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Reaching to Sounds Improves Spatial Hearing in Bilateral Cochlear Implant Users

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Objectives: We assessed if spatial hearing training improves sound localization in bilateral cochlear implant (BCI) users and whether its benefits can generalize to untrained sound localization tasks.

Design: In 20 BCI users, we assessed the effects of two training procedures (spatial versus nonspatial control training) on two different tasks performed before and after training (head-pointing to sound and audiovisual attention orienting). In the spatial training, participants identified sound position by reaching toward the sound sources with their hand. In the nonspatial training, comparable reaching movements served to identify sound amplitude modulations. A crossover randomized design allowed comparison of training procedures within the same participants. Spontaneous head movements while listening to the sounds were allowed and tracked to correlate them with localization performance.

Results: During spatial training, BCI users reduced their sound localization errors in azimuth and adapted their spontaneous head movements as a function of sound eccentricity. These effects generalized to the head-pointing sound localization task, as revealed by greater reduction of sound localization error in azimuth and more accurate first headorienting response, as compared to the control nonspatial training. BCI users benefited from auditory spatial cues for orienting visual attention, but the spatial training did not enhance this multisensory attention ability.

Conclusions: Sound localization in BCI users improves with spatial reaching-to-sound training, with benefits to a nontrained sound localization task. These findings pave the way to novel rehabilitation procedures in clinical contexts.

Key words: Active listening, Cochlear implant, Head movements, Reaching, Spatial hearing, Training, Virtual reality.

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INTRODUCTION

Cochlear implants (CIs) have become standard intervention for neurosensory deafness (Moore & Shannon 2009; Wilson 2019). Bilateral CIs (BCIs) are increasingly common, thus allowing partial access to interaural auditory cues (Aronoff et al. 2010; Gifford & Stecker 2020). Benefits of CIs for speech understanding are now well-established in children (Allen et al. 1998; Calmels et al. 2004), adults (Wilson et al. 1991; Stickney et al. 2004; Wilson 2017), and aging individuals (Forli et al. 2019). In addition, binaural hearing improves sound localization in the

Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and text of this article on the journal's Web site (www.ear-hearing.com). horizontal dimension for BCI users, compared to unilateral users (between group comparison) (Smulders et al. 2016), or to conditions in which one of the two CIs is switched off (within-group comparison) (Litovsky et al. 2009; Asp et al. 2012).

Yet, spatial hearing skills of BCI users are substantially poorer compared to listeners with normal hearing, when locating stationary (Kerber & Seeber 2012; Jones et al. 2014) as well as moving sound sources (Moua et al. 2019). A key factor causing such poor performance is the reduced availability of auditory cues. CIs limit input resolution in the temporal and frequency domains (Moore & Shannon 2009), alter sound levels through automatic gain control (AGC) (see, for instance, Dorman et al. 2014; Archer-Boyd & Carlyon 2019, 2021), and change the auditory cues by the effect of microphone filtering strategies (both related to noise reduction and to emphasize higher frequencies) (Seeber & Fastl 2008). In addition, the two CI processors work in isolation from one another, leading to independent acoustic streams to the brain (for discussion, see Verhaert et al. 2012; Rosskothen-Kuhl et al. 2021). Hence, BCI users can only access a degraded set of auditory cues to localize sound, among which the most salient ones are the interaural-level differences (ILDs) (Van Hoesel 2004; Grantham et al. 2007; Seeber & Fastl 2008; Grieco-Calub & Litovsky 2010).

All these limitations pertain to peripheral auditory signals. Can we rely on more central auditory learning processes to better use the degraded signal? Relearning spatial hearing skills is possible in deafened ferrets with BCI after multisensory training with interleaved auditory and visual stimuli (Isaiah et al. 2014). Training-induced improvements were observed in the responsiveness of auditory cortical neurons and in their sensitivity to ILDs. Improvement emerged also in behavior: both in the sound localization responses and in sound-evoked headorienting movements made by early-deafened ferrets with BCI (Isaiah et al. 2014). Studies with normal-hearing participants exposed to altered auditory cues also suggest that relearning spatial hearing is possible. Training protocols leveraging multisensory perception and active interactions with sounds proved effective in promoting adaptation to altered auditory cues and improved spatial hearing skills (Strelnikov et al. 2011; Carlile 2014; Mendonça 2014; Keating et al. 2015; Rabini et al. 2019; Valzolgher et al. 2020c). Finally, preliminary results in unilateral cochlear implant users (Luntz et al. 2005) and BCI users (Tyler et al. 2010) suggest that feedback-based training could also improve sound localization in this population. Yet, these pioneering works involved a limited number of participants and-critically-they did not explore if training effects could generalize beyond the trained task, which constitutes a hallmark of learning processes.

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1

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The aim of the present study was to assess whether spatial hearing can be trained in BCI users and whether training effects can generalize to untrained spatial auditory tasks. Building upon our previous work in normal-hearing adults listening with one ear plugged (Valzolgher et al. 2020c, 2022), we trained BCI users with a multisensory-motor task that combined reaching to near-by sounds, audiovisual feedback about sound position, and free-head movements. Reaching to sound could enhance spatial coding of sound position by incorporating the coordination of different effectors (eyes, head, hand) into a common reference frame (Cohen & Andersen 2002; Boyer et al. 2013). In addition, it could help directing attention toward the position occupied by the sound source and make the task more engaging, which is a fundamental feature in learning (Dehaene 2020). Finally, in monaurally plugged normal-hearing individuals, reaching to sounds encourage additional head movements in response to sounds, which appear to serve the purpose to explore the auditory scene more widely and to expose the unplugged ear to the sound sources (Valzolgher et al. 2020c).

To assess training specificity, we used a crossover experimental design (Fig. 1A; see Video File in Supplemental Digital Content 1, http://links.lww.com/EANDH/B44) in which we compared the experimental spatial training with a control nonspatial training that used the same stimuli and multisensory feedback, but different task demands (i.e., discrimination of amplitude modulations in the sound). Thus, all participants performed both the experimental training and the control one. Crossover paradigms are particularly suited for clinical applications (Senn 2002), because they permit the involvement of the totality of participants in the experimental training without the need of testing a control group (which could not benefit from training). Furthermore, taking advantage of this design, we minimized any potential intergroup differences. Specifically, we assessed if the improvement induced by the experimental training (spatial training) extends (i.e., generalizes) to a headpointing sound localization task, which entails different sound positions and requires localizing sounds using a different effector (the head instead of the hand). In addition, to probe generalization effects also when implicit sound localization is required, we tested participants in an audiovisual attention-orienting task, in which they were asked to judge the elevation of a visual stimuli while listening for a sudden sound.

Based on work by Valzolgher et al. (2020c, 2022), we predicted observing an improvement in sound localization across trials during the spatial training. In addition, we expected greater generalization effects after the spatial compared to the nonspatial training (as recently documented by Valzolgher et al. 2022, using a similar approach in normal-hearing adults listening with one ear plugged). Finally, because our apparatus allowed for unrestrained but measurable head movements, in line with Isaiah et al. (2014) we also studied changes in sound-related head-orienting movements. We predicted finding changes in sound-related head-orienting movements during (Valzolgher et al. 2022) and after training (Isaiah et al. 2014), consistent with the expected error reductions.

MATERIALS AND METHODS

Study Design

All participants (BCI users) took part in two experimental sessions, with at least 15 days of washout interval. Each session

comprised two testing phases and one training (Fig. 1A); they were identical in all respects except for the training task. Participants performed both training types, which were counterbalanced across participants in a within-subject crossover design. In one session, they engaged in the experimental spatial training task; in the other, they performed the control nonspatial training task. Testing phases included two auditory tasks: a head-pointing localization task (conducted in virtual reality (VR)) and an audiovisual attention-orienting task (conducted outside VR, see below). The head-pointing localization task differed with respect to training both in terms of targets spatial position and response effector (the head instead of the hand). The rationale was to minimize any potential effect of sensorimotor adaptation. The audiovisual attention-orienting task was instead an implicit sound localization task, in which sounds served as lateralized attention-orienting cues for the discrimination of visual targets (i.e., an audiovisual analog to the classic attention cueing paradigm) (see below for detailed descriptions of each tasks).

Participants

Twenty BCI participants (age: M = 45.6, SD = 13.1, 7 males, 15 right-handed) took part in the study (see the Materials for power calculation in Supplemental Digital Content 2, http://links.lww.com/EANDH/B43).

They were recruited at the otorynolaringology department of the civil Hospital Edouard Herriot in Lyon (France), and tested in a dedicated room inside the Hospital Edouard Herriot premises. Participants signed an informed consent before starting the experiment, which was conducted according to the criteria of the Declaration of Helsinki (1964, amended in 2013) and it was approved by the Ethical Committee (Ile de France X, N° ID RCB 2019-A02293-54), and recorded in clinicaltrials.gov (NCT04183348). All had normal or corrected-to-normal vision and reported no movement or vestibular deficit, nor neurological or psychiatric history. Age, sex and clinical data for individual BCI participants are provided in Table 1. During the experiment, participants used their daily sound processor settings (see Table 1 in Supplemental Digital Content 2, http:// links.lww.com/EANDH/B43 for details about CI model, processor strategy and microphone settings), to preserve the acoustic experience that each participant developed with the CIs.

Procedures

Testing Phases

Head-Pointing Sound Localization Task

This task was carried out entirely in VR, always using *real sounds* delivered in free field from predetermined positions computed on each trial based on the initial head position (Coudert et al. 2022; Valzolgher et al. 2020a,c). Our VR approach brings real sounds into visual VR and coordinates everything using Unity (see the Materials in Supplemental Digital Content 2, http://links.lww.com/EANDH/B43 for details about the apparatus and also Gaveau et al. 2020). Participants were immersed in a virtual room that matched the size of the real one but was devoid of any objects. Participants were instructed to localize sound sources and informed that sound could be presented anywhere in the surrounding space. At the beginning of each trial, participants were asked to direct their gaze in front of them, by aligning their head with a central fixation cross. When the



Fig. 1. Experimental procedure and setting. A, Schematic description of the overall crossover design. Each session (session 1 and session 2) comprised by two testing phases, with a training task in between. B, Testing phases. Top: schematic representation of the participant wearing the Head-mounted display (HMD) and holding the virtual reality (VR) controller during the head-pointing sound localization task. The eight spheres in front of the participant indicate predetermined speaker positions (not visible in the HMD). The hand holding the speaker represented near the red point was the experimenter's hand who move the speaker and bring it to the target position following instruction provided on a monitor. Bottom: schematic representation of the setting for the audiovisual attention-orienting task (conducted entirely outside VR). C, Training phase. Schematic representation of the participant wearing the HMD and holding the VR controller. The cylindrical speakers were visible only in VR (see inset) and indicated the possible sound positions during both training types. Inset: close-up of the scene as visible inside the HMD from participant's perspective. During the task participant saw a virtual scenario comprising a room, the speakers and the VR controller they were holding in their hand. See Video File in Supplemental Digital Content 1, http://links.lww.com/EANDH/B44 for animated description of the two training types.

correct posture was reached, the fixation cross turned from white to blue. In the meanwhile, the experimenter placed the speaker in one of the possible eight predetermined positions, using visual indications provided on a dedicated monitor (see Verdelet et al. 2019 and Gaveau et al. 2020 for a validation of this method and Valzolgher et al. 2020a,c for examples). The predetermined positions (shown in the top part of Fig. 1B) result from the combination of 4 different azimuths in front space $(-67.5^\circ, -22.5^\circ, 22.5^\circ, \text{ or } 67.5^\circ;$ with respect to the participant's body midline), a single distance (55 cm from the center of the head) and 2 different elevations (5° above and 15° below ear level). Target elevation was changed only with the purpose of introducing variability in the auditory stimulation, and the asymmetrical arrangement elevation positions resulted from the fact that the software for placing the speakers at predetermined positions was based on the position of the VIVE tracker located above the speaker, rather than the position of the

actual speaker. Crucially, the target sound was delivered only when the participant was in the correct start posture, and when the loudspeaker was positioned within a sphere with diameter of 5 cm centered on the predetermined location. This ensured that each stimulation position was fully replicable at the beginning of each trial. The target sound consisted of 3 sec of white noise, amplitude-modulated at 2.5 Hz, and delivered at about 65 dB SPL as measured from the participant's head. Participants were instructed to indicate sound position using their heads as a pointer. Note that head and trunk movements remained unconstrained during and after sound emission, allowing spontaneous active listening behavior. Note that participants were informed about their head projection due to a marker (white cross) and that they were only allowed to validate their response after the sound ended, by pressing a button on their handheld controller. To emphasize this instruction, the head projection marker (the cross) was white throughout the stimulation phase and

ID	Sex	Age, y	Etiology of deafness	Age at deaf diagnosis (y;m)	Age at first hearing aid (y;m)	Age at implantation (right ear)	Age at implantation (left ear)	Years with one CI	Years with two Cls
1	F	22	Unknown	0;5	0;7	2	15	13	7
2	F	65	Unknown	45	49	54	53	1	11
3	F	60	Genetic	10	10	40	51	11	9
4	F	46	Meningitis	1	5	39	44	5	2
5	F	47	Genetic	10	12	42	43	1	4
6	М	55	Genetic/sudden deafness	1	44	50	52	2	3
7	М	41	Ototoxicity	2	6	34	35	1	6
8	F	47	Genetic	16	21	42	39	3	5
9	М	32	Meningitis	2	2	3	28	25	4
10	М	25	Unknown	3	3	18	21	3	4
11	F	49	Unknown	13	30	39	39	0	10
12	М	59	Head trauma	52	No	53	53	0	6
13	F	47	Genetic	3	3	45	42	3	2
14	F	54	Genetic	42	42	50	51	1	3
15	М	24	Genetic	2;6	3	18	12	6	6
16	М	65	Otosclerosis	35	55	59	60	1	5
17	F	32	Otosclerosis of the cochlea	10	12	23	25	2	7
18	F	38	Genetic	13	18	26	30	4	8
19	F	51	Unknown	6	6	43	46	3	5
20	F	52	Genetic	6	23	43	51	8	1

TABLE 1. Biographic and anamnestic and clinical characteristics of CI participants

Cl indicates cochlear implant; F, female; M, male.

turned red only when response validation was allowed. Since the speaker was invisible in VR, participants did not have visual cues about its position. Each head-pointing sound localization task comprised 40 trials (five repetitions, for each of the eight sound positions) delivered in random order. Five practice trials were also introduced but discarded from the analyses. The task lasted approximately 15 min. See the Materials for details about the apparatus and general setting in Supplemental Digital Content 2, http://links.lww.com/EANDH/B43.

Audiovisual Attention-Orienting Task

This task was carried out entirely outside VR. Participants sat at a table placed inside the same room in which the VR experiments are carried out. Unlike the VR tasks, in this audiovisual attention-orienting task participants rested their heads on a chinrest facing the screen where visual stimuli were displayed; hence, head movements were not allowed. Participants were instructed to indicate the elevation of a visual disk (i.e., appearing on the screen either above or below their eye level) as quickly and accurately as possible. Crucially, in each trial a task-irrelevant sound was presented simultaneously from one of the loudspeakers flanking the screen, either on the same side as the visual disk (spatially congruent trials), or from the opposite side (spatially incongruent trials). Each trial started with a white fixation cross appearing in the center of the screen and remaining visible until response. After a random delay (450-600 ms), an auditory stimulus (white noise, duration 100 ms) was emitted from one of the two loudspeakers, at approximately 60 dB SPL as measured from head position. After 100 ms from sound delivery, the visual target was presented. This consisted of a white disk (20 pixels radius, 0.5° of visual angle), appearing on a black background for 140 ms in the upper or lower hemifield with respect to the horizontal meridian passing through visual fixation (1.15° above or below the meridian), either in the left or

right hemifield (10° from fixation). In half of the trials, the visual target and the sound appeared on the same hemispace (congruent trials), whereas on the remaining half, the visual target and the sound appeared on opposite hemispaces (incongruent trials). Participants were asked to keep their gaze towards central fixation throughout the task and to indicate as quickly and accurately as possible the elevation of the visual target. Up/down responses were given using the up/down arrows keys on an external keyboard, using the index/middle fingers of the right hand (Fig. 1B). Participants had a timeout of 2000 ms to give their answer and received feedback on accuracy (percentage of correct responses) and mean response time (in ms) only at the end of each block. Importantly, they were also explicitly informed that sounds were always entirely task-irrelevant. The audiovisual attention-orienting task comprised 128 trials (16 repetitions, for each of the four disk positions and each sound side, divided in two blocks of 64 trials each) delivered in random order. Eight practice trials were also introduced but discarded from the analyses. The task lasted approximately 10 min. See the Materials for details about the apparatus and general setting in Supplemental Digital Content 2, http://links.lww.com/EANDH/B43. **Training Tasks**

The training phases were carried out entirely in VR and took place in the same virtual room used for the other tasks detailed above. During both training tasks, the participant saw 13 virtual loudspeakers inside the Head-mounted display. The loudspeakers were arranged in a semicircle centered on the head (radius 50 cm), at -5° below ear level (due to the uncorrected offset between the tracker and the center of the speaker), and spanned between $\pm 72^{\circ}$ (with 12° of separation between each of them; see Fig. 1C and Video File in Supplemental Digital Content 1, http://links.lww.com/EANDH/B44). The target stimulus consisted of a white noise, with two possible amplitude modulations (2 or

3 Hz). Targets sounds were delivered from each of the virtual speaker in random order (12 repetition for each of the 13 speakers, resulting in 156 trials overall, divided into three blocks of 52 trials each). In each trial, a single sound was presented from one of the speakers. Sounds were delivered when the experimenter brought the real speaker into correspondence with one of the virtual ones, following a computer-controlled procedure based on continuous position tracking. Crucially, the same stimuli were delivered in the two training tasks, thus making the auditory component of the trainings identical in this respect (i.e., sounds with two amplitude modulations were delivered from positions that changed on a trial-by-trial basis). In addition, both training tasks involved a similar motor response: a reaching movement. However, in the spatial training the reaching movement served to indicate the perceived sound position, whereas in the nonspatial training served to indicate the perceived amplitude modulation in the target sound. Participants always held the controller with their right hand. At the beginning of each trial, the controller was positioned on their sternum. See the Materials in Supplemental Digital Content 2, http://links.lww.com/EANDH/ B43 for details about the apparatus and general setting.

Spatial Training

Participants were instructed to reach the speaker emitting the sound using the handheld VR controller. The sound lasted until the participant reached and "touched" the correct speaker. If they reached the wrong speaker, the correct speaker started flashing while the sound continued to play. Specifically, a series of red concentric circles (1024×1024 px, 2 circles per second) expanded intermittently, irradiating from the correct sound source (see Video File in Supplemental Digital Content 1, http://links. lww.com/EANDH/B44). The rationale for using wide concentric circles was to capture the participants' attention even in case they were looking away from the correct sound source (e.g., toward the opposite hemispace). The visual feedback and the target sound stopped only when the subject reached the correct speaker position with the controller. This has two implications: first, a sense of agency was associated with the correct response (Valzolgher et al. 2020a,b,c); second, whenever the wrong speaker was originally selected, a combination of visual and auditory signals guided the participant to the correct sound source. To enhance the feeling that the virtual speaker was touched, the controller always produced a brief vibration when coming into "contact" with one of the virtual speakers. This did not serve as feedback for performance, because the vibration occurred irrespective of whether the response was correct or incorrect. To prevent participants from colliding with the real speaker (held by the experimenter), the virtual speakers were always presented with a 5-cm offset in depth. The task lasted approximately 45 min (considering the breaks).

Nonspatial Training

Participants were instructed to identify whether the target sound contained a fast (3 Hz) or slow (2 Hz) amplitude modulation. For fast amplitude-modulated sounds, participants directed the controller in front of them, aiming to touch an invisible virtual button above the central speaker. For slow amplitudemodulated sounds, participants reached toward an invisible virtual button below the same central speaker instead. The position and effects of these virtual buttons was demonstrated to participants during the practice trials. A vibration from the controller always indicated that one of two buttons was correctly reached. As in the Spatial Training feedback procedure, a visual feedback was delivered in the case of wrong responses. This was a series of red concentric semicircles that expanded intermittently from above or below the central speaker to indicate the correct response. Recall that target sounds were presented from different spatial positions also during the nonspatial training, but this spatial information was totally task-irrelevant (see Video File in Supplemental Digital Content 1, http://links.lww.com/EANDH/ B44). The task lasted approximately 20 min (including breaks).

Statistical Analysis

Linear mixed-effect (LME) modeling was used for all statistical analyses. Statistical analyses were run using R (version 1.0.143). For the LME model, we used the R-packages emmean, lme4, lmerTest in R Studio (Bates et al. 2015; Fox & Weisberg 2020). The R-package car was used to obtain deviance tables from the LME models. When appropriate, we calculated Cohen's d_{av} as index of effect size (Lakens 2013). Data and R codes can be retrieved from osf.io/cqtmd.

The dependent variables considered in our analyses were sound localization azimuth error for the head-pointing sound localization task and for spatial training, and reaction time for the audiovisual attention-orienting task. Reaction time were instead analyzed for the audiovisual attention-orienting task. To study head movements, we extracted two dependent variables: number of head rotations and head-rotation extent (Valzolgher et al. 2020c).

RESULTS

Changes in Sound Localization and Head Movements During Spatial Training

Sound localization absolute error in azimuth at the beginning of the study was $24.1^{\circ} \pm 15.6^{\circ}$ (head-pointing sound localization before training in the first session), matching previous studies in documenting a low auditory spatial resolution, for example, when compared to normal-hearing performance (Kerber & Seeber 2012; Jones et al. 2014).

To examine if sound localization improved during the spatial training, we studied changes in absolute error in the horizontal dimension across successive trials using an LME model with trial number as fixed effect (Valzolgher et al. 2020c). To account for the variability related to individual participants and session in which the Spatial training was completed (first or second), we also included the participant (intercept and slope) and session (intercept) as random effects in the model. As shown in Figure 2A, BCI users reduced their absolute error across trials (main effect of trial number, X^2 (1) = 15.84, p < 0.001). Performance in the nonspatial training was near ceiling (mean number of errors = 1.4%; see cumulative discrimination error across participants in Fig. 2B). During the nonspatial training, participants were also faster in completing the trial compared to the spatial training (nonspatial: mean \pm SD = 1.68 \pm 0.25 sec; spatial training: mean \pm SD = 9.62 \pm 6.99; t (19) = 5.15, p < 0.001 on paired t-test; Cohen's $d_{av} = 2.19$).

During training the head was unrestrained and the target lasted until correct response, allowing active listening behavior (i.e., spontaneous head movements). To study head movements, we extracted two dependent variables: the number of head rotations and head-rotation extent (Valzolgher et al. 2020c) (see Materials for details in Supplemental Digital Content 2, http://links.lww.com/EANDH/B43). As expected by design, head-rotation patterns differed in the two training protocols: more head rotations occurred in the spatial (5.72 ± 3.24)

compared to the nonspatial training $(1.15\pm0.41, t (19) = 5.72, p < 0.001$ on paired t-test); furthermore, the extent of head rotations was larger during the spatial (89.06° ± 41.86°) compared to the nonspatial training (4.00° ± 1.91°, t (19) = 9.20, p < 0.001 on paired t-test). Interestingly, head-behavior evolved during the course of the spatial training tasks. BCI users progressively adapted their spontaneous head movements as a function of sound eccentricity: the number of head rotations diminished for central sounds (two-way interaction, X^2 (1) = 5.35, p = 0.02), while head-rotation extent increased for more peripheral sounds (X^2 (1) = 4.78, p = 0.03; see Materials in Supplemental Digital Content 2, http://links.lww.com/EANDH/B43 and Fig. 3).

Effects of Spatial Training on Head-Pointing Sound Localization

Figure 3A shows absolute localization errors in head-pointing sound localization across the two sessions of the experiment. The black line and circles indicate BCI users who performed the spatial training before the nonspatial training; the gray line and



Fig. 2. Participants' preformance during training. A, Reduction of absolute error in the horizontal dimension, as a function of trial in the spatial training. Linear regression (solid line), with 95% confidence intervals (dashed lines). B, Cumulative discrimination error across participants as a function of trials in the nonspatial training (i.e., number of participants who made a mistake in the trial).

circles indicate BCI users who completed the training in the reversed order. The spatial training improved performance to a greater extent compared to the nonspatial training, irrespective of the session in which it was completed.

To study the effect of spatial training on head-pointing sound localization, we entered absolute error in azimuth into an LME analysis with phase (pre or post training), training (spatial or nonspatial) and azimuth as fixed effects. We also included participant (intercept and slope) and testing session (intercept) as random effects, to account for the variability across participants and the order of training type. We found a main effect of training ($X^2(1) = 4.89$, p = 0.03). Crucially, the 2-way interaction between phase and training reached significance $(X^2(1) = 24.14, p < 0.001)$. The absolute error in azimuth decreased after the spatial (Pre: 25.2 ± 16.8 ; Post: 19.3 ± 11.1 ; t = 5.47, p < 0.001, Cohen's $d_{av} = 0.40$, Fig. 3B, C), but not after the nonspatial training (Pre: 22.8 ± 14.7 ; Post: 24.5 ± 17.2 , t = 1.48, p = 0.14, Cohen's $d_{av} = 0.11$, Fig. 3D, E). Density plots of raw data (responses) in azimuth as a function of target position and training are shown in Figure S1 in Supplemental Digital Content 2, http://links.lww.com/EANDH/B43.* For completeness, we also report the analyses on absolute error in elevation (Table 1 in Supplemental Digital Content 2, http:// links.lww.com/EANDH/B43).

To explore if participants who performed the spatial training in the first session (N = 10) maintained the improvement after the 2-weeks washout, we entered on their absolute errors in azimuth during the pretraining phase into an LME analysis with time (session 1 versus session 2) as fixed effects. Errors in the pre training phase were smaller on session 2 compared to session 1 ($X^2(1) = 4.64$, p = 0.03). Albeit this effect was small (3°), it may provide initial evidence that the error reduction induced by the Spatial training may persist after the 2-week washout.

Following Isaiah et al. (2014) we also studied immediate headorienting movements (i.e., movements occurring around 0.90 sec after the beginning of the sound), which reflect the first spontaneous orienting response toward the sound. Saccade-like headorienting response were more accurate after the spatial training, as revealed by the significant interaction between training and phase on response density at target location (F(1,19) = 6.52, p = 0.02, $n^2 = 0.11$; see Materials and Figure S1 in Supplemental Digital Content 2, http://links.lww.com/EANDH/B43).

Finally, we examined if training benefits were modulated by clinical variables. We correlate the training effect (difference in absolute error before and after the spatial training) with the participant's age at the moment of deafness diagnosis, years spent with one CI only and years spent with two CIs. No significant correlation emerged (all ps > 0.35).

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^{*}To examine to what extent changes in the amount of front-back confusions during the head-pointing task could impact on the observed training effects, we entered front-back confusions as variable in an LME with training and phase as fixed effects. We found a training by phase interaction $(X^2(1) = 8.61, p = 0.003)$. Before training, front-back confusions did not differ between spatial (12.2%) and nonspatial conditions (11.8%). After training, there were less front-back confusions in the spatial (4.6%) compared to the nonspatial condition (9.3%). Yet, this front-back confusion reduction did not fully explain our training related improvement. When we repeated the analysis of absolute azimuth error after removing all trials in which a front-back confusion was present, a training × phase interaction was still present $(X^2(1) = 14.64, p < 0.001)$.



Fig. 3. Performance in head-pointing sound localization. A, Absolute localization across the four testing sessions of the experimental design, separately for participants who completed the Spatial training on session 1 (gray) or session 2 (black line). Error bars represent standard errors. B–D, Absolute errors (in degrees) as a function of phase before and after the spatial (red, B) and nonspatial (blue, D) training. C–E, Training effect (deg): the difference between pre and post training session (pre-post) in absolute error as function of training task (C, spatial in red and E, nonspatial in blue). Positive values in (C) and (E) represent improvements after the training.

Audiovisual Attention-Orienting Task

To examine the effects of our training protocols on the audiovisual attention-orienting task, we entered the response time (ms) into an LME analysis with testing phase (pre or post training), training type (spatial or nonspatial), and congruency between sound and visual target position (congruent or incongruent). Again, participant number and session (intercepts) were treated as random effects.

We found a main effect of congruency (X^2 (1) = 30.45, p < 0.001) caused by faster visual discrimination responses when the auditory cue matched target side (congruent: M = 291.2 ms, SD = 79.2 ms) compared to when it occurred on the opposite side of space (incongruent trials: M = 307.3 ms, SD = 79.4 ms, Cohen's $d_{av} = 0.20$). We also found a 3-way interaction between testing phase, training type, and sound position (X^2 (1) = 4.90, p = 0.03). After the nonspatial training, audiovisual attention-

orienting effect decreased (Pre: M = 23.1 ms, SD = 17.8 ms; Post: M = 10.9 ms, SD = 20.5 ms; X^2 (1) = 4.25, p = 0.04, Cohen's d_{av} = 0.64), while it persisted after the spatial one (Pre: M = 11.9 ms, SD = 17.5 ms; Post: M = 18.4 ms, SD = 19.6 ms; X^2 (1) = 1.15, p = 0.28, Cohen's d_{av} = 0.35).

DISCUSSION

In the present study, we examined if the ability of bilateral CI users to localize sounds in the horizontal plane improves as a result of training. Specifically, we implemented a spatial training based on reaching-to-sound, audiovisual feedback, and free-head movements. During this training, we found that sound localization in BCI users improved rapidly across trials. After training, sound localization ameliorated also in an auditory spatial task performed using a different motor response with respect

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to the trained task (head-pointing instead of hand-reaching) and different sound-source positions. This generalization was significantly more pronounced compared to the one observed in a nonspatial control training task.

Our findings add to the clinical population of CI users training effects observed in animal models (Isaiah et al. 2014) and in normal-hearing human listeners (Strelnikov et al. 2011; Rabini et al. 2019; Steadman et al. 2019; Valzolgher et al. 2020b). Most notably, they go beyond early reports on training effects in CI users (Luntz et al. 2005) in two ways. First, they originate from a crossover experimental design, which allowed testing each participant in both training types, thus excluding potential confounding group differences when assessing training efficacy. Second, they show generalization of training effects to a different auditory spatial task. We additionally provided initial evidence that sound localization benefits partially persisted after the 2-week washout in participants who trained in the spatial task during the first session. This effect was, however, numerically small (3° on average); thus, it remains to be ascertained how long this improvement can really persist over time, and paraphs how much this transfer to daily life.

Finally, our study also probed training generalization effects in a task that required *implicit* sound localization, that is, the audiovisual attention-orienting task. We found that lateralized auditory cues were effective in orienting BCIs' visual attention. This finding is novel and adds to previous work in unilateral CI users, in which this audiovisual attention-orienting ability was absent (Pavani et al. 2017). Yet, no change in this task was observed after the spatial training. In fact, we observed a reduction of the attention-orienting effect after the nonspatial training. While this finding was unexpected and it will not be discussed further, it may suggest that repeated processing of nonspatial (rather than spatial) sound attributes could impact the ability to exploit sound position when orienting visual attention, at least in this clinical population.

While the spatial training produced a clear within-subject improvement, the BCI users in our study were fitted with different CI processors. This implies that the auditory cues available to each participant likely differed based on the various device brand and settings. Most notably, AGC types (i.e., which modulates the acoustic signal in amplitude, to compensate the reduced dynamic range of stimulated hearing provided by the implant), vary as a function of the manufacturer. AGC may distort ILDs across frequencies (which are fundamental for sound localization in CI users; see Dorman et al. 2014) in a more or less aggressive way as a function of the processor (and manufacturer) type and of the settings made by the hearing care professional. In the present experiment, the lack of synchronization of AGCs between bilateral CI processors (Pastore et al. 2021; Dwyer et al. 2021), the different duration of sound stimuli as a function of response time (Boyle et al. 2009), and the possible AGC distortions as a function of head movements (Archer-Boyd & Carlyon 2019; see also Archer-Boyd & Carlyon 2021) could have substantially distorted the available ILDs. Yet, irrespective of the modulations introduced by the CI processor our spatial training was robust enough to allow generalization of training effects from the training task (in which sound duration continued until response, 9.6 sec on average), to a test task (in which the sound lasted only 3 sec).

Our instructions allowed free-head movement during sound, and our VR apparatus permitted continuous measuring

of head movements. Several findings arose from this approach. First, during the spatial training, we observed that the number of head rotations diminished for central sounds compared to peripheral, across trial repetitions. BCI users appear to have learned to distinguish if sound came from the center or the periphery and thus, when sound sources were central, they did not need to move their heads, corroborating the improvement revealed by reduction of absolute errors across trials. Second, during the test task, we observed a training related improvement also in terms of the first head movement-orienting response. These immediate and spontaneous orienting movements of the head can reflect early encoding of sounds positions (Muir & Field 1979) and can be considered an implicit index of participants' ability to identify sound direction (also described as saccade-like head-response by Isaiah et al. 2014). Immediate head-orienting responses were more accurate in the spatial compared to the nonspatial training. This finding supports the training benefit documented using absolute errors as a dependent variable. Finally, a third observation concerns the potential role of head movements as effective behaviors strategies when relearning sound localization abilities (Valzolgher et al. 2020c). We showed that head movements in BCI users changed across trial repetition during the spatial training. Although this was not correlated to changes in performance (see Materials in Supplemental Digital Content 2, http://links.lww.com/EANDH/B43), this preliminary observation suggests that BCI participants may also adapt their headrotation behavior when relearning their spatial hearing skills, by making it more purposeful across trials. This finding adds to the literature showing that, compared to static listening conditions, moving the head while listening to sounds improves sound localization not only in normal-hearing participants (Pollack & Rose 1967; Perrett & Noble 1997a,b; Wightman & Kistler 1999; Vliegen et al. 2004; Brimijoin & Akeroyd 2012; Honda et al. 2013; McAnally & Martin 2014), but also in BCI users (Coudert et al. 2022; Mueller et al. 2014; Pastore et al. 2018). Future studies on spatial hearing relearning should examine further the spontaneous self-regulatory behaviors that participants implement during active listening, by adopting unconstrained head or even trunk movements and longlasting sounds, as here.

Limitations

Two methodological issues should be considered. First, our training protocols are likely not equally complex. Although neither task was speeded, while BCI users were relatively fast in responding to amplitude modulations in the target sound (1.7 sec on average), in the sound localization training they listened to each sound for a longer period before responding (9.6 sec). This raises the possibility that the greater efficacy of the spatial training could also reflect, to some extent, longer exposure to the sound. Second, head-pointing to sounds entails a motor response (i.e., head-turning) that is typically coupled with manual reaching movements. This may imply a partial overlap between the motor responses we adopted for the training and testing tasks. Future studies could examine the effects of a training performed with frontal and near sounds (as here), on test stimuli coming in back and/or far space. Changes in the acoustic features of training and test stimuli could also be implemented (syllables or words, as in Zheng et al. 2015, instead of broad band sounds as used here).

CONCLUSION

Using a novel spatial training approach based on reachingto-sounds, audiovisual feedback, and free-head movements during listening, we showed that training auditory skills in BCI users is possible. This improvement can be accounted for in terms of central cognitive processes and/or self-regulation strategies since the auditory input from the CI remained largely unchanged. Furthermore, it stresses the positive contribution that multisensory and motor processes can play in adapting to CI. While our approach to training proved successful, it clearly originated from an experimental more than a translational perspective. To assess the implications of our finding for clinical settings and real life, it would be important to expand our approach by testing the efficacy of the principles subtending our Spatial training by extending its duration and by testing further its generalization to a wider range of spatial locations and stimuli. Ultimately, the main aim remains to enhance spatial hearing in real life for CI users. Our findings can be seen as a first step towards expanding training approaches from speech perception alone to spatial hearing, after implantation. In this respect, they contribute to enrich the domain of actions that clinicians and patients themselves can undertake to improve their experience with the CIs.

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C.V., F.P., and A.F. conceptualized and design the experiment and managed funding acquisition and project administration. C.V., J.G., S.B., S.G., and M.T. performed the experiment. C.V. and F.P. analyzed data and wrote the paper. G.V. and R.S. worked on software. All authors discussed the results and implications and commented on the manuscript. F. P., A.F., and E.T. supervised the project and managed funding.

The authors have no conflicts of interest to declare.

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REFERENCES

- Allen, M. C., Nikolopoulos, T. P., O'Donoghue, G. M. (1998). Speech intelligibility in children after cochlear implantation. Am J Otol, 19, 742–746.
- Archer-Boyd, A. W., & Carlyon, R. P. (2019). Simulations of the effect of unlinked cochlear-implant automatic gain control and head movement on interaural level differences. *J Acoust Soc Am*, 145, 1389.
- Archer-Boyd, A. W., & Carlyon, R. P. (2021). Further simulations of the effect of cochlear-implant pre-processing and head movement on interaural level differences. *JAcoust Soc Am*, 150, 506.
- Aronoff, J. M., Yoon, Y. S., Freed, D. J., Vermiglio, A. J., Pal, I., Soli, S. D. (2010). The use of interaural time and level difference cues by bilateral cochlear implant users. *J Acoust Soc Am*, 127, EL87–EL92.

- Asp, F., Mäki-Torkko, E., Karltorp, E., Harder, H., Hergils, L., Eskilsson, G., Stenfelt, S. (2012). Bilateral versus unilateral cochlear implants in children: Speech recognition, sound localization, and parental reports. *Int J Audiol*, *51*, 817–832.
- Bates, D., Maechler, M., Bolker, B. M., & Walker, S. (2015). Fitting linear mixed-effects models using lme4. J Statist Softw, 67, 1–48.
- Brimijoin, W. O., & Akeroyd, M. A. (2012). The role of head movements and signal spectrum in an auditory front/back illusion. *Iperception*, *3*, 179–182.
- Boyer, E. O., Babayan, B. M., Bevilacqua, F., Noisternig, M., Warusfel, O., Roby-Brami, A., Hanneton, S., Viaud-Delmon, I. (2013). From ear to hand: The role of the auditory-motor loop in pointing to an auditory source. *Front Comput Neurosci*, 7, 26.
- Boyle, P. J., Büchner, A., Stone, M. A., Lenarz, T., Moore, B. C. (2009). Comparison of dual-time-constant and fast-acting automatic gain control (AGC) systems in cochlear implants. *Int J Audiol*, 48, 211–221.
- Calmels, M. N., Saliba, I., Wanna, G., Cochard, N., Fillaux, J., Deguine, O., Fraysse, B. (2004). Speech perception and speech intelligibility in children after cochlear implantation. *Int J Pediatr Otorhinolaryngol, 68*, 347–351.
- Carlile, S. (2014). The plastic ear and perceptual relearning in auditory spatial perception. *Front Neurosci*, 8, 237.
- Cohen, Y. E., & Andersen, R. A. (2002). A common reference frame for movement plans in the posterior parietal cortex. *Nat Rev Neurosci, 3*, 553–562.
- Coudert, A., Gaveau, V., Gatel, J., Verdelet, G., Salemme, R., Farne, A., ... & Truy, E. (2022). Spatial Hearing Difficulties in Reaching Space in Bilateral Cochlear Implant Children Improve With Head Movements. *Ear Hear*, 43, 192.
- Dehaene, S. (2020). *How We Learn: The New Science of Education and the Brain.* Penguin.
- Dwyer, R. T., Chen, C., Hehrmann, P., Dwyer, N. C., Gifford, R. H. (2021). Synchronized automatic gain control in bilateral cochlear implant recipients yields significant benefit in static and dynamic listening conditions. *Trends Hear*, *25*, 23312165211014139.
- Dorman, M. F., Loiselle, L., Stohl, J., Yost, W. A., Spahr, A., Brown, C., Cook, S. (2014). Interaural level differences and sound source localization for bilateral cochlear implant patients. *Ear Hear*, 35, 633–640.
- Forli, F., Lazzerini, F., Fortunato, S., Bruschini, L., Berrettini, S. (2019). Cochlear implant in the elderly: Results in terms of speech perception and quality of life. *Audiol Neurootol*, 24, 77–83.
- Fox, J., & Weisberg, S. (2020). Using Car and Effects Functions in Other Functions 3, pp. 1-5. https://mran.revolutionanalytics.com/snapshot/2020-05-18/web/packages/car/vignettes/embedding.pdf
- Gaveau, V., Coudert, A., Salemme, R., Koun, E., Desoche, C., Truy, E., Farne, A., Pavani, F. (2020). SPHERE: A novel approach to 3D and active sound localization. *bioRxiv*. Preprint posted online. March 20, 2020. doi: 10.1101/2020.03.19.998906
- Gifford, R. H., & Stecker, G. C. (2020). Binaural cue sensitivity in cochlear implant recipients with acoustic hearing preservation. *Hear Res, 390*, 107929.
- Grantham, D. W., Ashmead, D. H., Ricketts, T. A., Labadie, R. F., Haynes, D. S. (2007). Horizontal-plane localization of noise and speech signals by postlingually deafened adults fitted with bilateral cochlear implants. *Ear Hear*, 28, 524–541.
- Grieco-Calub, T. M., & Litovsky, R. Y. (2010). Sound localization skills in children who use bilateral cochlear implants and in children with normal acoustic hearing. *Ear Hear*, *31*, 645–656.
- Honda, A., Shibata, H., Hidaka, S., Gyoba, J., Iwaya, Y., Suzuki, Y. (2013). Effects of head movement and proprioceptive feedback in training of sound localization. *Iperception*, 4, 253–264.
- Isaiah, A., Vongpaisal, T., King, A. J., Hartley, D. E. (2014). Multisensory training improves auditory spatial processing following bilateral cochlear implantation. *J Neurosci*, 34, 11119–11130.
- Jones, H., Kan, A., Litovsky, R. Y. (2014). Comparing sound localization deficits in bilateral cochlear-implant users and vocoder simulations with normal-hearing listeners. *Trends Hear*, 18, 2331216514554574.
- Keating, P., Dahmen, J. C., King, A. J. (2015). Complementary adaptive processes contribute to the developmental plasticity of spatial hearing. *Nat Neurosci, 18*, 185–187.
- Kerber, S., & Seeber, B. U. (2012). Sound localization in noise by normalhearing listeners and cochlear implant users. *Ear Hear*, 33, 445–457.
- Lakens, D. (2013). Calculating and reporting effect sizes to facilitate cumulative science: A practical primer for t-tests and ANOVAs. *Front Psychol*, 4, 863.

- Litovsky, R. Y., Parkinson, A., Arcaroli, J. (2009). Spatial hearing and speech intelligibility in bilateral cochlear implant users. *Ear Hear*, 30, 419–431.
- Luntz, M., Brodsky, A., Watad, W., Weiss, H., Tamir, A., Pratt, H. (2005). Sound localization in patients with unilateral cochlear implants. *Cochlear Implants Int*, 6, 1–9.
- McAnally, K. I., & Martin, R. L. (2014). Sound localization with head movement: Implications for 3-d audio displays. *Front Neurosci*, 8, 210.
- Mendonça, C. (2014). A review on auditory space adaptations to altered head-related cues. Front Neurosci, 8, 219.
- Moore, D. R., & Shannon, R. V. (2009). Beyond cochlear implants: Awakening the deafened brain. *Nat Neurosci, 12*, 686–691.
- Moua, K., Kan, A., Jones, H. G., Misurelli, S. M., Litovsky, R. Y. (2019). Auditory motion tracking ability of adults with normal hearing and with bilateral cochlear implants. *J Acoust Soc Am*, 145, 2498.
- Mueller, M. F., Meisenbacher, K., Lai, W. K., Dillier, N. (2014). Sound localization with bilateral cochlear implants in noise: How much do head movements contribute to localization? *Cochlear Implants Int*, 15, 36–42.
- Muir, D., & Field, J. (1979). Newborn infants orient to sounds. *Child Dev*, 50, 431–436.
- Pastore, M. T., Natale, S. J., Yost, W. A., Dorman, M. F. (2018). Head movements allow listeners bilaterally implanted with cochlear implants to resolve front-back confusions. *Ear Hear*, 39, 1224–1231.
- Pastore, M. T., Pulling, K. R., Chen, C., Yost, W. A., Dorman, M. F. (2021). Effects of bilateral automatic gain control synchronization in cochlear implants with and without head movements: Sound source localization in the frontal hemifield. J Speech Lang Hear Res, 64, 2811–2824.
- Pavani, F., Venturini, M., Baruffaldi, F., Artesini, L., Bonfioli, F., Frau, G. N., van Zoest, W. (2017). Spatial and non-spatial multisensory cueing in unilateral cochlear implant users. *Hear Res*, 344, 24–37.
- Perrett, S., & Noble, W. (1997a). The contribution of head motion cues to localization of low-pass noise. *Percept Psychophys*, 59, 1018–1026.
- Perrett, S., & Noble, W. (1997b). The effect of head rotations on vertical plane sound localization. J Acoust Soc Am, 102, 2325–2332.
- Pollack, I., & Rose, M. (1967). Effect of head movement on the localization of sounds in the equatorial plane. *Percept Psychophys*, 2, 591–596.
- Rabini, G., Altobelli, E., Pavani, F. (2019). Interactions between egocentric and allocentric spatial coding of sounds revealed by a multisensory learning paradigm. *Sci Rep*, 9, 7892.
- Rosskothen-Kuhl, N., Buck, A. N., Li, K., Schnupp, J. W. (2021). Microsecond interaural time difference discrimination restored by cochlear implants after neonatal deafness. *Elife*, 10, e59300.
- Seeber, B. U., & Fastl, H. (2008). Localization cues with bilateral cochlear implants. J Acoust Soc Am, 123, 1030–1042.
- Senn, S. S. (2002). Cross-Over Trials in Clinical Research (Vol. 5). John Wiley & Sons.
- Smulders, Y. E., Van Zon, A., Stegeman, I., Rinia, A. B., Van Zanten, G. A., Stokroos, R. J., Hendrice, N., Free, R. H., Maat, B., Frijns, J. H. M., Briaire, J. J., Mylanus, E. A. M., Huinck, W. J., Smit, A. L., Topsakal, V., Tange, R. A., Grolman, W. (2016). Comparison of bilateral and unilateral cochlear implantation in adults a randomized clinical trial. *JAMA Otolaryngol Head Neck Surg*, 142, 249–256.

- Steadman, M. A., Kim, C., Lestang, J. H., Goodman, D. F. M., Picinali, L. (2019). Short-term effects of sound localization training in virtual reality. *Sci Rep*, 9, 18284.
- Stickney, G. S., Zeng, F. G., Litovsky, R., Assmann, P. (2004). Cochlear implant speech recognition with speech maskers. *J Acoust Soc Am*, 116, 1081–1091.
- Strelnikov, K., Rosito, M., Barone, P. (2011). Effect of audiovisual training on monaural spatial hearing in horizontal plane. *PLoS One, 6*, e18344.
- Tyler, R. S., Witt, S. A., Dunn, C. C., Wang, W. (2010). Initial development of a spatially separated speech-in-noise and localization training program. J Am Acad Audiol, 21, 390–403.
- Valzolgher, C., Alzhaler, M., Gessa, E., Todeschini, M., Nieto, P., Verdelet, G., Salemme, R., Gaveau, V., Marx, M., Truy, E., Barone, P., Farnè, A. & Pavani, F. (2020a). The impact of a visual spatial frame on real soundsource localization in virtual reality. *Curr Res Behav Sci, 1*, 100003.
- Valzolgher, C., Campus, C., Rabini, G., Gori, M., Pavani, F. (2020b). Updating spatial hearing abilities through multisensory and motor cues. *Cognition*, 204, 104409.
- Valzolgher, C., Verdelet, G., Salemme, R., Lombardi, L., Gaveau, V., Farné, A., Pavani, F. (2020c). Reaching to sounds in virtual reality: A multisensory-motor approach to promote adaptation to altered auditory cues. *Neuropsychologia*, 149, 107665.
- Valzolgher, C., Todeschini, M., Verdelet, G., Gatel, J., Salemme, R., Gaveau, V., Truy, E., Farnè, A., Pavani, F. (2022). Adapting to altered auditory cues: Generalization from manual reaching to head pointing. *PLoS One*, 17, e0263509.
- van Hoesel, R. J. (2004). Exploring the benefits of bilateral cochlear implants. *Audiol Neurootol*, *9*, 234–246.
- Verdelet, G., Desoche, C., Volland, F., Farnè, A., Coudert, A., Hermann, R., Truy, E., Gaveau, V., Pavani, F., & Salemme, R. (2019). Assessing spatial and temporal reliability of the vive System as a tool for naturalistic behavioural research. In 2019 International Conference on 3D Immersion (IC3D) (pp. 1-8). IEEE, Brussels, Belgium. https://doi.org/10.1109/IC3D48390.2019.8975994
- Verhaert, N., Lazard, D. S., Gnansia, D., Bébéar, J. P., Romanet, P., Meyer, B., Péan, V., Mollard, D., Truy, E. (2012). Speech performance and sound localization abilities in Neurelec Digisonic® SP binaural cochlear implant users. *Audiol Neurootol*, 17, 256–266.
- Vliegen, J., Van Grootel, T. J., Van Opstal, A. J. (2004). Dynamic sound localization during rapid eye-head gaze shifts. *J Neurosci*, 24, 9291–9302.
- Wightman, F. L., & Kistler, D. J. (1999). Resolution of front-back ambiguity in spatial hearing by listener and source movement. *J Acoust Soc Am*, 105, 2841–2853.
- Wilson, B. S. (2017). The modern cochlear implant: A triumph of biomedical engineering and the first substantial restoration of human sense using a medical intervention. *IEEE Pulse*, 8, 29–32.
- Wilson, B. S. (2019). The remarkable cochlear implant and possibilities for the next large step forward. *Acoust Today*, 15, 53–61.
- Wilson, B. S., Finley, C. C., Lawson, D. T., Wolford, R. D., Eddington, D. K., Rabinowitz, W. M. (1991). Better speech recognition with cochlear implants. *Nature*, 352, 236–238.
- Zheng, Y., Godar, S. P., Litovsky, R. Y. (2015). Development of sound localization strategies in children with bilateral cochlear implants. *PloS One*, 10, e0135790.