Auditory Localization and the Brainstem

Master thesis in Neuropsychology

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Abstract

The way sound is perceived and located in our brain varies due to various reasons. These would be the differences in the intensity or the time of the incoming sound stimuli, or due to personal differences of the listener. Previous research has proven the role of our brainstem in sound localization. The need to distinguish though whether the brainstem is the sole factor of this localization or if others, like attention, coexist, is highlighted. This review will analyze the theoretical base behind our sound perception, and its connection to our brainstem. Furthermore, it will propose in detail future scientific research which in turn would contribute greatly not only to the experimental but also to the clinical field, focusing on people with mild hearing disabilities.

Keywords:
brainstem, sound localization, mild hearing problems

Theoretical background

Sound localization refers to our ability to distinguish from which direction a sound is originating. In everyday life, finding the direction of the sound source is essential. Sound localization can help an animal in catching its prey or can aid a person in orienting to a talker of interest at a crowded party. A person's safe interaction in an environment can be affected when there is a low ability of sound localization. Lack of accurate sound localization can influence safe movement in public spaces, as, if a person cannot tell the direction of an approaching vehicle, with or without an accompanying horn or siren, it may lead to fatal consequences. But how does sound localization actually work? The idea is that a sound source coming from the right side of the head will be presented to have more intensity in the right ear. But, as the head stands in between the two ears, an acoustical or 'sound shadow' is cast, creating a difference in the sound intensity between the two ears. A sound coming from the right side of the head, will not have the same level of sound intensity to the right and left ears. The sound will be heard faintly lower to the left ear as the head is in the way.

Differences at the times of arrival (Interaural time difference, ITDs) and the intensity (Interaural level differences, ILDs) of stimuli at the two ears have as an outcome of this acoustical shadow. ITDs and ILDs are used to explain sound location in the horizontal plane. As mentioned above, when a sound is presented from the side of the head, the path from the source to the ear is interrupted by the listener's head (Middlebrooks & Green, 1991). The consequence is an interaural difference in sound pressure level (ILD) as the far ear would be effectively shadowed by the head and body. Furthermore, it leads to a difference between the time that sound enters one ear and the time it enters the other ear (ITD). ILDs change as a function of the position of a sound source relative to the head in the horizontal plane. The patterns of the ILDs are more irregular than interaural time difference (ITD) patterns as ILDs are significantly affected by the geometry of the head, outer ears, and shoulders. On the other hand, ITDs around the interaural axis are nearly spherically symmetric, are much less frequency-dependent, and never exceed values of 700ms or so. Specifically, for low-frequency tones and low-pass noise, both ILD and ITD show similar sensitivities. On the contrary, when high-frequency tones and noise are concerned, ILD can lateralize them, but ITD cannot. The reasons behind this difference in sensitivity are still unclear; a loss of phase-locking in the auditory nerve or a lower-frequency cutoff to the binaural system are two of the possible explanations (Macpherson & Middlebrooks, 2002).

To get more information regarding the meaning of this difference in sound perception, we first need to distinguish where this lateralization of the stimuli is represented in our brain. As Riedel & Kollmeier (2002) explain, it is known from previous neuroanatomical studies that left and right auditory fibers first intersect in the superior olive in the brainstem (Riedel & Kollmeier, 2002). Auditory information travels from the inner ear (cochlea) to the auditory cortex via the inferior colliculus. The latter is responsible for integrated sound localization and for generating the startle response, orienting the body toward relevant stimuli (Driscoll & Tadi, 2021). ILD and ITD are physiologically determined in the medial and lateral superior olives in the brainstem. By receiving inputs from both ears, these two constitute two of the most peripheral sites in the ascending auditory pathway (Tollin, 2003). The medial and lateral superior olives are regarded to be responsible for the initial encoding of ITDs and ILDs, respectively, resulting in spatial representation.

The fact that two mechanisms mediate auditory localization, is suggested because ILD and ITD represent the most important cues for directional hearing and localizing sound sources in the horizontal plane. In 1907, Rayleigh proposed the Duplex Theory which suggests that sounds are localized through a combination of ITDs and ILDs. Rayleigh was using pure tones such as tuning forks or singing flames but could not identify the boundary between low and high frequencies. Therefore, he suggested that this boundary was set at 500 Hz, with the ITD dominated at the low-pass stimuli (128 Hz) and the ILD dominated at the high-pass stimuli (above 500 Hz) (Hartmann et al., 2016). Since then, many attempts have been made in order to identify a boundary for pure tones. Sandel and others in 1955, as well as Mills in 1960, made comparisons of different ITDs and ILDs in the free field, resulting in an estimated boundary of about 1500 Hz (Hartmann et al., 2016). A revised version of Rayleigh's theory proposed by Macpherson and Middlebrooks in 2002, restates that in accordance with the Duplex Theory, a duplex rule applies to noise bands, in which 'the brain relies heavily on ITDs for low-frequency sounds, and ILDs for high-frequency sounds' (Macpherson & Middlebrooks, 2002) This translates into listeners giving high weight to ITD and low weight to ILD for low-pass filtered stimuli and the opposite for high-pass filtered stimuli. For example, when a sound played had a frequency less than 1500Hz the wavelength is greater than the time delay between the ears.

A need for further studies regarding the exact examination of how auditory spatial cues interact with each other and later, how they are processed in the brainstem, is highlighted. A research proposal would be to investigate whether people rely more on ILDs or ITDs when perceiving a sound and whether this ILD-ITD weighting in perception can be predicted by brainstem activity. It is already known that the sum of neuronal activity in the auditory brainstem and midbrain is quantified by the auditory brainstem response, a sound-evoked non-invasively measured electrical potential. The amplitude and latency of wave V (a peak of 5 ms after sound onset) are clinically used to estimate hearing sensitivity. The difference between the sum of the monaural and binaural auditory brainstem responses creates the binaural interaction component of the auditory brainstem response, or the binaural difference potential (Laumen, Ferber, Klump & Tollin, 2016). This binaural difference reflects the inhibition the input from each ear exerts on input from the other ear. The peak of the binaural interaction component curve shows at which ILD or ITD the binaural interaction is maximal, or at which ILD the brainstem thinks the sound is in the middle, centered position. The strongest interaction is typically observed for centered stimuli (0 dB ILD/0 µsec ITD) in the binaural interaction component, with the amplitude decreasing gradually with increasing lateralization (see *Figure 1*). ITD and ILD determine the latency of the most prominent peak of the binaural difference potential DN1.

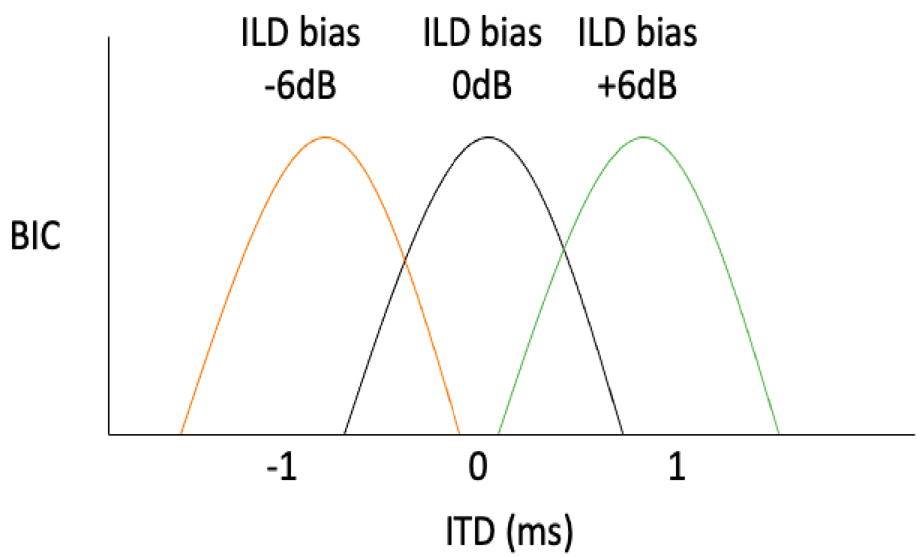

Figure 1: The difference between the sum of the monaural and binaural auditory brainstem responses from the binaural interaction component (BIC) of the auditory brainstem response. Depending on the ILD, the perceived sound location for different ITDs will be biased to the left (orange), right (green), or not biased (black).

Examining this further would lead to more information regarding the dual mechanisms that mediate localization. As explained above, Tollin (2003), proposed the two parallel ascending pathways, the medial and lateral superior olivary complexes, that travel through the brainstem and are believed to be responsible for encoding ITD and ILD (Tollin, 2003). Therefore, the question regarding the importance of the role of the brainstem in this ILD-ITD weighting emerges. Is the brainstem solely responsible during sound localization for encoding its binaural cues? That is to say, is it the main factor in ILD-ITD weighting?

Auditory Brainstem Response

When a stimulus is presented with an ILD and an ITD pointing towards the same location, a strongly lateralized percept is achieved (Schnupp, Nelken & King, 2012). ILD and ITD can act antagonistically, pointing in opposite directions, resulting in more central percepts of a stimulus when the ITD points left and the ILD points right, for example. The time-intensity-trading ratio expresses the weighing of ILD and ITD. The significant differences between antagonistic and synergistic responses imply that ILD and ITD are not processed independently in the brainstem (Riedel & Kollmeier, 2002). According to previous studies, a dynamic interplay between structures at different hierarchical levels, constitutes auditory perception. It is currently unclear which factors play major roles in this interplay (Lehmann & Schönwiesner, 2014). Questions arise regarding the influence of ILD/ITD trading on binaural perception. It is known that selective attention is the main mechanism that allows us to focus on a specific stimulus while filtering out an irrelevant one. But do different acoustic features, such as voice pitch, modulate differently the subcortical region in the brain? Does the direction of attention result in a different modulation of the brainstem? Specifically, what is the connection between behavior and the brainstem when coming to sound localization?

Discussion

A need for further studies is emphasized to shed more light on the role of ILD/ITD trading. The idea of a new study and its possible outcomes, alongside some future discussion points will be shortly presented below.

First, a research proposal would be to investigate whether binaural cue interaction can be explained by low-level interactions in the brainstem. The main hypothesis would be that the brainstem activity in response to sounds with various ILDs and ITDs is the main factor influencing the perceived sound location in the horizontal plane. To test that, two different measures would be needed, but first, an audiogram should be monitored to ensure the participants' healthy hearing capacity. With the use of an audiogram, only participants that score normally for their age group should be allowed to continue with the experiment. Then, the actual experiment would consist of a behavioral task to test how people perceive sound with varying ILD/ITD, and second, an EEG task, to measure the brainstem activity while listening to the same sounds as the behavioral task. If there is too much movement during the experimental process, the participant should also be excluded, as the movement interferes with the sounds coming from our task, therefore resulting in inaccurate EEG measurements. In both the perception and auditory brainstem response tasks, the center of the sound will be perceived when there is a positive bias on ILD, and a negative on ITD and vice versa (see *Figures 1 and 2*). For example, if we have a negative ILD, even if the sound comes from the right, the participants will say that it comes from the left. Therefore, a negative ILD creates a bias that sound is coming from the left, while a positive ILD creates a bias that sound is coming from the right due to the interaction with ITD. If the binaural interactions in the brainstem cannot explain the perceived sound location, other factors are contributing to how people perceive auditory locations. The two tasks are going to be described in more detail.

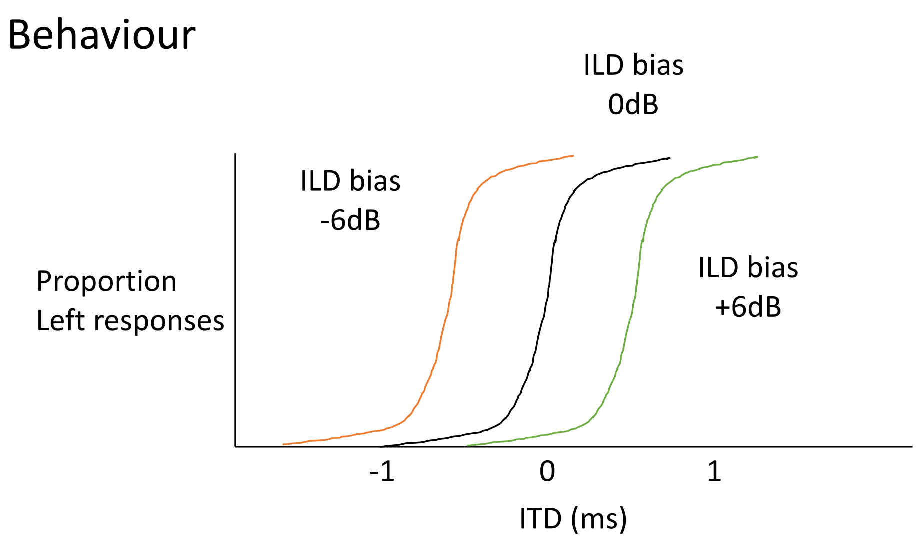

Figure 2. Depending on the ILD, the perceived sound location and proportion of left responses for different ITDs will be biased to the left (orange), right (green), or not biased (black).

Behavioral task

To investigate whether people rely more on ITD or ILD it would be interesting to vary ITDs and ILDs and combine them. ITD cues for sound location are derived from the interaural onset and phase differences. Sounds, consisting of a combination of 9 ITDs and 3 ILDs, will be presented and participants will be asked to indicate on a straight line (with a vertical line marking the center) whether they perceive the sound more to the left or the right. Combinations will be both agonistic, with ILD and ITD acting in the same direction, for example, both having positive values, and antagonistic, with ILD and ITD acting in opposite direction, for example, with ILD having a negative value, while ITD having a positive value. The antagonistic condition is supposed to result in a more centered image (Riedel & Kollmeier, 2002). The combinations of the presented sound would consist of 9 ITDs that would be presented in the timeslots of -1, - 0.6, -0.4, -0.2, 0, 0.2, 0.4, 0.6, and 1 ms, and 3 ILDs that would be presented in the volume of -6, 0 and 6 dB. The sound is going to be displayed through headphones and participants will indicate the perceived sound using a computer mouse (*Figure 3*). This way, an examination of how people trade ITD and ILD information (behavioral task) will be achieved. When there is no ILD bias (ILD = 0 dB), the expectation would be that when ITD has a negative value, participants will say that the sound is coming from the left, even if it is coming from the right ear. For example, when our center point is 0 ms, a negative ITD of -6 ms would create the perception of the sound arriving first on the left ear. On the contrary, when ITD has a positive value, participants would probably report sound coming from the right, although it is coming from the left ear (see *Figure 2*). The behavioral data would need to be fitted afterward with a psychometric function. The steepness of the graphic line is going to reflect the sensitivity to ILD and ITD, and the 50% point reflects the perceived center (PC).

Figure 3. An example of what the participants would see during the ITD task.

EEG task

The next step would be to record brainstem activity in response to the same ITD and ILD combinations using brainstem EEG. One electrode will be placed behind each ear and two electrodes will be placed on the forehead. Participants would be also listening to clicks, presented at 90dB (0 ILD), 84dB, and 96dB, while the EEG is conducted. The binaural difference potential would be analyzed by subtracting the sum of monaural auditory brainstem response wave V amplitudes from the binaural auditory brainstem response wave V amplitudes for each ILD and ITD combination to calculate the binaural interaction component. A peak detection would also be needed with the use of programming software, such as Matlab (see *Figure 4*). The resulting distributions of difference potentials should follow a normal distribution in which the mean reflects the perceived center in the brain stem (see *Figure 1*). After obtaining the results from both tasks we will be able to relate the perceived center obtained using psychophysics (behavioral task) and brainstem EEG.

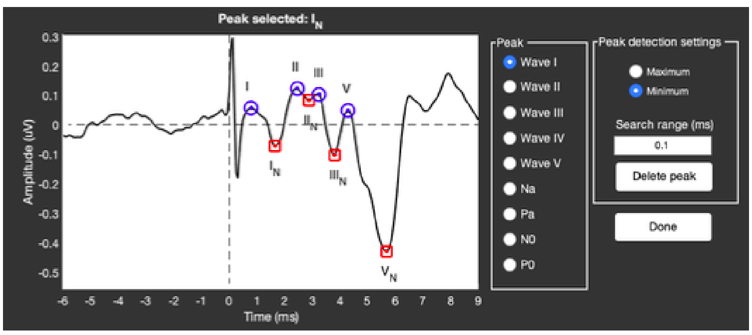

Figure 4. An example of what peak detection looks like.

Data Analysis

For the behavioral task, the proportion of 'perceived to the left of the center' responses will be calculated for each ITD and ILD combination and fitted with a cumulative Gaussian function. From this function, the perceived center (PC, 50% point) will be extracted. Using a one-way Repeated Measures ANOVA with the factor ILD bias and perceived center as a dependent variable we will test whether the perceived center shifts with ILD bias. Peak detection of wave V will be conducted using MATLAB programming. Furthermore, the BIC mean of the two electrode channels and signal-to-noise ratio (SNR) will be calculated. Finally, One-way ANOVA will be conducted to check the means of the differences between the two interventions. Due to the small sample size of this first phase of the study, correlation analysis will not be conducted.

Future outcomes

But what is the exact importance of all these findings, apart from understanding better our hearing system and its biases? A discussion point that derives from the expected results of the experiment described above, would be that if our brainstem is indeed the main factor influencing the perceived sound location in the horizontal plane, this would also shed some light on a better understanding of mild hearing problems. Provided that the behavioral and EEG tasks described above used the same ILDs and ITDs, and the results showed a similar pattern, then the neuroanatomical factor (the brainstem) is the one defining our sound perception and localization. This would result in thinking that behavior does not play the main role when it comes to hearing and that it is stipulated exclusively by the brainstem. Following this, it would be interesting to test how people with mild hearing problems would react to the EEG recording in comparison to normal hearing people. The next step to test this would be to gather a sample of healthy hearing and participants with affected hearing, expose them to the altered sounds, as described above, and measure their brainstem activity using the EEG.

Hearing impairments have a huge impact on an individual's daily life. These impairments could lead to limitations to everyday functions, activities, participation restrictions, or involvement in other social situations (Timmer et al., 2015). Previous research has also indicated a strong association between hearing impairment and daily-life fatigue (Burke & Naylor, 2020). Fatigue can have negative effects psychologically, implicating one's well-being, self-care, safety, cognitive functioning, and productivity. Factors that result in overall reduced quality of life. Similarly, people suffering from tinnitus have reported complaints regarding frequent sleep disturbances, like delayed sleep, morning awakenings, mid-sleep awakenings, as well as morning and chronic fatigue (Alster et al., 1993). Furthermore, its negative development is strongly correlated with stress, anxiety, emotional distress, and dissatisfaction with one's own life (Seydel et al., 2010). Despite that according to World Health Organization (WHO) adults facing mild hearing problems do not experience disability because of their hearing impairment, there is a wide range of negative effects that makes it difficult to accurately describe a patient's needs. A better, more accurate, and fast diagnosis is needed in order to understand each patient's needs and provide them with better, tailored treatment accordingly.

Various outcome measures can be used to assess the impact of mild hearing impairment on an individual. For example, a patient's speech perception is often assessed by speech audiometry, simulating conversation situations in everyday life, or self-report measures. Previous studies have shown a complex relationship between age and hearing ability. Specifically, age has a stronger influence on tasks that involve spatial or temporal processing (Timmer et al., 2015). Nevertheless, due to the heterogeneity of the symptoms and their impact, the current audiometric tools have been proven to be insufficient and insensitive for patients suffering from mild hearing impairments. When assessing hearing aid outcomes in adults with mild hearing impairment, the predicted outcomes are not always effective and sufficiently sensitive, due to their laboratory-based formation (Timmer et al., 2018). All these inconsistencies highlight the need for a more complex auditory function diagnostic test and hearing aid techniques respectively.

Large individual variability is being shown in many aspects when mild hearing impairment is concerned. Therefore, more evidence is needed to apply hearing threshold boundaries and gain a better understanding of the difficulties individuals face in everyday life. Research should aim to understand better the context of the listening environments and provide tasks both to healthy participants and the clinical population, to develop more accurate guidelines for clinicians. Following these thoughts, the proposed research design will firstly shed some light on healthy participants' sound localization and create a better clinical criterion regarding mild hearing problems as well.

For this purpose, a small sample size would be needed, as the first step to check our original hypothesis, before moving to the affected population. A sample of around 50 normal-hearing students, between 18 and 28 years old, could provide sufficient insight into the credibility of the experiment and its prospects. Some exclusion criteria would of course apply. Firstly, as mentioned above, an audiogram is essential in order to test one's eligibility for our study. If a participant scores below the average of their age group, then he or she can no longer participate. Second, participants having a historical or family background of tinnitus or another hearing disorder would be excluded from this first phase of the study, as it is desirable to test only normal hearing people. Lastly, participants with a diagnosis of attention-deficit hyperactive disorder (ADHD) should also be excluded, due to the stillness required for getting accurate results, without any movement and noise interventions. Furthermore, the sounds displayed can be considered quite disturbing for some people, therefore, it is wise to avoid the cause of any uneasiness or inconvenience.

If the original hypothesis is true, the measures are expected to show a similar pattern from both behavioral and EEG tasks. If the first results show indeed these similarities between the two tasks, it would mean that the brainstem is the main factor influencing sound localization. Then, a more elaborate study should be considered including different age groups. Normal hearing, of course, shows a decline due to aging, therefore during the audiogram, each age group is categorized based on the standardized norms, so any age bias should be prevented.

Of course, many ethical aspects of both research ideas should be taken into consideration before and while conducting the actual experiments. First, following the standard research procedure, an information letter should be given in advance, and the experiment should only begin after all participants' questions are answered and a signed informed consent has been given. At the end of the experiment, a debriefing letter should also be provided, to accurately explain the research questions and the methods used. The researcher should also give the contact details needed in case the participants have any further questions after the finish of the experiment. Second, during the audiogram, an indication of hearing loss may appear. Nevertheless, no official diagnosis is to be given at any point in the procedure. The researcher needs to keep in mind that the only use of the audiogram is as an inclusion or exclusion criterion for this study. The researcher is not an audiologist, who could sufficiently interpret the existence of a hearing abnormality. In the case of an abnormal indication, it is wise to advise the participant to visit a professional and get further tested. Then, it should be made clear to the participants from the beginning, that all information will be anonymized in the research and that they are allowed to stop taking part in the experiment at any time, without reasoning. The experiment would not harm the participants in any way. The tasks should be designed carefully, would be all non-invasive, and would not have any physical or mental consequences. Finally, the participants should not be deceived during the experiment and every question should be answered in the end.

Conclusion

To conclude this report, the further study of the role of the brainstem on sound localization would benefit scientific research and our knowledge of how sound is perceived in our lives. Most importantly though, it will lead to a better understanding of how hearing abnormalities should be addressed, in order to provide solutions for the patients. The clinical benefit of this research is highlighted, as well as the urgency to improve patients' life despite the heterogeneity of their situations.

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