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Hearing sounds in space: A neuro-cognitive investigation on the ability to associate auditory cues with external space

- PhD Thesis -

Doctoral Student Giuseppe Rabini [CIMeC]

Advisor Prof. Francesco Pavani [CIMeC]

Abstract

Sound localisation is one of the most representative function of the auditory system and, as such, it has been extensively investigated across species. Spatial hearing can be dramatically altered across the life span, yet research in humans have highlighted the remarkable capacity of the brain to adapt to changes of listening conditions, such as temporary ear plugging or long lasting hearing impairments. Although several investigations have examined accommodation to altered auditory cues (Chapter 1), a common theoretical framework seems to lack and a number of questions remain open. This limits the possibility to translate our current knowledge into concrete clinical applications for individuals who experience spatial hearing difficulties after hearing loss. The current dissertation reflects the attempt to answer specific questions regarding the process of sound localisation.

The first study (Chapter 2) aimed to investigate the relation between different reference frames in spatial hearing, namely egocentric and allocentric sound representation. We studies this topic in the context of a learning paradigm, assessing to what extent localisation of single sounds in simulated monaural hearing (unilateral ear plugging) can improve following an audio-visual spatial hearing training focused on egocentric sound processing vs allocentric sound processing. An untrained group was also included in the study. We found that localisation performance in the horizontal plane improved specifically in the side ipsilateral to the ear-plug for all groups. Yet, the trained groups showed a qualitatively different change of performance after four days of multisensory ego/allocentric training compared to the untrained group, providing initial evidence of the possible role of allocentric coding in acoustic space re-learning. These results further highlight the importance of including a testretest group in paradigms of sound localisation training.

The second study (Chapter 3) focused on a specific aspect of the phenomenological experience of spatial hearing, namely the subjective confidence about the perceived sound position. We examined the relation between objective localisation accuracy and subjective certainty while participants localised sounds in two different listening conditions – binaural or simulated monaural hearing. Results showed that overall subjective certainty on sound position decreased in the altered listening condition (unilateral ear-plugging). In simulated monaural hearing, localisation accuracy and spatial confidence dissociated. For instance, there were trials in which participants were accurate, but felt uncertain, and trials in which they were less accurate but expressed higher ratings of spatial confidence on sound position. Furthermore, subjective confidence increased as a function of time within the testing block, and it was related to the spatial distribution of the perceived sound-source position.

The third study (Chapter 4) exploited magnetoencephalography (MEG) to study the dynamics of the cortical network implied in active sound localisation. We implemented a novel apparatus to study sound localisation in MEG with real sounds in external space, and collected behavioural and subjective responses (i.e., accuracy and confidence, as in Study 2) during this altered listening condition. Results showed that participants were able to perceive the spatial difference between the positions of stimulation, thus proving the reliability of our novel setting for the study of spatial hearing in MEG. MEG data highlight a distributed bilateral cortical network involved in active sound localisation, which emerged shortly after stimulus presentation (100—125 ms). The network comprise the classical dorsal auditory pathway plus other cortical regions usually underestimated in previous literature – most

notably, regions in the central sulcus/precentral gyrus possibly involved in head movements. Connectivity analysis revealed different patterns of neural coupling, as a function of frequency band. In particular, coherence in high gamma revealed significant connections involving the parietal cortex and the posterior superior temporal cortex.

In the final chapter (Chapter 5), I summarise the main findings of the three studies, discuss their implications and outline potential future directions.

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Chapter 1

Background

The intent of this chapter is to give the reader the necessary information regarding the basic process of sound localisation and how the auditory system implements this function, from the initial sound waves reaching the ears to the complex auditory spatial percept. This theoretical chapter further aims to highlight the plastic properties of spatial hearing, presenting the different approaches used in previous studies investigating acoustic space accommodation to altered hearing conditions.

1.1 Sound localisation – Cue's extraction

Identifying the location of sound-sources location is a fundamental capacity for any cognitive system exploring the auditory environment in everyday life. Yet, this seemingly effortless ability entails remarkable challenges for the brain. Unlike visual and somatosensory systems, the auditory system does not map directly sound location on the primary sensory cortices (topographic mapping), which instead have a tonotopic organisation (Humphries, Liebenthal, & Binder, 2010; Romani, Williamson, & Kaufman, 1982; Saenz & Langers, 2014). Given the absence of this direct and univocal spatial relation, the system must exploits the anatomical conformation of our head and ears to infer sound-source coordinates (Middlebrooks, 2015a; Middlebrooks & Green, 1991; Schnupp, Nelken, & King, 2011). The interactions between sound waves, the head and the external ears give rise to specific auditory cues to localisation, which vary as a function of sound as well as head position in space. These cues allow the auditory system to define the location of auditory objects in three dimensions: azimuth (horizontal plane), elevation (vertical plane), and distance. In particular, binaural cues allow localisation in horizontal dimension, while monaural cues primarily contribute to localisation in the vertical plane, are fundamental front-back disambiguation and play a key role in distance estimation (see also Risoud et al., 2018).

Binaural cues involve a combined computation of the signals that reach the two ears. As reported for the first time by Lord Rayleigh (Rayleigh, 1907), two binaural cues are used for localisation in the horizontal plane: interaural time difference and interaural level difference. Given the spatial separation between the two ears, the distance between soundsource and each ear changes as a function of sound location and head posture. This determines systematic differences in time of arrival of the sound at the two ears (*interaural time difference, ITD*). Sound waves from a given source position reach the closer ear slightly before reaching the opposite ear, thus producing temporal difference of signal arrival. Interaural time difference are particularly useful for localisation of low-frequency sounds (< 1400 Hz), whose wavelengths are larger than the diameter of the head. This computation is extremely powerful and remarkable, as evidenced by the fact that the human auditory system can capture time delays of about 10-20 μ s for pure tone stimuli (Brughera, Dunai, & Hartmann, 2013).

The other binaural cue extracted by the auditory system results from the shadowing effect of the head on sound propagation between the two ears. When wavelengths are shorter than head's dimension (> 4000 Hz), the head acts as an obstacle on the sound wave pathway. Consequently, sound level at the ear closer to the position of the auditory source is higher compared to that measured at the opposite ear. The computation of the difference in sound level between the two ears gives rise to the binaural cue known as the *interaural level* difference (ILD), which is detectable till a disparity as low as 0.5 dB in humans (Van Opstal, 2016). Both cues provide essential information for sound localisation in the horizontal plane: ITDs are most informative for low frequencies below 1400 Hz, while ILDs are particularly accurate for high frequencies above about 4000 Hz, leaving an intermediate range in which binaural cues are more uncertain. The observation of the frequency-dependent efficacy of the binaural cues was proposed already by Lord Rayleigh in the "Duplex Theory", and was elaborated further during the 20th century (Macpherson & Middlebrooks, 2002; Mills, 1958). However, recent psychophysical investigations suggest that this frequency-dependent distinction of the two binaural cues is not so rigid, especially for complex sounds (van der Heijden, Rauschecker, de Gelder, & Formisano, 2019). Interestingly, it has recently been proposed that the auditory cortex retains an independent coding of ILDs and ITDs (Grothe, Pecka, & McAlpine, 2010) together with an integrated representation of the binaural cues (Edmonds & Krumbholz, 2014). Edmonds and Krumbholz hypothesised that the degree of integration might depend on the reliability of the different cues. When they carry consistent information they will be integrated in a common representation, otherwise the independent coding will prevail.

While combined information from both ears allow localisation of sounds in azimuth, information available at each single ear permits sound localisation on other dimensions – namely elevation, depth and the anterior-posterior axis. Already known from the beginning of the 20th century (Angell & Fite, 1901), the specific spectral composition of the sound reaching the single ear constitute the *monaural or "spectral" cues* to localisation. Depending on the position of the sound, the trunk, shoulders, head and anatomical conformation of the pinnae modify the acoustic spectrum of the stimulus. These directional-dependent spectral alteration of the sound occurring before it reaches the tympanic membrane are known as the Head Related Transfer Functions (HRTFs) (Colburn & Kulkarni, 2005). Given that anatomical conformation of the body, head and external ears are unique for each individual, also HRTFs are subject-specific (Carlile, Martin, & McAnally, 2005a). Accordingly, if a person is asked to judge sound position with a set of HRTFs of another individual, localisation errors along the vertical axis immediately arise (Middlebrooks, 1999; Wenzel, Arruda, Kistler, & Wightman, 1993). In normal-hearing listeners, both ears convey spectral information, originating distinct monaural cues for each ear. Notably, the overall single percept in elevation is derived from a partially asymmetrical integration of both monaural

cues, in which a major weight is given to the ear ipsilateral to the sound-source (Van Wanrooij & Van Opstal, 2005).

It is generally assumed that monaural cues have minimal contributions to sound localisation in the horizontal plane, at least under typical sensory conditions. Notable exceptions have been highlighted in studies investigating spatial hearing in blindness. Results showed that blind people are more sensitive to monaural spectral cues (Doucet et al., 2005; Voss, Lepore, Gougoux, & Zatorre, 2011), which can subtend their higher performance of localisation in horizontal plane. Given that blind are poorer than sighted individuals in localising sounds in elevation (Lewald, 2002b; Zwiers, Van Opstal, & Paige, 2003), it has also been suggested that higher reliance on spectral cues for the azimuth dimension, could detract from the individual's ability to exploit the same cues for elevation (Voss, Tabry, & Zatorre, 2015).

However, also in typical development a particular integration of spectral and binaural cues can occur. When sound-sources are located on the circumference of the so called "cone of confusion", where for each sound-position there is a potential mirror counterpart, individuals cannot say, for example, whether the sound is coming from the front or the back portion of space. In this situation, in which two distinct sources can have identical ILDs and ITDs but can be located in front or behind of the person, spectral cues are necessary to make a correct distinction (Carlile et al., 2005; see also Shinn-Cunningham, Santarelli, & Kopco, 2000). Aforementioned findings suggest that at least a partial *integration* of monaural and binaural auditory cues is a required step in the process of sound localisation.

Monaural cues contribute also to distance estimation, together with overall level of the sound, direct-to-reverberant energy ratio (DRR), dynamic cues and non-

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auditory/perceptual factors (for a detailed review on acoustic distance perception see Kolarik, Moore, Zahorik, Cirstea, & Pardhan, 2016). Higher frequencies content decrease as a function of distance. Stimuli in which lower frequencies predominate over higher frequencies content are perceived more distant from the subject (Musicant & Butler, 1980), unless the sound originates from more than 15 m from listener's position (Kolarik et al., 2016). However, in normal sighted and normal hearing humans distance evaluation, compared to azimuth and elevation estimation, is less accurate. In general, overestimations for sounds close to the participants, and underestimations for sounds farther from the subject are observed (Zahorik, 2002).

1.2 Accommodation to altered auditory cues

In the previous section, we described how typical human listeners extract relevant auditory cues for determining spatial coordinates of sound-sources in external space. We have outlined that binaural and monaural cues are functional for sound localisation in specific spatial dimensions. However, the dynamicity of our environment and the huge diversity of listening contexts (large vs. small rooms; in-door vs. out-door spaces) prevents stable hearing conditions. In addition, intact auditory localisation cues may not always be available (e.g. by a simple otitis, or by a more common condition of using a cell-phone while walking), or may be altered during development or adulthood. How can the auditory system react and adapt to these degraded information in order to maintain a correct perception of acoustic space?

Developmental studies in barn owls (Knudsen, Knudsen, & Esterly, 1984; Knudsen & Mogdans, 1992; Mogdans & Knudsen, 1992; Mogdans & Knudsen, 1993), ferrets (Keating & King, 2013; A J King, Parsons, & Moore, 2000) and rats (Popescu & Polley, 2010), reported a striking rewiring capability of the auditory system to compensate for degraded or limited localisation cues. Studies in barn owls suggested that alteration of binaural cues due to monaural ear-plugging induces a change in binaural sensitivity (binaural remapping) with a fundamental role of the first eight weeks of life in building efficient spatial maps. Conversely, studies in mammals (ferrets) indicated a weighting mechanism involving a recalibration of the intact spectral cues of the hearing ear.

Also in humans, the remarkable plasticity of the brain can be revealed in the context of spatial hearing. In adulthood, the investigation of these plastic processes has exploited so far the possibility to reversibly alter the auditory localisation cues, thus allowing the observation of learning and adaptive phenomena on spatial hearing. In the next paragraphs will focus on the studies which adopted the two most common procedures for binaural and monaural cues alteration. Different processes of accommodation has been observed, and specific hypotheses on the mechanisms responsible of the relative plastic changes has been proposed.

1.2.1 Binaural Cues perturbation: ear-plugging

Alteration of binaural cues is most commonly achieved by inserting a sound-attenuating earplug in one ear. This occlusion of one ear canal causes a change in the sound level reaching the two ears, affecting particularly ILDs, but also ITDs. Moreover, earplugs are most effective for high frequencies, thus impacting also on monaural spectral cues to some extent. It is important to emphasise that, although monaural ear-plugging usually aims to simulate a condition of unilateral hearing loss, it constitutes in fact a very different situation. The earplug, even if inserted correctly, allows some sound waves to pass through, providing to the auditory system a binaural, albeit heavily perturbed, stimulation. Moreover, the intact inner ear on the plug side may still receive acoustic information through bone conduction.

Notwithstanding these limitations, the simulated monaural hearing model has clear and replicable effects on spatial hearing. Behavioural consequences on sound localisation involve primarily the horizontal dimension, as reported systematically since the first studies on the topic (Angell & Fite, 1901; Flannery & Butler, 1981; Musicant & Butler, 1984b; Slattery & Middlebrooks, 1994). Monaural ear plugging causes an overall increase of sound localisation error, which is more pronounced in the space ipsilateral to the plug. The alteration of binaural cues also induces systematic localisation biases towards the hearing ear, with a clear divergence between actual position and perceived position of the sounds. However, unilateral plugging does not impact only horizontal localisation. For instance, Van Wanrooij and Van Opstal (2007) investigated the effects of monaural earplugs on 2D sound localisation, using different auditory stimulations. They reported an overall mislocalisation bias towards the unplugged side in the horizontal plane, thus confirming the critical role of binaural cues for spatial hearing in azimuth. Using low intensity sounds, for which binaural cues are basically absent, the authors also revealed that spectral cues of the hearing ear were implied in sound localisation in horizontal plane. This is important because it shows that, in a hearing context in which binaural cues are altered, ambiguous and unreliable, the intact

spectral shape cues acquire increasing relevance. Critically, they also showed a consistent and systematic impact of the ear-plug on elevation dimension, which was smaller than the effects on azimuth, but nevertheless present on both the plugged and unplugged side. The authors (Van Wanrooij & Van Opstal, 2007) thus proposed that localisation in elevation depended upon a combined analysis of spectral cues derived from both ears, with a weighting process regulated by the perceived (i.e. not actual) horizontal sound location, which in this case was strongly altered.

These findings highlight that our cognitive system relies on all available auditory cues when discriminating the azimuth and elevation components of sound-sources (Van Wanrooij & Van Opstal, 2007). Binaural and monaural cues are assumed to be *integrated* according to a sophisticated weighting process, dependent on the acoustic context and the relative reliability of the specific cues. The insertion of a unilateral earplug decreases the efficacy of binaural cues, increasing the weight of the intact monaural spectral cues for horizontal localisation. Concurrently, elevation judgements derives from a weighting process of spectral cues coming from both ears, which is influenced by the perceived horizontal position of the sound (Figure 1).



Figure 1. Cue-integration model for 2D sound localization. Under normal binaural hearing all available cues (ITD, ILD and spectral cues from both ears) are weighted to establish an azimuth percept (AZp), with major contribution of binaural cues, which are still reliable. Spectral cues from both ears contribute to determine the elevation percept (ELp), which is influenced by the perceived azimuth position (AZp). Under perturbed binaural hearing, the weights of the different cues will be balanced depending on the reliability of the cues. For instance, during monaural ear-plugging, binaural cues (ITD,ILD) are scarcely effective in estimate azimuth percept, and consequently the weight of spectral cues of the hearing hear increases to infer azimuth position of the sounds. Figure 1 adapted from Van Wanrooij and Van Opstal (2007)

The ear-plugging paradigm has been used in humans adopting either a *continuous* approach, in which the plug is worn all day for several consecutive days (Bauer, Matuzsa, Blackmer, & Glucksberg, 1966; Florentine, 1976; McPartland, Culling, & Moore, 1997), or implementing an *intermitted* approach in which the unilateral plug is worn only during the testing sessions and removed between sessions (Butler, 1987; Kumpik, Kacelnik, & King, 2010; Musicant & Butler, 1980; Strelnikov, Rosito, & Barone, 2011). In the continuous approach participants exploit their continuous dynamic interactions with the external environment for re-learning correspondences between auditory cues and space. However, in this more pervasive and more naturalistic approach, the identification of specific elements concurring to auditory localisation recovery remains uncertain. On the other hand, in intermitted approaches, only the specific characteristics of the implemented training promote sound localisation in monaural listening, with the risk of limited generalisation effects.

Early studies (Bauer et al., 1966; McPartland et al., 1997) reported that continuously wearing the ear-plug produced appreciable sound localisation improvements after 3 to 7 days, with acceleration of the process if combined with behavioural training (Bauer et al., 1966). Conversely, only 24 hours of continuous unilateral ear plugging did not cause any accuracy increase (Slattery & Middlebrooks, 1994).

Kumpik and co-workers (2010) tested three groups of participants in a training procedure: one group performed the training and testing sessions in a single day; the other two groups performed a training paradigm lasting 8 days, with different amount of trials per training session, 125 and 250 respectively. Results showed a performance improvement only in the groups trained for several days, which implied that a single training day may not be sufficient to trigger measurable adaptation processes. The recovery of performance towards that of pre-training phases has been attributed to *reweighting* of binaural and monaural auditory cues, with higher dependence on monaural spectral shape cues for azimuth localisation. This interpretation was supported by the fact that when spectral cues were cancelled out by adopting a trial by trial variation in the broadband sound spectrum, performance improvement did not occur, meaning that a specific adaptive *remapping* of the correspondences between ITDs and ILDs and external coordinates was not present.

Irving and Moore (2011) also combined continuous plugging with behavioural training, plugging participants for 5 consecutive days while concurrently engaging them in daily training sessions with response feedback. Again, results of performance improvement on the horizontal plane suggested a mechanisms of weighted integration of all available auditory cues, which exploited predominantly the spectral cues of the hearing ear. Minimal aftereffect were measured after plug removal (as observed also in Kumpik et al., 2010). Once the

unilateral earplug was removed, performance rapidly returned to that of normal binaural hearing. This could lead to conclude that remapping of binaural cues did not occur, and instead a reweighting process of binaural and monaural cues prevailed, favouring the weight of the intact spectral cues. An alternative view, however, is that remapping of binaural cues indeed occurred, but the auditory system is capable of building multiple and co-existing mappings between binaural cues and space.

The aforementioned findings are in line with results obtained testing adult ferrets plugged in one ear. Kacelnik and colleagues (2006) showed that accommodation to altered auditory cues by simple natural exposure to the environment does not lead to measurable improvements in ferrets, while the use of a training paradigm accelerated considerably the processing of acoustic space recovery. Importantly, the behavioural improvement was associated with a *cue-reweighting* process. The insertion of an ear-mould in the hearing ear of monaural plugged ferrets (a procedure that alters monaural cues without occluding the ear) disrupted the increased horizontal localisation performance achieved after training, bringing back accuracy levels to those measured the first moments after plug application. This demonstrates that animals learned to use spectral cues of the open ear to localise sounds when binaural hearing were perturbed.

In summary, *cue-reweighting* may be one of the key processes implied in accommodation to altered binaural cues, as also proposed by Keating and King (2015). *Cue-reweighting* refers to the mechanism though which under perturbed binaural hearing, the weights of available auditory cues is balanced depending on the reliability of binaural and monaural cues. Therefore, when binaural cues become uncertain, such as in condition of unilateral ear plugging, the system relies more on the intact spectral cues of the hearing ear

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to estimate sound position in horizontal plane. Adaptation to altered cues has been attributed to *cue-reweighting* particularly in ferrets (Kacelnik et al., 2006) and humans (Irving & Moore, 2011; Kumpik et al., 2010; Van Wanrooij & Van Opstal, 2007). Furthermore, also elevation perception is subject to process of *cue-reweighting* during monaural hearing, with greater dependence on the intact spectral cues of the earing ear compared to the spectral information coming from the occluded or altered shaped ear (unilateral ear-mould), (Hofman & Van Opstal, 2003; Van Wanrooij & Van Opstal, 2005, 2007).

Alteration of binaural hearing in humans was instead implemented by Trapeau & Schönwiesner (2015) through digital bilateral ear-plugging, which artificially shifted the natural ITDs of participants for seven consecutive days. Behavioural results, also validated by functional MRI data, highlighted an improvement on sound localisation in horizontal plane already after 48 hours, by simple natural exposure. In this case, the improvement was related to a process of *cue-remapping*, in which a different neural tuning of ITDs took place already at cortical level. Notably, adaptive re-weighting of binaural and monaural cues may scarcely explain the above findings, given that spectral cues of both ears were altered by the plugs. Moreover, a subgroup of participants were tested with 500 Hz low-passed filtered stimuli for which the contribution of ILDs and spectral cues were negligible. Localisation performance remain unchanged suggesting, again, a minimal contribution of spectral cues to the adaptation process occurred. Importantly, the new sound-space correspondence did not interfere with the old one, as proved by the absence of aftereffect after plugs removal. The crucial relevance of this findings in humans points to the intriguingly hypothesis that the human auditory system can create multiple correspondence between specific binaural cues (in this specific case ITDs) and coordinates in external space, after accommodation to perturbed hearing.

Therefore, acoustic space re-learning can be achieved also due to a second process called *cue-remapping* (Keating & King, 2015). *Cue-remapping* finds support already from the seminal study of Knudsen and colleagues (1984), and refers to the change in tuning of the neurons to specific ILDs/ITDs. While under normal hearing a specific ILD is associated with a particular spatial location, the same ILD under perturbed binaural hearing can point to another position. Thus the auditory system recalibrates the shifted tuning properties of the neurons to compensate for the effect of monaural occlusion/hearing deprivation. Cue remapping has been shown to be present in barn owls (Knudsen et al., 1984), as well as adult ferrets (Keating, Rosenior-Patten, Dahmen, Bell, & King, 2016) and humans (Keating et al., 2016; Trapeau & Schönwiesner, 2015).

Concerning studies with intermitted monaural occlusion, the time necessary for adaptation largely depended on the experimental paradigm adopted. For instance, in one early study, Musicant and Butler (1980) reported performance improvement after 60 days of sound localisation training. Butler (1987) provided participants with 95 training trials over 5 consecutive days, and observed accommodation results that lasted about 2 month after the training period. More recently, Strelnikov and colleagues (2011) showed that after five consecutive days of intermitted unilateral ear plugging participants who underwent an audiovisual training paradigm decreased their localisation errors in the horizontal plane. The reported improved performance, however, never reached pre-training level, highlighting the fact that complete creation of a new mapping between sounds and space requires more time to be accomplished at all, or that cue-reweighting cannot compensate entirely the auditory cue alteration. In this case, the authors focused on the role of multisensory audio-visual stimulation in promoting sound-space correspondences.

Training procedure with performance feedback in humans also proved effective (Keating et al., 2016). Interestingly, this study tried to disentangle the contribution of *cuereweighting* and *cue-remapping* in the process of accommodation to altered localisation cues, investigating performance improvement for specific stimuli. Less improvement was found for broadband noise with random spectral profile. This result indicated that, in order to accommodate to abnormal binaural cues, participants learn to rely more on spectral shape cues of the open ear (i.e. *cue-reweighting*), which in this case were disrupted. Yet, if adaptation derived only from a cue-reweighting process, localisation improvement for narrowband sounds (pure tones) would not be present. In fact, participants ameliorated their performance for both low and high frequency pure tones, suggesting that a recalibration of binaural cues (i.e. *cue-remapping*) was occurring. Thus, the authors showed that both processes of *cue-reweighting* and *cue-remapping* can contribute to acoustic space re-learning in the same individual, even though their reciprocal connection is still unclear. These results were further corroborated by an analysis on previous work on ferrets tested with intermitted unilateral ear-plugging (Keating, Dahmen, & King, 2015; Keating & King, 2013). Ferrets exhibited bot *cue-remapping* and *cue-reweighting*, and neurophysiological data points to independent neuronal coding for the two difference processes implied.

1.2.2 Monaural cues perturbation: ear-moulding and nonindividualised HRTFs

Understanding the consequences of spectral cue alteration and how human auditory system adapts to it is important for several reasons. First of all, the shape of human outer ear changes gradually during development, and consequently spectral shape cues change across the lifespan (Otte, Agterberg, Van Wanrooij, Snik, & Van Opstal, 2013). Secondly, spectral cues reweighting, as mentioned before, is fundamental in the process of acoustic space adaptation in monaural hearing. Finally, spectral cues are altered in every condition of hearing impairment supported by hearing aids (Byrne & Noble, 1998) or cochlear implants (Litovsky, Parkinson, & Arcaroli, 2009; Majdak, Goupell, & Laback, 2011; van Hoesel & Tyler, 2003).

As in the case of binaural hearing perturbation, different strategies have been used for the study of accommodation to altered monaural cues in normal-hearing participants. Two main methods allow alteration of spectral cues. The first method exploits the anatomical conformation of the pinnae in shaping spectral cues. Spectral cues are modified indirectly by changing the shape of the outer ear, by fitting in the concha cavity an ear-mould which alters the direction-dependent reflections, absorptions and diffraction of sound waves. The second method implies direct manipulation of the sound waves reaching the ear canal. In a context of a virtual environment delivered through headphones, spatialized sounds created with *nonindividualized* HRTFs are akin to the experience of localising with "the ears of a stranger". These two strategies impair sound localisation performance mainly in elevation.

Despite the fact that ear-moulding studies so far adopted different paradigms and focused on different aspect of acoustic space re-learning, common conclusion have been generally drawn. Hofman and collegues (1998) were among the first to demonstrate the ability of the mature auditory system to accommodate to modified spectral cues. They applied bilateral ear moulds to four normal hearing participants, testing sound localisation in 2D space (azimuth and elevation). Participants wore the moulds continuously during waking hours, for a period ranging from 19 to 39 days. Insertion of the moulds caused a dramatic decrease of performance in the vertical plane, leaving accurate localisation in azimuth. After a variable period of daily altered hearing experience with the moulds, participants regained localisation abilities in elevation. Notably, after removal of the moulds, performance was comparable to that of pre-moulding session, proving that the new sound-space association did not suppress nor interfere with the pre-existing one and that the different auditory cuespace correspondences can be retained in parallel (see also Carlile, Balachandar, & Kelly, 2014; Carlile & Blackman, 2014).

Results clearly showed high intersubjective variability of adaptation, which might be attributed to different factors, such as the participants' lifestyle, or specific interaction and auditory experience during the moulding period. However, a subsequent study highlighted a further possibility (Van Wanrooij & Van Opstal, 2005). The authors applied a single ear mould to 13 subjects over a period of at least 11 days, showing a relation between the magnitude of the mould effect on sound elevation perception and the subsequent degree of adaptation. Measuring subjective HRTFs with and without the moulds, the authors found that the more the two maps were dissimilar, the more participants improved after the adaptation period. Moreover, participants who's HRTFs change minimally with the mould did not show appreciable improvement effects. Contrasting results have been found instead by Trapeau and collaborators (2016). The authors showed that the auditory system can adapt to altered

spectral cues just after six days of continuous bilateral ear-moulding. However, the positive correlation between the degree of spectral degradation and the decreased performance on elevation judgement was preserved after the period of accommodation, such as participants whose spectral cues were disrupted the most showed slower and lower adaptation. Given these opposite and controversial results, the relation between auditory cues degradation and learning effects has yet to be ascertain properly. However, the hypothesis of a process in which higher acoustic cues perturbation lead to higher possibilities of learning new and efficient sound-space correspondences, seems to be the most supported at the moment (Van Opstal, 2016; Van Wanrooij & Van Opstal, 2005; see also Chapter 3 of this thesis).

Findings of Van Wanrooij and Van Opstal (2005) also indicates that adaptation to perturbed monaural spectral cues are ear-specific, suggesting that binaural weighting of monaural cues occurs after a spectral-to-spatial-mapping of each single ears, in accordance to the functional model proposed by Hofman and Van Opstal (2003). In particular, in the "spatial weighting scheme" (Figure 2) the overall elevation percept of a sound is the product of two different processing stage: the first in which spectral cues of the single ear are spatially coded in separate elevation percept, and a second stage in which those elevations are combined trough a binaural weighting process influenced by perceived target azimuth.



Figure 2. The spatial weighting scheme (Hofman and Van Opstal, 2003). As a first step, in order to estimate elevation, HRTFs from both ears are associated to spatial coordinate in a spectral-to spatial mapping process, independently. The second step requires a binaural weighting of the two independent perceived elevation. *Figure 2 adapted from Van Wanrooij and Van Opstal, 2005.*

The persistence of the new acoustic space mapping obtained after adaptation has been frequently reported (Carlile & Blackman, 2014; Hofman et al., 1998; Trapeau & Schönwiesner, 2015; Van Wanrooij & Van Opstal, 2005) and recently confirmed to be present even one month after a brief adaptation periods of six days (Trapeau et al., 2016). In that study, performance gain was retained after one week or one month and, most importantly, no aftereffects emerged in these testing sessions. Elevation accuracy resembled that of normal binaural hearing even at the very first trials after mould removal, indicating again that multiple maps could be retained by (and can be available for) the auditory system. The authors suggested a mechanisms of "many-to-one mapping" in which a single spatial location might be associated to many HRTFs configurations, similar to what was originally proposed by Hofman & Van Opstal (1998). Moreover, contrary to previous studies (Carlile et al., 2014; Hofman et al., 1998), they found decreased localisation also in horizontal dimension after bilateral ear moulding. Although perturbation in elevation was markedly most evident, degradation of azimuthal accuracy was dependent on it, in the sense that participants who showed lower accuracy in elevation showed also lower performance in horizontal plane. A process comparable to that proposed by Van Wanrooij & Van Opstal (2005) was advanced, in which an altered elevation percept can in turn influence a correct estimation of horizontal sound position.

How humans can learn to create and store new spatial maps, and particularly how they can create new associations between spectral cues (HRTFs) and spatial coordinates has been originally proposed by Van Opstal in his book (2016) through a computational neuralnetwork model. In this model, the spectral input originating by a sound with a specific position in elevation is compared to all stored sets of HRTFs through a correlative process. The sets that correlates the most with the given spectrum give rise to a spatial percept in vertical dimension. In the meantime, sensory feedback from vision and sensory motor system can be acquired, helping the selection of the appropriate map. A mismatch between the consequent elevation percept and the actual position of the sound leads to the creation of a new correspondence between the altered spectral cues and the specific sound location. Importantly, after the new maps is created, it does not interfere with previously generated maps, allowing the system to adaptively select the most appropriate map, depending on the hearing context (Figure 3).



Figure 3. Computational model of how the auditory system could learn and store a new set of HRTFs. The spectral input (Y) is compared to all stored HRTFs through a correlation process. The maximum correlation determines the elevation percept (\mathcal{E}_{perc}) and the subsequent response. If there is a mismatch between the elevation percept (\mathcal{E}_{perc}) and the percept determined by the visuo-motor system (\mathcal{E}_{Vis}), an error ($\Delta = \mathcal{E}_{perc} - \mathcal{E}_{Vis}$) informs the system to store the input spectrum (\mathcal{E}_{Tar}), as a results of a repetitive and long-term running average, as a new HRTF map, at the visuo-motor defined elevation. Importantly, the new map does not interfere with the original one. *Figure 3 adapted from Van Opstal, 2016*

While ear-moulding is a clever and efficient approach to alter direction-dependent monaural spectral cues to localisation, it is also an effortful and time-consuming method that few experimental laboratories can afford. An alternative approach is to create altered spectral cues is achieved by exploiting non-individualised HRTFs, and measuring adaptation effects of spatial hearing after different training paradigms (Majdak, Walder, & Laback, 2013; Mendonça, Campos, Dias, & Santos, 2013; Mendonça et al., 2012; Parseihian & Katz, 2012; Zahorik, Bangayan, Sundareswaran, Wang, & Tam, 2006). For instance, Parseihian and Katz (2012) trained listeners to localise sounds using non-individualised HRTFs in a virtual auditory environment. They reported improvement of accuracy, mainly in elevation, already after three training sessions of 12 minutes each. Participants have to actively move searching for target sounds, while listening to an audio feedback indicating the proximity to the sound
source. In this case, audio-proprioceptive information were exploited to promote acoustic space re-learning, that was however clearly incomplete after only three days. Also Zahorik and colleagues (2006) reported localisation improvement after brief training exposure (two sessions of 30 minutes each), specifically for front/back confusion errors. However, participants did not improve in elevation dimensions, suggesting that complete accommodation requires longer time and a more complex underlying process to be accomplished.

1.2.3 Non-auditory factors influencing acoustic space adaptation

Although spatial hearing builds primarily on fine interpretation of auditory cues, the development and re-learning of associations between auditory cues and space involves other sensory systems than just hearing, as well as the motor system. Sound localisation in everyday life occurs in a multisensory rich environment, hence information coming from multiple sensory systems concur in defining the spatial coordinates of heard sounds. In addition sound localisation is typically an active phenomenon – like all aspects of perception. For instance, localisation of sounds is usually accompanied by head orientation and eye movements, whose reciprocal position has to be accounted for by the audio-motor system (Goossens & van Opstal, 1999). Their position change continuously in relation to each other and in relation to the auditory target, characterising auditory space perception as a dynamic and active behaviour (Lambert, 1974). In natural environment auditory objects are usually paired with a visual counterpart, which rises the relevance of vision in acoustic space perception (King, 2009).

Increasing awareness of the influence of non-auditory factors in spatial hearing led to several attempts to exploit the same elements to restore sound localisation under perturbed hearing. The following paragraphs will outline the major non-auditory elements contributing to the promotion of accommodation to altered auditory cues, analysing their role and how they have been proved effective in specific training paradigms.

1.2.3.1 Vision

In typical development, sound localisation is inherently multisensory (Bruno & Pavani, 2018). Studies investigating the impact of vision in spatial hearing have shown that in multisensory contexts the influence of vision on audition can be substantial. In phenomena known as visual capture and ventriloquism, when the auditory and the concomitant visual stimuli are spatially separated, the location of sounds are systematically biased towards or attributed to the position of the visual source (Bertelson, 1999; Bertelson & Radeau, 1981; Chen & Vroomen, 2013). Moreover, pioneering studies in the 1980s showed that the use of distorted prisms produce recalibration of auditory spatial maps, with persistent biases in sound localisation in barn owls (Knudsen & Knudsen, 1985), ferrets (King, Hutchings, Moore, & Blakemore, 1988). Similarly, distorting prisms in humans led to short-term auditory spatial recalibration (Zwiers et al., 2003). In humans, presentation of continuous audio-visual discrepancies cause a transitory bias (ventriloquism aftereffect) in subsequent auditory-only localisation, with dislocation of the sounds in the direction of the previous experienced audio-visual pair (Frissen, Vroomen, de Gelder, & Bertelson, 2005; Lewald, 2002a; Radeau & Bertelson, 1974; Recanzone, 1998; Recanzone, 2009).

The general hypothesis is that the brain can calibrate the association between auditory cues and spatial location in external space, exploiting the more spatially reliable visuo-spatial information. When visual information is made uncertain and blurred, visual stimuli can instead be mislocalised towards the position of the sound, with audition capturing vision (Alais & Burr, 2004). These results suggest that predominance of vision for spatial processing is context-dependent and the brain integrates information coming from different senses relying on its degree of reliability (Battaglia, Jacobs, & Aslin, 2003; Heron, Whitaker, & McGraw, 2004).

Therefore, binding of different sensory information play a crucial role in acoustic space perception. Interestingly, this evidence could be exploited not only to influence spatial hearing, but also to facilitate the process of re-learning auditory cue-space correspondences. Increasing examples of training procedures built on the convergence of information across different sensory systems have been proposed in the last decades. There is now crucial evidence that multisensory training can facilitate unisensory learning (Shams, Wozny, Kim, & Seitz, 2011), with higher rates of learning when multisensory stimulation is used. Results show that sound localisation can be improved using a multisensory approach based on systematic associations between visual and auditory stimulation, both in monaurally plugged hearing humans (Strelnikov et al., 2011) and ferrets with bilateral cochlear implants (Isaiah, Vongpaisal, King, & Hartley, 2014). Multisensory stimulation has been further used to provide position feedback in different studies, in which participant's responses were followed by an audio-visual stimulation indicating the veridical position of the target (Shinn-Cunningham, Durlach, & Held, 1998; Zahorik et al., 2006). Other training paradigms used only visual stimulation as feedback after the participant's response, always indicating the real position of the sound (Bauer et al., 1966; Carlile et al., 2014; Kumpik et al., 2010; Mendonça et al., 2013, 2012). Intriguingly, Majdak and colleagues (2013) adopted a mix experimental design in which both visual and audio-visual positional feedback were employed. In a virtual environment, after the participant's response, a visual object appeared indicating the position of the target. Moreover, in order to emphasise the coupling between acoustic and visual spatial coordinates, the auditory target was further replayed together with the visual stimulus (multisensory stimulation) and participants has to point one more time in the target position. Despite the great impact of visual and multisensory (audio-visual) stimulation in training paradigms on sound localisation, a definitive answer about when and how visual stimuli should be delivered to obtain the maximum effectiveness, has yet to be ascertained. For instance, the different amount of efficacy of synchronous vs. delayed audio-visual stimulation is still uncertain in training paradigm on sound localisation. In general, a more fine-grained investigation of the effects of multisensory stimulation, which beneficial consequences might not be taken for grounded, seems to lack.

Although vision can help accommodation to altered auditory cues and it is a fundamental element in training procedures of hearing rehabilitation, it is not a necessary requirement for sound localisation per se, as mainly suggested by studies on blindness. On the one hand, seminal animal studies affirmed that visual stimulation is crucial for a typical development of auditory spatial maps in the superior colliculus (King & Carlile, 1993; Knudsen, 1988). On the other hand, humans with visual sensory deprivation from birth showed comparable or even superior abilities of sound localisation (Collignon et al., 2011; Collignon, Voss, Lassonde, & Lepore, 2009; Röder et al., 1999; Voss, Gougoux, Zatorre,

Lassonde, & Lepore, 2008; Voss et al., 2011), which suggests that visual input is not indispensable for developing proper spatial hearing skills.

1.2.3.2 Sensorimotor processes

The relation between sound localisation and head movements is present immediately after birth in humans. Head orienting toward sounds has been reported in the first 24 hours from birth (Clifton, Morrongiello, Kulig, & Dowd, 1981), in new-borns of a few days (Humphrey, Humphrey, & Muir, 1994; Muir & Field, 1979; Wertheimer, 1961), in infants of 1-3 months of age (Field, Muir, Pilon, Sinclair, & Dodwell, 1980), in 4-5 month age old (Muir & Clifton, 1985) and 6-9 months of age (van der Meer, Ramstad, & van der Weel, 2008). In adulthood, a certain degree of variability in head orientation behaviour has been shown (Fuller, 1992), but participants can direct the head to sound when instructed to do it (Brimijoin, Mcshefferty, & Akeroyd, 2012; Fuller, 1992; Fuller, 1996; Kim, Barnett-Cowan, & Macpherson, 2013). Interestingly, individual head movement tendency can be temporally modified. Evidence of plasticity in this sense has been shown through the use of aperture spectacles and cervical collar, in order to restrict the field of view and reduce the neck mobility, respectively. Findings highlighted a decreased tendency to head orientation with concomitant enhancement of ocular movements range after cervical collar removal. By contrast, after 9 days of restricted field view (20° through aperture spectacles) participants head movements propensity increased (Stahl, 2001).

The dynamic enhancement of content information of binaural and monaural cues through the displacement of the head can lead to several performance benefits. While Goossens and van Opstal (1999) did not find any advantage of head movements in sound localisation in azimuth or elevation discrimination, other studies suggest that head orientation promotes sound localisation in horizontal dimension (Perrett & Noble, 1997a; Thurlow & Runge, 1967) and reduces front/back confusion errors (Brimijoin & Akeroyd, 2012; J. Kim et al., 2013; Perrett & Noble, 1997b; Wightman & Kistler, 1999). Moreover, several pieces of evidence highlighted that also eye position influences the processing of localisation cues and auditory perception (Bulkin & Groh, 2006; Lewald & Getzmann, 2006; Razavi, O'Neill, & Paige, 2007a; Zwiers, Versnel, & Van Opstal, 2004). For instance, it has been shown that directional eye movement during the delay between two consecutive and spatially separated sounds significantly affect participant's sensitivity to the relative position of the sounds. Accordingly, performance on a same/different position task decreased when participant were instructed to change their fixation point between the delivery of the two sounds, clearly suggesting that eye movement have a impacting role in the perception of acoustic space (Pavani, Husain, & Driver, 2008).

The role of sensorimotor information in spatial hearing is further evident in approaches suggesting that audio-motor information can be sufficient for the development of spatial representation of sounds (Aytekin, Moss, & Simon, 2008; Bernard, Pirim, de Cheveigne, & Gas, 2012). In fact, the human brain is able to distinguish between changes in auditory input due to own subjective movement, through proprioceptive sensation, and changes due to external source movement. Aytekin and colleagues (2008) suggested a sensory-motor approach to sound localisation, in which a complex computational model is able to reliably estimate sound-source location through experience, continuously comparing its own orientation movement and the acoustic consequences of the movement itself. Learning is then achieved through the association between external sound position in space and relative audio-motor information. Notably, the experience-dependent nature of the sensory motor approach to sound localisation could be immediately translate to the context of accommodation to perturbed hearing, in which plastic processes can arose from self-generated actions and auditory-sensory-motor interactions.

Other studies focused on the potential of sensory-motor feedback in fostering acoustic space re-learning. In agreement with a previous study showing accommodation inside and outside the visual field after about 60 days of continuous ear-moulding (Carlile & Blackman, 2014), Carlile and collaborators (2014) investigated the role of sensory-motor feedback in promoting sound localisation. Over a period of 10 days, participants wore continuously bilateral ear-moulds and were assigned to one of four different groups. Each group performed daily a localisation task with nose-pointing response in a dark room, but with different subsequent feedback. The first group did not receive any feedback after localisation response (Control group). The second group was trained with a visual feedback indicating the veridical position of the sound, appearing after participant's response. The third group, the audiovisual-sensory-motor group (AVSM), after having indicated the perceived sound position, were provided with a visual feedback and with an auditory feedback indicating the ongoing distance from the target. Participants of this group were further encouraged to explore space with the head during the subsequent corrective localisation, thus exploiting sensory-motor feedback. The last group performed the same paradigm, but in this case the room lights were switched on, thus providing a richer visual reference frame. All groups showed improved performance after 10 days of ear-moulding, in accordance with findings of previous studies (Hofman et al., 1998; Van Wanrooij & Van Opstal, 2005). However, the AVSM group showed higher rate of improvement, particularly for what concerned front/back confusion errors. There were no difference between the groups who performed the training with or without light in the room. Therefore, as suggested by the authors, it seems that an active motor interaction with the acoustic environment may provide an effective tool to promote and accelerate the plastic process of learning auditory space.

Using virtual auditory environments, other studies exploited sensory-motor feedback during behavioural training paradigm, to promote accommodation to non-individualised HRTFs. In particular, different approaches has been used, such as space exploration through head re-orientation toward audio-visual target (Majdak et al., 2013; Zahorik et al., 2006); game-like scenarios in which participants has to actively find sound-sources around them through an hand-held tool (Ohuchi, Iwaya, Suzuki, & Munekata, 2005; Parseihian & Katz, 2012), or have to hit a moving sound with a hand-held tool as well (Honda et al., 2007).

The latest studies mentioned introduced a further element during training procedures, which is the action towards target sounds. Although during those actions, which required also a certain degree of whole-body movement, the contribution of sensory-motor feedback of the moving head was not negligible, the specific role of active body movement and interaction with the sound sources has yet to be defined properly. In fact, localise a sound reaching his veridical position require an additional step of motor action planning to specific spatial coordinates, that might have the potential, till largely unexplored, of further promoting adaptation to altered auditory cues.

1.2.4 A common framework - Functional models

In the previous sections I have outlined some of the models that have been proposed to capture sound-to-space mappings. These models often treated binaural auditory cues and monaural spectral cues separately, and did not aim to provide an overall framework of the functional mechanisms that relate auditory cues initially reaching the ears with the resulting spatial outcome.

In a recent review, Mendonça (2014) outlined a model aimed at explaining the continuous creation and adjustment of new "combination rules" for spatial hearing. This model focuses on the process of acoustic space adaptation adopting a functional perspective (for similar concepts see also Van Opstal, 2016). The model is presented schematically in Figure 4. The auditory cues resulting from a sound in space are combined following a specific rule to determine an auditory spatial percept. This combination rule seems to involve the integration of all auditory cues, even if the author do not specify this point in great details. The resulting percept is then compared with sensory (visual/sensorimotor) and response feedback, which can confirm or reject the sound-space correspondence. If there is a correspondence between acoustic percept and feedback the original combination rule is further strengthened. Otherwise, a new combination rule is created and tested. Through a recurrent process of trials and errors, new correspondences between auditory cues and space are progressively established. Again, the model assumes that multiple sound-space correspondences context.



Figure 4. Illustration of a hypothetical process of auditory adaptation through continuous sensory experience. The auditory cues characterising a sound in space are combined following a specific rule (1) to determine an auditory spatial percept (2). The resulting percept is then compared with environmental feedback (3). If there is a correspondence between acoustic percept and feedback the original combination rule is further strengthened (4). Otherwise, a new combination rule is created and a new correspondence between auditory cues and space is established. *Adapted from Figure 1 in Mendonça, 2014*

Although this model emphasises the contribution of multisensory information in the process of acoustic space-relearning, it presents several limitations, starting from missing information regarding the process of creation a combination rule from binaural and monaural cues, to the different potential role of distinct sensory feedback, to specifications about the creation of new combination rules.

In attempt to overcome these limitations and integrate previous models that specified in greater details the potential mechanisms of cue integration and sound-space correspondence updating (particularly the notions of *cue-reweighting* and *cue-remapping*, discussed above), I propose here a revised and extended version of Mendonça's model for acoustic space re-learning (see Figure 5). This revised functional model aims to highlight the different steps that may occur in the process of accommodation to perturbed hearing in the perception of acoustic space. We took inspiration by the existing proposals (see Keating & King, 2015; Mendonça, 2014; Van Opstal, 2016) and we further suggested the relevance of considering acoustic-space re-learning as a multifactorial and multisensory process. Given the growing evidences regarding the effectiveness of behavioural training paradigm in promoting spatial hearing recovery, the identification of the several elements that can potentially promote this process is, in our opinion, crucial and timely.

The starting point of the proposed model is the physical location of the auditory source in external space (*actual position of the sound*). This does not imply that the model assumes a purely feed-forward psychophysical chain, from sensory inputs to perception, as any listener surely has priors about the potential locations of sounds in the environment. These can be based on past experience, environmental statistics or task demands (e.g., see Parise et al., 2014). Yet, the model focuses on the auditory cues that the auditory system receives from the interactions of sound-waves with the trunk, head and outer ear - in Bayesian terms, the available 'evidence'.

This process of *Cues extraction* allows the gathering of binaural and monaural cues. Following Van Opstal (2016), the model assumes that HRTFs at each ears are compared to the relative stored maps (Van Opstal, 2016) and separate spatial percept in elevation are established (*Elevation percept left and right*). Notably, while Van Opstal described this *Signal Correlation Process* only for sets of HRTFs, findings from Trapeau and Schönwiesner (2015) suggest that it may also apply to binaural cues: sets of ITDs might be stored and retrieved in an hearing-context dependent manner. Therefore, we hypothesised that the *comparison of stored maps* could involve also binaural cues, leading to independent azimuth percept for ITD and ILD (*Azimuth percept ITD and ILD*). Further research should be done to corroborate or refuse this specific aspect of the model. In this phase, *Head movements* can intervene to promote *Cue extraction* and selection of the most appropriate stored maps. Head orientation can enhance auditory cue information and people can furthermore exploit this strategy to predict acoustic changes dependent on the specific head posture, helping again the *Signal Correlation Process*.

The subsequent step allows to estimate the *Perceived Sound Position*. Notably, here we focused on spatial perception in azimuth and elevation, however, the same binaural and monaural cues allow the perception of sound position also in the third dimension (distance). The overall perceived azimuth results from the weighting process that combines the two perceived azimuth, based on ITD and ILD; whereas the overall perceived elevation results from the weighting process that combines the two perceived elevations, based on HRTFs at the left and right ears (as suggested by Van Wanrooij and Van Opstal, 2007). Note that the model assumes that the weighting process for monaural cues is further influenced by the perceived azimuth position (Hofman & Van Opstal, 2003).

The resulting *Perceived Sound Position*, with its azimuth and elevation components, is *compared* with the non-auditory representation of the sound, which can be visual (i.e., the visual counterpart of the acoustic object), sensorimotor (e.g., sensorimotor feedback after reaching the sound source with the arm) or even memory related (e.g., comparison with the previously experienced position of the same sound). Similarly to what proposed in previous models (Mendonça, 2014; Van Opstal, 2016), the *Error Signal* produced by the *Comparison* process informs the auditory system about any significant mismatch between the *Perceived Sound Position* and the *Non-Auditory Sound Position*, thus triggering the adaptation

mechanism. The aforementioned non-auditory feedback (visual, sensorimotor, memory related), continuously help the system to refine the association between auditory cues and space under novel listening condition.

As anticipated earlier in this Chapter, adaptation in spatial hearing is assumed to exploit two distinct mechanisms: *cue-reweighting* and *cue-remapping* (Keating and King, 2015). Recent findings suggested that both processes may be present concomitantly in the same individual (Keating et al., 2016). In the proposed model, the consolidation of new maps (i.e., new associations between the auditory cues and spatial coordinates in external space) takes place with a process of *Cue-Remapping* that, expanding the proposal by Keating and King (2015), can be referred to both binaural and monaural cues. Once new combination rules are established through cue-remapping for a given hearing condition, they are stored in the system and (seemingly) they do not interfere with previously acquired maps (Hofman et al., 1998; Van Opstal, 2016), allowing individuals to adapt fluidly to different hearing contexts. Therefore, multiple and different stored maps can be established in the same listener, for what concern both monaural (HRTFs) (Hofman et al., 1998) and binaural (ILDs) (Trapeau & Schönwiesner, 2015) cues. In parallel, *cue-reweighting* can be involved in the weighting stage for azimuth and elevation estimation, leading to new perceived sound position as a result of continuous loops.

Although in previous paragraphs I have highlighted the role that sensory-related feedback (such as visual and sensorimotor feedback) in facilitating and promoting the processes of acoustic space re-learning, conceptual/informative feedback have also been exploited in training paradigms. After response, participants receive a feedback regarding their performance, which most of the time indicate the correctness of the response through

words or colours (Butler, 1987; Carlile & Blackman, 2014; Irving & Moore, 2011; Kumpik et al., 2010; Strelnikov et al., 2011). Other studies used pulsing sounds indicating the error magnitude as response feedback (Carlile et al., 2014; Parseihian & Katz, 2012). Although it is generally assumed that response feedback can induce faster adaptation, little evidence is currently present supporting this view (Mendonça, 2014). Furthermore, given that both sensory (audio-visual, sensorimotor) and informative (information about level of performance) feedback allow participants to monitor their success in achieving a goal (in spatial hearing training, localising a sound), they can be considered an example of reward – i.e., a key element driving human behaviour.

Although not explicitly detailed in the model, several *transversal components* may play a role in modulating the efficacy of adaptation mechanisms in spatial hearing. For instance, recent studies have highlighted a relation between visual mental imagery and sound localisation. Pairing a sound with an imagined visual stimulus, cause a mislocalisation of the sound towards the imagined visual position – a form of imagined ventriloquism (Berger & Ehrsson, 2013). The link between *visuo-spatial working memory* and sound localisation has been further reported in late-blind population (Tao et al., 2017). The authors measured visuo-spatial working memory abilities asking participants to retain and manipulate imagined spatial information. Next, participants were administered a sound localisation training that lasted 2 to 5 sessions. Results showed a positive correlation between performance on the matrix test and improvements in sound localisation. This behavioural finding was supported by an fMRI study that revealed enhanced functional connectivity between the precuneus and the lingual gyrus, suggesting that neural processing of sound location comprises an integration of visuo-spatial memory information in late-blind population. The absence of the

aforementioned connectivity pattern in early blind individuals indicated that prior visual experience modulates the neural network engaged in sound localisation and that when individuals can experience visual sensation, it is involved in the process of learning acoustic space. Although this relation has been reported testing blind people, these finding seems to highlight the possibility that sound localisation learning could be promoted by visual working memory ability also in sighted individuals. In general, the potentials of imagined visual representation of sound positions can be exploited in the presence of single and multiple stimuli, which could consequently provide benefit in both egocentric and allocentric spatial coding of sounds.

Another example of transversal components that could influence adaptation in spatial hearing is motivation. For instance, Bruns and colleagues (2014) demonstrated that motivation aspects, such as reward expectation, alter audio-visual spatial integration processes. In their experiment, participants were engaged in a sound localisation task in which they had to identify the correct position of a sound source while ignoring visual stimuli presented far from the auditory target (ventriloquism paradigm). The authors measured the ventriloquism effect as a function of reward: the amount of monetary reward was different between left and right hemi-field. They found that the ventriloquism effect was weaker for stimuli presented on the high-reward space compared to the low-reward one. Therefore participants, motivated by higher monetary reward expectation, localised more accurately the sounds coming from the respective hemifield, suggesting an impacting role of personal motivation in perceptual tasks. Thus, personal motivation could constitute, also in the context of acoustic space-relearning, a crucial factor in order to boost the potential of training procedures. Motivation could be functional in promoting re-learning because of its influence

on multisensory integration and, moreover, it could affect individual approach to the training consequently giving benefit to their performance outcomes.

Figure 5. A potential unified model of acoustic space re-learning. A full description of the model

is outlined in the section below.



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Chapter 2

Study 1

Interaction between egocentric and allocentric spatial coding of sounds revealed by a multisensory learning paradigm

The following study has been published on a peer-reviewed journal (Scientific Reports) in April 2019. The following contents are reported from the same journal article (here cited).

Rabini, G., Altobelli, E., & Pavani, F. (2019). Interactions between egocentric and allocentric spatial coding of sounds revealed by a multisensory learning paradigm. *Scientific reports*, 9(1), 7892.

2.1 Abstract

Although sound position is initially head-centred (egocentric coordinates), our brain can also represent sounds relative to one another (allocentric coordinates). Whether reference frames for spatial hearing are independent or interact remained largely unexplored. Here we developed a new allocentric spatial-hearing training and tested whether it can improve egocentric sound-localisation performance in normal-hearing adults listening with one ear plugged. Two groups of participants (N=15 each) performed an egocentric sound-localisation task (point to a syllable), in monaural listening, before and after 4-days of multisensory training on triplets of white-noise bursts paired with occasional visual feedback. Critically, one group performed an allocentric task (auditory bisection task), whereas the other processed the same stimuli to perform an egocentric task (pointing to a designated sound of the triplet). Unlike most previous works, we tested also a no training group (N=15). Egocentric sound-localisation abilities in the horizontal plane improved for all groups in the space ipsilateral to the ear-plug. This unexpected finding highlights the importance of including a no training group when studying sound localisation re-learning. Yet, performance changes were qualitatively different in trained compared to untrained participants, providing initial evidence that allocentric and multisensory procedures may prove useful when aiming to promote sound localisation re-learning.

2.2 Introduction

Accurate processing of sound source coordinates is central to our ability to perceive the 3D structure of the surrounding auditory scene (Bregman, 1990b, 1990a; Middlebrooks & Simon, 2017), discern signal from noise (Yost, 2017) and orient attention in space (Neupane, Woyke, & Wilde, 2014; Pavani et al., 2017). Sound localisation relies on the interpretation of auditory cues (interaural time and level differences, as well as monaural spectral cues) deriving from the interactions between sound waves, the head and external ears (Middlebrooks, 2015a; Middlebrooks & Green, 1991). Initial coding of sound position occurs in head-centred coordinates (Blauert, 1997), in an egocentric reference frame dependent on the head position on the trunk and listener's position in the environment. However, efficient interactions with the auditory environment require encoding of sound position also in a reference frame that remains stable when our head and our body change position. Such reference frame is termed allocentric (or world-centred) and it encodes the position of sounds with respect to other sound sources or external landmarks in the multisensory environment. This allocentric reference frame allows judgements on the relative positions of sounds, independent of the listener's position.

Coding of auditory space in different reference frames has previously been investigated in humans using electrophysiology, taking advantage of the Mismatch Negativity (MMN) response. In two studies using virtual sounds delivered through headphones¹¹ or free-field sounds¹⁰, Altmann and colleagues found evidence for head-centred (craniocentric) coding at the early processing stage corresponding to the MMN. However, a similar study conducted with free-field sounds by Schechtman and colleagues found that head-dependent and headindependent (Schechtman, Shrem, & Deouell, 2012) sound representations may in fact coexist, already at the processing stage captured by the MMN. The latter result is in agreement with research on ferrets, indicating that a majority of neurons in the auditory cortex is tuned to egocentric sound representation, and yet a restricted subsample of cells showing head-independent position coding also exists (Town, Brimijoin, & Bizley, 2017).

To the best of our knowledge, only one study has examined egocentric and allocentric sound coding using behavioural methods, focusing however on a special population. Studying sighted and blind individuals, Gori and colleagues (Gori, Sandini, Martinoli, & Burr, 2014) showed that congenitally blind people are highly accurate when asked to localise single sounds (an egocentric task), but they are impaired in a task that require a judgment on the relative distance between pairs of sounds (i.e., the auditory space bisection task, an allocentric task). This study revealed that sound localisation abilities in allocentric and egocentric reference frames can dissociate, at least in visually impaired people. In general, however, the issue of dissociation vs. interaction of egocentric and allocentric sound coding in humans remained largely unexplored. In the present study, we aimed to investigate this interaction in behaviour by testing if a training of sound localisation abilities performed in allocentric coordinates (auditory space bisection task) can improve spatial hearing performance in a pointing to sound task performed in egocentric coordinates.

Research on sound localisation training over the last decades has consistently revealed the auditory system plasticity when dealing with altered auditory cues (Wright & Zhang, 2006a). Studies in humans (Carlile, 2014; Keating & King, 2015; Mendonça, 2014; Shinn-Cunningham et al., 1998; Van Wanrooij & Van Opstal, 2005) as well as other animals (Kacelnik et al., 2006), showed that learning new correspondences between auditory cues and coordinates in space is possible, particularly when training paradigms are employed. The theoretical relevance of these findings resides in the identification of a perceptual ability which remains plastic beyond sensitive periods in the early stages of development (Ponton et al., 2001). Moreover, these observations have great clinical implications, as they open the possibility of training spatial hearing in adults with hearing loss, when binaural hearing is restored through hearing aids or cochlear implants. Several learning paradigms aimed at improving spatial hearing have adopted a multisensory approach (Mendonça, 2014). This approach builds on the notion that multisensory training can promote unisensory learning (Shams et al., 2011). In the case of audio-visual training, the hypothesis is that the brain can calibrate the association between auditory cues and spatial locations in external space, taking advantage of the more reliable visuo-spatial information. Support for this approach emerged from converging results in monaurally plugged hearing humans (Strelnikov et al., 2011) and in ferrets with bilateral cochlear implants (Isaiah et al., 2014). To date, however, all audiovisual training paradigms have been implemented in egocentric reference frame (Mendonça, 2014), with no attempt to exploit the same principles in the context of allocentric coding of sounds.

In audio-visual training paradigms the two multisensory events originate from identical positions in space (i.e., auditory and visual stimuli are spatially congruent). This perceptual coupling has been accomplished using either simultaneous or delayed multisensory stimulation. For instance, the audio-visual training developed by Strelnikov and colleagues (Strelnikov et al., 2011) consisted in single sounds delivered in free-field, and paired with simultaneous and spatially congruent visual events presented using LEDs. Participants were asked to localise each sound, using a laser pointer controlled by a central knob. Notably, in

order to avoid a complete reliance on visual information, the training session comprised occasional (15%) auditory-only stimulations. Differently, Majdak and co-workers (Majdak et al., 2013), implemented a virtual reality setup in which participants localised a single sound delivered though headphones in virtual auditory space, using a virtual reality laser pointer. No concomitant visual stimulation was delivered at this first stage. After the response, a red rotating cube was presented as feedback, to indicate the actual sound position (delayed spatially congruent stimulation). Finally, the sound was replayed once more from the same location, this time spatially and temporally coupled with the visual stimulus. Note that in both training studies, target sounds were localised with respect to the participant's body and required, in this sense, egocentric coding. An allocentric training would have require instead localisation of the sound with respect to a different object or landmark, or alternatively, the presentation of multiple sounds in different positions with a subsequent evaluation of their relative spatial location.

In the present work, we directly compared the efficacy of two multisensory trainings – one based on *allocentric* spatial processing, the other based on *egocentric* spatial processing – in promoting re-learning of correspondences between auditory cues and space. Following previous works, we altered spatial hearing by plugging one ear. Monaural listening deteriorates sound localisation performance (Flannery & Butler, 1981; Musicant & Butler, 1984a; Slattery & Middlebrooks, 1994) and proved an effective model for the study of auditory space re-learning (Musicant & Butler, 1980). One group of participants was trained using a multisensory (audio-visual) allocentric task, modelled on the auditory space bisection proposed by Gori and collaborators (Gori, Sandini, & Burr, 2012). Three bursts of white noise were presented in sequence, paired with spatial and temporally matching visual stimuli.

Participants in this group judged the relative position of the central sound with respect to the other two (see Fig. 1D). A second group of participants was trained using exactly the same audio-visual triplets, but was asked to perform an egocentric localisation task. A written instruction presented at the end of the trial instructed participants to point to one of the three sounds in the triplet. As in Strelnikov et al. (Strelnikov et al., 2011), in both training protocols audio-visual stimulation occurred in 75% of trials, whereas the remaining 15% consisted in auditory-only stimulation. Crucially, both groups were tested before and after training for their ability to localise a single auditory target delivered in front space. This egocentric sound localisation test was performed in both azimuth and elevation, because changes in performance following monaural plugging have been reported along the horizontal as well as vertical dimensions (Doucet et al., 2005; Van Wanrooij & Van Opstal, 2007). To assess training generalisation effects the stimulation used in pre- and post-training phases was a spoken syllable, instead of the white noise bursts used during training. Finally, a control group that did not perform any training was also included in the study to assess performance changes unrelated to training.

If allocentric and egocentric auditory spatial coding interact with one another, training benefits should transfer across *different* reference frames. This predicts that allocentric training should improve performance also in the subsequent egocentric task. Alternatively, partial segregation between allocentric and egocentric auditory spatial coding predicts that

only the group that performed both training and test within the *same* reference frame (i.e., the egocentric training group) can improve performance.



Figure 6. Apparatus, overall experimental procedure and tasks. (A) Participants sat in front of a matrix (5x12) of loudspeakers mounted on a rectangular panel, on which visual stimuli were projected when appropriate. Response were collected through mouse cursor or keyboard. (B) The experiment lasted five consecutive days, with testing sessions at day 1, day 3 and day 5, and training sessions from day 2 to day 5. (C) During testing sessions, participants completed an egocentric sound localisation task. In each trial, a spoken Italian syllable was presented from one speaker of the stimulation matrix and participants indicated the source of the sound by left-clicking with the mouse cursor in the correspondent position. (D) The AlloT Group performed the acoustic space bisection task. Three consecutive sounds (white noise) were presented at different horizontal positions and participants indicated if the second sound was closer to the first or third presented sound. During audio-visual trials (75% of total) a white dot appeared on screen to mark the exact position of each sound, together with lines connecting the dots to depict the spatial relationships between sounds. (E) The EgoT group received exactly the same audio-visual stimulation (with the only exception of lines connecting the dots) but was instructed to localise only one of the three presented sounds using the mouse.

2.3 Material and Methods

2.3.1 Participants

Forty-five normal hearing participants took part in the study and were assigned to one of three experimental groups: Allocentric Training Group (AlloT, N = 15, mean age = 23, *SD* = 2.7, 10 females), Egocentric Training Group (EgoT, N = 15, mean age = 24, *SD* = 3.9, 12 females), Control Group (Control, N = 15, mean age = 21, *SD* = 2, 12 females). All participants reported no history of auditory or neurological disease and had normal or corrected to normal vision. Pure tone audiometry (250, 500, 1000, 2000, 4000 Hz) was used to screen participants for hearing loss, and served to assess the efficacy of the ear-plug in each participant. The study was conducted according to the research ethics regulation of the University of Trento and in line with the Declaration of Helsinki (1964, amended in 2013).

Participants read and signed an informed consent before taking part in the experiment and received monetary reimbursement (7 ϵ /hour) or course credits for participation.

2.3.2 Apparatus

The experiment was administered in a reverberant room (4.2 x 5.0 m; mean background noise = 50 dB SPL). The experimental setup consisted in a custom-made rectangular wooden panel (95x60 cm) covering a visual angle of 43° , in which 60 round-shaped speakers (5cm diameter of Mylar; Pro Signal ABS-210-RC range 350–20,000Hz, 8K, 1W RMS Power) were mounted, arranged in a matrix of 5 rows and 12 columns (see Figure 7).



Figure 7. Schematic representation of the stimulation setup. A matrix of speakers, arranged in 5 rows and 12 columns, were fixed on a rectangular wooden panel, allowing sound presentation both in azimuth and elevation. Black circles represent auditory stimulation speakers with specific coordinates in horizontal and vertical plane. Visual stimuli were then projected on the white acoustically transparent fabric covering the speakers.

A white acoustically transparent fabric was placed in the frontal part of the panel, to prevent vision of the sound-sources and to serve as screen for projecting all visual stimulations. Visual stimuli were projected using an LCD projector (LG HW300G; resolution: 1280x 1024) connected to the stimulation PC (*Dell Precision T3400*). The panel was mounted on a wooden support and placed on a table 120 cm from participant's head, with its centre approximately at ear level (Figure 5A). The integrated sound card of the PC, connected to an external loudspeaker for sound amplification, was used for delivering all audio signals. Each signal was switched between 30 relays (NEC MR62-4.5 USB) by using the digital output of two National Instrument boards (NIusb-6259) to activate the desired speaker. Auditory stimulation was controlled using custom-made Matlab scripts (Mathworks R2015b, 32-bit).

2.3.3 Ear plugging method and audiometric testing

We used EAR Classic foam earplugs (3M PP 01 002; mean attenuation values as reported by manufacturing data: 30 dB, 24 dB, 22 dB for high, medium, low frequencies respectively; Single Number Rating = 32 dB) to simulate a unilateral conductive hearing loss and therefore decreasing spatial hearing abilities. The plug was always applied to the left ear. An intermitted approach (see Ref¹³ in main manuscript) was adopted, applying the plug at the beginning of each testing session and removing it at the end. Hearing threshold at the plugged ear was measured before each training session by audiometric test (Grason Stadler GSI 17 Audiometer) to quantify the plug-induced decrease of hearing threshold in each testing day. In the present experiment, mean attenuation value induced by the plug was 22.18 dB. Specifically, mean attenuation varied across frequencies tested (250 Hz: 14.52 dB; 500 Hz: 14.25 dB; 1000 Hz:18.89 dB; 2000 Hz: 29.64 dB; 4000 Hz: 33.61 dB; see also Fig. 2S). The experimenter explained the correct procedure for ear plugging (verbal instruction: "Roll the Ear Plug into a narrow tube. Put it in it, and hold it place for 20s with your fingertips") to each participant at the beginning of each experimental session to ensure an optimal fitting of the plug. During experiment, plugged ear was further covered with an ear muff (3M 1445, mean attenuation values of 32 dB, 29 dB, 23 dB for high, medium, low frequencies respectively; Single Number Rating = 28 dB, as reported by manufactory data), while the corresponding opposite muff was removed.

Figure 8 shows mean audiometric values for unplugged ears at day 1 (left and right) and plugged ear in all training and testing days (left), for each frequency tested (250, 500, 1000, 2000, 4000 Hz). Differently from common practice, we measured hearing threshold in the same reverberant room in which experiment was later administered.



Figure 8. Audiometric Test. Mean hearing threshold value for each frequency tested has been reported for right ear, left ear and left ear with the plug. For each frequency, hearing threshold of the plugged ear was clearly below 20 dB for left and right ear unplugged, and above 20 dB for left plugged ear. Error bars represent confidence intervals.

2.3.4 Procedure

The overall experimental protocol lasted five consecutive days (Figure 6B). Hearing thresholds were measured by audiometric test for each participant on day 1 for right and left ear in normal hearing condition and left ear in plugged condition. In addition, hearing threshold of the plugged ear was assessed at the beginning of each testing day to ensure that plugging was comparable across sessions.

On day 1, participants performed the test procedure in binaural (Binaural) and monaural hearing condition (Monaural day 1), in separate consecutive blocks. The same testing in monaural condition was repeated after two days (Monaural day 3) and on the last day (Monaural day 5). During the test procedure participants were administered a singlesound localisation task. We presented a stimulus (single spoken Italian syllable: counterbalanced number of occurrence between 'BA', 'RO' and 'GU', 500 ms duration) from a position of our stimulation setup and participants were required to localise the heard sound by moving a mouse cursor (hand icon, projected on the wide screen) to the location of the perceived sound, and validate their response with a left-click (Figure 6C). In each testing phase we presented a total of 180 trials, 3 for each possible position in randomised order. The entire session lasted about 15 minutes and was divided into two blocks of 90 trials each.

Training occurred from day 2 to day 5 (four sessions of training in total), always with the left ear plugged. For the AlloT group, training was modelled on the auditory space bisection task proposed by Gori and colleagues (Gori et al., 2012). Three consecutive sounds (white noise bursts, 500 ms each) were presented at different horizontal positions, at identical elevation. In each trial, sounds originated from three positions with same elevation but different azimuth. The first sound of the triplet was delivered with equal probability from the speaker located at -20°, -17° or -13° to the left of the participant, whereas the third sound was always delivered 9 speakers to the right of the first (e.g., first sound at -20°, third sound at 13°). Critically, the second sound was delivered at one of the intermediate positions between the first and the third, from immediately adjacent to the first to immediately adjacent to the third. In each trial, participants had to indicate whether the second sound, was closer to the first or to the third one. Responses were collected using the computer keyboard. Our choice to change the position of the first sound (unlike the classic procedure by Gori and collaborators (Gori et al., 2012) aimed to reduce the possibility that participants solved the allocentric task through egocentric strategies (Filimon, 2015), paying attention exclusively to the second sound while assuming that the first and third remained at identical positions throughout the experiment. Elevation of sound triplets changed unpredictably across trials (5 possible elevation levels), with each elevation sampled with equal probability within each block. The session was divided in 4 blocks of 60 trials each (total of 240 trials), for an overall duration of about 25 minutes.

In 75% of trials, a white dot (10 pixel diameter) appeared at the time of the auditory stimulation, indicating exactly the location of source location. To emphasise the spatial relation between the sounds a red line (2 pixels width) was presented to connect consecutive sounds (Figure 6D). In the remaining 25% of trials, sounds were presented without visual stimulation to prevent participants from solving the task only relying on visual stimulation. The percentage of audio-visual stimulation was based on the work of Strelnikov and colleagues (Strelnikov et al., 2011).

For the EgoT group, in each trial participants listened to three consecutive sounds (white noise bursts, 500 ms each) exactly as detailed above for the AlloT group. However, after presentation of the last sound (third) a visual instruction appeared on screen indicating which of the three sounds localise (e.g. 'S1', to indicate the first sound). Participants were required to point to target position using the mouse cursor that appeared on the white panel only at the moment of the response. As in the allocentric training, in 75% of trials a white dot indicated the position of each sound (Figure 6E). No red lines appeared connecting the dots. In the remaining 25% of trials, sounds were presented without visual stimulation. Again, participants received a total of 240 trials per session, divided in 4 blocks of 60 trials each. A single training session lasted approximately 25 minutes.

Three methodological aspects are worth noting. First, the auditory stimulation in both training procedures was completely identical, and the difference between training procedures concerned only the visual stimulation and the task. Although each individual sound likely

underwent an initial egocentric coding in both training procedures, critical to the allocentric training task was the spatial comparison between sounds, which entails an allocentric spatial representation. Second, to observe potential generalisation effects of the training paradigms we employed different stimuli and tasks between training and testing sessions, in line previous works (Mendonça et al., 2013; Watson, Carlile, Kelly, & Balachandar, 2017; Wright & Zhang, 2009). Third, unlike most of the previous works¹⁸, we introduced in the design a control group that did not take part in any training procedure (No Training group, NoT), but performed only testing of sound localisation at day 1, day 3 and day 5.

2.3.5 Data analysis

Our stimulation setup allowed the presentation of auditory stimuli both in azimuth and elevation, therefore we have been able to observe different degrees of performance in the two dimensions (see Table 1 and Table 2 for cumulative error measurements in all conditions). In the present work, we investigated performance through rms error and signed error, following Hartmann (Hartmann, 1983) (see also Grantham, Ashmead, Ricketts, Haynes, & Labadie, 2007; Pavani et al., 2017). The rms error represents the root mean squared difference between speaker position and subject's response. The Signed error represents mean difference between response and correct sound-source position and it could be either positive or negative. When considering azimuth, positive values indicate a rightward bias; when considering elevation, positive values indicate an upward bias. We calculated each error separately for each response component: azimuth and elevation. In case of sphericity assumption violations we adopted the Greenhouse-Geisser method of correction.

2.4 Results

Figure 9 shows rms error at the beginning of the protocol for both binaural and monaural listening conditions (day 1, shown with bold lines) and at the end of the protocol (day 5, shown with dashed lines). Performance is presented separately for each of the three groups as a function of horizontal speaker position (Figure 9 A-C) and vertical speaker position (Figure 9 D-F). In the following sections we describe (1) the ear-plug effects on sound localisation on day 1; (2) performance changes at day 5; (3) performance changes at day 3.



Condition - Binaural - Monaural_Day1 - Monaural_Day5

Figure 9. Performance in the sound localisation test. Rms errors for each listening condition (binaural, monaural day 1 and monaural day 5; for clarity performance on day 3 is not shown, see Table 1S and Table 2S for mean values) are displayed as a function of speaker position, separately for each group, for azimuth (A/B/C) and elevation (D/E/F). Thicker axes highlight horizontal speaker position (A/B/C) and vertical speaker position (D/E/F), respectively. Error bars show the standard error.

Table 1. Sound localisation performance in horizontal plane. Mean values (± SD) of rms Error and Signed Constant error in all experimental groups (Allocentric Training, Egocentric Training, No Training) in all listening conditions (binaural, monaural at day 1, day 3 and day 5).

	Allocentric Training Group				Egocentric Training Group				No Training Group				
	(N = 15)				(N = 15)				(N = 15)				
Error Measure	D'	Monaural			D'	Monaural			D'a and	Monaural			
	Binaurai	Day1	Day3	Day5	- Binaurai	Day1	Day3	Day5	Binaurai	Day1	Day3	Day5	
rms error D	3,901	14,690	12,909	13,210	3,573	14,12	12,877	13,407	4,262	13,781	12,011	12,779	
	(1,573)	(4,151)	(2,564)	(2,650)	(0,375)	(2,931)	(2,997)	(2,302)	(1,508)	(2,405)	(3,048)	(3,071)	
Signed constant	- 0,184	5,276	2,018	1,693	-0,531	4,973	2,429	1,590	0,031	5,462	2,961	2,906	
error E	(1,101)	(7,015)	(4,147)	(4,269)	(0,698)	(4,582)	(3,259)	(2,314)	(1,270)	(4,489)	4,383)	(5,275)	

Table 2. Sound localisation performance in vertical plane. Mean values (\pm SD) of rms error and Signed constant errorin all experimental groups (Allocentric Training, Egocentric Training, No Training) in all listening conditions (binaural,monaural at day 1, day 3 and day 5).

Allocentric Training Group					Egocentric Training Group				No Training Group				
(N = 15)					(N = 15)				(N = 15)				
Error Measure	D ' 1	Monaural			D '	Monaural				Monaural			
	Binaurai	Day1	Day3	Day5	Binaurai	Day1	Day3	Day5		Day1	Day3	Day5	
rms error D	8,020	9,140	9,648	9,771	8,801	9,438	9,518	9,214	8,021	9,496	9,626	9,810	
	(2,265)	(0,992)	(1,639)	(1,413)	(2,254)	(1,184)	(1,016)	(1,070)	(1,507)	(1,246)	(0,837)	(0,962)	
Signed constant	2,002	-0,328	-0,325	-0,335	2,959	0,634	1,295	0,686	2,518	0,279	-0,408	-0,242	
error E	(3,718)	(2,588)	(4,196)	(4,050)	(4,492)	(3,665)	(3,662)	(3,001)	(3,73)	(2,962)	(3,603)	(3,458)	

2.4.1 Ear-plug effects on sound localisation on day 1

To examine sound localisation performance on day 1, we entered rms errors in a mixed Analysis of Variance (ANOVA) with LISTENING CONDITION (binaural, monaural), STIMULATION SIDE with respect to the plugged ear (ipsilateral, contralateral), and STIMULATION ECCENTRICITY with respect to listener's body midline $(2^\circ, 6^\circ, 9^\circ, 13^\circ, 17^\circ, 20^\circ)$ as within-participant variables, and GROUP (AlloT, EgoT and NoT) as between-participants variable.
This analysis revealed a 2-way interaction between LISTENING CONDITION and STIMULATION SIDE (F(1,42) = 44.57, p < 0.001, $\eta^2 = 0.69$) and a significant 3-way interaction between LISTENING CONDITION, STIMULATION SIDE and STIMULATION ECCENTRICITY $(F(1.87,78.46) = 16.69, p < 0.001, \eta^2 = 0.28)$. None of these interactions was further modulated by GROUP (all F-values < 1). To study these interactions, we calculated the cost of monaural compared to binaural listening (from now on termed 'monaural listening cost') as the difference in rms error between the two conditions (positive values indicate worse performance in monaural listening). We found that monaural listening cost was overall larger for sounds delivered on the side ipsilateral to the plug $(12.4^{\circ} \pm 5.4)$ compared to the contralateral side ($5.9^{\circ} \pm 2.6$; see Fig. 10A). Interestingly, monaural listening cost varied substantially between-participants: some participants were minimally affected by the ear plug, whereas others localised all sounds towards the open ear. Finally, as revealed by the 3way interaction reported above, monaural listening cost increased as a function of eccentricity, particularly on the side ipsilateral to the plug (see Figure 9B). The omnibus ANOVA also revealed the main effects of LISTENING CONDITION, STIMULATION SIDE and STIMULATION ECCENTRICITY (all F-values > 30.00), as well as the two-way interactions STIMULATION SIDE* STIMULATION ECCENTRICITY and LISTENING CONDITION*STIMULATION ECCENTRICITY (all F-values > 14.00), which were subsidiary to the higher order interactions described above.

A similar ANOVA on mean signed error was run to examine systematic biases in sound localisation. This analysis revealed again a 3-way interaction between LISTENING CONDITION, STIMULATION SIDE and STIMULATION ECCENTRICITY (F(1.87,78.46) = 16.69, p < 0.001, $\eta^2 = 0.28$), which was not modulated by GROUP (F(3.74,78.46) = 0.48, p = 0.74, $\eta^2 = 0.28$)

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0.02). To study this interaction, we calculated the bias induced by monaural compared to binaural listening (from now on termed '*monaural listening bias*') as the difference in signed error between the two conditions (positive values indicate a bias towards the side contralateral to the plug). This bias is shown in Figure 9 as a function of eccentricity. It emerged as strong bias to respond towards the hearing side for sounds originating from the space ipsilateral to the plug (average bias: 13.58 ± 8.03 ; for all eccentricities t-test comparisons against zero p < 0.001). Interestingly, we also found a mild bias towards the body midline when responding to most eccentric sounds contralateral to the plug (-5.31 ± 4.66, -6.99 ± 5.13, -8.39 ± 5.04, for the three most eccentric positions, respectively; all t-test comparisons against zero p < 0.001).



Figure 10. Monaural listening bias as a function of stimulation eccentricity, divided by side of stimulation. Monaural listening bias represents the difference between signed error in monaural and binaural listening at day 1. Error bars show confidence intervals of the mean.

In the vertical plane, sound localisation in binaural listening was overall less precise compared to localisation in azimuth (rms error: azimuth = $3.7^{\circ} \pm 1.7$; elevation = $7.6^{\circ} \pm 3.2$; paired t-test, t(44) = 12.47, p < 0.001, Cohen's d = 1.86). To study whether alteration of binaural cues impacted also on sound elevation perception we entered rms error along the vertical dimension in a mixed ANOVA with LISTENING CONDITION (binaural, monaural), VERTICAL SPEAKER POSITION (-11°, -6°, 0°, 6°, 11°) as within-participants factors, and GROUP (AlloT, EgoT and NoT) as between-participants factor. This analysis revealed that rms error increased from binaural to monaural listening ($8.3^{\circ} \pm 2.0$, $9.3^{\circ} \pm 1.1$, respectively; F(1,42) = 14.33, p < 0.001, $\eta^2 = 0.25$). Localisation errors increased particularly for sounds above ear level (+5°: 5.6° ± 1.7 vs. 7.4° ± 2.3; +11°: 7.1° ± 3.4 vs. 11.3° ± 2.9), resulting in a significant two-way interaction between LISTENING CONDITION and VERTICAL SPEAKER POSITION (F(1.46, 61.33) = 15.95, p < 0.001, $\eta^2 = 0.27$). As for the analysis on the horizontal dimension, performance decrement determined by monaural plugging was comparable across groups (no main effect or interaction involving the GROUP factor emerged; all F values < 1).

A similar ANOVA on Signed Error in the vertical dimension, revealed an interaction between LISTENING CONDITION and VERTICAL SPEAKER POSITION (F(2.15, 90.31) = 55.98, p < 0.001, $\eta^2 = 0.54$). Sounds from above the horizontal midline were localised downward in binaural listening (-2.9° ± 3.7) and even more so in monaural listening (-7.3° ± 3.0; t(44) = 7.36, p < 0.001, Cohen's d = 1.1). By contrast, sounds from below the midline were localised upward in both binaural (7.7° ± 4.6) and monaural (7.7° ± 3.3) listening conditions alike (t(44) = 0.07, p = 0.942).



Figure 11. (**A**) Monaural listening cost in the horizontal plane as a function of Stimulation Side (Ipsilateral/Contralateral to the plug) and experimental group. (**B**) Monaural listening cost in the horizontal plane, irrespective of group, as a function of Stimulation Eccentricity and Stimulation Side. Error bars represent confidence intervals of the mean.

2.4.2 Change in performance at day 5

Changes in sound localisation performance in azimuth and elevation between day 1 and day 5 are shown in Figure 9, separately for the trained groups and the no-training group (compare solid and dashed lines depicting monaural listening conditions at day 1 and day 5, respectively).

To study the difference in monaural listening performance between the first and the last testing day, we entered rms errors in a mixed Analysis of Variance (ANOVA) with DAY (day 1, day 5), STIMULATION SIDE, STIMULATION ECCENTRICITY and GROUP as before. This analysis revealed a significant 2-way interaction between DAY and STIMULATION SIDE $(F(1,42) = 23.82, p < 0.001, \eta^2 = 0.36)$, as well as a 3-way interaction between DAY, STIMULATION SIDE and STIMULATION ECCENTRICITY ($F(2.81,118.10) = 9.56, p < 0.001, \eta^2 = 0.18$). None of the above interactions was further modulated as a function of GROUP (all F-values < 1).

To study these interactions, we calculated performance change as the difference in rms error between day 1 and day 5 (from now on termed '*Day1-Day5 Difference*'). On the side ipsilateral to plug, the rms error was smaller on day 5 (13.54 \pm 4.18) compared to day 1 (16.21 \pm 5.31; t-test: t(44) = 4.10, p < 0.001, Cohen's d = 0.61, corrected for multiple comparison; Day1-Day5 Difference = 2.67 \pm 4.37). By contrast, on the side contralateral to the plug, the rms error significantly increased from day 1 (9.87 \pm 2.44) to day 5 (11.05 \pm 2.73; t-test: t(44) = 2.73, p = 0.02, Cohen's d = 0.41, corrected for multiple comparisons using Bonferroni; Day1-Day5 Difference = -1.18 \pm 2.89; see Fig. 4A). Day1-Day5 Difference also changed as a function of eccentricity on both sides, but particularly on the side ipsilateral to the plug (see Figure 12B). The omnibus ANOVA revealed also the

significant main effects of STIMULATION SIDE and STIMULATION ECCENTRICITY (all F-values > 30.00) and the two-way interaction STIMULATION SIDE* STIMULATION ECCENTRICITY (F(1.83, 76.73) = 12.56, p < 0.001, η^2 = 0.23), both subsidiary to the higher order interactions described above.



Figure 12. (**A**) Day1-Day5 Difference in the horizontal plane as a function of Stimulation Side (Ipsilateral/Contralateral to the plug) and experimental group. (**B**) Day1-Day5 Difference in the horizontal plane irrespective of group as a function of Stimulation Eccentricity and Stimulation Side. Error bars represent confidence intervals of the mean. Positive values indicate performance improvement, negative values performance decrement.

A similar ANOVA performed on mean signed error was conducted to study if any systematic bias changed between day 1 and day 5. This analysis revealed the significant main effects of DAY (F(1,42) = 25.5, p < 0.001, η^2 = 0.375), STIMULATION SIDE (F(1,42) = 673.21, p < 0.001, η^2 = 0.94), STIMULATION ECCENTRICITY (F(4.05,170.25) = 12.49, p < 0.001, η^2 = 0.22), and the two-way interaction SIDE*ECCENTRICITY (F(1.85,170.25) = 77.74, p < 0.001, η^2 = 0.92). No higher order interaction emerged (all F-values < 1), as well as no main effect or interactions involving the between participants factor GROUP (all F-values < 1.1).

Overall, signed error changed between day 1 and day 5 (5.24 ± 5.37 , 2.06 ± 4.09 , respectively, t-test: t(44) = 5.14, p < 0.001, Cohen's d = 0.77). Similar to monaural listening at day 1, results on monaural listening at day 5 confirmed localisation bias toward the hearing side for sounds ipsilateral to the plug (9.99 ± 7.21), and a bias towards the midline for sounds originating from the space contralateral to the plug (-5.89 ± 7.12).

Interestingly, sound localisation performance in the vertical plane remained unchanged between day 1 and 5 (see lower panels in Figure 9). A mixed ANOVA on rms error, with DAY (day 1, day 5) and VERTICAL SPEAKER POSITION (-11°, -6°, 0°, 6°, 11°) as within-participants factors, GROUP (Allot, EgoT and NoT) as between-participants factor, revealed no significant main effect of DAY (F(1.527,61.081) = 1.54, p = 0.224, $\eta^2 = 0.04$) or GROUP (F(2,40) = 0.39, p = 0.68, $\eta^2 = 0.02$), nor any two-way or three way interactions (all F-values < 1.4).

Dependent Variable	Stimulation	Stimulation Eccentricity						
	Side	2 °	6 °	9 °	13°	17 °	20 °	
Monaural listening cost	Contralateral	5.67 (3.51)	4.07 (2.85)	4.15 (3.16)	5.58 (3.84)	7.31 (4.75)	9.60 (5.09)	
	Ipsilateral	7.42 (4.27)	8.91 (4.42)	10.82 (5.02)	13.59 (6.22)	16.40 (7.29)	18.23 (7.59)	
Day1-Day3 Difference	Contralateral	0.59 (3.37)	0.36 (2.34)	-0.05 (3.37)	-0.13 (4.31)	-1.94 (5.10)	-1.44 (5.01)	
	Ipsilateral	1.37 (3.33)	1.76 (4.14)	3.37 (3.59)	3.20 (5.11)	2.76 (5.92)	3.55 (6.04)	
Day1-Day5 Difference	Contralateral	0.88 (3.60)	-0.34 (3.25)	-0.83 (3.64)	-1.45 (4.20)	-2.71 (4.98)	-2.61 (5.68)	
	Ipsilateral	1.57 (4.19)	2.34 (4.55)	2.68 (4.45)	2.59 (5.17)	6.41 (6.34)	3.41 (6.02)	

Table 3. Mean values $(\pm sd)$ of Monaural listening cost, Day1-Day5 Difference and Day1-Day3 Difference computed onrms error, reported as a function of Stimulation Side (Ipsilateral/Contralateral to the plug) and Stimulation Eccentricity.

2.4.3 Change in performance at Day 3

Having established that monaural listening performance in rms error changed between the first and the last day of our protocol, we investigated whether this dependent variable changed even after two days, namely at day 3. To this aim, we entered azimuthal rms errors in a mixed Analysis of Variance (ANOVA) with monaural testing DAY (day1, day 3), STIMULATION SIDE with respect to the plugged ear (ipsilateral, contralateral), and STIMULATION ECCENTRICITY with respect to listener's body midline (2° , 6° , 9° , 13° , 17° , 20°) as within-participant variables, and GROUP (AlloT, EgoT and NoT) as between-participants variable (see Tables 3 for mean values).

This analysis revealed a 2-way interaction between DAY and STIMULATION SIDE $(F(1,40) = 12.18, p = 0.001, \eta^2 = 0.23)$ and the 3-way interaction DAY*STIMULATION SIDE*STIMULATION ECCENTRICITY (F(2.58,103.26) = 6.53, p < 0.001, $\eta^2 = 0.14$). None of these interactions were modulated by GROUP (all F-values < 1s). To study these interactions, we calculated localisation performance difference in the horizontal plane between the first (day 1) and the third (day 3) testing day in monaural listening as the difference in rms error

between the two testing days (from now on termed 'Day1-Day3 Difference'). On the ipsilateral side, rms error reduced on day 3 (13.27 ± 4.54) compared to day 1 (16.21 ± 5.31 ; t-test: t(42) = 4.18, p < 0.001, Cohen's d = 0.64, corrected for multiple comparisons using Bonferroni; Day1-Day3 Difference = 2.50 ± 3.92). On the side contralateral to the plug, however, no change in rms error emerged from day 1 (9.87 \pm 2.44) to day 3 (10.32 \pm 2.38) (t-test: t(42) = 1.03, p = 0.62, Cohen's d = 0.16, corrected for multiple comparison; Day1-Day3 Difference = 0.03 ± 2.24). Day1-Day3 Difference increased as a function of eccentricity in the plugged side, whereas in the unplugged side reached significance only for one eccentricity. The main effects of DAY, STIMULATION SIDE and STIMULATION ECCENTRICITY (all F-values > 10.00) as well as the two-way interactions STIMULATION SIDE* STIMULATION ECCENTRICITY (F(1.84, 73.57) = 13.50, p < 0.001, $\eta^2 = 0.25$) reached significance, but were subsidiary to the higher order interactions described above. In the vertical plane localisation performance did not change between day 1 and day 3. Rms error in the vertical plane was studied using an ANOVA with DAY (day 1, day 3) and VERTICAL SPEAKER POSITION (-11°, -6°, 0°, 6°, 11°) as within-participant factor, and GROUP (Allot, EgoT and NoT) as between-participants factor. The analysis revealed no significant main effects or interaction involving the GROUP variable (all F-values < 1.5) (Figure 13).



Figure 13. (**A**) Day1-Day3 Difference in horizontal plane as a function of Stimulation Side (Ipsilateral/Contralateral to the plug). Day1-Day3 Difference, calculated as the difference between rms error in monaural listening at day 1 and day 3, is shown separately for each experimental group. (**B**) Day1-Day3 Difference in horizontal plane is shown as a mean of all groups, as a function of Stimulation Eccentricity and divided by Stimulation Side. Error bars represent confidence intervals of the mean.

2.4.4 Follow-up analysis

The first follow-up analysis stem from the observation that monaural listening cost in horizontal dimension at day 1 was substantially different across participants (Figure 12). We asked whether such variability at day 1 could predict performance changes observed at the end of our protocol (day 5). To this aim, we analysed the relation between *monaural listening cost* at day1 and *Day1-Day5 Difference* using Pearson correlations. Correlation plots are shown in Figure 14, separately for the three groups. In both training groups a significant relation between monaural listening cost and Day1-Day5 Difference in azimuth due to monaural plugging on day 1, the more they changed localisation performance after training (AlloT Group: r = 0.74, p = 0.002). By contrast, Day1-Day5 Difference was unrelated to

monaural listening cost in the No Training group (r = -0.079, p = 0.78). An ANCOVA with DAY1-DAY5 DIFFERENCE as dependent variable, GROUP (AlloT, EgoT and NoT) as independent variable and MONAURAL LISTENING COST as covariate, showed a significant 2-way interaction between GROUP and MONAURAL LISTENING COST (F(2,39)=5.69, p=0.007, η^2 =0.14).



Figure 14. (A-C) Relation between monaural listening cost and Day1-Day5 Difference as a function of group. The trained groups (AlloT and EgoT, panels A and B, respectively) show a positive and significant correlation between monaural listening cost at day 1 and the performance difference between day 1 and day 5. No such relation emerged for the No Training group (C).

The second follow-up analysis stem from the observation that Day1-Day5 Difference on horizontal plane was positive on the plugged side (suggesting performance improvement), but negative on the unplugged side (suggesting performance decrement). One interpretation for this unexpected finding is that recalibration of auditory space between day 1 and 5 emerged as overall shift of responses towards the unplugged side – rather than a re-learning of auditory-cue space correspondences. If this is the case, Day1-Day5 Difference on the plugged side should correlate with Day1-Day5 Difference in the unplugged side across participants. We tested this hypothesis using correlations (Pearson) and found no relation between ipsilateral improvement and contralateral decrease, neither when treating all participants together (r = 0.03, p = 0.86) nor when splitting them as a function of group (AlloT: r = 0.27, p = 0.34; EgoT: r = -0.15, p = 0.58; NoT: r = -0.07, p = 0.080).

2.5 Discussion

In the present study, we examined the relation between allocentric and egocentric reference frames in spatial hearing, in the context of multisensory guided training of sound localisation. First, we confirmed that the method adopted for auditory cues alteration (monaural ear plugging) can effectively impair sound localisation abilities in the horizontal dimension. In addition, we extended this classic finding by showing that sound localisation impairments emerged also in the vertical dimension, and by documenting substantial inter-participants variability in the monaural listening cost determined by the ear-plug. Second, after four days of protocol (day 5), we measured performance improvements on single sound localisation on the side ipsilateral to the plug (left), which emerged together with concomitant performance decrements on contralateral space (right). Notably, these performance changes emerged only in the horizontal dimension, whereas monaural sound localisation in the vertical dimension remained entirely unaffected. Third, we found that performance changes occurred with comparable strength in all tested groups – i.e., irrespective of whether participants were trained or untrained. From a theoretical perspective, this finding implies that listeners can

change their sound localisation performance even in absence of error feedback signal. From a methodological point of view, it stresses the importance of including a no training group when assessing the efficacy of sound localisation training methods. Finally, we proposed a new audio-visual protocol based on allocentric coding of sound, extending the principles of multisensory stimulation previously implemented only using egocentric procedures. In the following sections, we will discuss each of these novel contributions in details.

In agreement with previous findings we show performance decrement from binaural to monaural listening (ear-plugging), mostly in the space ipsilateral to the plug. However, the impact of monaural plugging on sound localisation performance was markedly different between participants. Inter-individual variability of the consequences of ear plugging has been reported previously (Kumpik et al., 2010), but its origin remains to be ascertained. It could reflect inter-individual efficacy of the plug, different sensitivity to auditory cues alteration, or a combination of the two. An interesting finding of the present study is the impact of this inter-individual variability of the plug-effect (which we termed 'monaural listening cost') on performance change after four days of training (which we termed 'Day1-Day5 Difference'). Although sample size of each experimental group was limited, it is noteworthy that in our two trained groups the magnitude of training effects was linearly related with the amount of sound localisation deficit induced by the plug (see Fig. 5 A-C). Participants who were more affected by the ear plug changed their performance post-training to a greater extent, compared to participants who were minimally affected by monaural occlusion. Intriguingly, this positive relation was completely absent in the control group which just repeated the test after 2 and 4 days. Given the limited number of participants in each group (N = 15), these correlation results should be taken with caution. Yet, positive

relations between earplug effect and training benefit have previously been reported in humans with similar sample sizes (Van Wanrooij & Van Opstal, 2005), (but see Trapeau & Schönwiesner, 2015 for contrasting results). In particular, in a study on spatial hearing relearning after monaural ear-moulding, Van Wanrooij and Van Opstal (Van Wanrooij & Van Opstal, 2005) showed that participants whose spectral cues were disrupted the most achieved better post-training results (N=11), and learned at faster rates compared to participants who were minimally affected by monaural ear-moulding. The functional model proposed by Van Opstal (2016) assumes that a new correspondence between auditory cues and space is stored whenever a discrepancy is detected between the spatial outcome of an existing sound-space correspondence (SSC) and the actual stimulus position, leading to the consolidation of new SSC with repeated exposures. In this context, the observed relation between monaural listening cost and Day-Day5 Difference might be interpreted as the consequence of the perceived discrepancy between the response and the actual sound position. This discrepancy was only experienced during training and was clearly largest for those participants who were maximally affected by the plug. Indeed, no such relation between ear-plug effect and change in performance between day 1 and day 5 was detected in the no-training group (which never received feedback).

This finding suggests that qualitative differences might exist between the trained groups and the no-training group, despite the quantitatively comparable performance. Performance changes in individuals with altered auditory cues who received no error-feedback signal has been recently documented using other methods. Zonooz and colleagues (Zonooz, Arani, & van Opstal, 2018) tested sound localisation in the vertical plane using spectrally poor (band limited) sounds in trained vs. untrained participants. While

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performance improvements were larger in participants trained with visual feedback, even those participants who did not received performance-related feedback showed soundlocalisation improvements in vertical plane. Performance changes in the no-training group are compatible with the theoretical framework provided by Keating and King (Keating & King, 2015). The authors proposed that adaptation to altered sound localisation cues can result from two different (though not mutually exclusive) mechanisms: cue-reweighting and cue-remapping. Cue-reweighting is a fast adaptation process, in which the relative contribution (i.e., weight) of the available auditory cues is changed to accommodate the intervening modulations (e.g., ear-plugging, as here). Instead, cue-remapping is a slowly emerging adaptation phenomenon in which a new correspondence between available auditory cues and space is progressively encoded. The observed differences between trained and un-trained participants may relate to these two different adaptation mechanisms. Specifically, the no-training group may have primarily changed its performance exploiting a fast cue-reweighting mechanism. By contrast, the sensory feedback provided in the audiovisual trainings may have triggered a slower process of sensory recalibration, in which new sound-space correspondences started to emerge from a combination of cue-reweighting and cue-remapping processes. This suggests that longer and more consistent training procedure may be essential to achieve proper cue-relearning. In this sense, it is possible that our short training (25 minutes per sessions, for 4 consecutive days) captured only the intermediate phase of the entire adaptation process, in which cue-reweighting – but not a full and stable cue-remapping mechanism - has been accomplished. This could also partially explain the combination of ipsilateral improvement and contralateral decrement measured in the trained group.

The present study also introduced a novel training approach based on audio-visual coding of sounds in *allocentric* coordinates. Previous research exploring the effects of training in the context of reversibly altered auditory cues almost exclusively adopted an egocentric frame of reference (for a review see Mendonça, 2014). One notable exception is a study conducted by Gori and colleagues (Gori, Vercillo, Sandini, & Burr, 2014), conducted with blindfolded hearing participants tested in binaural listening. The procedure entailed an auditory spatial bisection task similar to the one adopted here, as well as training sessions aimed at improving allocentric coding using multisensory feedback. Specifically, the experimental set-up comprised nine speakers, each associated with one vibrotactile stimulator placed on the forearm of the participant. Speakers and vibrotactile stimulators were kept spatially aligned throughout the task. The tactile feedback group listened to triplets of acoustic stimuli (as in the present work), paired with delayed (200 ms) spatially-congruent tactile stimulation. During training, participants were required to attend the multisensory stimulation but performed a different task, which consisted in detecting an occasional higher tone. Performance in the auditory bisection task improved in the tactile feedback group, but not in participants who received only a verbal feedback about sound position, or participants who received no feedback.

While this audio-tactile study highlights the potentials of multisensory stimulation in promoting allocentric auditory space perception, two differences with the current work are noteworthy. First participants were not explicitly required to perform an allocentric coding of sounds during training, unlike our audio-visual allocentric task. Second, in Gori et al. (Gori, Vercillo, et al., 2014) stimuli and task remained identical throughout the experiment, limiting our understanding of generalisation of training effects. Conversely, our study

introduces, for the first time, an allocentric training procedure based on *relative* position of multiple sounds for the purpose of changing auditory space mapping. Importantly, the structure of our paradigm, with differences between training and test sessions both in terms of stimulation (spoken syllables, rather than white noise bursts) and task (localisation of a single stimulus, rather than egocentric/allocentric processing of triplets of sounds) allows assessing learning generalisation effects. Generalisation effects have strong implications for translational application of training procedures to applied or clinical settings, and are thus considered a key requirement when assessing the efficacy of training procedures (Mendonça et al., 2013, 2012; Wright, Sabin, Zhang, Marrone, & Fitzgerald, 2010; Wright & Zhang, 2009). Our novel allocentric training procedure also extends to allocentric coding the multisensory training principles (R. S. Kim, Seitz, & Shams, 2008; Lehmann & Murray, 2005; Lovelace, Stein, & Wallace, 2003; Shams & Seitz, 2008) for the purpose of acoustic space re-learning. We provided participants a visual counterpart not only of the position of the sounds, but also of the spatial relationship between them. The rationale for adding lines between the dots (Figure 1D) was to emphasise visuo-spatial encoding of the acoustic scene. In addition, we reasoned that they could promote the use of visuo-spatial mental imagery (Cornoldi & Vecchi, 2004) during the response phase, in agreement with the evidence that vision can facilitate allocentric representations of space (Pasqualotto, Spiller, Jansari, & Proulx, 2013). We acknowledge, however, that the effectiveness of the added lines connecting the dots should not be taken for granted, as a proper control condition is missing in the present paradigm.

In conclusion, our work constitutes a first attempt to address a largely unexplored aspect of sound localisation abilities – namely the interaction between egocentric and

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allocentric representations. Addressing this domain is important because it could potentially introduce a novel approach to auditory spatial training. In vision, studies on egocentric vs. allocentric space coding have shown partial dissociation (Feigenbaum & Morris, 2004; Grimsen, Hildebrandt, & Fahle, 2008; Iachini, Ruggiero, & Ruotolo, 2014; Kesner, R.P., Farnsworth, G., DiMattia, 1989; Pizzamiglio, Guariglia, & Cosentino, 1998; Ruggiero, Ruotolo, & Iachini, 2009) as well as interactions (Burgess, 2006; Fink et al., 2003; Klatzky, 1998; S.F.W. Neggers, Van der Lubbe, Ramsey, & Postma, 2006; Sebastiaan F.W. Neggers, Schölvinck, & van der Lubbe, 2005) between these representations. Likewise, integration and interaction between different reference frames has been proposed to be necessary for an efficient tactile localisation (Heed, Buchholz, Engel, & Rö Der, 2015). To the best of our knowledge, our study provides the first investigation aimed at assessing such interaction between reference frames in the auditory domain. It has been recently proposed that egocentric and allocentric representations may be linked in a hierarchical manner, with egocentric processing involving only a subpart of the wider neural network subtending allocentric processing (Zaehle et al., 2007). If this is the case, exploiting allocentric training could foster space re-learning to a greater extent and prove more effective compared to training based on egocentric space representations. Testing this hypothesis was beyond the scopes of the present work, and it implies testing the efficacy of egocentric and allocentric training on sound localisation tests conducted on both reference frames (i.e., egocentric and allocentric). Yet, this follow-up study could exploit the current findings to further understand the contribution of allocentric auditory space processing in sound localisation re-learning.

Chapter 3

Study 2

Certain but incorrect: On the relation between subjective certainty and accuracy in sound localisation

The following study has been submitted as a paper on a peer-reviewed journal and it is currently under review. The following contents are reported from the un-reviewed manuscript sent to the journal (Experimental Brain Research).

3.1 Abstract

When asked to identify the position of a sound, listeners can report the location they perceive as well as their subjective certainty about this spatial judgement. Yet, research to date focused primarily on reports of perceived location (e.g., accuracy and precision of pointing responses), neglecting instead the phenomenological experience of subjective spatial certainty. The present study aimed to investigate (1) changes in subjective certainty about sound position induced by listening with one ear plugged (simulated monaural listening), compared to typical binaural listening; (2) the relation between subjective certainty about sound position and localisation accuracy. In two experiments (N=20 each), participants localised single sounds delivered from one of 60 speakers hidden from view in front space. In each trial, they also provided subjective ratings of spatial certainty about sound position. In binaural listening, participants were mostly accurate and certain about sound position. Instead, monaural listening decreased accuracy and it reduced subjective certainty overall, even in the absence of feedback on performance. Interestingly, accuracy and certainty dissociated in monaural listening, with trials in which participants were subjectively certain but incorrect, as well as trials in which participants were uncertain but correct. Subjective certainty rapidly increased as a function of time during the monaural listening block. In addition, it changed as a function of perceived location of the sound source. We discuss these novel findings suggesting that the neglected study of subjective certainty about sound position could shed light on the changes occurring in sound-to-space mapping.

3.2 Introduction

When we listen to a speaker in a quiet room, most often we can report its direction and we are certain about our perceptual experience. On the contrary, when an ambulance approaches us in the street, we can mistake its direction and we know that we have little certainty about our perceptual judgement. To date, research on spatial hearing has focused extensively on objective reports of perceived location (e.g., accuracy and precision of pointing responses), neglecting instead the phenomenological experience of subjective spatial certainty about sound position. Yet, individuals are typically aware of their perceptual experiences and, when asked, they can express confidence ratings about their perceptual performance (Van Overschelde, 2008). This topic has been investigated mainly in vision research, within the "Realism of Confidence" framework (Adams & Adams, 1961), which refers to subjective rating of confidence in sensory discrimination. Conversely, research in audition has scarcely explored subjective confidence about auditory perception. The present study investigates the relation between sound localisation accuracy and subjective spatial certainty about sound position in human listeners. To modulate spatial accuracy and certainty, we tested participants in the atypical condition of listening with one ear plugged, and compared it with the more usual binaural listening.

Although seemingly straightforward, sound localisation is a complex perceptual process in which the auditory system interprets subtle auditory cues to infer the spatial coordinates of sounds. Sensory information coming from both ears (binaural cues) and from each ear independently (monaural cues) support acoustic space perception (Middlebrooks, 2015b; Middlebrooks & Green, 1991). Sounds originating from a specific source reach the two ears with different time and intensity, producing auditory cues useful to localise sounds

in the horizontal plane: Interaural Time Differences (ITDs) and Interaural Level Differences (ILDs). The computation of binaural cues is highly developed in the human auditory system, which can capture time delays in the order of 10-20 μ s (Brughera et al., 2013) and intensity difference of about 0.5 dB (Van Opstal, 2016). Furthermore, as sound waves are filtered and modified by the head and the shape of outer ear, spectral auditory cues arise. These cues are specific for each ear and each individual (Carlile, Martin, & McAnally, 2005b) and allow localisation in the vertical plane (Musicant & Butler, 1984a), distance estimation (Kolarik et al., 2016) and front-back disambiguation (Carlile & Pralong, 1992).

In typical listening conditions, auditory cues are efficiently exploited and sounds are localised with good accuracy and precision. Yet, a number of temporary or permanent conditions can alter auditory cues and make sound localization uncertain. One of such examples is simulated monaural listening, typically achieved by plugging and muffing one ear to hearing individuals. Although ear-plugging does not completely eliminate binaural hearing, it induces asymmetrical auditory cues with three main consequences for spatial hearing: first, it decreases accuracy, particularly in azimuth and in the space ipsilateral to the plug; second, it induces localisation biases towards the hearing ear; third, it increases error variability (Flannery & Butler, 1981; Musicant & Butler, 1984b; Slattery & Middlebrooks, 1994; Van Wanrooij & Van Opstal, 2007; Rabini, Altobelli & Pavani, 2019).

Even in the absence of feedback, participants report being aware of the altered hearing condition that results from having one ear plugged. Hence, simulated monaural listening should in principle affect subjective certainty about perceived sound position. Error variability, which has been interpreted as an indirect index of sensory uncertainty, in indeed increased in simulated monaural listening (Ege, Van Opstal, & Van Wanrooij, 2018; Garcia, Jones, Rubin, & Nardini, 2016). However, to what extent subjective certainty on sound position decreases from binaural to monaural listening conditions remains, to the best of our knowledge, a largely unexplored issue (but see Zacharov, Pedersen, & Pike, 2016 for researches in the field of virtual sounds reproduction). Likewise, it is unknown whether any expected decrease in spatial certainty relates with decreased localisation accuracy (i.e., trials with larger localisation error are also characterised by low perceived confidence) or instead it is independent from localisation performance (i.e., localisation errors are not necessarily paired with low confidence judgements).

In the present work, we addressed both these issues by asking participants to listen to single sounds delivered from hidden speakers in front space and perform two consecutive tasks: first, a sound localisation task; second, a confidence rating judgement, indicating subjective certainty about each sound-source position. On a trial-by-trial basis, participants indicated the position of the sound using a cursor (*accuracy measurement*), and next they answered the question "How much were you confident about the position of this sound in space?" (*confidence measurement*; for a similar design see also Fleming and colleagues, 2010). Across blocks, these consecutive tasks were performed in binaural listening and with one ear plugged. The study comprised two experiments, conducted on different participants. In Experiment 1, participants judged both sound azimuth and elevation; in Experiment 2, they judged only sound azimuth, because sound elevation was always made unambiguous using visual cues. Feedback on sound localisation performance was never provided.

As to our first question (does subjective certainty decreases from binaural to simulated monaural listening conditions?), we expected that performing sound localisation with one ear-plugged would decrease confidence ratings, particularly for sounds ipsilateral

to the plug. As to our second question (does the expected decrease in confidence reflects the degree of localisation accuracy?) we anticipated two possible scenarios for the monaural earplugged condition. The first scenario is that confidence and localisation accuracy are primarily correlated, i.e., participants express lower confidence ratings particularly for sounds they localise with less accuracy. A second scenario is that confidence ratings will dissociate from localisation accuracy, i.e., participants would remain confident even for sounds they localise with less accuracy. This alternative scenario could arise if participants fail to perceive that the correspondence between auditory cues and space has changed by effect of the ear-plug, and they remain confident about a perceptual solution that has become, in fact, erroneous. Recall that participants never received feedback about their localisation performance. Hence, the only pieces of information that can challenge their confidence in sound-source position are: (1) their semantic knowledge of the listening context (one ear has been plugged) and (2) the alteration of the overall perceptual auditory experience.

3.3 Material and methods

3.3.1 Participants

Forty hearing participants took part in the study, 20 participants were recruited in Experiment 1 (15 females, mean age = 21.8 ± 2.91) and a different sample of 20 participants participated in Experiment 2 (18 females, mean age = 22.7 ± 2.39). Hearing threshold assessment was performed by pure tone audiometry (Grason Stadler GSI 17 Audiometer; tested frequencies: 250, 500, 1000, 2000, 4000 Hz). Audiometric test was delivered also in the simulated

monaural listening condition, to control in each participant the efficacy of the ear-plug. All participants had normal or corrected to normal vision and reported no history of auditory, neurological or psychiatric disease. Before the experiment, participants read and signed an informed consent received course credits and or gadgets of our lab (https://r.unitn.it/en/cimec/cats) for participation. The study was approved by the Ethic Committee at the University of Trento (Protocol number: 2018-002) and was conducted in line with the Declaration of Helsinki (1964, amended in 2013).

3.3.2 Apparatus and Stimuli

The experiment was administered in a 4.2 x 5.0 m reverberant room. Auditory stimuli were delivered by 60 small round-shaped speakers (5cm diameter of Mylar; Pro Signal ABS-210-RC range 350–20,000Hz, 8K, 1W RMS Power) mounted on a rectangular wooden panel and arranged in a grid of 12 columns and 5 rows. In this matrix, speakers were placed horizontally at approximately $\pm 2^{\circ}$, $\pm 6^{\circ}$, $\pm 10^{\circ}$, $\pm 13^{\circ}$, $\pm 17^{\circ}$ and $\pm 20^{\circ}$ with respect to participant's body midline (positive indicates speakers to the right), and at 0° , $\pm 6^{\circ}$ and $\pm 11^{\circ}$ elevation with respect to the participant's ear level (positive indicates speakers above). A sound-transparent white curtain covered the entire speaker matrix, preventing any visual cue about their position and allowing the projection of visual stimuli and instructions on top of the speaker matrix. To this purpose, an LCD projector (LG HW300G; resolution: 1280x 1024) was mounted behind the participant (as in Rabini et al., 2019). Participants sat at about 120 cm from the speaker matrix, which was fixed on wooden stands and placed on a table. Although head movements were not physically constrained, participants were instructed to keep the head still and fixate a white dot at the beginning of each trial. The entire experiment was managed

by a PC (Dell Precision T3400) and controlled by custom-made Matlab scripts (Mathworks R2015b, 32-bit).

Three different Italian syllables ("BA", "RO", "GU"; 500 ms long) spoken by a female speaker (recorded using a Blue Snowball iCE Condenser Microphone), were used as auditory stimuli in the localisation task, selected randomly in each trial. Responses were collected through mouse cursor and keyboard (see Rabini et al., 2019) (see Study 1).

3.3.3 Procedure

In both experiments, the entire experimental paradigm lasted approximately 45 minutes. Each experiment was divided in two consecutive blocks in which participants were tested in a binaural and in a simulated monaural listening condition. In the simulated monaural listening condition, participants wore a single ear-plug (EAR Classic foam earplugs, 3M PP 01 002) and a single ear muff (3M 1445) on the same ear. The experimenter verbally instructed each participant on the correct method of plug-insertion, to achieve optimal fitting of the plug (as in Rabini et al., 2019). Hearing threshold were measured through pure tone audiometry on both the unplugged ear and, before simulated monaural listening block, on the plugged ear. In binaural listening, hearing threshold were below 25 dB SPL for both ears, for each frequency tested in each experiment. Simulated monaural listening caused a drop in hearing threshold at the plugged ear, which changed to above 20 dB SPL for each frequency tested in each experiment, but particularly for high frequencies. Half of participants was plugged on their left ear, remaining half was plugged on their right ear. Order of listening condition (binaural and simulated monaural) was counterbalanced between participants.

In the sound localisation task, in any given trial a single sound was presented from one speaker of the matrix (3 trials for each of the 60 speakers, for a total of 180 trials for each listening condition). Participants were instructed to indicate the perceived position of the sound using a mouse cursor. In Experiment 1, each trial started with a white fixation dot (1 s duration), followed by the auditory stimulus (500 ms duration). At the end of sound delivery a hand-shape mouse cursor appeared on the white panel covering the speaker matrix; participants moved the cursor to the position of the target sound and confirmed their choice by pressing the left button of the mouse. No visual feedback was given during or after response. In Experiment 2, participants were informed about sound elevation at the beginning of each trial using visual instructions (see below), and responses were restricted to the horizontal dimension. In each trial, after the fixation dot (1 s duration), a white and empty rectangle was presented on the front screen to indicate the elevation of the upcoming target (i.e., a specific row of the unseen speaker matrix). This cue to elevation remained visible during sound presentation and response phase. After stimulus presentation (500 ms duration), a white line appeared inside the rectangle (same height as the rectangle), and participants moved the line to mark the horizontal position of the sound, confirming final desired position by pressing the left button of the mouse. Thus, despite the auditory stimulation was identical to Experiment 1, participants only indicated the horizontal component of sound position. This eliminated any uncertainty in the vertical dimension.

After each sound-localisation response, participants rated their subjective certainty about sound position in space (confidence ratings), answering the question "How much were you certain about sound position?" The question was displayed on the panel and participants responded using a keyboard. In Experiment 1 confidence ratings were given on a discrete

scale, ranging from 1 to 4, in which 1 indicated low confidence on sound position and 4 indicated high confidence on sound position. In Experiment 2 confidence ratings were given on a continuous scale. A vertical white segment was presented at the centre of the screen, with a horizontal red segment in the middle to serve as indicator. Participants moved the red segment upward or downward using the keyboard arrows to indicate their perceived spatial confidence (the upper extreme indicated complete certainty about sound position, whereas the lower extreme indicated complete uncertainty). Note that the orientation of this confidence line was orthogonal to the azimuthal position of judged sounds.

Data availability statement. A public data repository is available at the following link. Database: OSF, https://osf.io/esb5w/

3.4 Results

3.4.1 Ear-plug effect on sound localisation

To describe accuracy and variability for the horizontal (Experiment 1 and Experiment 2) and vertical components of the response (Experiment 1), we used the *rms error* (root mean squared of the difference between response and target position), and the *variable error* (standard deviation of the mean response for each speaker considered), following the guidelines by Hartman and colleagues (1983; see also Grantham, Ashmead, Ricketts, Haynes, & Labadie, 2007; Pavani et al., 2017). We considered as target position the coordinates (x, y) of the centre of the loudspeaker, whereas response position was indexed by the coordinates (x, y) of the mouse-click during the response phase. All dependent variables were analysed using Analysis of Variance (ANOVA), adopting the Greenhouse-Geisser correction method in case of sphericity assumption violations. Because analyses were

identical in Experiment 1 and Experiment 2, for ease of comparison they will be presented together, with between experiments statistical comparisons when appropriate.

3.4.1.1 Rms Error

We started by investigating whether plugging different ears (left vs. right) influenced sound localisation accuracy in the monaural condition, considering the horizontal plane alone. We entered mean rms error for each participant in a repeated measures ANOVA with LISTENING CONDITION (Binaural, Monaural) and STIMULATION SIDE (Ipsilateral, Contralateral) as within subject factors, and PLUGGED EAR (Right, Left) as between subjects factor. Note that collapsing trials as a function of stimulation side and elevation resulted in 90 trials per cell of the experimental design (i.e., 3 trials for each speaker location x 6 speakers on each side x 5 vertical rows). Neither the main effect of PLUGGED EAR (Exp.1, F(1,18) = 0.16; Exp.2, F(1,18) < 0.001, nor the interactions involving this factor (Exp.1 all F-values < 0.3; Exp.2 all F-values < 0.5) reached significance. In other words, compared to binaural listening, plugging the left or the right ear reduced accuracy in a comparable fashion (see Figure 14a and 14b). Based on this preliminary finding, with the aim to simplify our experimental design and analyses, we recoded localisation stimulation and responses as ipsilateral and contralateral to the plugged side (see also by Gougoux and colleagues, 2005). A 2x2 repeated measures ANOVA with LISTENING CONDITION (Binaural, Monaural) and STIMULATION SIDE (Ipsilateral, Contralateral) as within subject factors showed a significant main effect of LISTENING CONDITION (*Exp. 1*, F(1, 19) = 147.722, p < 0.001, $\eta^2 = 0.886$; *Exp. 2*, F (1, 19) = 309.92, p < 0.001, $\eta^2 = 0.94$) and STIMULATION SIDE (*Exp. 1*, F(1,19) = 9.69, p = 0.006, $\eta^2 =$ 0.34; *Exp.2*, F(1,19) = 7.59, p = 0.01, $\eta^2 = 0.28$), as well as a significant two-way interaction

(*Exp.1*, F(1, 19) = 7.85, p = 0.011, $\eta^2 = 0.29$; *Exp.2*, F(1, 19) = 11.20, p = 0.003, $\eta^2 = 0.37$). Figure 15c and 15f show mean accuracy in binaural and monaural listening conditions. Decreased accuracy in the simulated monaural condition is evident, particularly on the side ipsilateral to the plug. A direct comparison between the two experiments (using an ANOVA with LISTENING CONDITION, STIMULATION SIDE and EXPERIMENT) revealed no main effect or interaction involving EXPERIMENT (F<1.75). This indicates that providing a visual cue on vertical position of sounds did not affect localisation accuracy in azimuth for Experiment 2.



Figure 15. Sound localisation performance (rms error) in the horizontal plane in Experiment 1 (a, b, c) and Experiment 2 (d, e, f). Performance of participants plugged to the left and right ear are shown separately in plot (a, d) and (b, e), respectively. Localisation performance of all participants, recoded as ipsilateral vs. contralateral to the plugged ear, are presented in plot (c) and plot (f). Error bars indicate confidence intervals.

Having established that the impact of simulated monaural listening was comparable irrespective of plugged ear side, we turned to investigate whether order of condition (Binaural-Monaural vs. Monaural-Binaural) influenced sound localisation performance. We computed a repeated measures ANOVA with LISTENING CONDITION (Binaural, Monaural) and STIMULATION SIDE (Ipsilateral, Contralateral) as within subject factors, and BLOCK ORDER (Binaural-Monaural, Monaural-Binaural) as between subject factor. We found a significant main effect of BLOCK ORDER (*Exp. 1*, F(1, 18) = 8.25, p = 0.01, $\eta^2 = 0.314$; *Exp. 2*, F(1, 18) = 7.02, p = 0.01, $\eta^2 = 0.28$), and the interaction LISTENING CONDITION * BLOCK ORDER (*Exp. 1*, F(1, 18) = 6.14, p = 0.02, $\eta^2 = 0.029$; *Exp. 2*, F(1, 18) = 4.17, p = 0.056, $\eta^2 = 0.011$). Participants that performed the simulated monaural condition as first block showed higher *rms error* irrespective of stimulation side, in Experiment 1 as well as in Experiment 2 (Table 4), compared to participants who performed the binaural condition as first block.

Table 4. Mean confidence ratings, rms error (azimuth), variable error (azimuth) and normalised confidence (0-100 scale) in binaural and simulated monaural listening condition, as a function of stimulation side. Note that *Mean confidence* refers to ratings given on a discrete scale from 1 to 4 in Experiment 1. In Experiment 2, *Mean confidence* refers to ratings given on a continuous scale from 0 to 100%. *Normalised confidence* refers to confidence ratings expressed in a 0-100% scale.

Experiment	Listening	Side	Mean	rms Error	Variable	Normalised
	Condition		confidence	(deg)	Error (deg)	confidence
Experiment 1	Binaural	Contralateral	2.94 (0.51)	3.96 (1.09)	2.09 (0.64)	73.51 (12.68)
(<i>n=20</i>)		Ipsilateral	3.02 (0.48)	3.98 (1.10)	1.92 (0.70)	75.54 (12.11)
	Simulated	Contralateral	2.51 (0.54)	10.12 (2.79)	4.39 (1.90)	62.82 (13.43)
	Monaural					
		Ipsilateral	2.44 (0.56)	14.04 (5.54)	4.64 (2.02)	60.97 (14.25)

Experiment 2	Binaural	Contralateral	81.52 (12.96)	3.99 (1.28)	1.79 (0.28)	81.52 (12.96)
(<i>n=20</i>)		Ipsilateral	81.17 (13.25)	3.78 (0.74)	1.95 (0.47)	81.17 (13.25)
	Simualted	Contralateral	66.02 (14.25)	10.97 (2.46)	4.68 (1.50)	66.02 (14.25)
	Monaural					
		Ipsilateral	61.06 (17.35)	15.26 (4.73)	5.21 (1.71)	61.06 (17.35)

In Experiment 1, we also analysed responses in elevation, computing *rms error* on the vertical component of the responses. A repeated measures ANOVA, with LISTENING CONDITION (Binaural, Monaural) and POSITION (High, Centre, Low) as within-subject factor showed a main effect of both factors (LISTENING CONDITION: F (1, 19) = 10.24, p = 0.005, $\eta^2 = 0.35$; POSITION: F(1.15, 23.93) = 4.78, p = 0.035, $\eta^2 = 0.201$), as well as a significant two-way interaction (F (1.26, 31.95) = 10.45, p = 0.002, $\eta^2 = 0.355$). Simulated monaural listening decreased accuracy compared to the binaural condition, mainly in the upper portion of space (binaural = 7.37 ± 2.93, monaural = 10.62 ± 3.76).

3.4.1.2 Variable error

To investigate changes in response precision from binaural to simulated monaural listening, we entered the *variable error* as dependent variable in a repeated measure ANOVA with LISTENING CONDITION (Binaural, Monaural) and STIMULATION SIDE (Ipsilateral, Contralateral) as within subject factors.

In Experiment 1, the significant main effect of LISTENING CONDITION (F(1, 19) = 40.45, p < .001, $\eta^2 = 0.68$) revealed different error variability between the two conditions, irrespective of stimulation side (STIMULATION SIDE: F(1, 19) = 0.1; LISTENING CONDITION x STIMULATION SIDE: F(1, 19) = 2.93). Similarly, in Experiment 2, there was a main effect of

LISTENING CONDITION (F(1, 19) = 96.67, p < .001, η^2 = 0.84), but no effect of stimulation side (STIMULATION SIDE: F(1, 19) = 4.00, p = 0.06, η^2 = 0.174; LISTENING CONDITION x STIMULATION SIDE: F(1, 19) = 1.1). Thus, in both experiments we found an overall increase of error variability in monaural compared to binaural listening, which was no related to stimulation side.

Variable error in the vertical plane for Experiment 1, was examined using a repeated measures ANOVA with LISTENING CONDITION (Binaural, Monaural) and POSITION (High, Centre, Low). The main effect of POSITION (F(2, 38) = 2.96, p = 0.06, $\eta^2 = 0.14$) and two-way interaction LISTENING CONDITION*POSITION (F(2, 38) = 3.04, p = 0.06, $\eta^2 = 0.14$) only approached significance, suggesting that error variability in elevation was comparable in binaural and monaural conditions.

3.4.2 Ear-plug effect on confidence ratings

After completing the sound localisation task, participants explicitly judged their subjective certainty on sound position on a discrete 4-point scale in Experiment 1, and on a continuous scale 0-100% in Experiment 2. For between-experiments comparisons, we conducted all analyses on normalised confidence ratings (expressed on 0-100% confidence scale). A repeated measures ANOVA with LISTENING CONDITION and STIMULATION SIDE revealed a significant main effect of LISTENING CONDITION (*Exp. 1*, F(1, 19) = 43.73, p < .001, $\eta^2 = 0.697$; *Exp. 2*, F(1, 19) = 31.14, p < .001, $\eta^2 = 0.621$). A significant two-way interaction also emerged (*Exp. 1*, F(1, 19) = 7.77, p = 0.012, $\eta^2 = 0.29$; *Exp. 2*, F(1, 19) = 106.49, p = 0.005, $\eta^2 = 0.341$), indicating that confidence decreased from binaural to simulated monaural listening, particularly on the side ipsilateral to the plug (Monaural condition: *Exp. 1*, t (19) = 2.17, p = 0.012, p = 0.012, p = 0.0012, p

0.043, Cohen's d = 0.4; *Exp.2*, t(19) = 3.96, p < .001, Cohen's d = 0.89; see Table 5S). Interestingly, significant positive correlations between confidence rating in binaural and simulated monaural listening conditions emerged for both experiments (*Exp.1*, Pearson's r = 0.79, p < .001, R² = 0.62; *Exp.2*, Pearson's r = 0.52, p = 0.02, R² = 0.27), suggesting that participants were overall consistent when expressing confidence ratings across listening conditions (Figure 16b and 16d).

Finally, direct comparison between normalised confidence ratings in the two experiments, using an ANOVA with LISTENING CONDITION and EXPERIMENT as factor, revealed a significant main effect of EXPERIMENT (F(1, 38) = 10.29, p = 0.003, $\eta^2 = 0.213$). Confidence ratings on sound position was higher in Experiment 2 compared to Experiment 1, irrespective of listening condition (Binaural: *Exp.1* = 66.11 ± 16.3, *Exp.2* = 81.34 ± 13.1; Monaural: *Exp.1* = 49.2 ± 18.4, *Exp.2* = 63.54 ± 15.6). This is compatible with the fact that in Experiment 2 only azimuth was uncertain, whereas elevation was always determined through visual cues.



Figure 16. Mean confidence ratings in binaural and simulated monaural listening condition, as a function of stimulation side (Ipsilateral/contralateral to the ear-plug), in Experiment 1 (a) and Experiment 2 (c). Plot (b) and plot (d) represent the positive linear correlation between confidence ratings given in binaural and monaural condition, in Experiment 1 and Experiment 2, respectively. Error bars indicate confidence intervals of the mean.

3.4.3 Relation between localisation accuracy and confidence ratings

To study the relation between localisation accuracy and subjective certainty on sound location, we examined single trials in each participant to determine if accuracy (i.e., difference between response and target position) and confidence ratings were above or below the individual mean. Based on this evaluation, we assigned each trial to one of four categories: i) trials with high accuracy and high confidence (highA-highC); ii) trials with high accuracy but low confidence (highA-lowC); iii) trials with low accuracy but high confidence (lowA-highC); and iv) trials with low accuracy and low confidence (lowA-lowC).

The number of trials in each of the four categories changed as a function of listening condition (as shown in Figure 3, separately for the two experiments). The number of trials was used as dependent variable and entered in a repeated measures ANOVA with ACCURACY-CONFIDENCE RELATION (highA-highC, highA-lowC, lowA-highC, lowA-lowC) and LISTENING CONDITION as within-subject factors. This analysis revealed a significant main effect of the ACCURACY-CONFIDENCE RELATION ($Exp.1: F(1.36, 25.9) = 27.61, p < .001, \eta^2 = 0.59; Exp.2: F(2.16, 41.14) = 91.58, p < .001, \eta^2 = 0.83$), as well as a significant interaction ACCURACY-CONFIDENCE RELATION * LISTENING CONDITION ($Exp.1: F(2.18, 41.55) = 74.98, p < .001, \eta^2 = 0.79; Exp.2: F(1.48, 28.09) = 80.18, p < .001, \eta^2 = 0.81$). To explore this two-way interaction, we ran separate ANOVAs for the two listening conditions (i.e., we considered only ACCURACY-CONFIDENCE RELATION as factor).

In the binaural listening condition, categories of accuracy-confidence relation were not equally distributed (*Exp.1*: F(1.26, 24.01) = 92.02, p < .001, $\eta^2 = 0.83$; *Exp.2*: F(1.28, 24.28) = 155.6, p < .001, $\eta^2 = 0.89$). As expected, the categories of higher accuracy were the most represented, with the majority of trials falling in the category of high accuracy and high confidence. Notably, also in this typical hearing condition there were trials in which accuracy and confidence ratings were dissociated (see Figure 17). In the simulated monaural listening condition, the overall picture was considerably different. Again, trials were not equally distributed across categories (*Exp.1*: F(1.17, 22.23) = 5.74, p = 0.02, $\eta^2 = 0.23$; *Exp.2*: F(1.25,
23.80) = 9.81, p = 0.003, $\eta^2 = 0.34$). The most represented category was the one of low accuracy and low confidence, in which participants were wrong and highly uncertain about target locations. Notably, however, other associations between accuracy and confidence emerged in a consistent number of trials (66% in Experiment 1; 64% in Experiment 2; see Figure 17). In particular, two dissociation patterns were observed in which participants were accurate but poorly confident, or inaccurate but confident.

In the final two sections, we report post-hoc analyses to explore to what extent accuracy and confidence during simulated monaural listening changed as a function of time in the block (section 3.4.3.1) or spatial distribution of the responses (section 3.4.3.2). For clarity, we restricted these post-hoc analyses to Experiment 2 only, where accuracy and confidence can unequivocally refer to the dimension affected by monaural plugging (horizontal plane).



Figure 17. Mean number of trials belonging to different levels of accuracy-confidence relation in the two experiments. Trials were assigned to the following categories: high accuracy and high confidence (highA-highC), high accuracy and low confidence (highA-lowC), low accuracy and high confidence (lowA-highC) and low accuracy and low confidence (lowA-lowC), separately for binaural and simulated monaural listening condition.

3.4.3.1 Change in accuracy and confidence as a function of time

To inspect how accuracy changed as a function of time, we divided the simulated monaural listening block in 10 bins. In each bin (n = 18 trials), we computed the difference between high and low accuracy trials, and divided this value by the sum of the two. This produced a normalised index that revealed which type of trial prevailed in each bin (where -1 indicates that all trials were low accuracy; +1 all trials were high accuracy). As shown in Fig. 4a, at all bins accuracy remained below zero, i.e., low accuracy trials prevailed throughout the simulated monaural listening block, and no linear increment was detected ($R^2 = 0.06$, F(1,8)

= 1.61, p = 0.24). A similar procedure was adopted to inspect the temporal distribution of trials with high/low confidence (where -1 indicates that all trials were low confidence; +1 all trials were high confidence). Again, at all bins confidence remained below zero, i.e., low confidence trials prevailed throughout the simulated monaural listening block (see Figure 18b). However, a clear linear increase in confidence was detected revealing that participants became progressively more confident on sound position as the block evolved ($R^2 = 0.56$, F(1,8) = 12.42, p = 0.007).



Figure 18. Plot (a) and (b) represents the normalised index (range [-1 +1]), separately for accuracy (a) and confidence (b), calculated by dividing the monaural block in 10 bins of 18 trials each. Accordingly, negative values reflect a prevalence of lower accuracy/confidence ratings over higher accuracy/confidence ratings, in each bin. We renamed the Y axes in order to clarify figure interpretation. Linear regression values are shown in both plots.

3.4.3.2 Change in accuracy and confidence as a function of responses space

To inspect how accuracy and confidence changed as a function of response space, we studied how trials of the four categories (i.e., highA-highC; highA-lowC; lowA-highC; lowA-lowC) were represented at each response location. For clarity, we clustered all responses into the regions of space corresponding to actual speaker locations. This analysis was performed on *response* space rather than *stimulation* space, because only the former indicates where each sound was actually perceived.

When participants were *more confident*, the majority of responses were directed to the *periphery* – particularly in the space contralateral to the plug (left). This response pattern was somewhat similar for trials with higher accuracy (Figure 19; highA-highC) and trials with lower accuracy (Figure 19; lowA-highC). This similarity was confirmed by a correlation analysis between the number of highA-highC and the number of lowA-highC trials at each response position (r = 0.55, p = 0.067). By contrast, when participants were *less confident*, the majority of responses were directed to the *centre*. This pattern was again similar irrespective of accuracy level (compare Figure 19, highA-lowC, and Figure 19, lowA-lowC). This similarity was again confirmed by a correlation analysis between the number of hogh A-lowC trials at each response position (r = 0.62, p = 0.032). This

finding suggests that a possible relation may exist between confidence level and the portion of space towards which participants direct their responses.



Figure 19. Spatial distribution of trials falling in the four categories of accuracy-confidence relation along the horizontal plane, considering perceived sound position. Error bars represent confidence intervals of the mean. Low confidence ratings were overall related to perceived sound position towards the centre, whereas high confidence ratings were overall related to perceived sound positions, regardless the level of accuracy.

3.5 Discussion

In simulated monaural listening conditions, existing correspondences between auditory cues and external space become less reliable, and the quality of the hearing experience changes. Studies to date focused almost exclusively on the objective errors measured when listeners are asked to localise sounds, largely neglecting the subjective dimension subtending this perceptual experience. The main goal of the present study was to investigate subjective certainty about sound position during altered hearing, and explore the relation between this phenomenological report and the objective sound localisation performance. To this aim, we devised a task in which participants localised a single sound in binaural listening or in a monaural ear-plugged conditions, and successively rated their subjective certainty about its perceived spatial origin, on a trial-by-trial basis. In two experiments, we found that: (1) simulated monaural listening affects subjective certainty about sound position, even in the absence of feedback on performance; (2) spatial accuracy and subjective spatial certainty often dissociate from one another, when listening with one ear plugged; (3) subjective certainty rapidly increased during the simulated monaural listening condition; (4) a relation may exist between subjective certainty and the portion of space towards which participants direct their responses. In addition, we report two novel observations on the effects of monaural plugging on accuracy, which provide useful methodological indications for the implementation of this model of altered hearing.

3.5.1 Decreased localisation accuracy under simulated monaural listening

As expected, localisation accuracy decreased in simulated monaural listening compared to typical binaural listening. In both experiments, monaural ear-plugging resulted in worse localisation performance in the horizontal plane for all tested positions, but particularly for sounds ipsilateral to the ear-plug (Flannery & Butler, 1981; Musicant & Butler, 1984b; Van Wanrooij & Van Opstal, 2007). This proves that our manipulation was successful in perturbing the existing correspondences between auditory cues and space, causing discrepancies between actual and perceived sound positions.

Two novel findings concerning this ear-plug perturbation effects are worth mentioning: (1) they were comparable irrespective of plugged side (left or right ear); (2) they were influenced by order of listening conditions (binaural and monaural). In the majority of previous studies, the same ear was plugged to all participants (Belendiuk & Butler, 1975, 1977; Butler, 1971; Butler & Flannery, 1980; Musicant & Butler, 1980, 1985; Rabini et al., 2019). The few studies in which the plugged ear was randomised between participants (Hebrank & Wright, 1974; P. Hofman & Van Opstal, 2003; Morimoto, 2001; Van Wanrooij & Van Opstal, 2007) did not comment on this methodological choice, leaving open the possibility of potential performance differences as a function of plugged side. Here we showed that, in both experiments, localisation accuracy was entirely comparable between left-plugged and right-plugged participants. We also counterbalanced the order of listening conditions, and studied the effect of this manipulation on ear-plug perturbation effects. We found that participants who started the experiment with the binaural listening condition

showed smaller localisation errors compared to participants who started the experiment with the simulated monaural listening condition. This advantage of starting with the binaural condition might reflect easier familiarisation with the task and/or better priors for sound source position related to this listening condition. Previous studies have shown that sound localisation accuracy is higher when participants can visually explore the stimulation setting before blindfolded testing (Tabry, Zatorre, & Voss, 2013; Tonelli, Brayda, & Gori, 2015). Moreover, recent findings suggest that sound localisation might be shaped by the perceived spatial range of target presentation (Ege, Van Opstal, & Van Wanrooij, 2019), indicating that the mere experience of the spatial distribution of target sounds can have an impact on spatial hearing abilities. Interestingly, comparing horizontal localisation in Experiment 1 (azimuth and elevation both unknown) and Experiment 2 (only azimuth unknown), we did not find any significant difference. This observation might suggests that a visual prior on the elevation of sounds do not necessarily change localisation performance in horizontal plane. Alternatively, it could result from our choice of target stimuli, as the prevalence of low frequencies in our auditory stimuli (vowels) could have limited the use of monaural spectral cue for localisation in azimuth, in both experiments.

Concerning localisation in vertical plane, results from Experiment 1 indicate that monaural ear-plugging decreases performance also in this spatial dimension. These results are in agreement with the notion that localisation in the vertical plane entails binaural weighting of monaural cues (Hofman & Van Opstal, 2003; Van Wanrooij & Van Opstal, 2005). Spectral cues from both ears concur to create the overall elevation percept. When binaural weighting is changed (as in monaural ear-plugging), the perception of sounds position in elevation is also altered.

3.5.2 Decreased confidence ratings under simulated monaural listening

Monaural ear-plugging caused a general decrease in subjective certainty about sound position, even in the absence of feedback on localisation performance. Previous works have related certainty on sound location performance with response *precision*, as indexed by performance variability (Ege et al., 2018; Garcia et al., 2016). When localisation error increases together with error variability, precision is lower and uncertainty is higher. Accordingly, Denison (2017) proposed that "perceptual precision better characterises the uncertainty of perceptual experience".

In both experiments of the present study we measured a general increase of error variability in the horizontal plane from binaural to monaural hearing condition, thus showing lower precision in simulated monaural listening. The variability of localisation error, is however an *implicit* measure of spatial uncertainty. Here we used confidence ratings as an *explicit* measure of subjective spatial certainty (for a terminology-related debate about perceptual uncertainty and perceptual confidence see Denison, 2017; Morrison, 2016, 2017). Note that, unlike studies investigating confidence levels about the perceptual decision itself (see Fleming et al., 2010), here we were interested in the subjective spatial certainty about sound position, not in the subjective judgement about the trial-by-trial performance. In this respect our subject confidence measure is more akin to the notion of 'localizability' adopted in previous works on the qualitative aspects of spatial hearing obtained with virtual sounds

reproduction (Zacharov, Pedersen, & Pike, 2016). Using the Spatial Audio Quality Inventory (SAQI, Lindau et al., 2014) these authors defined 'localizability' as "the degree of precision to which the position and extend of source or ensemble can be identified" (Zacharov et al., 2016). Our notion of subjective certainty aimed to capture a similar subjective feeling, but applied here to real rather than virtual sounds.

Although subjective certainty generally decreased in simulated monaural listening condition at single subject level, participants remained overall consistent in their confidence ratings about sound position throughout the experiment. Results of both experiments showed a positive correlation between mean confidence ratings in binaural and simulated monaural listening condition. Considering this observation is crucial for studies on perceptual confidence, in which a subjective bias in providing explicit confidence ratings should be considered.

Our results highlighted that in Experiment 2 confidence ratings were generally higher (both in binaural and monaural condition) compared to Experiment 1. One interpretation of this finding is purely methodological: we used different evaluation scales in the two experiments (discrete vs. continuous), and hence the registered difference could have emerged as a consequence of type of measurement. However, an alternative interpretation is that the experienced subjective certainty increased in Experiment 2 because only horizontal sound was unknown. Confidence ratings are linked to specific decision boundaries (Denison, 2017), and as such they depend upon the specific questions posed by the experimenter. In Experiment 1, where both azimuth and elevation were unknown, decision boundaries for confidence ratings likely reflected a combination of uncertainty along these two dimensions. By contrast, in Experiment 2, where only azimuth was unknown, decision boundaries for confidence ratings were unequivocally related to the horizontal dimension alone.

3.5.3 Localisation errors are linked to different degrees of explicit spatial uncertainty

One important motivation for the present work was to examine the relation between subjective certainty and localisation accuracy. To this aim, we studied the link between accuracy and confidence ratings on a trial-by-trial basis in each participant. As expected, for the majority of binaural trials participants were accurate and certain, whereas in monaural trials the scenario was markedly different, with all combinations between confidence ratings and accuracy more evenly represented. We divided trials in which accuracy and confident corresponded (accurate and confident; or inaccurate and not confident), as well as trials in which the two measures dissociated (accurate but not confident; inaccurate but confident). We believe the latter combinations, which together accounted for 47% of monaural trials in either experiment, are particularly interesting because they may reflect objective and subjective performance when sound-to-space correspondences are made unreliable. Participants may feel the perceptual solution is unreliable, and yet the correspondence proved effective; or, vice versa, participants may retain (or develop) confidence in a correspondence which is, in fact, incorrect.

Post-hoc analyses on changes in subjective certainty and accuracy as a function or time or perceived sound location were also informative. Confidence ratings increased rapidly

during the monaural testing session, whereas accuracy remained more stable across monaural trials. This suggests that the adaptation process triggered by repeated exposure to simulated monaural listening (Carlile, 2014; Mendonça, 2014; Van Opstal, 2016), could impact on subjective certainty about sound position earlier than it impacts on accuracy. In this sense, processes of sensory plasticity under altered hearing, regarding sound localisation performance, could potentially be capture by the increasing sense of certainty on sound position over time. Consequently, a speculative hypothesis is that confidence ratings could index early mechanisms of adaptation to altered hearing (e.g., cue-reweighting) whereas accuracy could index later adaptation mechanisms (e.g., cue-remapping). We also observed that monaural trials with higher and lower confidence ratings, were not randomly distributed. Sounds associated with lower confidence ratings were mostly perceived as originating from the central positions. Conversely, sounds associated with higher confidence ratings were localised towards the periphery. In both cases, this pattern emerged irrespective of accuracy levels. It could be argued that when sounds are perceived as coming from the periphery the relative spatial confidence is higher due to the fact that for these positions the auditory cues are typically (i.e., in binaural listening condition) more reliable and informative (note that the most peripheral speakers were located at $\pm 20^{\circ}$), contrary to the more central locations. These speculative interpretations should be addressed in future empirical studies, yet they suggest that trial-by-trial subjective confidence could prove informative for revealing updating of sound-to-space correspondences.

3.6 Conclusions

The present study expands the previous literature on the effects of reversible monaural earplugging, by adding novel results on a key phenomenological feature of this altered auditory experience - the subjective certainty about sound position. We showed that the decreased performance in simulated monaural listening reported in previous studies is paired with a decay in subjective spatial confidence about sound position, even when no feedback about localisation performance is provided. Results also showed that subjective certainty can dissociate from localisation accuracy. This dissociation emerges at the single trial level (e.g., trials that are accurate but uncertain, or vice versa) and in the way each measure evolves during the monaural block (i.e., rapid increases for subjective certainty, but not for accuracy). Finally, a relation may exist between subjective certainty and the portion of space towards which participants direct their responses. As a methodological note, we also documented the comparable effects of plugging the left vs. right ear, and we highlighted the relevance of taking into account order of listening conditions between participants. Given that subjective outcomes of sensory processes are fundamental to guide behaviour, we suggest that investigating the self-reported confidence about sound position in space could tell us more about the possible behavioural consequences of certain/uncertain localisation in everyday life, finally pointing to future directions for the study of this component also the in hearing impaired population.

Chapter 4

Study 3

Cortical dynamics in a sound localisation task:

an MEG study with sounds in external space

4.1 Abstract

In the auditory domain, the perception of the spatial features of an acoustic object is achieved by a complex network of brain structures, from subcortical to cortical brain regions. In humans, the tonotopic organisation of the auditory cortex does not allow a fine-grained spatial coding of sound at cortical level, yet a broad network of regions identifiable along the dorsal auditory stream have been consistently reported. In the present study we focused on the network subtending active sound localisation, further investigating its dynamics, using MEG. We delivered, for the first time, real external spatialized sounds, directly in the MEG shielded room, designing a stimulation setting completely non-ferromagnetic. Participants were required to localise a single sound on a trial by trial basis. Moreover, we asked participants to rate their subjective certainty (confidence) on sound position, in each trial.

Participants showed a good and reliable level of localisation performance, even though the listening condition in the MEG cabinet was clearly altered. Confidence on sound position was variable and dissociated in several aspects from localisation accuracy. MEG data highlighted a rich bilateral cortical network underpinning active sound localisation, as early as 100 ms after stimulus onset. This network mainly comprise the primary and associative auditory cortices (Heschl's gyrus, superior temporal gyrus and sulcus, planum temporale), and the parietal cortex (intraparietal sulcus). In frontal regions, identifiable source activations were confined to the right inferior frontal gyrus, whereas in the left hemisphere emerged a dominant activation of the anterior insula. Interestingly, we reported persistent source activation in the central sulcus-gyrus and in multimodal areas such as the cingulate cortex and the parietal-occipital sulcus. Connectivity analysis highlighted a complex pattern of

connections as a function of frequency band, with a dominant role of the parietal cortex, as well as the central sulcus.

4.2 Introduction

The ability to perceive and represent acoustic space is one of the remarkable results of brain development, in humans as wells as other animals. While visual and somatosensory systems map directly the stimulus location on the sensory receptive surface and subsequently on the respective sensory cortices (topographical maps), the auditory system does not. The tonotopic organisation of the cochlea and the human auditory cortex (Romani et al., 1982) does not permit a direct mapping of acoustic space coordinates at cortical level. Therefore, the auditory system must infer the spatial position of sounds through auditory cues, derived from the interactions of sound waves with the listener's head and outer ear. Auditory cues originating from differences of sounds at the two ears, termed binaural cues (interaural time differences, ITDs; and interaural level differences, ILDs), allow localisation in the horizontal plane. By contrast, auditory cues reaching each ear separately, termed monaural or spectral cues, are functional to localise sounds in elevation, depth and disambiguate front/back confusion errors (Middlebrooks, 2015; Middlebrooks & Green, 1991). Psychophysical studies suggested that a weighting process of both binaural and spectral cues concur to the complex perception of sound position in azimuth and elevation (Van Wanrooij & Van Opstal, 2007; see Chapter 1). The weights of these cues seem to be balanced according to the hearing status of the listener and the different degree of reliability of the acoustic cues in any particular condition. Thus, coding of sound-source location entails an association between the available auditory cues and the coordinates in external space (Mendonça, 2014; Van Opstal, 2016), as also proposed by studies on acoustic space re-learning (Carlile, 2014; Hofman et al., 1998; Kumpik et al., 2010; Wright & Zhang, 2006b). In addition, data regarding current head position concur to the perceptual process of sound localisation, as originally outlined by Wallach (1940) and further investigated in several experiments (Brimijoin, Boyd, & Akeroyd, 2013; Brimijoin, McShefferty, & Akeroyd, 2010, 2012).

A considerable amount of work has described the neural mechanism of auditory cues processing in the brain-stem, in the first stages of sound processing (Grothe, Pecka, & McAlpine, 2010b). Likewise, a parallel line of research has also investigated the cortical regions primarily involved during a sound localisation task (Ahveninen, Kopčo, & Jääskeläinen, 2014; van der Heijden, Rauschecker, de Gelder, & Formisano, 2019). Neuroimaging studies have identified a broad cortical network involved in acoustic space perception, adopting different experimental approaches that ranged from passive listening to unattended sounds changing spatial location (e.g., Brunetti et al., 2005; Deouell, Heller, Malach, D'Esposito, & Knight, 2007; Deouell, Parnes, Pickard, & Knight, 2006) to intentional localisation of attended sounds. In this network, three nodes have been consistently reported: the posterior part of the superior temporal gyrus (pSTG) and the planum temporale (PT), the parietal cortex (mainly IPL), and the dorsolateral prefrontal cortex (Ahveninen et al., 2006; Barrett & Hall, 2006; Brunetti et al., 2005; Deouell et al., 2007; Getzmann & Lewald, 2010; Kopčo et al., 2012; Krumbholz et al., 2005; Tata & Ward, 2005; Warren, Zielinski, Green, Rauschecker, & Griffiths, 2002).

The role of planum temporale in spatial hearing has been demonstrated in passive listening paradigms (Deouell et al., 2007, 2006), fMRI paradigm with in-ear recorded spatialized stimuli (Battal, Rezk, Mattioni, Vadlamudi, & Collignon, 2019) and it has been corroborated by studies that exploited TMS (Ahveninen, Kopčo, & Jääskeläinen, 2014) and tDCS (Lewald, 2019) to investigate the causal role of the posterior part of the auditory cortex in spatial hearing. Arnott and colleagues (2004) highlighted the role of the inferior parietal

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lobule (IPL) and superior frontal sulcus (SFS) in the perception of acoustic space. Interestingly, each study reporting SFS activation, reported also activation in IPL, suggesting a possible coupling between those regions in auditory spatial tasks. Involvement of inferior parietal cortex has been shown also using PET (Zatorre, Bouffard, Ahad, & Belin, 2002) and TMS (Karhson, Mock, & Golob, 2015). Notably, the causal role of IPL in spatial hearing has also been shown to be related to individual localisation improvement after short behavioural training (Du et al., 2015b).

This cortical network for sound localisation has been identified also in studies that contrasted attention to spatial vs. non-spatial features of sounds (Alain et al., 2001; Alain, 2008; De Santis, Clarke, & Murray, 2006; Zatorre, 2001), and it has been conceived originally as a feedforward 'dorsal' network, starting from early sensory auditory area and extending to higher-order processing regions (van der Heijden, Rauschecker, et al., 2019), distinct from a more 'ventral' cortical network involved in sound identification. This dualpathway model is analogue to the well-known model of the "what" (object identity) and "where" (object location) processing streams in vision (Rauschecker & Tian, 2000). Interestingly, a recent review on the topic (van der Heijden, Rauschecker, et al., 2019) has emphasised the potential dynamicity of the spatial hearing network during active localisation (Figure 20). The authors suggested that the evidence about the sharpened tuning activation of the primary auditory cortices during auditory spatial processing (Van Der Heijden, Rauschecker, Formisano, Valente, & De Gelder, 2018) might be supported by feedback signals from frontal cortices. In particular, the dorsolateral prefrontal cortex (dlPFC) might constitute the origin of the top-down modulation over auditory cortices (Fritz, David, RadtkeSchuller, Yin, & Shamma, 2010; Goldman-Rakic, 1996; Jiang, Chevillet, Rauschecker, & Riesenhuber, 2018; van der Heijden, Rauschecker, et al., 2019).



Figure 20. **Cortical network of active, goal-oriented, sound localisation processing.** The blue areas indicate auditory cortical regions, with darker blue representing increased spatial sensitivity. The red areas are sensorimotor regions of the auditory dorsal stream. The solid arrows signal functional cortico-cortical (feedforward) connections. The dashed arrows indicate two potential routes for feedback connections to explain the sharpening of spatial tuning in the primary auditory cortex (PAC) during active sound localization. Arrow 1 reflects a direct feedback route for top-down modulation of activity in the PAC by the dorsolateral prefrontal cortex (dlPFC). Arrow 2 reflects an indirect feedback route in which top-down modulations of PAC activity by the dlPFC are mediated by the planum temporale (PT), the area that is traditionally implicated in spatial processing. IPL, inferior parietal lobule; PMC, premotor cortex.

Picture and description from van der Heijden et al., 2019

Relevant to our project, only very few studies so far have examined the cortical dynamics of the neural network involved in spatial hearing. One first notable exception is the study by Brunetti and colleagues (2005), which combined fMRI and MEG to investigate the cortical response to sounds changing randomly in spatial location while participants were passively listening to its. fMRI group analysis revealed three main activation areas comprising the posterior part of the superior temporal gyrus (CSTG), Heshl's gyrus, and supramarginal gyrus, with a general right hemisphere dominance (also reported in Palomaki,

Tiitinen, Makinen, May, & Alku, 2002). The involvement of the supramarginal gyrus in the inferior parietal cortex was particularly evident when sounds originated from different spatial sources vs. the presentation of a single sound. MEG findings rather allowed the description of a specific temporal flow of information between the three regions of interest. Specifically, activation pattern started in the Heschl's gyrus (N1 source, mean peak latency 139 ms), and then moved to the caudal region of STG (mean peak latency 156 ms) and the supramarginal gyrus (mean peak latency 162). A second relevant work was conducted by Ahveninen and collagues (2006). They exploited the potentials of fMRI-MEG combination, focusing on the "what" and "where" streams of non-primary auditory cortices. The authors implemented an adaptation paradigm in which participants attended either to spatial or phonetic features of a sequence of sounds. Results showed a modulation of selective attention in neural adaptation to specific attributes of the sounds (spatial vs. phonetic). Spatial differences between probes and adaptors elicited stronger activation of the posterior N1 response, especially in cortical areas posterior to Heschl's gyrus: planum temporale (PT) and posterior superior temporal gyrus (pSTG). Notably, the non-primary posterior "where" pathway responded 30 ms earlier than the opposite anterior "what" pathway. Moreover, additional cortical areas have been reported in response to spatial feature of sounds compared to identity features, comprising parietal and frontal lobe (DLPFC) regions.

In the present work we intended to deepen current knowledge about cortical dynamics of spatial hearing, not only defining the cortical regions involved in active sound localisation, but also describing their reciprocal interaction. An innovative aspect of our study is the fact that we delivered real spatialized sounds in the MEG cabinet, through a custom made arrays of completely non-ferromagnetic sound sources. For each speaker, the target sound (50 ms

long air puff) was created by the transition of an air flow (2 bar pressure) into a small plastic tube. We arranged six speakers around participant's position in a semi-circular fashion, thus obtaining six possible real azimuth locations (with equal elevation). In order to increase task difficulty and therefore error variability, we covered the real sound sources, further defining 18 total positions (6 real and 12 fake), labelled through alphabetic letters ranging from A to R (see Figure 22). In each trial we presented a single sounds (coming from one of the six real sources), and participants had to localise the sound indicating the alphabetic letter indexing source position. Moreover, we asked participants to rate their subjective certainty on sound position (Rabini, Lucin & Pavani, 2019 submitted). Although behavioural performances are typically describe in terms of accuracy and precision, under altered listening conditions the different levels of accuracy might relate to different degrees of subjective certainty (confidence) about sound-source position (see Chapter 3). For instance, we can have high confidence about the position of a sound in space and be at the same time highly accurate in our judgement, as well as be completely wrong. Seemingly, we can have low confidence about sound-source position (guessing), making a wrong judgement, as well as be objectively highly accurate (Rabini, Lucin & Pavani, 2019 submitted). In the present study we asked participants to estimate explicitly their confidence about the position of sounds in space trial by trial (as in Fleming et al., 2010), while engaged in a sound localisation task. Immediately after, they gave their confidence rate (Likert scale, from 1 to 6) about sound-source position, thus answering the question "How much were you certain/confident about the position of this sound in external space?"

In the present work, i) we aimed to find the cortical network previously described by several contributions; ii) we expected to observe a dynamic propagation of the network starting from auditory cortices and expanding along the dorsal pathway, as also shown by the cited MEG studies; iii) we tried to show the connectivity pattern emerging between pairs of regions of interest, using measures of cortical coherence in different frequency bands; iv) we combined neural and behaviour data investigating whether our index of connectivity can capture the different degrees of accuracy and confidence, or both, emerged in the sound localisation task.

4.3 Material and Methods

4.3.1 Participants

Sixteen normal hearing participants took part in the study (12 females; age = 26.5 ± 4.7). All participants reported no history of auditory or neurological disease and had normal or corrected to normal vision. Pure tone audiometry (250, 500, 1000, 2000, 4000 Hz) was used to screen participants for hearing loss.

The study was conducted according to the research ethics regulation of the University of Trento (code: 2018-002) and in line with the Declaration of Helsinki (1964, amended in 2013). Participants read and signed an informed consent regarding the experiment and the MEG procedure before taking part in the experiment and received monetary reimbursement (15 \in /hour) or course credits for participation.

4.3.2 Apparatus

Following the idea of adopting an experimental approach as ecological as possible, we used real spatialized sounds (not virtual), inside the MEG shielded room. Accordingly, we built our own "speaker array", creating a stimulation setting completely non-ferromagnetic.

4.3.2.1 Sound Sources

Each sound source was composed of a plastic (hydraulic) pipe (20 cm length, 5 cm diameter) mounted on a second (hydraulic) plastic pipe (100 cm length, 5 cm diameter), which constituted its support (see Fig. 21). The sound source (little pipe) was plugged to the support so that the pipe exit (actual sound source position) was at 192 cm height from the floor, which was approximatively the height of participant's ear ones positioned (seated) on the MEG chair. In this way, we ensured to have all sound sources approximatively at ear level (zero degrees in elevation from participants head position).

Each source was plugged through a pressure connector (PG6-4) to a plastic tube (4 mm internal diameter), which was connected to a pneumatic stimulator device. The pneumatic device was managed with Matlab, and allowed the injection of air inside our stimulation pipes. The air (2 bar pressure), travelling through the pipe, generated an air puff (using the same mechanic principle of the pipe organs), which has been used as auditory stimulus (Figure 21).



Figure 21. Sound Source. We created the sound sources with a plastic pipe plugged on a second plastic pipe support. Through a tiny (4mm diameter) tube connected to a pneumatic device (managed with Matlab), we injected pressured air (2 bars) in the sound source pipe, thus creating an air-puff (as it works for pipe organs), which constituted our stimulus (50 ms duration).

4.3.2.2 Setting

The entire setting (placed inside the shielded room) comprehended six real sound sources, arranged in a semicircle at 150 cm from participant's position (Figure 22). Note that the whole setting had to be highly portable as well as precisely reproducible. In order to rigorously maintain the positions of stimulation across participants, we built a wooden arc in which we crave squared wholes, the centre of which corresponded to -25° , -15° , -5° , $+5^{\circ}$, $+15^{\circ}$, $+25^{\circ}$ (from participants location, see Figure 23), in which we further positioned the stimulation pipes.



Figure 22. Picture of the stimulation setting skeleton. Six sound sources (plastic pipes) were positioned at 150 cm from participant's position, arranged in a semicircle covering an arc from -25° to $+25^{\circ}$. Each pipe was plugged to tiny plastic tubes connected to a pneumatic device, which was placed outside the MEG cabinet and delivered the pressured air.



Figure 23. Setting. Panel (**A**) represents a schematic visualisation of the actual sound source positions $[-25^{\circ} \text{ to} + 25^{\circ}]$, placed at 150 cm from participants head position. Panel (**B**) represents a schematic representation of the "Real" and "Fake" stimulation position. The frontal part of the setting was covered with a black sound-transparent curtain. Consequently we placed alphabetic letters labels over the position of the pipes and between them, in order to simulate more ("fake") stimulation positions, enhancing response possibility and error variability. Total number of possible response solution for the participants were 18 (letter A to R), of which 6 "Real" and 12 "Fake". Participants were not told about the exceeding positions and the difference with the real one.

In order to hide the position of the pipes and increase response variability, we covered the frontal part of the setting with a black sound-transparent curtain. Moreover, we applied alphabetic letters (A to R) labels over and between the position of the "real" sound sources (pipes), obtaining a total of 18 possible positions: 6 "Real" and 12 "Fake" (Figure 23; see also Figure 22). Also the posterior and upper sides of the setting were properly covered to avoid participants to see the real composition of the apparatus ones entering the shielded room (Figure 24).



Figure 24. The stimulation setting was totally covert to avoid participants to see the structure of the apparatus, thus having important priors on possible sound source positions. In particular, the frontal side of the setting was covered with a black sound-transparent curtain which hided the plastic pipes. Moreover, alphabetic letters label indicating "Real" and "Fake" position were placed over and between the stimulation pipes, in order to increase the number of possible responses and thus error variability.

A transparent rectangular rigid-plastic sheet was placed at about 100 cm from the participants head and it was fixed on custom-made wooden boards (Figure 22, Figure 24). Visual stimulation was back-projected on it using Matlab (Mathworks R2017b, 32-bit) and the Psychophysics Toolbox Version 3 (Brainard & Vision, 1997).

We used a Propixx DLP projector (VPixx technologies) with a refresh rate of 60Hz and a resolution of 1280×1024 pixels ($21.7 \times 13.16^{\circ}$).

A MEG-compatible eye-tracking device (Eyelink 1000 plus, SR Research Ltd., Ottawa, Canada) allowed to continuously monitor eye position binocularly at 1000 Hz, and it was placed between the stimulation set-up and the MEG chair, at 100 cm from participant's position.

4.3.3 Stimuli

As mentioned in previous paragraphs, auditory stimuli were created through air injection inside the plastic pipes. The stimuli used in the present work were 50 ms long air puffs, characterised by low frequencies content, as shown in the spectrum represented in Figure 25 and Figure 26. Mean stimulus intensity was 55 dB SPL at participant's head position (measured at 150 cm from source position).

Recordings of sounds has been done outside the shielded room for technical constrains, therefore the reported measures are not precisely that of inside the MEG cabinet, but they are still reliable. Comparably, we measured (this time inside the MEG cabinet, with a MEG compatible microphone connected to the MISC channels) the delay of auditory stimulation: specifically we measured the delay between the Matlab trigger for stimulus onset and the effective appearance of the sound directly outside the stimulation pipe, and we did it separately for each sound source position [-25°: 0.03 s \pm 0.001; -15°: 0.029 s \pm 0.002; -5°: 0.029 s \pm 0.002; +5°: 0.029 s \pm 0.002; +15°: 0.032 s \pm 0.002; +25°: 0.031 s \pm 0.001].



Figure 25. Experimental auditory stimulus. A 50 ms long air puff has been used as auditory stimulus in each trial. In the figure are represented the time-frequency spectrogram and the raw amplitude spectra of the sound created by air travelling though one of the plastic pipes of the experimental setting.



Figure 26. Experimental stimuli. Time-amplitude course, spectrogram (Time-frequency) and frequency power estimation in three separate rows respectively, for each sound-source.

Visual stimuli consisted of instructions before the task and a white fixation cross (10 pixel width) during the experiment at appropriate time points. The screen background was kept black coloured. In this way, the fixation cross was clearly visible on the transparent plastic sheet, and the projector's light was not disturbing for the participants.

4.3.4 Paradigm

Each trial started with a white fixation cross displayed on a black uniform background. After a variable (random) interval between 0.5 and 1.0 s, a single auditory stimulus was played (0.05 s duration). After 2 s from stimulus offset the fixation cross disappeared and participants were allowed to give their answer, by verbal response. Participants were instructed to keep strict eye fixation on the white cross until it disappeared. We acknowledge that eye movements and sound localisation are strictly related and eye movements in response to sounds are a natural behaviour in humans (Arnott & Alain, 2011; Ege et al., 2018; Gruters et al., 2018; Pavani et al., 2008; Razavi, O'Neill, & Paige, 2007b). However, in the present study we restrict eye movements to avoid signal contamination after auditory stimulation and try to capture the pure spatial response to sounds cleaned from visual feedback and searching strategies.

In each trial a single sound was played from one of the sources (pipes) in a random and counterbalanced order. The tasks of participants were double: localise the heard sound and express their certainty on the position of this sound. In order to localise the sound participants had to indicate (by verbal response) the alphabetic letter (A-R) indexing the position of the perceived sound source. After that, they had to rate their spatial certainty (confidence) on sound position on a Likert Scale ranging from 1 to 6 (1: completely uncertain, 6: completely certain). Note that our question was not related to participant's confidence on their performance, but in their subjective certainty on sound position.

In other words, after fixation cross offset, participants had to answer two questions: 1) Where did the sound come from? And 2) How much were you certain about the position of the sound in space?

As previously mentioned, participants answered by verbal response. The communication between participants (MEG cabinet) and the experimenters (MEG lab, outside the shielded room) was allowed by the standard Elekta Speaker installed in the shielded room. Experimenter listened to participants through an intercom unit, and they manually inserted the responses in the custom made Matlab script running on the Stimulation PC managing the experiment.

Inter-trial interval (ITI; time from response registration to fixation cross onset) was 1.5 s. We presented 12 trials for each position in each run (72 trials per run), testing 8 runs for each participants. The total amount of trial was 576 (96 for each position).

At the beginning of each run, participants performed a calibration procedure for eye-tracking data registration. Due to technical issues, eye-tracking data were recorded for 8 subjects out of 16.

4.3.5 MEG Data acquisition

MEG data were recorded at the Center for Mind/Brain Sciences (CIMeC, University of Trento), using a Neuromag VectorView MEG scanner system with 306-channels (204 first order planar gradiometers and 102 magnetometers; Elekta-Neuromag Ltd., Helsinki, Finland), with a sampling rate of 1000 Hz. The MEG system was located in a magnetically (two layers) shielded room (AK3B, Vakuumschmelze, Hanau, Germany). Participants position on the MEG chair was carefully checked at the beginning of the experiment ensuring that the upper part of the head was at close contact with the dewar. During testing, head position was recorded at the beginning of each experimental block.

Before starting the experiment, participants were instructed to keep the initial position as much as possible avoiding body, head (primarily) and limb movements, during the task. Participants were told to further avoid muscular activity of the mouth during the trial and specifically when fixation cross was at screen. Comparably, participants were instructed to avoid eye blinks and keep strict fixation on the cross when it was displayed. Eye movements were allowed during the response phase and before fixation cross onset.

Immediately before the experiment, in a separate room, head shape of each subject was recorded in order to co-register the MEG's SQUID with the individual anatomy of the participant. A Polhemus Fastrak digitizer (Polhemus Inc., Vermont, USA) has been used to digitalise three fiducial points (nasion, pre-auricular left and pre-auricular right), five head-position induction coils (HPI, attached to the forehead and mastoids) and a grid of minimum 500 additional points covering the head of participants. Landmarks and head-position induction coils were digitized twice to ensure that their spatial accuracy was less than 1 mm. Synchronisation between MEG data recording and experiment timing was implemented through trigger delivery at fixation cross onset and offset, stimulus onset and offset and response recording.

We further used vertical and horizontal electro-oculogram (EOG) to record eye-related blinks and movements.

4.3.6 MEG data processing

MEG data pre-processing analysis was performed using the Brainstorm toolbox of Matlab (Tadel, Baillet, Mosher, Pantazis, & Leahy, 2011).

The standard structural surface reconstruction pipeline of the FreeSurfer software package (Dale, Fischl, & Sereno, 1999) has been used to produce 3D models of the head surface, the brain and the skull of each individual subject. The anatomical models were then co-registered to the MEG sensors by marking fiducial points (nasion, pre-auricular left, pre-auricular right, anterior/posterior commissure and interhemispherical point) on the MRI scans. We followed this procedure for participants who have already done an MRI scan at CIMeC (13 subjects). For the remaining participants (three), we created a pseudo-individual anatomy, warping an anatomy template (ICBM152) to fit the shape of the digitalized head points individually recorded before starting the experiment.

MEG data pre-processing started by checking head position at the beginning of each experimental run and by visually detecting bad channels using a python based tool for bad channels detection and data navigation (MEG lab, CIMeC, University of Trento). The bad channels detected in this phase have been excluded from subsequent analyses.

MEG data were then filtered with the Elekta Neuromag MaxFilter function (Elekta Neuromag MaxFilter 2.2), using the temporally non-extended spatial Signal Source Separation method (SSS) (S. Taulu & Simola, 2006; S. Taulu, Simola, & Kajola, 2005; Samu Taulu & Kajola, 2005).

Working on continuous data, trigger delays were corrected adding an offset to the stimulus onset trigger recorded and saved in the MEG data. We applied specific offset depending on the specific sound source, as explained in the Material and Method section (mean trigger delay was 0.03 s).

We used a semi-automatic method to detect artifacts and reject bad trials. First, eye-blinks and saccades were detected through automatic functions of Brainstorm (Detect Blinks, Detect

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Saccades) applied to continuous raw data and based on EOG signals. We then imported epochs from raw data, starting from -200 ms to +1900 ms from corrected stimulus onset, applying a baseline correction (DC offset) from -200 ms to -1 ms pre-stimulus onset. Given the high variability of eye-blinks/saccade behaviour of participants in our sample, we first visually inspected the data marking as bad all trials containing blinks and saccades, aside from other artifacts. If, in a specific subject, the total percentage of rejected trials was above 20%, we run Independent Component Analysis (ICA) on its raw data, setting 20 as maximum number of component to be extracted (default option). We then selected only the components related to eye-movements (mainly eye-blinks, 1 or 2 components) and applied the relative projections to raw data in order to correct the MEG signal for this specific artifacts. In a second pre-processing step we re-imported the epochs of this participants, as described above, and visually inspected each epoch marking bad trials with residual artifacts (deflections larger than 3000 fT/cm as in (Salminen, Jones, Christianson, Marquardt, & McAlpine, 2018)), which have been rejected from the subsequent analysis steps. On average, $11\% \pm 7$ of the trials were rejected for each subject.

4.3.7 Source Reconstruction and ROI definition

Individual source reconstruction was computed with the Brainstorm toolbox of Matlab (neuroimage.usc.edu/brainstorm/). A model of overlapping spheres was used to perform the forward problem. Noise covariance was computed using empty-room MEG recordings acquired before participant's testing. For some participant, in case empty-room recording of its testing day was not available, noise covariance was estimated from the more recent empty-room recording (the day before).
Source estimation was performed through minimum norm imaging method, with current density map as measure and constrained dipole orientation (Constrained: normal to cortex). Before averaging across subjects, each subject's averaged (across all trials) source was projected on a standard anatomical template (MNI/ICBM152).

Averaged source data of each subject were then baseline normalised through z-score transformation (Baseline: -200 ms, -1 ms) and absolute values were successively calculated on its. As the last stage we calculated a group source activity map by averaging individual data at source level.

Regions of interest (ROIs) were subsequently selected based on the Group source activation (grand average) in specific time window as suggested by previous literature regarding the neural network involved in spatial hearing. Moreover, other regional foci of activation were selected as region of interest based on evoked source activity. ROIs selection has been implemented using Brainstorm (Matlab), by selecting the activation peak for each region as seed and extending the area of that region in order to comprehend 20 vertices each. For the subsequent ROI analysis, activity (time series) of each significant region of interest was extracted on a trial by trial bases for each individual subject.

4.3.8 Connectivity analysis

As a measure of coupling between cortical regions we estimated *coherence*, calculated on ROIs time series originated through the source analysis procedure described above. We considering all valid trials for each participants, independently of testing block and sound source position. We computed trial by trial coherence, separately for pre-stimulus baseline (from -0.2 to 0 s) and post-stimulus period, avoiding evoked response activity and thus

considering induced activity in a time window ranging from 0.35s to 0.85 s after stimulus onset.

This analysis was performed using the FieldTrip toolbox of matlab, first implementing FFT algorithm, using a multitaper time-frequency transformation (mtmconvol) based on Slepian sequence, with epochs zero-padded in order to obtain Fourier coefficients with frequency resolution of 0.5 Hz, from 1 to 100 Hz.

The coherence coefficients obtained, for each ROI pair, were then averaged across selected frequency bands (theta: 4-7 Hz, alpha: 8-13 Hz, beta: 14-29 Hz, low gamma: 30-59 Hz and high gamma: 60-90 Hz), at individual level.

Before grand averaging and statistical testing we used the Fisher transform (Enochson & Goodman, 1965) in order to stabilise the variance of the distribution of individual coherence. In order to test, in this preliminary analysis, the statistical significance of the coherence measures, we compared the post-stimulus coherence with the pre-stimulus baseline coherence, in each individual ROI-ROI pair, using a parametric paired sample t-test. Consequently, we obtained, separately for each frequency band, a range of significant cortico-cortical couplings. Coherence were calculated between all possible pairs of ROIs within each brain hemisphere.

4.3.9 Behavioural data analysis

Behavioural data were first analysed considering all trials for each participants, in other to show the specific behavioural performance on sound localisation with the new setting we adopted in the MEG cabinet. Given the novelty of the stimulation setting and the particular acoustic condition of the MEG shielded room, we had to prove that participants perceived the difference in sound source location, with a reasonable degree of variability. Clearly, typical binaural hearing was altered, therefore we expected to measure altered localisation performance.

We characterised localisation performance through the error system introduced by Hartman and colleagues (Hartmann, 1983) and adopted in other studies (Grantham et al., 2007; Rabini et al., 2019). Three error indexes represents localisation errors (rms error), localisation bias (signed error) and error variability (variable error). Greenhouse-Geisser method of correction was used in case of sphericity assumption violation.

Considering confidence ratings, we first calculated a mean confidence rating based on stimulation position. Second, we collapsed confidence ratings following the perceived sound source position. Accordingly, we investigated whether spatial certainty on sound position (confidence) was differently related to stimulation position and perceived sound position.

In a second step of analysis, when we related behavioural performance with neural signature of sound localisation (MEG signal), we computed localisation accuracy calculating an absolute error (Response position – Stimulation position) on a trial by trial bases. In this analysis, we considered only the valid trials that survived the MEG data pre-processing step, thus the data that were used for MEG data analysis.

In order to investigate the relation between confidence and accuracy, we computed raw accuracy (i.e., difference between response and target position) and confidence in a trial by trial base, further determining their level as above or below the mean (for each individual subject). Based on this evaluation, we assigned each trial to one of four categories: i) trials with high accuracy and high confidence (highA-highC); ii) trials with high accuracy but low

confidence (highA-lowC); iii) trials with low accuracy but high confidence (lowA-highC); and iv) trials with low accuracy and low confidence (lowA-lowC).

4.4 Results

4.4.1 Behavioural data

4.4.1.1 Localisation accuracy and spatial confidence

Figure 27 shows performance of each participant in the sound localisation task. In the plots, response position is shown as a function of stimulation position. The diagonal line represents the ideal match between response and stimulation position, i.e., perfect localisation performance. As can be seen, mean values (darker points) approximate the diagonal line for most participants, suggesting that sound direction was reliably perceived with our setting. Still, localisation errors were consistently present, as expected in this altered binaural listening condition.



Figure 27. Sound localisation performance. Responses in the sound localisation task are displayed as a function of stimulation position, separately for each participant. The diagonal line represents perfect matching between response and stimulation position. Although the hearing condition in the MEG room can be considered an unusual or even altered listening situation (head in the MEG helmet, high reverberation), participants clearly perceived the difference in sound-source direction. Black dot represent mean responses for each stimulation position, grey dot represent individual trials.

We investigated whether localisation changed as a function of sound source eccentricity, on both left and right side. To this aim, we computed a repeated measure ANOVA on rms error with STIMULATION SIDE (left, right) and STIMULATION ECCENTRICITY (5°, 15°, 25°) as within subject factors. The analysis revealed a significant main effect of STIMULATION ECCENTRICITY (F(1.27, 19.12) = 7.55, p = 0.009, $\eta^2 = 0.15$), caused by higher rms error in peripheral compared to central positions (-25°: 13.15 \pm 5.18, -15°: 8.46 \pm 3.12, -5°: 9.11 \pm 2.84, 5°: 7.16 \pm 2.76, 15°: 10.16 \pm 3.44, 25°: 10.99 \pm 5.39). A two-way interaction STIMULATION SIDE* STIMULATION ECCENTRICITY was also found (F(2, 30) = 7.91, p = 0.003, $\eta^2 = 0.04$). Post-hoc pairwise comparisons revealed that while in the right side of stimulation there was a significant difference in rms error between the lower (5°) and the higher (25°) eccentric positions (t(15) = 3.26, p = 0.032, Cohen's d = 0.82, Bonferroni corrected), in the left side significant differences were present between eccentricity 5° and eccentricity 25° (t(15) = 3.44, p = 0.019, Cohen's d = 0.86, Bonferroni corrected), as well as between eccentricity 15° and eccentricity 25° (t(15) = 3.99, p = 0.004, Cohen's d = 0.99, Bonferroni corrected).

A similar ANOVA conducted on signed error showed a significant main effect of STIMULATION SIDE (F (1, 15) = 122.66, p < 0.001, η^2 = 0.66) and STIMULATION ECCENTRICITY (F (2, 30) = 16.7, p < 0.001, η^2 = 0.03). A significant two-way interaction also emerged (F (1.30, 19.54) = 7.57, p = 0.008, η^2 = 0.04). The difference in sign error between left and right stimulations, indicates a strong localisation bias towards the midline (which increases as a function of stimulation eccentricity), with positive signed error for sounds coming from the left (-25°: 10.96 ± 5.23, -15°: 5.33 ± 3.86, -5°: 6.97 ± 3.30), and negative signed error for sounds coming from the right (5°: -3.15 ± 4.33, 15°: -8.13 ± 4.16, 25°: -7.66 ± 6.04).

Finally, response precision was investigated considering the variable error. Using again the repeated measures ANOVA, we found a significant main effect of STIMULATION ECCENTRICITY (F(1.30, 19.54) = 7.57, p = 0.008, $\eta^2 = 0.04$), suggesting increased variability of localization error towards the most peripheral positions (-25°: 6.91 ± 2.19, -15°: 5.93 ± 1.83, -5°: 5.52 ± 1.15, 5°: 5.37 ± 1.51, 15°: 5.53 ± 1.26, 25°: 6.99 ± 2.58).

Having assessed accuracy and precision in estimating sound direction with our setup, we examined the confidence expressed by participants on their response (see Chapter 3).

Figure 28 shows that participants expressed comparable confidence ratings for each sound-source position. Nonetheless, confidence ratings were entered into an ANOVA with STIMULATION SIDE and STIMULATION ECCENTRICITY as within-subject factors, a significant main effect of STIMULATION SIDE (F(1, 15) = 7.01, p = 0.018, $\eta^2 = 0.009$) emerged, caused by higher confidence for sounds coming from the left compared to the right side (mean difference= 0.172, t(15) = 2.65, p= 0.018, Cohen's d = 0.662, Bonferroni corrected).



Figure 28. Confidence ratings in the sound localisation task. Confidence ratings (subjective certainty on sound position) are displayed as a function of stimulation position, separately for each participant. Although listening condition, visual stimulation and auditory stimulation (different stimulation position) remained constant throughout the entire experiment, the expression of confidence ratings on sound position showed a certain degree of variability. Black dots represent mean confidence rating, separately for each position of stimulation, whereas grey dots represent individual trials.

4.4.1.2 Accuracy-Confidence relation

As shown in Chapter 3, it is not always the case that sounds localised with higher accuracy are also those for which participants express higher confidence judgements – particularly under altered listening conditions. To investigate the relation between accuracy levels and confidence, we categorised each trial depending on their level of accuracy/confidence (above or below the mean calculated for all trials in each participant, as in Chapter 3). We then used the number of trials falling within each category (highA-highC, highA-lowC, lowA-highC, lowA-lowC) as dependent variable.

A repeated measure ANOVA with ACCURACY (high, low) and CONFIDENCE (high, low) as within-subject factors revealed a significant main effect of ACCURACY (F(1,15) = 9.16, p = 0.008, $\eta^2 = 0.087$), as well as a significant two way interaction ACCURACY and CONFIDENCE (F(1,15) = 5.07, p = 0.04, $\eta^2 = 0.045$). A significant difference emerged only between highA-highC and lowA-highC categories (t(1,15) = 3.74, p = 0.005, Cohen's d = 0.93, Bonferroni corrected; see also Figure 29). This indicates that responses with higher confidence were associated more with higher than lower accuracy responses. Conversely, were participants were less certain about their responses the proportion of higher and lower accuracy trials was comparable.





Figure 29. Mean number of trials assigned to distinct categories depending of their level of raw accuracy and confidence (above/below the individual mean). Trials were assigned to the following categories: high accuracy and high confidence (highA-highC), high accuracy and low confidence (highA-lowC), low accuracy and high confidence (lowA-highC) and low accuracy and low confidence (lowA-lowC). Grey points represent mean number of trials of single participants. Error bars show standard error.

4.4.1.3 Change in accuracy and confidence as a function of time

Chapter 3 showed that confidence, but not accuracy, rapidly change during simulated monaural listening. To investigate whether this occurred also in the altered listening condition in the MEG room, we computed a mean accuracy (Response location – Stimulation location) and mean confidence for each experimental run (8 total runs, 72 trials for each run). We then examined the relation between experimental block and accuracy/confidence using linear modelling. As shown in Figure 30a, no linear relation emerged for error measures over time (F(1,6) = 1.26, $R^2 = 0.17$, p = 0.30) suggesting no significant changes in localisation

accuracy from the first to the last testing block. By contrast, a positive and significant relation emerged for confidence ratings (F(1,6) = 188.2, $R^2 = 0.97$, p < 0.001). As shown in Figure 29b, confidence rating significantly increased as a function of time (blocks) during the experimental session.



Figure 30. Change in accuracy and confidence as a function of time (experimental blocks). Plot (a) shows raw localisation error in degrees (Response location – Stimulation location) as a function of experimental block. Plot (b) shows confidence ratings as a function of experimental block. Darker dots represent group mean values, whereas grey points represent mean values at single subject level

4.4.2 MEG data

4.4.2.1 Evoked response and Source activity

Figure 31 shows grand averaged (across all positions of stimulation and subjects) auditory evoked response to acoustic stimuli (all MEG magnetometers and gradiometers). Epochs were defined as time intervals between -200 ms and 1900 ms from stimulus onset. A first visible evoked response was detectable already a 40 ms after stimulus onset. As expected, the principal component in response to the presented sound emerged around 100 ms from stimulus onset (N1m).



Figure 31. Grand Average auditory evoked response to sound stimulation (50 ms air puff). The evoked response was computed on all trials for each participants. Epoch's length was defined from -0.2 to 1.9 seconds after auditory stimulation. The main component, as expected, appeared at around 100 ms from stimulus onset.

Grand average time course of evoked response further highlights a prominent evoked responses at around 200 ms and 300 ms, followed by sustained activity up to the end of the epochs.



Figure 32. Grand Average source activity maps during the sound localisation task. Source activity was averaged across all valid trials and all participants at selected peak latencies. Visualisation threshold was set at z-score between 2 and 20, and source activity was overlaid on a template brain.

HG, Heschl's gyrus; PT, planum temporale; STS-STG, superior temporal sulcus/gyrus; pIPS/aIPS, posterior/anterior intraparietal sulcus; IFG, inferior frontal gyrus; central CS, ventral central sulcus; Cing, cingulate cortex; PT-O-S, parieto-occipital sulcus.

Figure 32 shows grand averaged (across stimulation positions and subjects) images of cortical source activity at different time sections (from 40 ms to 300 ms post stimulus onset).

Averaged source activity reveals a distributed cortical network in response to sounds, when participants are engaged in sound localisation. At around 40 ms, when the first detectable response was visible, a significant bilateral activation of Heschl's gyrus (HG) and superior temporal cortex (medial and posterior STS-STG) emerged. At 100 ms, in correspondence with the main auditory evoked response, source activity extended to include the planum temporale (PT), the posterior intraparietal sulcus (pIPS) in the inferior parietal lobule, and the ventral part of the central sulcus/gyrus (ventral CS) in both hemispheres. At 125 ms, this primarily dorsal auditory network further extended bilaterally to the anterior part of the intraparietal sulcus (aIPS) in the superior parietal lobule, and left anterior insula (aIns). Interestingly, sustained activation also extended to the cingulate cortex (Cing) and parieto-occipital sulcus (PT-O-S) in extra striates visual cortices, again in both hemispheres. In the frontal lobe, we mainly detected source activity at the level of the inferior frontal gyrus, in the right hemisphere (IFG).

We selected the mentioned brain areas as specific regions of interest (ROIs) for further analyses. The MNI coordinates of the peak in each of these regions are reported in Table 5.

Aroa	MNI co	ordinate	s (mm)
Alea	x	У	Z
L Heschl's gyrus	-47	-28	11
L planum temporale	-47	37	16
L middle superior temporal S-G	-53	-31	1
L posterior superior temporal S-G	-53	-46	7
L posterior intraparietal S	-33	-59	38
L anterior intraparietal S	-38	-34	39
L ventral central S	-59	-7	17
L dorsal central S	-21	-30	57
L anterior insula	-41	13	-3
L cingulate cortex	-14	-40	48
L parieto-occipital S	-20	-65	18
R Heschl's gyrus	48	-14	10
R planum temporale	43	-27	13
R middle superior temporal S-G	53	-28	2
R posterior superior temporal S-G	46	-42	15
R posterior intraparietal S	38	-47	44
R anterior intraparietal S	37	-30	39
R ventral central S	58	-5	20
R dorsal central S	30	-28	57
R inferior frontal G	42	21	20
R cingulate cortex	16	-38	45
R parieto-occipital S	8	-63	21

Table 5. MNI coordinates (mm) of the region of interest (ROIs) identified in the localisation task at Group level. Regions

 of interest were found in both hemispheres, comprising a distributed (dorsal) neural network.

4.4.2.2 ROIs peak latency and amplitude

For each selected ROI in both hemispheres we extracted individual time series data, from the average response (all trials) of each participant. Group mean peak latency and amplitude was then computed on the averaged time series of each ROI.

Averaged time series for each ROI were then individually plotted and grouped anatomically (temporal lobe, parieto-occipital lobe, frontal lobe, other ROIs).

In the temporal lobe, significant brain activity started as soon as 40 ms after stimulus onset, mainly in bilateral HG and STS-STG regions. Prominent peaks of averaged time series were found around 100 ms in the primary auditory cortex (right HG: 104 ms, left HG: 104 ms) and associative cortices represented by superior temporal gyrus/sulcus in their medial and posterior parts (right mSTS: 101 ms, left mSTS: 104 ms ; right pSTS: 98 ms, left pSTS: 11 ms) and planum temporale (right PT: 101 ms; left PT: 106 ms), a region frequently reported in spatial hearing literature (van der Heijden, Rauschecker, et al., 2019). Figure 33 shows mean time series of selected ROIs in the temporal lobe (right/left HG, right/left mSTS-STG and pSTS-STG, right/left PT).

Temporal Lobe



Figure 33. Averaged Time series of Temporal Lobe's ROIs. Time series for each region of interest were averaged across all trials and all participants. Black arrows indicates the latency of the identified local peak (maximum). HG, Heschl's gyrus; PT, planum temporale; STS-STG, superior temporal sulcus/gyrus; PT, planum temporale.

It is worthy to highlight the specific activation flow in the auditory cortices, as displayed in Figure 34. Foci of activations moved from primary auditory cortex to associative auditory cortex, as a function of time. Specifically, at around 100 ms source activity was prominent in Heschl's gyrus, whereas already at 140 ms in the left hemisphere and at 200 ms in the right hemisphere, it moves towards the planum temporale (see Table 6).



Figure 34. Source activity in the auditory cortices. Two regions of interest in the auditory cortex, namely HG (Heschl's gyrus) and PT (plunum temporal), are displayed over grand average source activity maps separately for each hemisphere (left: a, b, c; right: d, e, f) at selected latencies (left: 100 ms (a), 140 ms (b); right: 100 ms (d), 200 ms (e)). Panel (c) and (d) show sagittal and coronal view of source activity at 100 ms, for left (c) and right (f) Heschl's gyrus.

In the sound localisation task, source activity slightly moved from primary auditory cortex (HG) to secondary cortex, as a function of time after auditory stimulation.

ROI	Hemisphere	Time Interval [ms]	Mean Amplitude
	Right	80-120	11.37 (5.81)
		180-220	5.56 (3.16)
Heschl's gyrus (HG)	Left	80-120	8.51 (7.31)
		130-170	4.93 (3.61)
	Right	80-120	9.99 (6.53)
Planum temporale (PT)		180-220	6.02 (4.32)
	Left	80-120	8.05 (7.90)
		130-170	5.24 (4.29)

Table 6. Mean amplitude of bilateral Heschl's gyrus (HG) and planum temporale (PT) time series (computed on groupROIs time series), at selected time intervals (left: 80-120 ms and 130-170 ms; right: 80-120 ms and 180-220 ms).



Figure 35. Time series amplitude of Heschl's gyrus (HG) and plunum temporale(PT), separately for selected time intervals (20-60, 80-120, 130-170, 180-220, 230-270, 280-320). Plot (a) shows averaged amplitude of ROIs HG and PT, highlighting the difference between the two regions of interest in each hemisphere. Plot (b) shows averaged amplitude of ROIs HG and PT within each hemisphere, highlighting the difference in source activation of the same ROI, separately for each hemisphere. Error bars show standard error of the mean.

Interestingly, mean amplitude of the ROI's time series in the right hemisphere was constantly higher throughout the time course, and in particular in the 80-120 time window (HG: right= 11.37 ± 5.81 , left= 8.51 ± 7.31 ; PT: right= 9.99 ± 6.53 , left= 8.05 ± 7.90) (Figure 34).

In the parietal lobe, principal source activations lied in the inferior and superior parietal lobule (IPL/SPL) and specifically in the intraparietal sulcus (IPS). Two distinct foci of activation emerged in both hemispheres, which we labelled anterior (aIPS) and posterior (pIPS) intraparietal sulcus. Source activation of pIPS peaked at 102 and 107 ms in the right and left hemisphere, respectively. The anterior part (aIPS) reached it maximum peak slightly later in the right hemisphere (104 ms) and was even further delayed in the left hemisphere (196 ms) (Figure 36).



Figure 36. Source activation in the right parietal cortex at 100 (a) and 200 (b) ms post sound stimulation. Grand average source maps show consistent detectable source activation starting from 100 ms in the posterior part of the intraparietal sulcus (pIPS). At 200 ms, instead, prominent and extended activation emerged in the anterior part of the IPS.

ROI	Hemisphere	Time Interval [ms]	Mean Amplitude
	Right	80-120	5.37 (5.16)
		180-220	3.56 (2.19)
posterior intraparietal sulcus (pIPS)	Left	80-120	4.09 (3.43)
		180-220	2.95 (1.53)
	Right	80-120	3.92 (1.77)
anterior intraparietal sulcus (aIPS)		180-220	3.88 (2.83)
antenor intrapanetar solicus (an S)	Left	80-120	3.11 (1.72)
		180-220	4.57 (2.53)

Table 7. Mean amplitude of bilateral posterior intraparietal sulcus (pIPS) and anterior intraparietal sulcus (aIPS) time series

 (computed on group ROIs time series), at selected time intervals (80-120 ms and 180-220 ms).

As shown in Table 7 and Figure 37, source activity amplitude slightly increased or appeared sustained for aIPS and clearly decreased for pIPS as a function of time. This observation is corroborated by previous studies (Alain, Shen, Yu, & Grady, 2010) suggesting that different cognitive processes are subtended by distinct parietal activation during auditory spatial tasks.



Figure 37. Time series amplitude of anterior (aIPS) and posterior (pIPS) intraparietal sulcus, separately for selected time intervals (20-60, 80-120, 130-170, 180-220, 230-270, 280-320). Plot (a) shows averaged amplitude of ROIs aIPS and pIPS, highlighting the difference between the two regions of interest in each hemisphere. Plot (b) shows averaged amplitude of ROIs aIPS and pIPS within each hemisphere, highlighting the difference in source activation of the same ROI, separately for each hemisphere. Error bars show standard error of the mean.

Grand average source activation further highlighted sustained activity in brain regions broadly corresponding to bilateral parieto-occipital sulcus (PT-O-S), with peak latencies at 105 and 106 ms in the right and left hemisphere, respectively. Figure 38 shows mean averaged time course over all participants, separately for each selected region of interest in the parieto-occipital cortex.





Time [ms]

Figure 38. Averaged Time series of Parietal-Occipital Lobe's ROIs. Time series for each region of interest were averaged across all trials and all participants. Black arrows indicates the latency of the identified local peak (maximum). aIPS, anterior intraparietal sulcus; pIPS, posterior intraparietal sulcus, PT-O-S, parieto-occipital sulcus.

Frontal activation in auditory spatial task are often reported and associated to the dorsolateral prefrontal cortex (dlPFC) (van der Heijden, Rauschecker, et al., 2019). In the present study we found a defined activation source in the right inferior frontal gyrus (rIFG), which peaked at 100 ms (mean amplitude in the 80-120 ms time interval: 3.28 ± 1.91) with consequent sustained mean amplitude (Figure 40).

ROI	Hemisphere	Time Interval [ms]	Mean Amplitude
Inferior frontal avrus (IEG)	Right	80-120	3.28 (1.91)
		180-220	2.99 (1.70)
	Right	80-120	5.64 (2.69)
ventral central sulcus (ventral CS)		180-220	3.20 (1.84)
ventral central solicus (ventral CO)	Left	80-120	3.94 (3.08)
		180-220	2.98 (1.80)
	Right	80-120	3.62 (3.06)
dorsal contral sulous (dorsal CS)		180-220	2.71 (1.72)
	Left	80-120	2.58 (1.48)
		180-220	2.47 (1.31)

 Table 8. Mean amplitude of bilateral ventral (ventral CS) and dorsal (dorsal CS) central sulcus, and inferior frontal gyrus

 (IFG) time series (computed on group ROIs time series), at selected time intervals (80-120 ms and 180-220 ms).

Most interestingly, we reported two distinct foci of activation in the central sulcus/gyrus in response to spatialized sounds.

We identified a ventral and a dorsal activation in the central sulcus (ventral CS and dorsal CS), bilaterally. Mean amplitude for each ROI are shown in Table 8. Maximum peak latencies were detected in the 100-130 ms window after stimulus onset (right, ventral CS; 105 ms, dorsal CS: 103 ms; left, ventral CS: 103 ms, dorsal CS: 122 ms).

Figure 39 highlights the two foci of activation detected in the central sulcus. This source activity is comparable to that of other studies (Prudente et al., 2015) investigating the role of head movements, that is known to play a critical role also in sound localisation (Perrett & Noble, 1997).



Figure 39. Grand average source activity maps in the bilateral central sulcus. Central and dorsal components of central sulcus brain activity is highlighted both in the template visualisation than in the coronal section of each respective hemisphere (b). Visual representation of the homunculus (from Prudente et al., 2015) in which red and black arrows indicate ventral and dorsal brain regions involved in head movement and head movement programming. Red stars indicate the location of the homologous regions found in the study of ().



Frontal Lobe

Figure 40. Averaged Time series of Frontal Lobe's ROIs. Time series for each region of interest were averaged across all trials and all participants. Black arrows indicates the latency of the identified local peak (maximum). Ventral CS, ventral central sulcus; dorsal CS, dorsal central sulcus; IFG, inferior frontal gyrus.

Finally, activation identified in the bilateral posterior cingulate cortex (Cing) peaked at 105 ms in the right hemisphere (mean amplitude in the 80-120 time window: 5.05 ± 2.06) and 110 ms in the left hemisphere (mean amplitude in the 80-120 time window: 4.67 ± 2.8).

Interestingly, the region of interest including the anterior part of the left Insula, which had a sustained activation starting from 100 ms post stimulus onset (mean amplitude in the 80-120 ms time interval: 4.52 ± 3.61) showed its maximum peak (time series averaged across participants), at 503 ms post stimulus onset. Figure 41 shows average time series for each of the aforementioned regions of interest.



Time [ms]

Figure 41. Averaged Time series of left and right cingulate cortex (Cing) and left anterior insula (aIns) Time series for each region of interest were averaged across all trials and all participants. Black arrows indicates the latency of the identified local peak (maximum).

4.4.2.3 Cortical coupling

The results of the functional connectivity analysis on coherence are presented in Figure 42 and Tables 9-12. In the figure, separately for each frequency band, we showed the significant connections emerged in the connectivity analysis. In the tables, significant coherence values are highlighted in light yellow and dark yellow depending on their level of statistical significance: p < 0.01 dark yellow, 0.01 light yellow. As outlined in the figure/tables, we reported a wide range of significant regional coupling (computed as pre-stimulus vs. post-stimulus coherence) between different nodes of our identified network, with specific configurations as a function of frequency band and brain hemisphere. In the following description, we highlighted the strongest values of coherence (<math>p < 0.01).

Table 9. Coherence values in the right hemisphere, for each frequency band, separately. Theta (4-7 Hz), Alpha (8-13 Hz), Beta (14-29 Hz), low Gamma (30-59Hz), and high Gamma (60-90 Hz). Dark yellow highlights significant value with p< 0.01. Light yellow highlights significant values with 0.01

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9		1	0.254	0.315	0.190	0.175	0.324	0.125	0.274	0.372	mSTS			-	0.246	0.301	0.190	0.175	0.139	0.286	0.366		mSTS			0.184	0.308	0.171	0.154	0.219	0.154
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Table 10. P values relative to coherence measurements in the right hemisphere, for each frequency band, separately. Theta (4-7 Hz), Alpha (8-13 Hz), Beta (14-29 Hz), low Gamma (30-59Hz), and high Gamma (60-90 Hz). Dark yellow highlights significant value with p< 0.01. Light yellow highlights significant values with 0.01

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0.874 C P.C P.C P.C P.C P.C P.C P.C P.C P.C P

Table 11. Coherence values in the left hemisphere, for each frequency band, separately. Theta (4-7 Hz), Alpha (8-13 Hz), Beta (14-29 Hz), low Gamma (30-59Hz), and high Gamma (60-90 Hz). Dark yellow highlights significant value with p< 0.01. Light yellow highlights significant values with 0.01



0.267

0.115

Table 12. P values relative to coherence measurements in the lefthemisphere, for each frequency band, separately. Theta (4-7 Hz), Alpha (8-13 Hz), Beta (14-29 Hz), low Gamma (30-59Hz), and high Gamma (60-90 Hz). Dark yellow highlights significant value with p< 0.01. Light yellow highlights significant values with 0.01



0.267 0.424

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Figure 42. Functional connectivity results. Significant coherence between ROIs is represented through coloured and curved connections, as a function of brain hemisphere (left, right) and frequency band (theta, alpha, beta, low gamma and high gamma). Thickness of links between ROIs represents post-stimulus coherence values.

In the low frequency theta band, in the left hemisphere we reported strong

significant coupling between HG and aIPS (t(15) = 3.07, p = 0.008), aIPS and mSTS-STG (t(15) = 3.06, p = 0.008) and dorsal CS and Cing (t(15) = 2.67, p = 0.01) and between P-O-S and dorsal CS (t(15) = 2.19, p = 0.04) (Figure 42, Table 11, Table 12).

In the alpha band, in the left hemisphere we reported strong significant coherence between pIPS and aIns (t(15) = 3.41, p = 0.003), PT and aIns (t(15) = 3.19, p = 0.006) and between dorsal CS and Cing (t(15) = 3.17, p = 0.006) (Figure 42, Table 11 and Table 12).

Considering the beta band, we found strong significant coherence between aIPS and Cing (t(15) = 3.15, p = 0.006), in the right hemisphere (Figure 42, Table 9, Table 10). In the left hemisphere we reported significant coupling between HG and ventral CS (t(15)=, p=), aIPS and dorsal CS (t(15) = 2.82, p = 0.01), and between aIPS and mSTS-STG (t(15) = 2.93, p = 0.01 (Figure 41, Table 11, Table 12).

In the high gamma frequency band, in the right hemisphere strong significant coherences were found between PT and pIPS (t(15) = 3.03, p = 0.008), between ventral CS and pIPS (t(15) = 3.35, p = 0.004), and between ventral CS and aIPS (t(15) = 2.81, p = 0.01) (Figure 42, Table 9, Table 10). In the left hemisphere, we found significant coherence between PT and aIns (t(15) = 3.41, p = 0.003), PT and Cing (t(15) = 2.64, p = 0.01) and between aIns and ventral CS (t(15) = 2.89, p = 0.01) (Figure 42, Table 11, Table 12).

4.4.2.4 Relation between coherence and behaviour

In order to test whether the measured coherence reflects some aspect of behavioural performance, we computed two Pearson correlation analyses: one between coherence and performance accuracy, the other between coherence and confidence ratings expressed in the sound localisation task.

For each participant, we divided raw localisation error and confidence ratings, expressed for each trial, in quartiles. The first quartile grouped trials with low Accuracy/Confidence; the second trials with medium low Accuracy/Confidence; the third trials with medium high Accuracy/Confidence; the fourth trials with high Accuracy/Confidence. Next, we computed coherence between the data within each cluster, following the same procedure we adopted for the previous analysis of coherence. As last step, we investigated the distribution of the obtained values of coherence as a function of accuracy/confidence level.

First of all, we inspected possible correlations between those regions that exhibited the strongest significant results (p < 0.01) from the coherence analysis. In particular, we focused, in the high gamma frequency band, on the coherence involving the parietal cortex. Considering the interaction between posterior IPS and planum temporale, we did not find any significant correlation between accuracy levels and coherence (r = -0.028, p=0.826), nor for the relation between degrees of confidence ratings and coherence (r = -0.028, p = 0.824). Comparable results emerged when considering the relation between posterior IPS and Central CS: neither the correlation between accuracy and coherence (r = -0.014, p = 0.941) nor the correlation between confidence and coherence (r = -0.093, p = 0.46) reached significance. In an exploratory manner, we investigated also the correlations involving the pairs with a comparable significant level of coherence (p<0.01) in all other frequency bands. Again, all correlations failed to reach significance (all p > 0.4), for both accuracy and confidence.

4.5 Discussion

The present work was designed to study the dynamics of the cortical network subtending active sound localisation, by showing how this network unfolds in time and by studying the connectivity between its nodes. To this aim we created a novel setup that allowed the presentation of real sounds in external space in MEG, and collected behavioural and neural data while participants performed an active sound localisation task. We found that active sound localisation is supported by a wide and bilateral cortical network, mainly regions within the dorsal auditory pathway for sound processing. This network starts as early as 40 ms in auditory cortices, but already at 100-125 ms involves regions across all brain lobes. Functional connectivity analysis also revealed significant cortical coupling between different nodes of this network, from associative auditory regions to parietal and frontal areas.

4.5.1 Real sounds in external space in MEG

The first innovative element of our study is the design of a stimulation setting completely non-ferromagnetic, which allowed sound stimuli delivery in external space. We built a semicircular array of plastic tubes, in which we injected pressured air exploiting a pneumatic device, thus creating real spatialized sounds (50 ms air puff). Previous studies either used
one of two common practices in order to investigate spatial hearing in neuroimaging paradigms. A first solution has exploited virtual sounds with manipulated ILDs and ITDs, delivered through MEG compatible headphones in the shielded room (Brunetti et al., 2005; Régis Trapeau & Schönwiesner, 2018; Trapeau & Schönwiesner, 2015). An alternative strategy, more ecological and optimised for each individual, recorded directly in the ear-canal of each individual the signal generated by sounds coming from different position outside the shielded room. Then, for each individual, the specific sounds were re-presented in the MEG cabinet, through the compatible headphones. In this way, the specific spectral cues arising from the particular configuration of the outer ear of each participant are highly preserved (Battal et al., 2019; Pavani, Macaluso, Warren, Driver, & Griffiths, 2002).

The present work is, to the best of our knowledge, the first MEG study using real sound in external space, in a sound localisation paradigm. Our participants listened directly to the sounds coming from different position in the (also visible) external space. We believe the acoustic context inside the MEG shielded room should be considered as an altered – or at the very least atypical – listening condition. The narrow dimension of the room, with a consistent degree of reverberation, together with the fact that participants head was almost entirely inside the MEG helmet, led to an altered listening experience, which cannot be considered entirely comparable with the typical binaural listening. Therefore, as a first step, we investigated whether participants were able to perceive the spatial separation between the sounds delivered from different positions. Note that we used six real stimulation position, covering the sources in order to increase task difficulty and, consequently, error variability. Moreover, our setting spanned a range of possible positions from -25° to +25°, a very narrow portion of the frontal horizontal field. Behavioural results showed that participants were able

to localise the sounds along all the stimulation space, albeit with detectable amount of errors. In particular, our experimental sample showed a strong localisation bias towards the centre, with higher variability for the most extreme positions. These results are compatible with the altered hearing condition in which participants were immerse, and they could be also related to other documented altered hearing conditions. For instance, during simulated monaural listening (one ear-plugged), participants usually exhibit a localisation bias towards the hearing ear, that is, in almost the cases, a bias towards the centre (Musicant & Butler, 1984; Rabini et al., 2019). Nonetheless, this results are compatible with the notion that humans are more precise in localising sounds in the central median portion of space, in horizontal plane (Dingle, Hall, & Phillips, 2010). Taken together, the results on the localisation task outlined the effectiveness of our experimental setting as a viable mean for running scientific experiments on spatial hearing using MEG.

As in the second experiment of this thesis (Study 2), we again asked participants to rate their spatial certainty on sound position, after each localisation response. The results point to similar effects to those found when testing participants under simulated monaural listening (Study 2). The different degrees of localisation accuracy were related to distinct level of subjective spatial certainty, showing that accuracy and confidence could dissociate also in this study. Moreover, similar to Study 2, subjective confidence on sound position increased as a function of time (experimental blocks), whereas localisation accuracy remained almost stable across the experiment. Notably, while with an ear plugged (Study 2) participants immediately recognised the altered acoustic situation in which they were tested, in the MEG room this effect was not so evident. The increasing confidence on sound position in both experiments might thus suggest that subjective certainty on sound position could be

related to task familiarisation, rather than awareness of the atypical listening condition per se. Given that this variable is still under-investigated in spatial hearing we could only speculate on its meaning. However, this study constituted a further attempt to investigate the subjective experience of the perceptual outcome of our auditory system, in spatial hearing.

4.5.2 Early activation of the cortical network for active sound localisation

Most importantly, MEG data recordings during the localisation task allowed us to observe the brain "in action", while engaged in an active auditory spatial task with real stimuli in external space. Neuromagnetic evoked activity was observed as early as 40 ms after stimulus onset in auditory cortices, with the highest and most consistent peak at about 100 ms, as reported in studies on non-human primates (Mazzoni, Bracewell, Barash, & Andersen, 1996) and humans (Burtthompson & Mason, 1996; Spierer, Bellmann-Thiran, Maeder, Murray, & Clarke, 2009; Spierer, Murray, Tardif, & Clarke, 2008). This predominantly evoked response, with a similar time course, was found in different sub regions of the primary and associative auditory cortex and parietal cortex. We reported also consistent foci of activation in the cortical regions of the central sulcus, the posterior cingulate cortex and the parietaloccipital sulcus. The right inferior frontal gyrus and the left insula further exhibited a consistent auditory evoked response. Two other visible peaks emerged at about 200ms and 300 ms after stimulus onset, with lasting induced response until the end of the epochs, when participants were allowed to respond.

In the auditory cortices, the first hub of the cortical network involved in spatial hearing, we recorder source activity from the primary sensory and associative cortices, namely the Heschl's gyrus, the superior temporal gyrus and sulcus, and the planum temporale. In particular, we have been able to show a propagation of source activity from the HG to the planum temporale, as a function of time. This difference was visible already at 200 ms post stimulation. The critical role of the auditory cortices in spatial hearing has been first shown by studies reporting impaired sound localisation performances after lesions of the auditory cortex in animals (Jenkis and Merzenich, 1984; Kavanagh and Kelly, 1987; Malhotra et al, 2004) and humans (Sanchez-Longo and Forster, 1958; Klingon and Bontecou, 1966; Zatorre and Penhune, 2001; Zimmer, Lewald, and Karnath, 2003).

Although it is not the object of our experimental question, is worth to mention that several models for auditory spatial coding has been proposed in neurophysiological and psychophysical studies in humans (Middlebrooks, 2014), ranging from a two-channel representation (Salminen, Tiitinen, Miettinen, Alku, & May, 2009; Salminen, Tiitinen, Yrttiaho, & May, 2010), to a three-channel representation (Briley, Goman, & Summerfield, 2016a; Dingle et al., 2010; Dingle, Hall, & Phillips, 2012, 2013) of acoustic space in auditory cortices. The two-channel model postulates that spatial information in auditory cortex is based on a population rate code knows as the hemifield code (Phillips, 2008; Salminen, May, Alku, & Tiitinen, 2009; Salminen, Tiitinen, et al., 2009; Spierer, Bellmann-Thiran, Maeder, Murray, & Clarke, 2009b), both in animals (McAlpine, 2005; Stecker, Harrington, & Middlebrooks, 2005; Werner-Reiss & Groh, 2008) and humans (Briley, Kitterick, & Summerfield, 2013; Derey, Valente, De Gelder, & Formisano, 2016; Magezi & Krumbholz, 2010; Salminen, Tiitinen, & May, 2012). Accordingly, neurons in auditory cortex are tuned to broad portions of space, identifiable along the horizontal dimension (Salminen, Tiitinen, et al., 2009). Specifically, auditory cortices in both hemisphere comprise different population

of neurons responding preferentially to the left and to the right side of the space, with a bias toward the contralateral stimulation (Briley, Goman, & Summerfield, 2016b). For instance, Salminen and colleagues (2009) implemented an MEG adaptation paradigm, in order to assess neural cortical tuning for spatialized sounds. When probe and adaptor were located in the same hemifield, the amplitude of N1m component was significantly reduced. The three-channel model offers an alternative solution. Accordingly, a third population of neurons, tuned to azimuthal space around the midline, is present in bilateral auditory cortex (Briley et al., 2016a; Dingle et al., 2010).

Finally, spatial tuning of auditory cortex seems to vary as a function of task-specificity, with a higher sharpening during explicit sound localisation task than during idle listening (Lee & Middlebrooks, 2011). The bilateral spot identified as the planum temporale belong to the well-known auditory dorsal pathway, and it has been frequently reported in studies of requiring spatial processing of sounds (Arnott et al., 2004; Battal et al., 2019; van der Heijden, Rauschecker, et al., 2019).

The auditory spatial network further comprise the parietal cortex (van der Heijden, Rauschecker, et al., 2019), whose critical role in sound localisation has been reported starting from lesion studies, with damaged dorsal auditory regions (Clarke et al., 2000; Bellman et al., 2001). Here we reported activation in the inferior and superior parietal lobules, bilaterally, and specifically in the intraparietal sulcus. Interestingly, two distinct foci emerged and seemed to have a slightly different time course in term on response amplitude. We found an early consistent activation of the posterior part of the intraparietal sulcus, followed by propagation of the source activity towards a more anterior part. Parietal cortex has been usually detected in auditory spatial tasks, although with less consistency during passive listening (Zatorre, 2002). Our results confirm and expand previous findings investigating the role of the parietal cortex in this network (Alain, He, & Grady, 2008; Alain, 2008), by suggesting that different partitions of the IPS could intervene in different phases of the task. In particular, Alain and colleagues (2010) showed a dissociation between response-related and memory-related activity in the inferior parietal cortex, which was distinguished in a posterior and anterior localisation of source activity. We capture a similar anterior-posterior shift in the IPS response, which may reflect the design of our localisation task. Participants listened to single spatialized sound in each trial, but were allowed to respond only after 2 seconds from stimulus offset – a time window in which they had to keep sound position in memory. It thus could be suggested that the different loci found in the intraparietal sulcus could reflect different stages of spatial processing, from posterior IPS (stimulus encoding) to anterior IPS (stimulus maintenance) (see also Proskovec, Wiesman, Heinrichs-Graham, & Wilson, 2018).

Somewhat unexpectedly, we were not able to fully capture the contribution of dIPFC in sound localisation. Although previous investigations have highlighted the contribution of this frontal brain region in auditory spatial tasks (Arnott & Alain, 2011; Arnott et al., 2004) we identified reliable activation only in the right IFG, which is usually associated with stimulus identity processing, belonging to the ventral stream (Bushara et al., 1999). Yet, given that we did not have a control condition for this task, it is possible that its role can be associated to the complex processing of the sound, irrespective of its spatial attributes.

Intriguingly, the cortical network we revealed included well-localised regions within the central sulcus-gyrus bilaterally. Our hypothesis is that this activation might reflect cortical processing associated to head-movements. Using an isometric head-orientation task in fMRI,

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Prudente and co-workers (2015) refined previous findings on head-movements identifying the cortical regions associated to muscular activity of the neck regions, specifying its location in the motor homunculus. Those regions partially overlap to those found in the present study, suggesting that we might have captured a fundamental component of the sound localisation process related to head-movement (or programmed head-movement). Moreover, as evidenced by the coherence analysis described in the next section, we reported important connectivity between this nodes and parietal/ posterior auditory cortices. Several studies investigated the role of head movement in spatial hearing (Brimijoin & Akeroyd, 2012; Brimijoin et al., 2013; Wallach, 1940; Wightman & Kistler, 1999), with however few effective attempts with neuroimaging techniques. The isometric approach could potentially be an optimal solution, and our findings suggest that this could be a promising way to investigate the role of head-related movements in sound localisation.

We reported also source activity in the left anterior insula, which has been previously reported in earlier studies (Alain, McDonald, Kovacevic, & McIntosh, 2009; Arnott et al., 2004; Du et al., 2015), but whose role is far to be ascertained.

Strong activation has further been reported in the bilateral posterior cingulate cortex, a findings which not entirely unexpected, giving the crucial role of this cortical region in aspects related to decision conflicts (Botvinick, 2007) (emphasised in our protocol by increased difficulty of the task related to the altered hearing condition). Similar activation had been reported in a sound localisation paradigm investigating spatial hearing in blind humans (van der Heijden, Formisano, et al., 2019). The authors suggested that, in the typical population, the activation of the posterior cingulate cortex might be linked to visuo-spatial processing of sound location.

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4.5.3 Connectivity within the network, preliminary findings

To further characterise the dynamics of this cortical network, we implemented a preliminary functional connectivity analysis of spectral coherence. In the right hemisphere, considering the core auditory cortex (Heschl's gyrus), we found significant coherence with the cingulate cortex (theta and low gamma bands) and with the dorsal CS (alpha and high gamma bands). The planum temporale was functionally coupled with the dorsal and ventral regions of CS (theta and beta bands, respectively) and, notably, with the pIPS (high gamma band). Source activity in posterior IPS was coupled with the middle and posterior part of the STS-STG (high gamma and beta bands, respectively), whereas the anterior part of the IPS was significantly connected to the IFG and cingulate cortex (beta band), as well as with the middle STS-STG and the dorsal CS (high gamma band). Interestingly, in the left hemisphere, we found several significant connectivity pattern involving the anterior insula, and in particular the coherence with anterior and posterior IPS in the alpha band.

These connectivity results – encompassing primarily PT, pIPS, aIPS, STS and Cing in the right hemisphere – appear to capture well the dorsal network for sound localisation and, possibly, the indirect route for feedback modulation postulated by van der Heijden and colleagues (2019). Yet, our findings failed to highlight strong connectivity with the frontal regions, which were limited to the significant coherence found between IFG and aIPS (beta band) and between IFG and cingulate cortex (theta band). Instead, connectivity results revealed a predominant role of the central sulcus in his ventral and dorsal parts, with significant coherence pattern in different frequency bands. For example, in the high gamma frequency band, in the right hemisphere, dorsal CS was significantly coupled with HG,

mSTS-STG and aIPS, while the ventral CS showed significant coherence with anterior and posterior IPS.

Taken together, the connectivity results outlined a connected network mainly in the high gamma frequency, with predominant role of the parietal cortex and the posterior auditory cortex, two nodes of the core auditory spatial network. Given that connectivity results emerged after computing a difference between short pre-stimulus baseline (200 ms) and short post stimulus period of induced activity (500 ms), we cannot exclude that the limited coherence in low frequency bands (theta, alpha) could be contaminated by the short duration of the time intervals we choose for the analyses. However, results on high gamma band are compatible with studies investigating auditory spatial working memory (Kaiser, Heidegger, Wibral, Altmann, & Lutzenberger, 2008; Kaiser, Rieder, Abel, Peters, & Bledowski, 2017; Lutzenberger, Ripper, Busse, Birbaumer, & Kaiser, 2002), and with studies highlighting other oscillatory dynamics in specific frequency band, during auditory spatial working memory tasks (Kaiser, 2015; Kaiser, Heidegger, Wibral, Altmann, & Lutzenberger, 2007; Proskovec et al., 2018). Therefore, the connectivity analysis of the present study should be deepen in order to compare the dynamics of the cortical network identified in the present study with that of the aforementioned researches.

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4.5.4 Conclusions

In the present study, we showed the cortical network subtending active sound localisation, adopting a novel approach, which combined the use of real sounds in external space with the high temporal and spatial resolution of MEG.

Although some aspects of our data analysis are, at this stage, still preliminary, several observations confirms previous literature on spatial hearing (e.g. activation of the dorsal auditory pathway from the early stages of acoustic processing) and are here enriched by description of the dynamics of the network and by connectivity measures showing cortical coupling between core nodes.

Moreover, MEG data analysis revealed source activation in cortical regions that remained partially neglected. In particular, the central sulcus/precentral gyrus which could reflect the contribution of head movements (or programmed head movements) in the process of sound localisation, being also actively involved in the network as shown by the connectivity analysis. Secondly, the role of visual information suggested by activation of multimodal areas such as the superior temporal sulcus and the parieto-occipital sulcus. These results show that the auditory network can rapidly extend to visual and multimodal cortical regions if the task requires this processing. In addition, the role of the cingulate cortex, which might highlight a process of decisional conflict that was certainly present in our task of sound localisation in altered hearing condition.

Finally, our novel approach might be suitable for investigating new questions related to head movements or the role of visual information in spatial hearing. Again, the flexibility of our stimulation setting (it is possible to change both the horizontal and vertical position of the sources depending on the experimental paradigm) might be useful to test the different models proposed for the cortical coding of sound position in the auditory cortex. Accordingly, models of two-channels (Stecker et al., 2005) or three-channels (Dingle et al., 2010, 2012) coding of azimuth sound position might be easily proved in a more ecological context with real sounds in external space.

Chapter 5

General Conclusions

The present thesis explored the field of acoustic space perception investigating the perceptual process of sound localisation in different aspects. In particular, I studied this topic under typical and altered (one ear-plugged) listening conditions, exploiting behavioural and neuroimaging techniques.

The first study (Chapter 2) describes a first attempt to investigate the reciprocal relations between egocentric and allocentric coding of sounds in spatial hearing. I tested the hypothesis that these two spatial representations can interact by exploiting a learning paradigm on sound localisation. In particular, I examined if a behavioural training based on allocentric coding of sound could influence subsequent egocentric sound coding. Results showed that after four consecutive days of audio-visual training (in simulated monaural hearing condition), trained groups improved in egocentric spatial coding of sounds specifically in the azimuth space ipsilateral to the ear-plug. This performance change was comparable irrespective of whether participants performed the training in an egocentric or allocentric reference frame. Although comparable improvements emerged also in a group of subjects that did not perform any training procedure, changes in this group were qualitatively different from that of trained groups. These results indicate that the auditory system can rapidly adapt to altered hearing conditions in tasks of sound localisation, possibly reweighting the contribution of the available auditory cues (Van Wanrooij & Van Opstal, 2007). The present findings further indicate the implementation of audio-visual paradigm on sound localisation could be a suitable method to study the potential interactions between egocentric and allocentric coding of sounds.

Previous works on adaptation to altered spatial hearing, exploited behavioural training paradigms that only focused on egocentric sound coding (Mendonça, 2014). In this respect, the innovative approach introduced in Study 1 could prompt future research focused on more complex representation of sounds, namely allocentric coding. By studying to what extent training procedures based on coding sounds in one reference frame (e.g., allocentric) could transfer to spatial coding in another frame of reference (e.g., egocentric) could inform

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about the reciprocal interactions occurring between these two spatial coding. Interestingly, results from a parallel line of investigation developed in our lab suggest a possible asymmetry in the relations of these two reference frames in spatial hearing (Valzolgher, Campus, Rabini, Gori & Pavani, in preparation). Participants were tested in a task of single sound localisation (egocentric) and tasks requiring allocentric coding of sounds (e.g., spatial auditory bisection task), before and after 3 days of behavioural training on sound localisation performed in egocentric frame of reference. While in Study 1 of the present thesis the effects of an allocentric training percolated to the subsequent egocentric task, in this other study the effects of the egocentric training remained confined to the egocentric task. None of the allocentric tasks improved, suggesting a possible dissociation between the effects of training based on egocentric vs. allocentric coding of sounds in ameliorating the respective spatial processing. Proving that training on sound localisation performed in a specific reference frame can have broader vs. selective effects on spatial hearing, could guide the implementation of training paradigms in applied settings (e.g., adaptation to non-individualised HRTFs) or clinical settings (e.g., learning to localise sounds with bilateral hearing aids or cochlear implants).

The second study (Chapter 3) constitutes a first attempt to link the perceptual processes of sound localisation with its cognitive outcome for awareness, which is the subjective (and conscious) certainty on sound position. More specifically, I studied the relation between objective sound localisation accuracy and the subjective certainty on sound position under normal and altered hearing condition (simulated monaural listening). I found that the explicit subjective certainty about sound position varied as a function of listening condition (binaural vs. simulated monaural). In particular, under altered hearing, confidence

on sound location decreased compared to binaural condition and it dissociated from localisation accuracy. Moreover, confidence increased as a function of time and appeared to be related to the perceived position of the sounds. In particular, confidence – but not accuracy – increased as a function of time during the experiment. (Convergent findings in this direction emerged also in Study 3). These results suggest that in altered hearing conditions, components related to both the familiarisation with the task and familiarisation with the listening condition might be taken into account when interpreting the development of confidence rating on sound position over time. Moreover, these results indicate that, especially in altered hearing conditions, localisation performance and subjective experience of sound position can dissociate. This shed light on a different, phenomenological, aspect of sound localisation which remained largely overlooked until recently.

Subjective certainty about sound location has been largely neglected in the literature on sound localisation, despite the potential contribution of this variable in guiding human behaviour. Our investigation started the experimental research in this direction, suggesting future applications focusing on the relation between confidence on sound position and the relative decision-related behaviour. Findings of our study further highlight a complex relation between perceptual performance and subjective certainty on sound position under altered hearing, which in almost the cases dissociated: confidence on sound localisation does not predict the level of accuracy of sound localisation performance. Note that this phenomenological aspect has never been investigated in clinical populations with hearing impairment; it would be interesting to examine whether different relations between objective performance and subjective confidence on sound position between objective performance and subjective confidence on sound position between objective performance and subjective experience on sound location emerge in these atypical contexts. In this regard, studying the level of subjective confidence on sound position before and after a training paradigm on sound localisation could further inform about the significance of this index to signal re-learning of correspondences between auditory cues and space. A speculative hypothesis is that confidence on sound position might reflect the strength of the association between auditory cues and coordinates in external space, in specific listening conditions.

The third study (Chapter 4) examined the dynamics of the cortical network involved in active sound localisation. This final study exploited the spatio-temporal resolution of MEG to show a broad and connected cortical network subtending active sound localisation. We reported source activation in the classical auditory dorsal stream encompassing the core and posterior auditory cortex, the planum temporale, the intraparietal sulcus and the right inferior frontal gyrus. Other regions of interest – less expected but in hindsight of great interest – emerged as early as 100 ms after stimulus onset, comprising the central sulcus / precentral gyrus, the cingulate cortex, the parietal-occipital sulcus and the left anterior insula. Coherence analysis further revealed that the intraparietal sulcus and the central sulcus are particularly connected to a consistent part of the cortical network highlighted. These results indicate that active sound localisation is supported by a widespread network identifiable along the dorsal auditory stream, which also comprises other regions such as the central sulcus/precentral gyrus, which appears to play a pivotal role in this complex process.

Our experimental design and the innovative use of a completely non-ferromagnetic setting in the shielded room, open to the possibility to study spatial hearing in a more ecological manner, while also exploiting neuroimaging techniques such as MEG. For instance, our setting and the results of our study will allow to examine the role of the motor

component related to planned (but not executed) head-movements in the perceptual process of sound localisation. Moreover, relation between egocentric and allocentric coding of sounds at cortical level could be investigated with the present setting, exploiting the presence of multiple sound-sources and their customisable manipulation. In this regard, a direct link between study 1 and study 3 could be pursued in future researches. As a final note, the connectivity approach and the presentation of real sounds could be also applied to the study of adaptation to altered hearing condition. For instance, differences in connectivity pattern between a pre-training and post-training period could be captured with the setting ad experimental approach adopted in our MEG study.

5.1 The Big Picture

In the present thesis I investigated the process of sound localisation in order to explore the human ability of perceiving the surrounding acoustic space. Although sound localisation is frequently investigated by a fine-grained psychoacoustic perspective, the studies developed in our project are grounded on a cognitive vision of this auditory perceptual process. Taken together, the three studies I have presented in this thesis highlight the complexity and multi-level nature of acoustic space perception, pointing to complementary aspects of this cognitive process. In this multi-level perspective can be read the present thesis in its entirety, with each study that fits into a specific level of representation of the perceived sound source position. In all studies spatial hearing has been investigated by means of sound localisation tasks.

At the *first level*, the MEG study allowed to shed light into the spatio-temporal dynamics of the cortical network subtending single sound localisation, mainly answering the

question on how our brain processes single sound location involving complex cortical interacting networks. In other terms, we looked at the egocentric representation of sounds, at cortical level. This study revealed the brain in action, replicating and expanding previous neuroimaging findings on the cortical regions involved during sound localisation (van der Heijden, Rauschecker, et al., 2019). I confirmed the existence of an auditory dorsal network involved in spatial hearing. In addition, I showed that cortical areas adjacent to central sulcus (e.g., pre-central cortex) may be pivotal, both in term of evoked responses and connectivity patterns. The first level of spatial representation of auditory stimuli thus highlighted the dynamics and the sensorimotor nature of spatial coding of sounds at the cortical level, further suggesting the presence of visual and multisensory (audio-visual) influences on this cognitive process (see cortical activation in posterior cingulate cortex, parietal-occipital sulcus, but also posterior STS). In this regard, the aforementioned elements need to be taken into consideration in a functional model of sound localisation, as the one outlined in Chapter 1 by our group.

At the *second level*, I moved from neural to cognitive representations of sounds. The *first level* allowed to investigate how our brain processes single sound location with respect to our own position, in an egocentric frame of reference. However, in the complex and multi-object environment of everyday life, sounds position could be defined also with respect to other objects, in an allocentric spatial representation. Consequently, we expanded our perspective to examine the different spatial representation of auditory stimuli, focusing in particular on the relation between egocentric and allocentric coding of sounds (Study 1). This higher-level representation has been scarcely investigated, yet several interesting cues arose also from our behavioural study, which suggested that a possible influence of allocentric

coding on egocentric sound source representation might exist. Results from Study 1 together with additional findings from our laboratory suggest that a hierarchical organisation of spatial representations of sound could explain a possible dissociation between the reciprocal effects of egocentric and allocentric coding of sounds: a training based on allocentric spatial coding appears to have an effect on egocentric representation of sounds (Study 1), but not vice versa (Valzolgher et al., in preparation).

At the *third level*, I moved from cognitive to metacognitive spatial representation, formulating novel questions about the quality of the perceived sound source position (awareness of the spatial percept). I investigated the degree of confidence explicitly reported by participants about the perceived location of the sounds. Study 2 and Study 3 allowed to show that the explicit degree of confidence on sound position change of a function of hearing condition. In addition, they showed that when participants were accurate in localising sound, they were not necessary confident about their perceive position, and vice versa. This phenomenological aspect has been largely neglected until now (but see questionnaires about spatial quality of sounds in virtual environments, Lindau et al., 2014), even though it could constitute a critical aspect to consider when investigating human behaviour in natural environment. In this respect, it is important to emphasise that whenever we do not have environmental feedback about our own performance, we usually rely on the confidence we have in our perception to take subsequent decisions and/or adjust our behaviour. In this sense, investigating the degree of confidence on perceived sound source position might capture a crucial aspect of spatial representation of sounds in external space. An intriguingly hypothesis, is that perceived confidence on sound position, in absence of external feedback, could constitute an internal, implicit, feedback allowing the consolidation or the modification of specific sound-space correspondences (spatial maps). In this sense, we could potentially consider subjective certainty as an internal brain signal informing about the solidity of the actual spatial mapping. As such, we should measure it at cortical level, and the connectivity approach could be an interesting tool to accomplish this goal. According to this hypothesis, a wrong correspondence between auditory cues and space could be also consolidated, leading however to high ratings of perceived confidence on sound position. On the other hand, low confidence ratings on sound position would suggest an unstable and less defined correspondence between acoustic cues and coordinates in external space. Future studies in this direction have the potential to inform and refine the existing models of adaptation to altered hearing condition, including the variable of spatial confidence in the dynamic process of acoustic space re-learning.

In summary, I tackled the topic of acoustic space perception from different angles, investigating sound localisation at distinct cognitive levels, from the cortical representation of sound source coding, to the complexity of the cognitive representation of sounds in different reference frames, to the conscious strength of this representation. One of the major contributions of the present thesis is the multi-level approach to spatial hearing outlined in previous sections, which I believe necessary when investigating perceptual processes in a neuro-cognitive perspective.

5.2 Outside the laboratory

The present thesis highlighted the potential of exploiting behavioural training-based paradigm to shed light on human cognition. We exploited it in Study 1, but it is perfectly

suited to be used in future advance of Study 2 and Study 3. This approach grounds on one of the most fascinating features of human brain, which is plasticity. Our brain is able to recalibrate itself due to experience and this is particularly evident after sensory impairment. Investigating human cognition and perception exploiting this natural feature could be extremely powerful both for basic research and for clinical application. Simulation of sensory impairment (as we did with simulated monaural listening in Study 1) as a model to study specific perceptual processes, allows the development of basic cognitive and neuroscientific research, whereas the application of the knowledge gained from basic research allows the implementation of rehabilitation procedure in clinical population. The present thesis had the appealing aim to set the path to move in this (long and difficult) direction.

Again, each study points to different clinical and applicative scenarios. At the *first level*, Study 3 suggests that sound localisation is implemented in the brain by an intrinsic interplay between auditory, sensorimotor and multisensory regions. The connectivity approach proposed in our study could reveal important network alterations in people suffering from hearing impairment or hearing degradation, such as elderly individuals, pointing to the relevance of cortical coupling in constructing our sense of auditory space. Moreover, investigating the effects of behavioural trainings on the cortical network subtending spatial coding of sounds could potentially highlight changes in functional connectivity between cortical regions pivotal for this perceptual and cognitive process.

At the *second level*, the investigation of different cognitive representations of auditory space has been scarcely investigated in hearing-impaired population (e.g., CI users, elderly, people with hearing aids). Moreover, Study 1 suggests that a behavioural training based on allocentric coding of sound could be effective in improving subsequent egocentric coding. If

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confirmed, these results will open a new methodological approach, which exploits the more complex and hierarchically higher allocentric representation in paradigms of accommodation to altered auditory cues.

Finally, at the *third level*, Study 2 suggests that human awareness of spatial representation of sounds is highly variable, especially after auditory cues alteration. However, the metacognitive representation of sound source position, indexed by explicit confidence has never been investigated in people with altered hearing. Furthermore, the study of this phenomenological aspect both in hearing impaired population and within paradigm of behavioural trainings aiming to improve auditory localisation abilities could shed light on the nature of this metacognitive variable, and its role in the construction and consolidation of new sound-space correspondences (auditory spatial maps).

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