain amount of time to alter and learn to interpret the degraded sound signals coming from the CI (Kral et al., 2006). Three phases of neuroplastic adaptation after the implantation of a CI exist (Kral et al., 2006): The first fast phase encompasses the first few weeks after implantation and shows no sensitive phase. This is followed by the second phase which comprises the first months up to four years and shows adaptational processes (Kral et al., 2006). The last phase is the longest one and is related to increased higher order cortical activation (Kral et al., 2006). The patients with an implanted CI could now in a first step adapt the new auditory quality provided by the CI. In a second step, they could then learn how to reinterpret auditory spectral cues such as interaural time differences and interaural level differences with a CI. That such a process must occur over the first months after implantation becomes especially clear when looking at the continuously decreasing localization error in the single-source condition. The auditory brain may thus have learned to reinterpret the reliability of these spectral cues under these new circumstances and may have even developed new strategies in terms of cue reliability (see Dahmen and King, 2007).

Hansen et al. (2013) examined sound localization in a group of 29 postlingual SSD-patients about to receive a unilateral CI. A horizontal arc of 108° with 8 loudspeakers was used to present everyday sounds. Subjects had to point to the loudspeaker where they thought the sound originated from. Hansen et al. (2013) also report decreased sound localization ability of some patients within the early postoperative period (between 3rd and 6th month). This is an interesting observation which was also replicated in this study. The decrease in the magnitude of the localization error is not a linear process and it tends to increase marginally for some positions. Hansen et al. (2013) explain this finding with the lack of experience of the auditory system at this point. In the present study, the localization error for the contralateral and the semi-contralateral positions increases between the 3 months and 6 months assessment (see also Figure 11 and 12), however, their magnitude is marginal.

The present results show that unilateral CI implantation can help to improve sound localization in SSD-patients. Other studies have also confirmed that a CI can improve sound localization in SSD-patients: Arndt et al. (2011a) compared the effectiveness of different hearing devices such as bone-anchored hearing aid, conventional contralateral routing of signal and CIs in 11 unilateral deaf subjects. Their experimental setup comprised a horizontal semicircle with seven different loudspeakers. Patients were asked to identify the loudspeaker from which an isolated sound originated. After 12 months with a unilateral CI, patients showed a reduction of the median localization error by 15.0° in comparison to patients with a conventional contralateral routing of signal device (39.9° median localization error) or patients equipped with a bone-anchored hearing aid (30.4° median localization error). The study of Arndt et al. (2011a) investigated the effectiveness of different hearing aid devices in relation to each other. In the present study, in the single-source condition the reduction of the median localization error from preoperatively to the $\geq$12 months postoperative measurement was 26.3° (difference of averaged median localization error of all five positions before implantation 51.7°, at the $\geq$12 months time point 25.4°). The present study is therefore able to replicate a similar magnitude of the reduced localization errors for the CI.

The capability for auditory reorganization strongly depends on the time-point of onset of deafness. In a study analyzing 7 postlingual and 3 prelingual SSD-patients receiving a CI with a similar experimental setup as the one applied in the present study, only the postlingually deaf patients showed a marked improvement in sound localization. In contrast, the prelingual SSD-patients showed no relevant improvement after CI implantation (Firszt et al., 2012). When the auditory system has never undergone an appropriate auditory developmental environment enabling its functionality (see Dahmen and King, 2007), later CI implantation will thus not result in a comparable effect as CI implantation in postlingually deaf individuals. Interestingly, also in postlingual SSD-patients, there appears to be a time limit until which implantation is helpful in restoring binaural input. It has indeed been speculated, that SSD-patients should receive their CI implantation within 10 years of deafening of the one ear (Arndt et al., 2011a). Longer time periods without stimulation of the auditory nerve seem to lead to permanent damage. While the statistical analysis of the present study was performed on the cohort of SSD-patients as a whole, when looking at the one patient with postlingual SSD of more than 20 years separately, indeed less improvement in sound localization ability after implantation could be observed than in those whose duration of SSD was shorter.

As already discussed in the first study presented (see 4.1), the validity of the measurement technique has limitations since it not only measures where the subject localizes the sound source but also how well subjects can imagine the current position of the swivel in space which represents an abstract mathematical skill combined with proprioceptive abilities. Since the swivel has no integrated - for example haptic - feedback for the central position, subjects do not know where the swivel is currently located. The lack of feedback in terms of location of the swivel might thus have resulted in a continuous production of additional target deviations since subjects had no access to calibration of auditory space. Also, from a physical point of view, the target positions were not equally reachable. While the 0° and ±45° positions could easily be reached, the extreme positions (±90°) could not be comfortably reached without turning of the upper body, thus possibly leading to a larger target deviation than at the 0° or the ±45° positions.

It can be summarized that postlingual SSD-patients can benefit from a unilateral CI. Unilateral CI implantation can lead to improved sound localization in both a single-source setting as well as a multiple-sources setting. The rehabilitative effects are thereby strongest for the ipsilateral positions and become functionally relevant between 3 and 6 months after surgery. Overall, there appears to be an effect that a unilateral CI enables postlingual SSD adults to localize sounds binaurally again. It is important to notice that not every patient is likely to benefit from the implantation. The success of a unilateral CI seems to depends highly on the duration of deafness of the affected ear, the etiopathology of deafness and the remaining abilities of the normal hearing ear.

4.4 Conclusion and future outlook

This thesis investigated auditory neuroplasticity in three studies. In the first study, cross-modal organization of a visually deprived sensory cortex was shown in the shape of auditory neuroplasticity. This auditory neuroplasticity was shown to enable blind subjects to perform on a comparable level in the localization of target sounds within a complex acoustic setting. The following study investigated in how far a congenital auditorily deprived brain can be trained to seeing “faster”. From the three different tested visual paradigms, it was interestingly in the most difficult task, the video synopsis task, in which deaf subjects performed significantly better. This is a highly interesting finding since it confirms that neuroplasticity can be trained (Herholz and Zatorre, 2012; Hertrich et al., 2009; Dietrich et al., 2013a) and trainability was indeed shown for the most challenging task within a very short training period. Additionally, the understanding of the film is not a perceptual task only but instead a higher-order cognitive function which requires a semantic understanding of the film. The final study investigated long term adaptation abilities in the paired auditory modality of postlingual SSD-patients. In the patients of this study, the modality had initially undergone adequate development but in adulthood its functionality was severely reduced due to the loss of input of one of its peripheral sensors. This study showed that when a modality is exposed to an adequate auditory environment during the developmental phase and later in adulthood loses part of its functionality, this modality can regain part of its functionality again.

All three studies show that the auditory brain is a highly adaptable system whose cross-modal plasticities extend well into adulthood. It needs to be pointed out however, that two of the three studies presented here did not result in clear effects but only numerical trends due to their small sample size. This issue of being partly underpowered can clearly be attributed to the rareness of the investigated conditions and thus the difficulty of recruiting patients qualifying for inclusion. This problem is of a general nature and affects many clinical studies working on this topic. It would thus be of great value for the scientific community to establish a registry that covers subjects with certain uncommon etiologocies across Germany or even across Europe. This course of action is already quite common in other disciplines of medicine (for example the international spine registry 'Spine Tango', hosted at www.eurospine.org/spine-tango.htm).

When examining the effects of training on the visual processing speed in deafs, in the meta-contrast masking experiment, central and peripheral visual presentations were tested. A common issue in tasks working with vision in deafs is a missing standard for the peripheral visual field in deafs. When tested on a computer screen, its dimensions range from 3° (Chen et al., 2006) to 20° (Colmenero et al., 2004). Using a large half-circular screen that covers the whole visual field, so that subjects submerge in the visual presentation, might first of all help to define a standard for the peripheral visual field of deafs. Additionally, by retesting all of the here used paradigms, this altered mode of presentation might yield clearer results concerning the numerical trends of this study. This approach sounds rather promising since the most difficult task of the second study resulted in a highly significant difference between deaf subjects and controls while being presented centrally. It would be fascinating to know if these results would change with both modes of presentation. Again, it was the most diffciult task of the second study that yielded a highly significant effect after training. Therefore, interesting new insights could be gained by finding other cognitively demanding tasks and presenting them centrally and peripherally.

The third study investigated the overall spatial auditory perception that resulted from the normal hearing ear and the implanted ear. When looking at the experimental setup of the present study, two interesting extensions might result in further insights into the auditory rehabilitational processes of SSD-patients. The first extension is to retest this experimental setup with different hearing conditions. In the presented experimental setup, the auditory percept was tested when subjects could use both ears (that is the normal hearing ear and the implanted ear). Additionally, the experimental setup could be extended to also test the auditory percept when subjects can only use their normal hearing ear for the localization of the target sounds. The implanted ear would have to be blocked for this testing. The final step would test the auditory abilities of subjects when they are only allowed to use the CI with the normal hearing ear being blocked. This type of testing would allow a more detailed understanding of the ongoing ear-specific reorganizational process throughout auditory rehabilitation. The second extension is to test the auditory abilities of SSD-patients over time in a moving and three dimensional sound scene. A stationary and horizontal auditory scene is already more challenging than the isolated horizontal presentation of a single target sound. However, auditory scenes of daily life are most often composed of moving auditory objects in three dimensional space, for example the sound of a falling mug. Investigating these factors could yield a better understanding of the time points when certain aspects of auditory perception such as movement of auditory objects become a viable source of auditory information for SSD-patients again.

It is well known that the left and right hemisphere have different functions in processing auditory stimuli (for example Devlin et al., 2003; Binder et al., 2000; Schönwiesner et al., 2006). It can therefore be speculated that the side of implantation affects the degree of neuroplasticity and therefore the long-term development of auditory perception. Additional studies examining the role of laterality of the CI would prove quite fruitful towards establishing an optimal protocol for CI implantation and especially subsequent auditory rehabilitation training in case of SSD.

One thing that appears to be a common denominator among all three studies is the importance of behavioral relevance. Blind subjects are unlikely to point with a fixed pointing procedure without any sort of audio-motor feedback to an isolated target sound. Deaf subjects showed their best performance for a “real-world” task whereas neither the meta-contrast experiment nor the object recognition experiment showed a significant performance difference between groups. The localization of both an isolated target source as well as a target source among multiple distractors is a highly relevant task for humans and it has even a higher behavioral relevance when one ear is deaf. Enhanced processing on neural levels certainly represent fascinating findings. And coming back to the cause for neuroplasticity mentioned at the beginning, neuroplasticity has a profound biological meaning since it enables the individual to survive in its changing environment. Survival is dependent on the behavior of the individual. Relevance, however, only comes into play, when these neural enhancements will result in measurable behavioral changes (see also Pavani and Bottari, 2012). The three studies of this thesis showed that in blind, deaf and SSD-affected individuals quantitatively measurable behavioral relevant reorganization occurred due to cross-modal neuroplasticity.

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