Early visual cortex response for sound in expert blind echolocators, but not in early blind non-echolocators

Alessia Tonelli a,b,*, Claudio Campus a, Monica Gori a

a UVIP, Unit for Visually Impaired People, Istituto Italiano di Tecnologia, Genova, Italy
b Department of Translational Research of New Technologies in Medicine and Surgery, University of Pisa, Pisa, Italy

ABSTRACT

Echolocation is a perceptual and navigational skill that can be acquired by some individuals. Regarding blind people, this skill can help them “see” the environment around them via a new form of auditory information based on echoes. Expert human echolocators benefit from using this technique not only in controlled environments but also in their everyday lives. In the current study, we investigate the effect of echolocation on blind people’s auditory spatial abilities at the cortical level. In an auditory spatial bisection task, we tested people who are early blinds and early blind expert echolocators, along with sighted people. Our results showed that there is similar early activation (50–90 ms) in the posterior area of the scalp for both early blind expert echolocators and sighted participants, but not in the early blind group. This activation was related to sound stimulation, and it is contralateral to the position of the sound in space. These findings indicate that echolocation is a good substitute for the visual modality that enables the development of auditory spatial representations when vision is not available.

1. Introduction

Several studies have demonstrated that during human development, vision plays an important role in helping other sensory systems, such as audition, create a homogeneous and coherent representation of space (Gori et al., 2012; Knudsen and Brainard, 1991). However, researchers have not gained consensus regarding what happens to spatial perception abilities when visual modality is absent. Some studies have demonstrated that, despite the absence of vision, blind individuals have enhanced spatial auditory skills (Collignon et al., 2013; Roder et al., 1999). Since blind people rely more on hearing in mapping space and navigating, it is likely that they are able to develop expertise in using audition for spatial representation. This expertise can cause a reorganization at the cortical level resulting in the visual areas being colonized by auditory processing. In agreement with these ideas, it has also been shown that some enhanced skills in blind individuals have been associated with the remaining senses recruiting the visual cortex (Collignon et al., 2009; Striem-Amit and Amedi, 2014; Striem-Amit et al., 2012, 2015; Weeks et al., 2000). For example, the accuracy in auditory localization tasks correlates with the magnitude of one’s visual cortical activation (Gougoux et al., 2005; Voss et al., 2011).

Nonetheless, studies have demonstrated that when blind people are required to locate a sound on the vertical plane (Lewald, 2002; Zwiers et al., 2001) or in auditory spatial bisection tasks (Gori et al., 2014; Vercillo et al., 2017, 2018), their performance is worse than sighted controls. Moreover, congenitally blind people engaging in a complex spatial auditory task do not benefit from recruiting the visual cortex (Campus et al., 2019). This result is because vision can be important for calibrating the other senses to process specific aspects of spatial information. When vision is not available, the remaining senses are not able to develop spatial representation correctly.

Echolocation is the ability to detect silent objects in the environment using self-generated sounds. It is well known in the animal world (Jones, 2004; Yan and Suga, 1996), such as bats or whales; however, little is known about the abilities of humans for echolocation (Kolarik et al., 2014; Thaler and Goodale, 2016). At the behavioral level, it has been demonstrated that, compared to blind no-echolocators, blind echolocators have better performances in navigation tasks (Thaler et al., 2020), and localization (Rice and Feinstein, 1965; Stroffregen and Pittenger, 1995; Teng et al., 2012; Thaler et al., 2011; Wallmeier et al., 2013). Alternatively, at the neural level, researchers have discovered that there is functional recruitment of the visual areas that are specific for echoes (Arnott et al., 2013; Thaler et al., 2011, 2014). Moreover, echolocation can also offer real-life advantages to blind people, such as fostering social inclusion. An online survey has shown that blind echolocators achieve a higher salary and have more mobility in unfamiliar places. This result provides evidence that echolocation may play a role for those with vision loss (Thaler, 2015).

In a recent study, Vercillo et al. (2015) tested the auditory spatial abilities of people who are early blind expert echolocators by having...
them perform a complex spatial auditory task (an auditory spatial bisection task). In this task, participants were asked to listen to three consecutive sounds, and they had to judge whether the second sound was closer in space to the first or the third sound. This type of task to be executed needs two steps: first, the ability to localize in space every single sound; second, the ability to relate sounds among them, allowing the person to construct a spatial metric. Compared to early blind people who are not echolocators (Gori et al., 2014), these early blind expert echolocators performed the spatial task with similar precision to the members of the sighted group. Interestingly, no difference was found among the three groups in a simple localization task respect to the midline. Based on this result, we could hypothesize that the use of echolocation leads to a further reorganization at the cortical level for complex auditory tasks.

The starting point of the present study is to test whether the difference in behavior between early blind expert echolocators and early blind participants, naïve to echolocation, is present at the cortical level.

In two recent studies, Campus et al. (2019, 2017) investigated the cortical processing of people participating in the audio-space bisection task; first, they examine sighted individuals and, subsequently, they considered the congenital blinds. In analyzing the position of the second sound in space, they found a correlation between the performance in the auditory spatial bisection task and the ERPs (Event-Related Potential) response in the posterior region of the scalp contralateral to the position of the sound. This correlation was present early in the processing stage. It appeared in time windows within 50–90 ms from the onset of the second sound. This posterior response and the correlation was not present in early blind individuals.

In the present work, we used the same paradigm as Campus et al. (2019, 2017). During an auditory spatial bisection task, we recorded and compared ERPs and psychophysical responses in groups of early blind expert echolocators (EBEE), early blind (EB) that do not use echolocation in everyday life, and sighted people (S).

We hypothesized that if echolocation has a functional role upon the development of audio-space representations, this should produce an effect on the cortical reorganization of EBEE, resulting in a cortical response in an audio-space bisection similar to the one found in sighted individuals.

2. Materials and methods

2.1. Participants

In total, 10 early blind participants (see Table 1 for clinical details) and five sighted (S - (three females, two males: mean age of 41.8 years, SD = ± 14.6 years) controls were tested. Of the early blind participants, five were EBEE (three females, two males; mean age of 41.6 years, SD = ± 20.43 years) while the other five had no knowledge of how to use echolocation (EB - three females, two males; mean age of 47.6 years, SD = ± 13.74 years). The division between EBEE and the EB was carried out using a qualitative questionnaire. The questionaire helped us to assess how much echolocation participants used in their everyday lives and was administered in a session prior to this experiment. As first question, we asked all participants who are blind, whether they used echolocation, preceded by an explanation of what echolocation was. Afterward, we continued with the rest of the questionaire only for those participants who had answered affirmatively. For further information about the results, see the supplementary materials.

We acknowledge that the sample of echolocators presented in this study is not very large and may not be representative of the general population of the echolocators. To the best of our knowledge, there is only one study that has addressed, even if marginally, the point of representativeness (Thaler, 2013), which estimates the use of echolocation technique by 20%–30% of the blind population. However, this estimate has been extrapolated from anecdotal reports dating back to the 1920s, and to date there are not statistics available. This limitation is due to the peculiar nature of the topic and to the intrinsic difficulty for a robust definition of expert echolocators.

Moreover, our sample size is similar to other studies present in the literature (e.g. Norman and Thaler, 2019; Teng et al., 2012; Vercillo et al., 2015).

All participants reported normal hearing, and they gave written informed consent. The study was approved by the ethics committee of the local health service (Comitato Etico, ASL 3, Genova), and it was conducted in line with the Declaration of Helsinki.

2.2. Stimuli

To deliver the sounds to the participants, we used a set of 23 loudspeakers (width of 7 cm each); these were placed on the horizontal axis at the level of the lower hemi-field. The array of speakers covered a range of ±25° of visual angle (with 0° representing the central speaker, negative values on the left and positive values on the right). All participants sat at a distance of 180 cm from the central loudspeaker.

Each sound was a 500 Hz pure tone that had a duration of 75 ms (60 dB SPL) (Fig. 1).

The temporal interval between the sounds was always 500 ms. The first and the third sounds were always delivered at −25° (left side) and +25° (right side) degrees, respectively. In turn, the second sound could occur from either −4.5° or 4.5° in space (Fig. 1). These values corresponded to approximately 75% of the correct answers for the auditory spatial bisection thresholds that were used in previous studies, which were tested with both sighted and EB participants (Campus et al., 2017; Gori et al., 2014). A total of 120 trials were performed for each position of the second sound (−4.5° or 4.5°).

2.3. Procedure

Participants sat in front of the set-up. During the task, the experimenter asked them to keep their heads in a still position while fixating straight ahead. The task was to listen to three consecutive sounds and to report whether the second sound was more distant to the first or the

Table 1

| Participant | Age at test (y.o.) | Gender | Pathology | Age complete blindness | Braille reading | Mobility skill |
|-------------|-------------------|--------|-----------|------------------------|----------------|---------------|
| #EBEE1      | 53                | M      | Retinopathy of Prematurity | Birth        | Yes             | Good mobility skills |
| #EBEE2      | 29                | F      | Retinopathy of Prematurity | Birth        | Yes             | Good mobility skills |
| #EBEE3      | 26                | M      | Leber’s Amaurosis          | Birth        | Yes             | Good mobility skills |
| #EBEE4      | 27                | F      | Retinopathy of Prematurity | Birth        | Yes             | Good mobility skills |
| #EBEE5      | 72                | F      | Depth damage of vision in both eyes | Birth | Yes | Good mobility skills |
| #EB1        | 32                | F      | Retinopathy of Prematurity | Birth        | Yes             | Good mobility skills |
| #EB2        | 64                | F      | Atrophy of the eyeball    | Birth        | Yes             | Good mobility skills |
| #EB3        | 60                | M      | Fibroplasia retrolentale  | Birth        | Yes             | Good mobility skills |
| #EB4        | 42                | M      | Retinopathy of Prematurity | Birth        | Yes             | Good mobility skills |
| #EB5        | 40                | F      | Congenital cataracts and malformation of the lens | Birth | No | Good mobility skills |
third (Fig. 1). Participants pressed a button to answer. In order to bypass potential spurious neural responses, participants were asked to answer immediately after the last sound. The experiment lasted approximately 105 min total, within which 45 min was used for the actual experiment.

2.4. EEG data collection and preprocessing

To record participants’ EEG we used the Biosemi Active Two EEG System with 64 active electrodes. To reduce the induced noise between the electrode and the amplification/digitization system (BioSemi Active Two, BioSemi B.V. Amsterdam) we used preamplifiers in each electrode. This allowed high electrode impedances. We kept the electrode offsets below 35 mV. Then we applied a first-order analog anti-aliasing filter with a half-power cutoff at 3.6 kHz. The data was sampled at 2048 Hz (down sampled at 512 Hz with a decimation factor of 1/4 after recording) with a bandwidth of DC to 134 Hz when using a fifth-order digital sync filter. Each active electrode was measured online with respect to a common mode sense (CMS) active electrode that produced a monopolar (non-differential) channel.

Two additional electrodes were positioned on the external canthi for the EEG recording. Particular care was taken to ensure that participants did not touch any of the electrodes. Eye movements produce a moving dipole source, which generates positive and negative peaks when differentiating the two EOG electrodes; respectively, this reflects eye movements toward the right and left. Via visual inspection, we identified the trials showing horizontal ocular movements in order to discard them. We calculated the difference between the left and right EOG and averaged the signal in synchronisation with the first or second sound presentation in order to exclude potential spurious effects as the result of ocular movements. Then, we compared the amplitude of ocular movements between conditions. No significant modulation occurred due to the physical or relative spatial position of S2.

EEG was filtered between 0.1 and 100 Hz. Next, segments with eye movements were removed by visual inspection, while non-stereotypical (e.g., movements, muscle bursts) high-amplitude artifacts were removed using an automated artifact rejection method called Artifact Subspace Reconstruction (ASR - Mullen et al., 2013); this is available as a plug-in for the EEGLAB software (Delorme and Makeig, 2004). ASR computes the principal components, which then span a lower-dimensional subspace. Subspace components are compared to the properties/results of decomposition from the baseline EEG (the algorithm identifies components from the reference EEG data). By activating the components, the root mean square amplitude is estimated along with their means and standard deviations (Delorme and Makeig, 2004; Mullen et al., 2013). Given these statistics, a threshold matrix is calculated. During the processing stage, we obtain these components to be compared with the threshold matrix to decide whether their variance lies below it. In the subspace, we reconstruct the data. To identify the corrupted subspaces, we used a sliding window of 500 ms and a threshold of three standard deviations. We choose this threshold to minimize the influence of occasional large-amplitude noises or artifacts, such as bursts that originated from muscle contraction. Furthermore, channels were removed if their correlations were less than 0.85 based on an estimation of other channels or if their line noise relative to the signal was more than four standard deviations from the channel population’s mean. We removed time windows when the fraction of corrupted channels exceeded the threshold of 0.25, after applying the mentioned above criteria. Other parameters were kept as default.

The EEG data were further cleaned using independent component analysis (Delorme and Makeig, 2004). We used two EEGLAB toolboxes, namely SASICA (Chaumon et al., 2015) and IC_MARC (Freilich et al., 2015), to select artefactual components; in turn, we kept all the parameters as default. For the component rejection, the criteria reported in the corresponding validation papers were followed mainly based on abnormal topographies and/or spectra. The joint use of ASR and ICA permitted a good signal to noise ratio that was efficient in removing two different kinds of artifacts: ASR in removing transient artifacts (e.g., short muscle contractions) and ICA to remove stereotyped repeated artifacts (e.g., cardiac or long-lasting muscle activities). After applying ASR, the runica function of the EEGLab toolbox automatically estimated the rank of the data and, when required, it performed a preliminary dimensionality reduction with PCA before extracting the independent components.

Data was then referenced to the average of the left and right mastoids.
2.5. Sensor Level Analysis

To obtain ERPs, the EEG data were averaged in synchronization with the onset of the first or second sound. As such, we considered a period of 200 ms before the first sound onset as a baseline. We were having a clean baseline before the first sound helps to avoid any possible sound effects due to late cognitive processes that are related to the previous sounds.

Following previous studies by (Campus et al., 2019, 2017), we considered electrodes linked to visual processing (O1, O2 in occipital areas), as they could reveal possible contralateral responses with respect to the spatial position of sounds. In agreement with previous studies in which a specific ERP component was present for the sighted group but not for the EB people group, a time window was defined between 50 and 90 ms after the sound considered. The time windows have been associated with the spatial bisection task (Campus et al., 2019, 2017) and with studies evaluating the classical C1 ERP component elicited by visual tasks (Di Russo et al., 2002; Röder et al., 1999; Stolarova et al., 2006).

2.6. Source Level Analysis:

In order to reconstruct the cortical generators of the ERP components that were affected by the experimental factors, we employed a distributed source analysis using the Brainstorm software (Tadel et al., 2011). Next, data were re-referenced to the common average among all channels (Tadel et al., 2011). Then, cortical current source distribution within the brain was represented through 15,002 elementary dipoles that were obtained by sampling a tessellated cortical mesh template surface derived from the standard 1 mm resolution brain of the Montreal Neurological Institute (which had a non-linear average of 152 participants, processed with FreeSurfer 5.3 ICBM152 (Fonov et al., 2009). To avoid misleading over-interpretation, we did not fix the dipole orientations to the cortex surface; rather, these were left free to assume whichever (unconstrained) orientation. The EEG forward modeling of volume currents was completed with a three-layer (head, outer and inner skull) symmetric boundary element model (BEM) generated through OpenMEEG (Gramfort et al., 2011). To estimate the sensor variance, a diagonal noise covariance matrix was then computed for each participant using the pre-stimulus interval. The intensities of sources were estimated through the sLORETA approach (Pascual-Marqui, 2002). This technique is robust to noise in recorded data, and it models model approximations with fair spatial resolution. Besides, the depth weighting used in this approach alleviates the natural bias of the basic minimum norm estimation approaches toward superficial currents. Brainstorm’s default parameter settings were used for both the source reconstruction and the BEM creation.

The source activation was averaged for each participant and each condition within the selected time windows. Subsequently, the norm of the vectorial sum of the three orientations was calculated at each vertex.

3. Results

Behavioral analyses.

To analyse the behavioral data, we calculated the sensitivity ($d'$) of the performance for all three groups. For each participant, we calculated the hit rate (H), i.e., the proportion of trials where the participant responded correctly on what was the more distant interval, and the false alarm rate (FA), i.e. when the participant’s response did not correspond to the more distant interval. Afterward, we applied the followed formula to calculate the $d'$:

$$d' = z(H) - z(FA)$$

in which is the $z$-value for the given probability.

As shown in Fig. 2, it is clear that the group of EBEE and S have the same performance with a high level of sensitivity in performing the task; in contrast, the performance of the EB group is far below them. To confirm these results, we ran a two-sample perturbation test using Welsh’s t ($B = 10000$) and using the Bonferroni correction for multiple comparisons. We found a significant difference between EBEE and EB (Welsh-t = 11.5, $p < 0.01$) and S and EB (Welsh-t = 5.45, $p < 0.01$), while there was no difference between S and EBEE (Welsh-t = 0.72, $p = 1$). The results confirm that what had already been found by Vercillo et al. (2015).

ERPs analyses.

The spatial bisection task is a complex auditory task that to be performed requires the creation of a metrical representation of the space. The first step to test if a metric representation has been created by participants is to look at the ERPs responses of the second sound (Campus et al., 2019). Thus, for all groups, we analyzed the ERPs of the second sound, whereas the first sound was used as a control. The results highlight a gain modulation at the level of the occipital (O1 and O2 – Fig. 3) regions as well as three significant time windows (Fig. 3). The earliest time window considered occurs at 50–90 ms after the sound onset. Given the small number of samples for each group, on the mean ERPs amplitude comparisons we ran a two-way ANOVA using a permutation test with between factor Groups (EBEE vs EB vs. S) and within factors Positions second sound ($–4.5°$ and $+4.5°$) and Sounds (First sound and Second sound). We ran an ANOVA for both channels, O1 and O2. For the O1 channel, there was a significant main effect for the Sound ($p < 0.01$), the Position ($p < 0.01$) and the interaction between Sound, Position and Group ($p < 0.01$). The same result was also obtained for the ANOVA that was run on the O2 channel; there was a significant main effect for the Sound ($p < 0.01$), the Position ($p < 0.01$) and the significant interaction between Sound, Position and Group ($p < 0.01$).

Fig. 4 represents the scalp topography of the mean ERP’s amplitude in the 50–90 ms time window. In Fig. 4, a different pattern of activation appears between the EBEE and EB groups and between the EB and S groups. The S and EBEE groups show a contralateral activation of the visual area that is relative to the position of the second sound; this is not present in the EB group. Subsequently, we ran a two-sample perturbation test using Welsh’s t ($B = 10000$) with a Bonferroni correction for multiple comparisons for the results of channels O1 and O2. For the O1
Fig. 3. Group average of un-subtracted ERPs for EBEE (in green), EB (in cyan), and S (in blue) participants. The data in the upper row are an example of the occipital right scalp (O1) related to the position in space of the second. The bottom row represents an example of the occipital left scalp (O2) for the two positions of the second sound. The grey rectangle highlights the ERP activation in the time range between 50 and 90 ms. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

Fig. 4. Averaged ERPs’ scalp maps in the time windows between 50 and 90 ms for each group. (A) Shows the activation of EBEE (first row), EB (second row) and S individuals (last row) for the first sound. Conversely, for the second sound, the first sound does not elicit any early activation in the posterior part of the scalp. Subsequently, (B) shows the different activation pattern between EBEE (first row), EB (second row) and S individuals in the last row for the second sound. While early EB generally show a low activation at the posterior level of the scalp, EBEE have a focal activation contralateral to the spatial position of the sound in the posterior side of the scalp as do S participants.
channel, we found a significant difference between the EBEE and the EB in both $-4.5^\circ$ condition ($t = -34.11, p < 0.01$) and the $+4.5^\circ$ condition ($t = 17.78, p < 0.01$). The same results were found between the S and EB groups in both the $-4.5^\circ$ condition ($t = 38.7, p < 0.01$) and $+4.5^\circ$ condition ($t = 31.24, p < 0.01$); however, there was no difference between the groups S and EE. For the O2 channel, the results were similar to the O1 channel: there were significant differences for the $+4.5^\circ$ conditions between the EBEE and EB groups ($t = 46.44, p < 0.01$) and between the S and EB groups ($t = 50.11, p < 0.01$). The same results were present for the $-4.5^\circ$ condition (EBEE and EB: $t = 20.11, p < 0.01$; S and EB: $t = 31.04, p < 0.01$). The data of each participant are shown in Fig. 5.

Another gain modulation of the ERPs signal was observed later in time between 110 and 170 ms (P140, see Fig. 2). This latter activation was not contralateral to the position of the second sound; rather, it was widespread over the entire occipital area. This highlights a stronger activation in the EBEE and S groups. Furthermore, there is a third-time window that shows a different modulation between 200 and 400 ms of the neural activity between the two groups (Fig. 2). This later activation seems to occur in agreement with the auditory-evoked contralateral occipital activation (ACOP) that has been previously observed in sighted individuals between 250 and 400 ms (Hillyard et al., 2016; McDonald et al., 2013). Like the early response, the ACOP was more pronounced and lateralized in EBEE and S individuals; in contrast, in EB participants, it was lower and not lateralized (see Fig. 2).

4. Source analysis

Since scalp information cannot ensure that the occipital cortex is involved in the generation of the component within a range of 50–90 ms, we ran a source-level analysis. For each participant and condition, the average source modulation within the time window 50–90 ms was computed. This was then calculated as the norm of the vectorial sum of the three orientations at each vertex. Fig. 6 shows the average activation for each group. Both sighted, and EBEE participants showed a cortical activation of the visual cortex contralateral to the physical position of the second sound, while the EB showed a lower level of bilateral cortical activation.

5. Discussion

In this study, we test the influence of echolocation on people’s spatial acoustic representation at the cortical level. Vercillo et al. (2015) compared the behavioral performance of these same three groups of participants (EBEE, EB, and S) in an auditory bisection task. The results showed that the behavior of the EBEEs was similar to that of sighted participants when compared to EBs. This supports the idea that echo-location has an influence on the representation of the auditory space. In this study, we demonstrated that the different behavior by the EBEEs and EBs is associated with different cortical processing of the auditory stimuli in the posterior areas of the scalp.

EBEEs show a clear activation of posterior areas associated with the second sound, similar to the activation of sighted people; in contrast, the EB does not show this same pattern. In particular, we found an early occipital activation (P70) in both EBEE and sighted people that is contralateral to the position of the second sound. More importantly, this same early activation was found by Campus et al. (2017) in sighted participants. The authors suggested that the P70 component is specifically elicited by the construction of a spatial metric that mimics the C1 component that is usually related to the early responses of the striate visual cortex for visual stimuli, suggesting that it is possible to find the same activation elicited by an auditory response. The authors specify that this occur when the activation is modulated by the construction of a spatial metric. More generally, they speculated that the cortical activation that underlies the C1 ERP component could play a fundamental role in constructing the metrics in the space domain. This explanation is linked to the hypothesis of cross-sensory calibration that was proposed by Gori et al. (2008, 2014). The hypothesis notes that during development, the visual system calibrates the other senses to process specific aspects of spatial information because vision is the most accurate sense and, therefore, it is best able to perceive the spatial properties of the environment. Consequently, in people who are blind, the lack of visual information during the early stages of development does not allow the remaining senses to benefit from the visual experience. Our results suggest that the use of echolocation can provide a solid foundation for the development of spatial representation when visual input is not available.

Regarding the bisection task, we would like to point out that apparently it could be comparable to a simple localization task, since the “target” sounds are only two and symmetrically located along the midline, however, it is not the case. First, behavioral studies have already carried out this comparison in both early blind (Gori et al., 2014) and expert echolocators (Vercillo et al., 2015), finding that in a localization task there is no difference in performance between sighted and people who are blind (regardless of the use of echolocation), while a difference was found in the bisection task. Moreover, at the neural level previous studies have shown activation of primary visual cortex for auditory localization in group of blind participants (Gouguix et al., 2005; Leclerc et al., 2006; Röder et al., 1999), nevertheless, none of the studies reported an early occipital activation such the one described here and in previous studies investigating auditory spatial bisection (Campus et al., 2019, 2017). Second, the delivery given to the participants on the type of task to perform and the experimental paradigm itself were created in order to prevent the bisection task from being performed as a localization task, despite the two “target” sounds. In the first case, the experimenter explicitly explained to the participant to judge which distance was longer, whether it was between the first and second sounds or between the second and third sounds. Finally, the participants before starting the task did not have the opportunity to see (in the case of sighted people) or explore haptically (blind people) the array of speakers, and they were not aware of being seated in the middle of the array of speakers.

Fig. 5. The ERPs for each participant (symbols) in the time windows between 50 and 90 ms. In group EB (in cyan), regardless of whether the second sound is closer to the third or the first sound, O1 and O2 present the same kind of activation. Conversely, both group S (in blue) and EBEE (in green) have greater responses when the electrode considered is contralateral to the position of the sound. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)
Summarizing, all the instructions provided focused the participants to the construction of a metric, and not to solve the task by only considering the second sound. Therefore, these findings strongly point to the specificity of the spatial bisection and seem to robustly exclude that the participants performed a pseudo-localization task, instead genuinely performed a bisection task through the construction of a metric representation of space.

The majority of studies that investigate the neural basis of echolocation use neuroimaging techniques like PET or fMRI. They mainly focus on how the brain responds to the presence of echoes. In one of the first studies, Thaler et al. (2011) measured the brain activity of two echolocators while they were listening to sound clicks with and without echoes. The researchers found an increased activation for echoes at the level of the visual brain areas compared to people in the sighted controls. Moreover, another two studies (Arnott et al., 2013; Thaler et al., 2011; Wallmeier et al., 2015) found that echo-related activation is contralateral to the position of the silent object; this reflects that there is a “retinotopic” organization in response to the echoes in V1.

More recently, a new study by Norman and Thaler (2019), in addition, to find evidence for a retinotopic-like organization of sound echoes in expert echolocators who are blind, they found the same evidence of spatial mapping of source sounds comparing blind to sighted controls. The authors propose that the retinotopic map of the primary visual cortex undergoes a reorganization into expert blind echolocators to allow the same retinotopic organization to be used not only for sound echoes but also for simple acoustic localization. The spatial mapping found for sounds and sound echoes can be equivalent to the visual space in sighted people, taking advantage of the retinotopic organization of early visual cortex that in people who are blind lack of visual inputs.

Therefore, we can infer that the visual cortex in EBEEs plays a fundamental role in spatial representation. In turn, this cortical organization can support the development of spatial representations, which is useful for solving the space bisection task investigated in the current study. Evidence suggests that echolocation shares some characteristics with vision at the behavioral level. It has been shown that trained blind echolocators may experience the “size-weight illusion” (Buckingham et al., 2015); i.e., in using echolocation, they judge small objects to be heavier compared to bigger objects, even if the two objects weigh exactly the same amount. Furthermore, echolocation may be subjected to “size constancy” (Milne et al., 2015): this is a perceptual phenomenon in which objects appear to have the same physical size independent of the size of the visual angle subtended, which in turn changes with distance.

Thanks to this “visual background”, EBEE may be better able to learn some spatial properties that are challenging for EB.

These results in EBEE suggest that they have a different representation of space compared to EB. Although some works have shown similarities between sighted people and EBEE (Cuturi and Gori, 2017; Vercillo et al., 2015), to date, it is not clear which cortical mechanisms are associated with the “substitution” of vision thanks to the echolocation of developing space representations.

A possible explanation is that echolocation provides sensory-motor feedback due to the primary use of echolocation in navigation (Kolarik et al., 2014). Routine use of this skill allows people who are blind to create a representation of space that goes beyond their peri-personal space. During navigation, self-generated clicks provide sensory feedback (echoes) that are associated with motion, which creates an auditory-motor association similar to visual-motor association. In contrast, it has been demonstrated that non-self-generated clicks can be used by echolocators to perceive space (Supa et al., 1944; Thaler and Castillo-Serrano, 2016). As such, it is not clear why the blind population to perceive space cannot use everyday echoes (such as the sounds of footsteps). These results suggest that the brains of echolocators can be “reorganized” because echolocation signals allow them to develop a spatial representation that can be activated for mouth or non-mouth clicks. However, this is the case only in echolocators.

Fig. 6. The average source analysis activation for the time window between 50 and 90 ms. The left side of the figure presents the source analysis for the long distance condition – when the second sound is closer to the third. The right side shows the short distance condition – when the second sound is closer to the first. For each group and position, the right-back and left-back cortical activation has been represented.
Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.neuropsychologia.2020.107617.

References

Arnott, S.R., Thaler, L., Milne, J.L., Kihl, D., Goodale, M.A., 2013. Shape-specific activation of occipital cortex in an early blind echolocation expert. Neuropsychologia 51 (5), 938–949. https://doi.org/10.1016/j.neuropsychologia.2013.01.024.

Buckingham, G., Milne, J.L., Byrne, C.M., Goodale, M.A., 2015. The size-weight illusion induced through human echolocation. Psychol. Sci. 26 (2), 237–242. https://doi.org/10.1177/0956797614561267.

Campus, C., Sandini, G., Amadeo, M.B., Gori, M., 2019. Stronger responses in the visual cortex of sighted compared to blind individuals during auditory space representation. Sci. Rep. 9 (4), 1935. https://doi.org/10.1038/s41598-018-37281-x.

Campus, C., Sandini, G., Concetta Morrone, M., Gori, M., 2017. Spatial localization of sound elicits early responses from occipital visual cortex in humans. Sci. Rep. 7 (1), 10415. https://doi.org/10.1038/s41598-017-0941-z.

Chaumont, M., Bishop, D.V.M., Busch, N.A., 2015. A practical guide to the selection of independent components of the electroencephalogram for artifact correction. J. Neurosci. Methods 250, 47–63. https://doi.org/10.1016/j.jneumeth.2015.02.025.

Collignon, O., Dormal, G., Albouy, G., Vandewalle, G., Voss, P., Phillips, C., Lepore, F., 2013. Impact of blindness onset on the functional organization and the connectivity of the occipital cortex. Brain 136 (9), 2769–2783. https://doi.org/10.1093/brain/awt176.

Collignon, O., Voss, P., Lassonde, M., Lepore, F., 2009. Cross-modal plasticity for the spatial processing of sounds in visually deprived subjects. Exp. Brain Res. 192 (3), 343–358. https://doi.org/10.1007/s00221-008-1553-z.

Cuturi, L.F., Gori, M., 2017. The effect of visual experience on perceived haptic verticality when tilted in the roll plane. Front. Neurosci. 11, 687. https://doi.org/10.3389/fnins.2017.00687.

Delorme, A., Makeig, S., 2004. EEGLAB: an open source toolbox for analysis of single-trial EEG dynamics including independent component analysis. J. Neurosci. Methods 134 (1), 9–21. https://doi.org/10.1016/j.jneumeth.2003.10.009.

Di Russo, F., Martínez, A., Sereno, M.I., Pitzalis, S., Hillyard, S.A., 2002. Cortical sources of the early components of the visual evoked potential. Hum. Brain Mapp. 15 (2), 95–111. https://doi.org/10.1002/hbm.10101.

Donev, V., Evans, A., McKinstry, R., Aloni, C., Collins, D., 2009. Unbiased nonlinear average age-appropriate brain templates from birth to adulthood. Neuroimage 47, S102. https://doi.org/10.1016/j.neuroimage.2009.07.008.

Fries, L., Andersen, T.S., Møller, V.S., Feng, W., Martinez, A., McDonald, J.J., 2016. Cross-modal reorganization of visual systems in congenitally blind humans. Brain 139 (1), 288–293. https://doi.org/10.1093/brain/awt013.

Fonov, V., Evans, A., McKinstry, R., Aloni, C., Collins, D., 2009. Unbiased nonlinear average age-appropriate brain templates from birth to adulthood. Neuroimage 47, S102. https://doi.org/10.1016/j.neuroimage.2009.07.008.

Gorga, M., Sandini, G., Martinoli, C., Burr, D., 2012. Development of visuo-auditory integration in space and time. Front. Integr. Neurosci. 6 (September), 77. https://doi.org/10.3389/fnins.2012.00077.

Gori, M., Sandini, G., Martinoli, C., Burr, D., 2014. Impairment of auditory spatial localization in congenitally blind humans. Brain 137 (1), 288–293. https://doi.org/10.1093/brain/awt013.

Gougoux, F., Zatorre, R.J., Lassonde, M., Voss, P., Lepore, F., 2005. A functional neuroimaging study of sound localization: visual cortex activity predicts performance in early blind individuals. PLoS Biol. 3 (2), e27. https://doi.org/10.1371/journal.pbio.0000027.

Gosnell, G.W., Fairhall, A.L., 1995. Visual instruction of the neural map of auditory space in the developing optic tectum. Science 265 (5195), 85–87. https://doi.org/10.1126/science.2655209.

Kolarik, A.J., Cirstea, S., Pardhan, S., Moore, B.C.J., 2014. A summary of research investigating echolocation abilities of blind and sighted humans. Hear. Res. 310, 60–68. https://doi.org/10.1016/j.heares.2014.01.010.

Leclerc, C., Saint-Amour, D., Lavoie, M.E., Lassonde, M., Lepore, F., 2000. Brain functional reorganization in early blind humans revealed by auditory event-related potentials. Neuroreport 11 (3), 545–550.

Lewald, J., 2002. Vertical sound localization in blind humans. Neuropsychologia 40 (12), 1868–1872. https://doi.org/10.1016/S0028-3932(02)00071-4.

McDonald, J.J., Stormer, V.S., Martinez, A., Feng, W., Hillyard, S.A., 2013. Salient sounds activate human visual cortex automatically. J. Neurosci. 33 (21), 9194–9201. https://doi.org/10.1523/JNEUROSCI.5902-12.2013.

Milne, J.L., Anello, M., Goodale, M. a, Thaler, L., 2015. A blind human expert echolocator shows size constancy for objects perceived by echo. Neurocase 21 (4), 465–478. https://doi.org/10.1177/1355479414556493.

Moss, C.F., Bohn, K., Gilkinson, H., Surlyke, A., 2006. Active listening for spatial orientation in a complex auditory scene. PLoS Biol. 4 (4), e79. https://doi.org/10.1371/journal.pbio.0040679.
Mullen, T., Kothe, C., Chi, Y.M., Ojeda, A., Kerth, T., Makeig, S., Cauwenberghs, G., Trypios, P., 2013. Real-time modeling and 3D visualization of source dynamics and connectivity using wearable EEG. 2013 35th Annual International Conference Of The IEEE Engineering In Medicine And Biology Society (EMBC), 2184–2187. https://doi.org/10.1109/EMBC.2013.6609688.

Norman, L.J., Thaler, L., 2019. Retinotopic-like maps of spatial sound in primary visual cortex of blind human echolocators. Proc. Biol. Sci. 286 (1912), 20191910. https://doi.org/10.1098/rspb.2019.1910.

Pascual-Marqui, R.D., 2002. Standardized low-resolution brain electromagnetic tomography (sLORETA): technical details. Suppl D: In Methods and Findings in Experimental and Clinical Pharmacology, vol. 24, pp. 5-12. https://doi.org/10.4161/pdr.24.3.4163.

Pascual-Marqui, R.D., 2002. Standardized low-resolution brain electromagnetic tomography (sLORETA): technical details. Suppl D. In: Methods and Findings in Experimental and Clinical Pharmacology, vol. 24, pp. 5-12. https://doi.org/10.4161/pdr.24.3.4163.

Rice, C.E., Feinstein, S.H., 1965. Sonar system of the blind: size discrimination. Science 148 (3673), 1107–1108. https://doi.org/10.1126/science.148.3673.1107.

Röder, B., Teder-Salejarvi, W., Sterr, A., Rosler, F., Hillyard, S.A., Neville, H., 1999. Improved auditory spatial tuning in blind humans. Nature 400 (6740), 162–166. https://doi.org/10.1038/22106.

Siemers, B.M., Schnitzler, H.-U., 2004. Echolocation signals reflect niche differentiation among echolocating bats. Brain Res. Brain Res. Rev. 488. https://doi.org/10.1016/j.cognition.2003.12.001.

Stolarova, M., Keil, A., Moratti, S., 2006. Modulation of the C1 visual event-related potential by conditioned stimuli: evidence for sensory plasticity in early affective perception. Cerebr. Cortex 16 (6), 876–887. https://doi.org/10.1093/cercor/bhj031.

Stromfroegen, L.E., Pittenger, J.B., 1995. Human echolocation as a basic form of survey data. Front. Physiol. 4 (Dec), 98. https://doi.org/10.3389/fphys.2013.00098.

Thaler, L., Arnott, S.R., Goodale, M.A., 2011. Neural correlates of natural human echolocation in early and late blind echolocation experts. PloS One 6 (5), e20162. https://doi.org/10.1371/journal.pone.0020162.

Thaler, L., Castillo-Serrano, J., 2016. People’s ability to detect objects using click-based echolocation: a direct comparison between mouth-clicks and clicks made by a loudspeaker. PloS One 11 (5), e0154668. https://doi.org/10.1371/journal.pone.0154668.

Thaler, L., De Vos, R., Kish, D., Antoniou, M., Baker, C., Hornikx, M., 2018. Human echolocators adjust loudness and number of clicks for detection of reflectors at various azimuth angles. Proc. Biol. Sci. 285 (1873), 20172735. https://doi.org/10.1098/rspb.2017.2735.

Thaler, L., Goodale, M.A., 2016. Echolocation in humans: an overview. Wiley Interdisciplinary Reviews: Cognit. Sci. 7 (6), 382–393. https://doi.org/10.1002/wi ris.1406.

Thaler, L., Milne, J.J., Arnott, S.R., Kish, D., Goodale, M.A., 2014. Neural correlates of motion processing through echolocation, source hearing, and vision in blind echolocation experts and sighted echolocation novices. J. Neurophysiol. 111 (1), 112–127. https://doi.org/10.1152/jn.00501.2013.

Thaler, L., Zhang, X., Antoniou, M., Kish, D.C., Cowie, D., 2020. The flexible action system: click-based echolocation may replace certain visual functionality for adaptive walking. J. Exp. Psychol. Hum. Percept. Perform. 46 (1), 21–35. https://doi.org/10.1037/xhp0000597.

Vercillo, T., Milne, J.L., Gori, M., Goodale, M.A., 2015. Enhanced auditory spatial localization in blind echolocators. Neuropsychologia 67, 35–40. https://doi.org/10.1016/j.neuropsychologia.2014.12.001.

Vercillo, T., Tonelli, A., Gori, M., 2017. Intercepting a sound without vision. PloS One 12 (5), e0177407. https://doi.org/10.1371/journal.pone.0177407.

Vercillo, T., Tonelli, A., Gori, M., 2018. Early visual deprivation prompts the use of body-centered frames of reference for auditory localization. Cognition 170, 263–269. https://doi.org/10.1016/j.cognition.2017.10.013.

Voss, P., Lepore, F., Gougoux, F., Zatorre, R.J., 2011. Relevance of spectral cues for auditory spatial processing in the occipital cortex of the blind. Front. Psychol. 2 (March), 1–12. https://doi.org/10.3389/fpsyg.2011.00048.

Wallmeier, L., Geidle, N., Wiegbre, L., 2013. Echolocation versus echo suppression in humans. Proc. Biol. Sci. 280 (1769), 20131428. https://doi.org/10.1098/rspb.2013.1428.

Wallmeier, L., Kish, D., Wiegbre, L., Flanagan, V.L., 2015. Aural localization of silent objects by active human biosonar: neural representations of virtual echo-acoustic space. Eur. J. Neurosci. 41 (5), 533–545. https://doi.org/10.1111/ejn.12843.

Weeks, R., Horwitz, B., Aziz-Sultan, A., Tian, B., Wessinger, C.M., Cohen, L.G., Hallett, M., Rauschecker, J.P., 2000. A positron emission tomographic study of motion processing through echolocation, source hearing, and vision in blind echolocation experts and sighted echolocation novices. J. Neurophysiol. 111 (1), 112–127. https://doi.org/10.1152/jn.00501.2013.

Vercillo, T., Milne, J.L., Gori, M., Goodale, M.A., 2015. Enhanced auditory spatial localization in blind echolocators. Neuropsychologia 67, 35–40. https://doi.org/10.1016/j.neuropsychologia.2014.12.001.

Vercillo, T., Tonelli, A., Gori, M., 2017. Intercepting a sound without vision. PloS One 12 (5), e0177407. https://doi.org/10.1371/journal.pone.0177407.

Vercillo, T., Tonelli, A., Gori, M., 2018. Early visual deprivation prompts the use of body-centered frames of reference for auditory localization. Cognition 170, 263–269. https://doi.org/10.1016/j.cognition.2017.10.013.

Voss, P., Lepore, F., Gougoux, F., Zatorre, R.J., 2011. Relevance of spectral cues for auditory spatial processing in the occipital cortex of the blind. Front. Psychol. 2 (March), 1–12. https://doi.org/10.3389/fpsyg.2011.00048.

Waller, L., Geidle, N., Wiegbre, L., 2013. Echolocation versus echo suppression in humans. Proc. Biol. Sci. 280 (1769), 20131428. https://doi.org/10.1098/rspb.2013.1428.

Waller, L., Kish, D., Wiegbre, L., Flanagan, V.L., 2015. Aural localization of silent objects by active human biosonar: neural representations of virtual echo-acoustic space. Eur. J. Neurosci. 41 (5), 533–545. https://doi.org/10.1111/ejn.12843.

Weeks, R., Horwitz, B., Aziz-Sultan, A., Tian, B., Wessinger, C.M., Cohen, L.G., Hallett, M., Rauschecker, J.P., 2000. A positron emission tomographic study of auditory localization in the congenitally blind. J. Neurosci. 20 (7), 2664–2672. https://doi.org/10.1523/JNEUROSCI.20-07-02664.2000.

Yan, J., Suga, N., 1996. Corticofugal modulation of time-domain processing of biosonar information in lats. Science 273 (5278), 1100–1103. https://doi.org/10.1126/science.273.5278.1100.

Zwiers, M.P., Van Opstal, A.J., Cruijssen, J.R.M., 2001. A spatial hearing deficit in early-blind humans. RC142 J. Neurosci. 21 (9), RC142. https://doi.org/10.1523/JNEUROSCI.21-09-J0002.2001.