Changes in the Human Brain Cortex in Response to Learning Click-Based Echolocation: A Virtual Navigation Paradigm

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Submission Date:	28th March 2019

Abstract

Traditionally, sensory areas within the human brain are viewed as being tied to specific modalities. However, an emerging perspective suggests the brain may be organised in a flexible way, with sensory areas being driven by the task at hand. To investigate the functional organisation of the brain, we trained sighted people in echolocation related tasks and examined BOLD activity associated with the processing of echoic information before and after training. We then compared this activity to that observed in expert echolocators completing the same task. Despite sighted participants showing an improvement in echolocation ability, the brain regions recruited by expert echolocators and sighted participants appear to be somewhat different. When we isolated the processing of echoes, we found an increase in BOLD activation in the occipital cortex of expert echolocators, but not in sighted participants after training. Despite this, both groups displayed common activations within the primary auditory cortex. Similar results were also found when we compared the processing of all sounds to silence. When we investigated the processing of spatially coherent routes, compared to scrambled routes, we found activations within the occipital cortex of expert echolocators and sighted participants as a result of training. Our results suggest that the brain of expert echolocators may be organised in a flexible way, with sensory areas, such as the primary 'visual' cortex being recruited for the processing of auditory information. Furthermore, recruitment of the calcarine cortex in sighted people, after training, may hint at the possibility that the sighted brain is also organised in a flexible way, with areas typically devoted to vision, namely the occipital cortex, possibly processing spatial information conveyed by echoes.

Acknowledgements of Contribution to Thesis Work

All MRI procedures were developed by Lore Thaler.

All MRI scanning was undertaken by Roger Blacklock and Liam Norman. Assistance provided by Caitlin Dodsworth for 10 sighted participants. Assistance provided by Greg Van-Dongen and Laura Naysmith for four sighted participants.

Programs for spatial navigation tasks were developed by Lore Thaler and coded by Liam Norman.

Sound Editing software was coded by Lore Thaler.

Four sighted participants were recruited and trained completely by other MSc students, Greg Van-Dongen and Laura Naysmith.

Ten sighted participants were recruited and trained completely by Caitlin Dodsworth.

Training protocols were developed by Lore Thaler, with contributions from Caitlin Dodsworth, Greg Van-Dongen and Laura Naysmith.

Statement of Copyright

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1. Introduction

A major problem in neuroscience lies in understanding the functional organisation of the brain. The functional specialisations of sensory areas were traditionally viewed as being tied to specific modalities, for example, higher-order areas of the 'visual' cortex were associated with selectivity to objects or faces. A radically different and emerging view is that the brain is organised by task, rather than by sensory modality (Amedi, Hofstetter, Maidenbaum & Heimler, 2017; Maidenbaum, Abboud & Amedi, 2014; Pascual-Leone, Amedi, Fregni & Merabet, 2005). This idea is supported by the fact that in blind individuals higher-order 'visual' areas, such as the visual word form area or the lateral occipital complex, can process the same information as conveyed by sound, (Amedi, Stern, Camprodon, Bermpohl, Merabet, Rotman et al., 2007; Striem-Amit, Cohen, Dehaene & Amedi, 2012), while 'auditory' areas can process visual motion (Lomber, Meredith & Kral, 2010). These findings support the view that the brain might be organised flexibly by task, and not by modality.

Echolocation is a term that was coined by Griffin (1944) whilst describing the ability of bats, marine mammals and people to obtain spatial information about obstacles or prey in the dark. Echolocation relies on the generation of sound, and the comparison of the outgoing sound with the returning echo (Jones, 2005). This use of reflected sound allows individuals to gain information about their surrounding environment.

In recent years, research concerning human echolocation has gained momentum, with particular focus on echolocation using mouth-clicks (Kolarik, Cirstea, Pardhan & Moore, 2014; Thaler & Goodale, 2016). This research has confirmed that whilst click-based echolocation is a skill that is currently only used by a few blind people, often referred to as expert echolocators, it can be learned by anyone, including sighted people (Ekkel, van Lier & Steenbergen, 2017; Hausfeld, Power, Gorta & Harris, 1982; Schenkman & Nilsson, 2010; Teng, Puri & Whitney, 2012; Tonelli, Brayda & Gori, 2016). As a consequence, click-based echolocation is a suitable paradigm to investigate to what degree the human brain might be organised by task or by modality, as people who are new to this skill will have a good baseline for comparison. Furthermore, the comparison of ‘expert echolocators’ and people who have newly learned this skill enables us to answer questions about long term plasticity.

To address these questions, we used a virtual navigation paradigm. There is considerable literature about navigation and virtual navigation using the visual modality, (Hildreth, Beusmans, Boer & Roydon, 2000; Spriggs, Kirk & Skelton, 2018; Thorndyke & Hayes-Roth, 1982), and whilst vision is the most common modality used to navigate by people who are sighted, previous research has shown that it is not essential and can also be achieved through other senses.

One study used a sensory substitution device, the virtual EyeCane, to investigate navigation in the absence of vision (Levy-Tzedek, Maidenbaum, Amedi & Lackner, 2016). It is based on the physical EyeCane which uses infrared sensors to obtain distance information. The device emits a series of beeps; the closer the device is to an obstacle, the higher the frequency of beeps presented. In a virtual environment, participants were represented by an avatar holding the EyeCane and were asked to navigate eight environments. A training phase was employed in which participants made use of visual and auditory information whilst exploring two environments. During the testing phase, only auditory information was available (Levy-Tzedek et al., 2016). Using auditory information to navigate resulted in a longer path length and completion time, along with an increased number of collisions and pauses (Levy-Tzedek et al., 2016). It seems that relying on auditory information to navigate may be more difficult, but it is possible after training. Importantly, the training effects were always measured within the same eight environments, so it is not clear to what degree participants really learned to navigate using auditory information and to what degree they may have acquired ‘automated’ responses, allowing them to successfully navigate through the space.

Navigation has also been investigated using a visual to tactile SSD called the Tongue Display Unit (TDU) which converts visual information into tactile pulses on the tongue (Kupers, Chebat, Madsen, Paulson & Ptito, 2010). In this experiment, the tongue was constantly stimulated, with outer electrodes representing walls and a singular electrode representing the participants position (Kupers et al., 2010). In a virtual task, blind and blindfolded-sighted participants were required to use the computer keyboard to navigate two routes, 15 times per day for four days (Kupers et al., 2010). Initially, results showed that blind and blindfolded sighted participants were equally as good at using the TDU to navigate, however by the end of the training period blind participants outperformed blindfolded sighted participants (Kupers et al., 2010). Although navigational ability was investigated, this was always within the same routes. Again, it is possible that participants may have learned a specific set of responses, allowing them to successfully complete a route, rather than to actually navigate. Despite this, these results suggest that both blind and sighted people are able to learn to navigate using an alternative modality.

In addition to behavioural training using the TDU, the neural networks associated with navigation were investigated (Kupers et al., 2010). A passive fMRI procedure was employed, in which participants were presented with a route and a scrambled route and had to decide which of the two presentations had been a route (Kupers et al., 2010). Despite no behavioural difference in performance between blind and blindfolded sighted whilst scanning, blind participants showed an increase in blood-oxygen-level-dependent (BOLD) signal in the right parahippocampus, parietal cortex, precuneus, anterior cingulate cortex, pre-frontal cortex, cerebellum and occipital cortex (Kupers et al., 2010). In contrast, blindfolded-sighted participants performing the task displayed increased BOLD activity in the parietal cortex, precuneus, anterior cingulate cortex and cerebellum, but activity in the occipital cortex and parahippocampus was absent (Kupers et al., 2010). This suggests that the neural networks underpinning these navigational abilities may be different in blind and blindfolded-sighted participants. However, it is also possible that training with the TDU was not long or thorough enough to permit measurable neuroplastic changes in sighted people. As such, it is an open question to what degree the changes measured in sighted participants, compared to blind participants, were due to differences in the long-term changes in relevant sensory areas as a result of changes in sensory processing, as opposed to training with the TDU.

A further comparison was made between blind participants performing the navigational task using the TDU and sighted participants completing the task with visual information only (Kupers et al., 2010). Similar BOLD activations were present in both groups, including the right parahippocampus, parietal cortex, precuneus, anterior cingulate cortex, pre-frontal cortex, and occipital cortex (Kupers et al., 2010). This seems to suggest that the same neural networks, which are used for navigation using vision, are recruited by blind individuals when using the TDU to navigate.

With respect to the neural correlates of click-based echolocation, research is limited, but has consistently shown that blind echolocation experts show activations in occipital cortex, including early visual areas (calcarine cortex; BA17) for the processing of echoes (Arnott, Thaler, Milne, Kish & Goodale, 2013; Milne, Arnott, Kish, Goodale & Thaler, 2015; Thaler, Arnott & Goodale, 2011; Wallmeier, Kish, Wiegrebe & Flanagin, 2015). At present, it is an open question to what degree these activations are due to expertise in echolocation or long term changes in brain function due to blindness.

We employed a 10-week echolocation training programme in sighted individuals. We trained participants to complete echolocation tasks and monitored their accuracy in a virtual navigation task, as well as their accuracy in determining the size and orientation of objects using their own mouth-clicks. The latter tasks were used to provide more comprehensive training to facilitate comparison to echolocation experts who use their own mouth-clicks. It is expected that echolocation ability will improve over 20 training sessions and participants will become increasingly accurate in all tasks.

The comparison of brain activity during a virtual navigation task, before and after training, will allow us to investigate changes in brain activity in response to learning about echo-acoustic information. Specifically, fMRI will highlight which areas of the brain are recruited for processing echo-acoustic information in sighted people. This can then be compared to activity shown by expert echolocators when performing the same tasks. This may reveal whether sensory areas are tied to specific modalities, or if the brain is organised in a more flexible way, with sensory areas being driven by the task. Furthermore, it will allow us to determine to what degree the changes in brain activity observed in sighted people match activations found in expert echolocators.

2. Materials & Methods

All testing procedures were approved by Durham University Ethics Committee. Participants were presented with an information sheet (appendix A) and privacy notice (appendix B). Informed consent was obtained (appendices C & D) and all subjects were screened to ensure suitability for fMRI (appendix E). A debrief followed the experiment (appendix F).

2.1. Participants

Fourteen sighted novices (8 males) aged 21-71yrs participated. All reported to have no prior echolocation experience and normal or corrected to normal vision. Hearing ability was measured with pure tone audiometry (0.25-16kHz) for both ears. A total of 5 expert echolocators (experience in echolocation for more than three years and daily use of it) also took part. Characteristics are shown in table 1.

Table 1. *Characteristics of Expert Echolocators*

Subject	Sex	Age (y)	Cause of Blindness
1	M	36	Lost sight gradually from birth due to glaucoma. Only bright light detection since early childhood. Used echolocation on a daily basis since 12yrs.
2	F	43	Vision loss at birth due to Leber's Congenital Amaurosis. Used echolocation since 31yrs.
3	M	24	Sudden vision loss at 12yrs, with normal vision prior to this. Used echolocation on a daily basis since vision loss. Eyes removed at 19yrs.
4	M	59	Vision loss since birth due to retinal detachment. Bright light detection only. Use of echolocation since 6yrs.
5	M	51	Enucleated in infancy due to retinoblastoma. Used echolocation since infancy.

2.2. Virtual Navigation Task

A virtual navigation task was created and used to train echolocation ability in sighted participants over a 10-week period. A variation of this task was also used to prepare participants for the task they would complete during fMRI, and to assess navigational abilities and associated BOLD responses during fMRI in expert echolocators and in sighted participants, before and after training.

2.2.1. Virtual Navigation – Training Task

In order to create the computer based virtual navigation training task, three physical mazes were created. Sound recordings were made within these mazes and then used to populate six virtual mazes (i.e. three original and three mirror versions) on the computer. The virtual mazes were navigated by sighted blindfolded participants across 20 sessions, two sessions per week, spread over a 10-week period. The aim was to train participants to navigate using echo-acoustic information.

2.2.1.1. Sound Recording & Editing

Sound recordings were created in an anechoic chamber at Durham University Psychology Department. The walls, door and ceiling were lined with acoustic absorption foam wedges to reduce reverberations and absorb frequencies above 315Hz. A 300 x 300cm grid was mapped onto the floor of the anechoic chamber and subdivided into $25cm^2$ squares. Three physical mazes were created using poster boards mounted on metal poles.

Eight sound recordings were made in a clockwise direction at 0^o, 45^o, 90^o, 135^o, 180^o, 225^o, 270^o and 315^o at each intersection point of the grid within each maze (see Figure 1), with a north facing start point. A speaker (Visaton SC5.9 ND) mounted in front of the mouth of a manikin was used to play click-sounds (see Norman & Thaler 2018 for anthropometric measurements of the manikin). The speaker was driven by a laptop (Dell Studio 1558; Intel i3 CPU 2.27GHz; 4 GB RAM; Windows 7 pro 64 bit), external sound card (Soundblaster; creative labs model sb1240) and amplifier (Kramer 900N). Sounds were produced by Audacity 2.0.2. The clicks and returning echoes were recorded by microphones, placed inside the manikin's ears, and a digital recorder (DPA SMK-SC4060 miniature microphones; DPA microphones, Denmark; TASCAM DR100-MKII recorder; TEAC Corporation, Japan; 24 bit and 96 kHz).

We recorded a T-maze, U-maze and Z-maze. Detailed information about each maze is presented in figure 1. The end point of each mazes was created using corrugated plastic sheets, as opposed to poster boards that comprised the remaining walls of the maze.

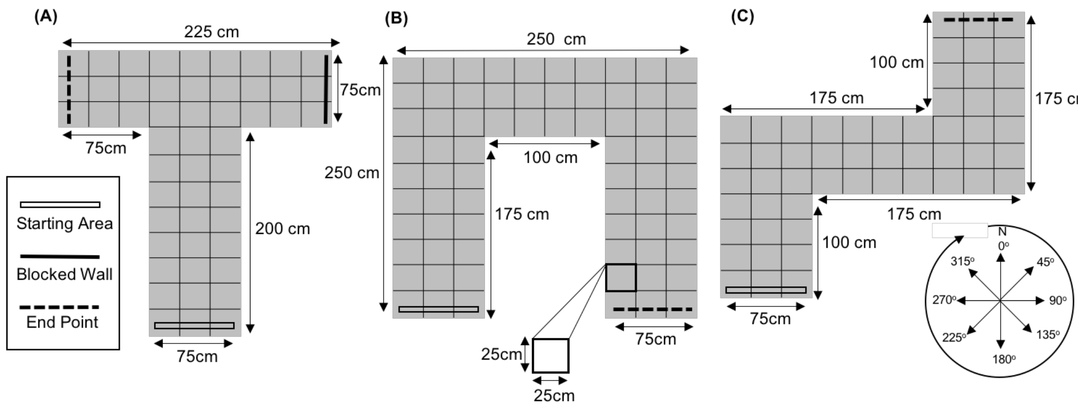

Figure 1. **(A).** Illustration of T-maze and recording positions. The solid black line denotes the blocked wall to the right. **(B).** Illustration of U-maze and recording positions. **(C).** Illustration of Z-maze and recording positions. In all diagrams, the black box represents starting area and the black dashed line symbolises the end point which was made from corrugated plastic sheets. Eight sound recordings (0^o-315^o) were made at each grid intersection in each route. All diagrams contain dimensions of each physical route.

The recorded sounds were processed using MATLAB R2012b. The result was a single sound and returning echo for each position and angular orientation within a maze. To create mirror images of each maze, channels and locations were reassigned. The result was 6 distinct virtual mazes, shown in figure 2.

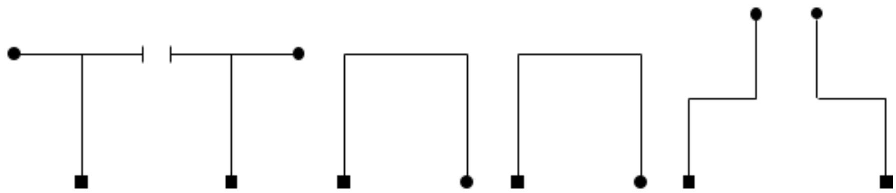

Figure 2. Line drawings illustrating the six mazes used to train echolocation ability in the virtual navigation task. Mazes were also presented prior to fMRI and during fMRI. The square represents the starting position and the circle denotes the goal position within each maze. The dashed line (T-maze only) signifies a blocked wall.

2.2.1.2. Set Up & Computer Program

Psychophysics toolbox (Brainard, 1997) and MATLAB R2018b were used to run the experiment on a laptop (Dell Latitude E7470; Intel Core i56300U CPU 2.40; 8GB RAM; 64-bit Windows 7 Enterprise) with external sound card (Soundblaster; creative labs model sb1240). Echolocation stimuli were presented through headphones (Etymotic ER4B).

To navigate, participants used the computer keyboard. Pressing any key would start a trial. Each press of the 'W' key would move the participant one step forward in the virtual maze and pressing the 'S' key would result in one step backwards. Upon pressing the 'A' key, the participant would rotate 45^{o} in an anti-clockwise direction and each 'D' press would rotate the participant 45^{o} in a clockwise direction. An example of how the computer program works is shown in figure 3.

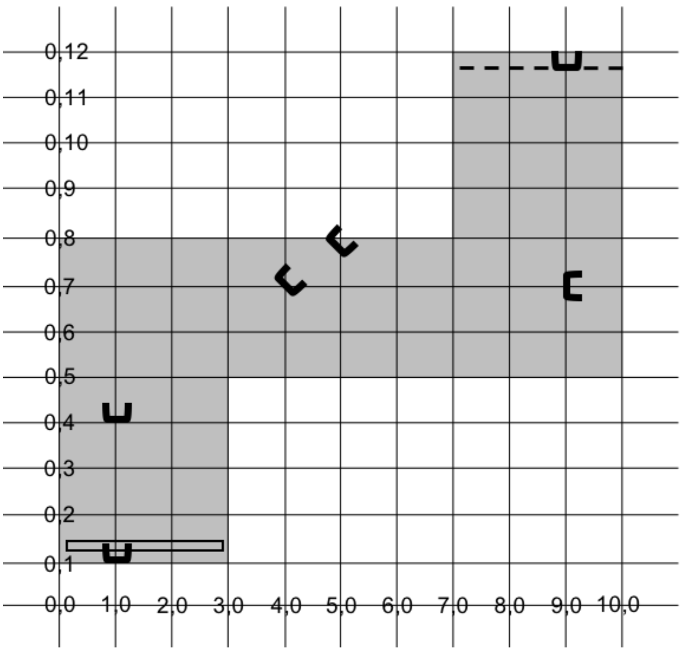

Figure 3. A demonstration of how participants were represented during the virtual navigation training task and how they would successfully navigate from the start to the end of a maze. The black box represents the area in which participants could enter the maze and the black dashed line shows the end point. In this example, the participant is positioned at 1,1. To get to 1,4, the participant would press the 'W' key three times. Upon pressing the 'D' key once, followed by the 'W' key four times, the participant would move to 5,8. One press of the 'S' key would result in the participant moving back to 4,7. One press of the 'D' key would rotate the

participant 45^{o} right, and five presses of the 'W' key would take the participant to 9,7. To get to the end point of the route, the participant would press the 'A' key twice to rotate 90^{o} left and the 'W' key five times.

2.2.1.3. Procedure

All sighted participants were asked to wear a blindfold and to close their eyes when completing the virtual navigation task. Each participant was assigned to one of two groups. One group started with T-maze (right turn), U-maze (right-right turn), and Z-maze (right-left turn). The other group started with the mirror version of each maze. First a demo trial was completed in order to gain familiarity with the controls and the task. To successfully complete the task, sighted participants had to navigate from the start to the end of each virtual maze, within 3 minutes. All sighted participants completed 20 sessions in total. Sessions 1-18 consisted of 18 trials, with each of the three mazes being presented six times. Sessions 19 & 20 contained 36 trials, of which 18 trials contained mazes which had been previously navigated and 18 trials contained mazes which were 'new' (i.e. the three mirror versions that they had not trained with in sessions 1-18). The purpose of this manipulation was to determine if people had successfully learned to navigate using echo-acoustic cues or if they had just learned 'stereotypical' responses. In the latter case, their performance for the novel mazes should be worse than for the trained mazes.

Participants could enter each maze at one of four positions in sessions 1-14, and they always faced straight into the maze (i.e. at 0^{o}). In sessions 15-20, participants could enter the maze at one of four positions and one of 3 orientations (0^{o}, 45^{o} or 315^{o}) meaning there were 12 different possible start conditions. All starting locations and orientations were randomised and participants were not informed. If a collision occurred (i.e. participants bumped into a wall) an error tone would be presented in sessions 1-14. In addition to this, in sessions 15-20, participants would receive a 15s time out in which they would not hear any echolocation stimuli and would be unable to move.

Expert echolocators did not take part in this task.

2.2.2. Virtual Navigation – Pre fMRI

The pre fMRI virtual navigation task was designed to introduce echolocation stimuli and prepare participants for the task during fMRI. The goal of this task was to determine if participants could discriminate between sounds with echoes and sounds without echoes, if participants could discriminate between 'routes' and 'scrambled' routes through mazes, and if participants were able to discriminate between different types of routes. Whilst the virtual navigation training task (2.2.1.1) had permitted participants to navigate by themselves through the various mazes, the pre-fMRI navigation task was a 'passive' task, during which participants only listened to sequences of sounds without pressing any keys. Only at the end of each sequence, participants responded as to what they had perceived.

2.2.2.1. Sound Recording & Editing

The same sounds used in the virtual navigation training task (2.2.1.1) were also used for the pre fMRI task.

Two samples were created for each of the six mazes by selecting recordings corresponding to a specific sequence of locations and orientations within that maze. The resulting sound files were 10.53s in length and contained 18 clicks and echoes, each separated by 600ms, and there were twelve sound files in total. These twelve files were assigned to one of three categories: (1) single turn route (2) two turn route with both turns going into the same direction, (3) two turn route with both turns going into different directions. Scrambled stimuli for each of the six routes were also created in order to create sound files that had exactly the same acoustic information (i.e. timing, clicks and echoes), but that did not convey a coherent route. To do this, the individual click-echo sounds in each route sound file were randomly shuffled and pieced together so that there was no coherent route. In order to create a secondary set of control stimuli, i.e. stimuli with clicks but not containing any echoes, a sound recording was used during which the manikin had been placed facing the foam padded wall in the anechoic chamber. This sound was then repeated at the same temporal sequence as sounds in 'route' and 'scrambled' sound files.

In total, five types of sound stimuli were created: routes (single-turn; two-turns-same; two-turns-different), scrambled routes and clicks with no echoes.

Due to the way in which stimuli were created, stimuli containing echoes (both 'route' and 'scrambled' stimuli) were of higher RMS intensity than stimuli not containing echoes (data not shown).

2.2.2.2. Set Up & Computer Program

A laptop (Dell Latitude E7470; Intel Core i56300U CPU 2.40; 8GB RAM; 64-bit Windows 7 Enterprise) and MATLAB version R2018b were used to run the pre fMRI task. All audio stimuli were presented via an external sound card (Soundblaster; creative labs model sb1240) and amplifier (Kramer 900N) over MR compatible insert earphones (model s-14 sensimetrics, Malden, MA). Audio stimuli had been equalised for the nonlinear frequency response of the headphones using filters provided by the manufacturer. There were 30 trials per block, in which each of the five types of echolocation stimuli were presented 6 times in a random order.

2.2.2.3. Procedure

Five expert echolocators and all sighted participants completed two practice sessions on two separate days before scanning. Each session contained one practice block. Sighted participants completed four sessions in total; two before the pre-training scan and two before the post-training scan. Initially, all participants were presented with an example of each type of echolocation stimuli over MR compatible insert earphones (model s-14, sensimetrics, Malden, MA) and received feedback. Sighted participants and expert echolocators with any residual visual sensitivity were asked to wear a blindfold and close their eyes. When experimental trials commenced, participants were asked to respond verbally as to which type of echolocation stimuli they had heard. This response was recorded by the experimenter. The next trial followed immediately. Each practice session took a maximum of 20 minutes to complete.

2.2.3. Virtual Navigation – During fMRI

All participants completed a virtual navigation task during fMRI. The aim was to determine which areas of the brain were recruited for the processing of echo-acoustic information for navigation in sighted participants and expert echolocators.

2.2.3.1. Sound Recording & Editing

The same procedure for recording and editing sounds as the pre fMRI virtual navigation task (2.2.2) was adopted. As a result, the stimuli used were exactly the same.

2.2.3.2. Set up & Computer Program

Pre-recorded routes, with a fixed duration of 10.53s, were presented to participants via insert earphones (model s-14, sensimetrics, Malden, MA). A computer, external sound card (Soundblaster; creative labs model sb1240) and amplifier (Kramer 900N) were used to play the sounds. Each run contained 9 routes, 9 scrambled routes, 9 recordings containing no echoes, and 11 silent events. The presentation order was in blocks, so that three sound trials were followed by one silent trial. Sound events within each block were counterbalanced across runs. Each run started with two silent trials and ended with one silent trial. Each sound trial was followed by a tone to indicate a response was required via an MRI compatible response pad (Fiber Optic Button Response System, Psychology Software tools, Pennsylvania, USA).

2.2.3.3. Procedure

Five expert echolocators took part in one scanning session, whilst all sighted participants completed two scanning sessions; one prior to training and one after training. Immediately before scanning, participants were made familiar with examples of the echolocation stimuli and received feedback. During scanning, sighted participants and expert echolocators with residual vision were asked to wear a blindfold and close their eyes. Echolocation stimuli were presented to participants and participants had to respond, via an MR compatible keypad on their right hand, as to which type of stimuli they heard. The button below the thumb denoted clicks with no echoes, the index finger signified a single turn route, the middle finger indicated route containing two-turns in the same direction, the ring finger signified a route containing two-turns in different directions and the little finger was to be pressed when a scrambled route was presented. Each run contained 38 trials, and all participants completed 6 runs per scanning session.

2.3. fMRI Data Acquisition

Imaging for all participants was performed at Durham University Neuroimaging facility (James Cook University Hospital, Middlesbrough, UK). A 3-Tesla whole body MRI system (Magnetom Tim Trio, Siemens, Erlangen, Germany) with a 32 channel head coil was used. To acquire functional data a sparse sampling design was used in combination with a single shot gradient echo-planar pulse sequence. Repetition time (TR) was 13s (11s silent gap and 2s slice acquisition). Thirty-eight volumes were acquired across the whole brain with a 64x64 matrix size and 192 degrees FOV, which led to in-slice resolution of 3mm x 3mm. Slice thickness was 3.5mm. Echo time (TE) was 30ms and flip angle (FA) was 90^{o}.

2.3.1. fMRI Data Analysis: Pre-Processing & Co-Registration

Data were analysed using Brain Voyager QX versions 2.1.3, 2.15 and 2.8 (Brain Innovation, Maastricht, The Netherlands). Functional runs for all expert echolocators and sighted participants were subjected to slice scan time correction (tri-linear sinc), temporal high pass filtering (cut-off at 2 sines/cosines) and 3D motion correction (sinc). To align the functional to the anatomical data, the first volume of the motion corrected functional run which was closest to the anatomical was aligned to the anatomical scan. The anatomical image was then co-registered to the run using an initial and fine tuning (rigid body) alignment. Each functional run was pre-processed so that it was aligned to the first volume of the motion corrected functional closest to the anatomical. The ACPC was manually found for each anatomical scan and was transformed into Talairach space. VTC pre-processing was conducted and all data were spatially smoothed (Gaussian Kernel with FWHM 6x6mm).

2.3.2. fMRI Data Analysis: Whole Brain

A whole brain analysis was undertaken for five expert echolocators and fourteen sighted participants using a random effects approach (RFX) for each group separately. To control the rate of type I errors in the statistical maps created, we applied a cluster size threshold (Forman et al., 1995). Cluster threshold values were estimated in volume space using the BrainVoyager Cluster Threshold Estimator Plugin (Goebel, Espodito & Formisano, 2006).

Echolocators completed one scanning session, whereas sighted participants completed one scan prior to training and one post-training, with the aim of comparing brain activity before and after learning to echolocate. This post-pre analysis will then be compared to BOLD activity shown by expert echolocators when completing the same task.

2.3.2.1. BOLD Activity Related to Processing Echolocation Stimuli Compared to Silence: Sound > Silence

To compare brain activity in sighted participants related to the processing of echolocation sounds compared to silence we computed ($Route_{post\ -\ pre}$) + ($Scrambled_{post-\ pre}$) + ($No\ Echo_{post\ -\ pre}$) > Silence. As a result, BrainVoyager ran the contrast as ($Route_{post}$ + $Scrambled_{post}$ + $No\ Echo_{post}$ - $Route_{pre}$ - $Scrambled_{pre}$ – $No\ Echo_{pre}$). We applied a general linear model (GLM) to the 6 time course runs (z-transformed) for each anatomical scan. A group analysis of data from sighted participants (n=14) was conducted using RFX at $p < .05$ (statistical threshold $t_{(13)} = 2.161$, cluster threshold 31). A group analysis of expert echolocator data (n=5) was also conducted using RFX at $p < .05$ (statistical threshold $t_{(4)} = 2.790$, cluster threshold 102). We computed (Route + Scrambled + No Echo) > Silence, and BrainVoyager ran the contrast as (Route + Scrambled + No Echo).

2.3.2.2. BOLD Activity Related to Processing of Echoes Compared to No Echoes: Echo > No Echo

To compare brain activity in sighted participants related to the processing of echoes, compared to no echoes, in the post-training scan compared to the pre-training scan we computed ($Route_{post\ -\ pre}$) + ($Scrambled_{post\ -\ pre}$) > ($No\ Echo_{post\ -\ pre}$). Brain Voyager then ran this contrast as ($Route_{pre}$ + $Scrambled_{pre}$ + $No\ Echo_{post}$ > $No\ Echo_{pre}$ + $Route_{post}$ + $Scrambled_{post}$). Again, we applied a GLM to the 6 time course runs (z-transformed) for each anatomical scan. A group analysis of data from sighted participants (n=14) was conducted using RFX at $p < .05$ (statistical threshold $t_{(13)} = 2.161$, cluster threshold 31). To compare brain activity in expert echolocators related to the processing of echoes compared to no echoes we computed (Route + Scrambled) > No Echo and BrainVoyager ran the analysis as (Route + Scrambled). A conjunction analysis was added to compare the processing of echoes (Route + Scrambled) to silence. A GLM was applied to the 6 time course runs (z-transformed) for each anatomical scan. A group analysis of expert echolocator data was also conducted using RFX at $p < .05$ (statistical threshold $t_{(4)} = 2.790$, cluster threshold 102).

2.3.2.3. BOLD Activity Related to Processing of Routes Compared to Scrambled Routes: Route > Scrambled

To compare active voxels, in sighted participants, when routes were presented, compared to scrambled routes, in the post-training scan compared to the pre-training scan we computed ($Route_{post\text{-}pre}$) > ($Scrambled_{post\text{-}pre}$) and BrainVoyager ran the contrast as ($Route_{pre}$ + $Scrambled_{post}$ > $Scrambled_{pre}$ + $Route_{post}$). We applied a GLM to the 6 time course runs (z-transformed) for each anatomical scan. A group analysis of data from sighted participants (n=14) was conducted using RFX at $p < .05$ (statistical threshold $t_{(13)} = 2.161$, cluster threshold 31). To compare brain activity in expert echolocators when routes were presented, compared to scrambled routes, we computed (Route > Scrambled) and this is how BrainVoyager ran the contrast. A conjunction analysis was added to compare the processing of routes (+ Route) to silence. A GLM was applied to the 6 time course runs (z-transformed) for each anatomical scan. A group analysis of expert echolocator data was also conducted using RFX at $p < .05$ (statistical threshold $t_{(4)} = 2.790$, cluster threshold 102).

2.3.3. fMRI: Additional Exploratory Analyses

Additional exploratory data analyses were undertaken for fourteen sighted participants (post-pre) and five expert echolocators (single session) using an RFX for each group separately. We compared BOLD activity when processing sounds compared to silence (Sound > Silence), echoes compared to no echoes (Echo > No Echo) and routes compared to scrambled routes (Route > Scrambled), using the same computations as the whole brain analysis (2.3.2). The analysis was undertaken at $p < .05$, using the same statistical thresholds ($t_{(13)} = 2.161$ for sighted participants; $t_{(4)} = 2.790$ for expert echolocators), however the cluster thresholds (31 for sighted participants; 102 for expert echolocators) were removed for both groups.

2.4. Active Echolocation Tasks

In addition to virtual computer based tasks, we also used active echolocation tasks to train echolocation ability. These tasks are described as 'active' as participants were required to produce their own mouth-click and interpret the returning echoes. We used a size and orientation perception task, as well as a real-world navigation task. For size and orientation tasks testing was undertaken in the same anechoic room used to make recordings for the virtual navigation task. The accuracy of responses given were recorded. For the real-world navigation task sighted participants used mouth clicks to find their way in a level section of the psychology department. Sighted participants, and expert echolocators with residual vision, were asked to wear a blindfold and close their eyes when completing the tasks. Sighted participants competed 20 sessions of these tasks, two sessions per week, across a 10-week period. Where time permitted, expert echolocators completed a single session for each task.

2.4.1. Size Discrimination Task

Stimuli: An illustration of the apparatus and procedure used to train echolocation ability is shown in figure 4. Participants stood in the centre of the room and the apparatus was placed such that two disks, made from acrylic, faced the participants at a distance of 33cm from the tragus. The height was adjusted so that the mouth was in line with the centre of the two horizontal poles. The task was to identify if the larger of the two disks (the reference disk) was located at the top or the bottom position. The reference disk was 25.4cm in diameter, and the remaining five disks measured 22.9cm, 17.5cm, 13.5cm, 9cm and 5.1cm in diameter. Disk placement was randomised and the reference disk appeared on the top and bottom equally often.

Three expert echolocators completed one session consisting of 60 trials. All sighted participants completed 20 sessions, each with 30 trials. If sighted participants scored 90% or above in two consecutive sessions, the framework was moved an additional 33cm away.

Procedure: Two practice trials were performed to ensure familiarity with the task and procedure and test trials followed. Participants were asked to occlude their ears with their fingertips whilst the experimenter placed each disk on the framework. Once disks had been placed, the experimenter stepped behind the participant and a shoulder tap was used to signal to participants that they could unblock their ears. Before clicking, the participant made a judgment as to whether the reference disk was on the top or bottom (pre-click judgment). Then, participants were given 14s to make mouth clicks to determine the location of the reference disk (click-judgment). Responses were given via hand signal, specifically participants would point to the ceiling if they thought the reference disk was on the top, or to the floor if they thought it was on the bottom. If a response was not given in 14s, participants were prompted to answer by another shoulder tap. Feedback was given. Trial sequence is shown in figure 4.

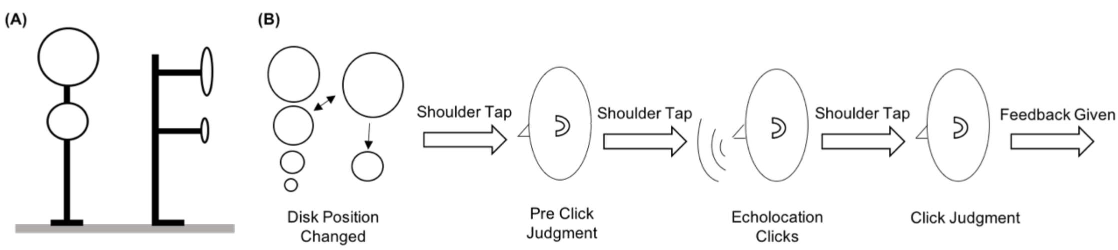

Figure 4. **(A).** Illustration of the apparatus used to train echolocation ability in the size discrimination task, consisting of a weighted metal base, supporting a vertical steel pole. Attached were two horizontal poles. Circular disks cut from acrylic were mounted on to the horizontal poles. Illustrated from a front and lateral view. **(B).** Trial sequence for the size discrimination task.

2.4.2. Orientation Discrimination Task

Stimuli: The apparatus illustrated in figure 5 was used to train echolocation ability. Participants stood in the centre of the room and the apparatus was placed such that the acrylic board, which measured 80cm x 20cm, was placed 33cm from the tragus. The height of the framework was adjusted so that the mouth was in the centre of the board. The goal of the task was to identify the orientation of the board as being horizontal, vertical, left-side-up or right-side-up, as shown in figure 5. The orientation was randomised so that each was presented equally often.

Five expert echolocators completed one session with 40 trials. All sighted participants completed 20 training sessions, each with 24 trials. If sighted participants were over 90% accurate in two consecutive sessions, the apparatus was moved an additional 33cm away.

Procedure: Two practice trials were undertaken to gain familiarity with the task and test trials followed. Participants occluded their ears with their fingertips whilst the orientation of the board was manipulated. Once the board had been placed the experimenter stepped behind the participant and a shoulder tap indicated that they could unblock their ears and begin clicking. Participants were given 20s to make a response, if a response was not provided then a shoulder tap was used as a prompt. A verbal response was given and feedback was provided. The trial sequence is shown in figure 5.

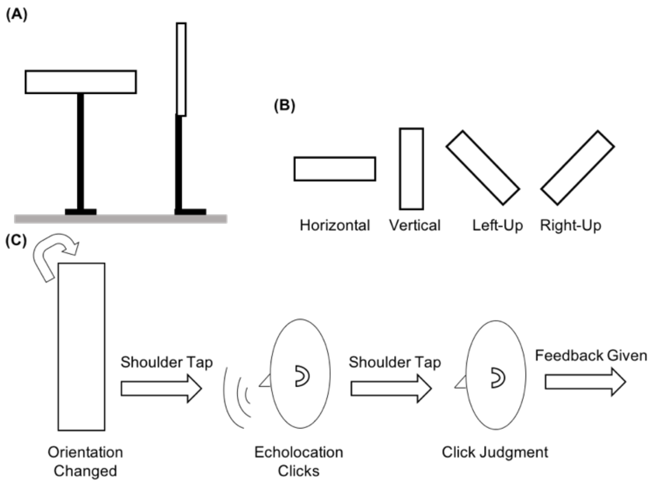

Figure 5. **(A).** Illustration of the apparatus used to train echolocation ability in the orientation discrimination task. A rectangular board cut from acrylic, measuring 80cm x 20cm, was mounted to a vertical steel pole and supported by a weighted metal base. Shown as oriented horizontally in the front view and vertically in the lateral view. **(B).** An illustration of the possible orientations of the board. **(C).** Trial sequence for the orientation discrimination task.

2.4.3. Real World Navigation Task

The goal of the task was for participants to learn about various spatial environments. Participants were carefully monitored by an experimenter at all times and were asked to complete similar tasks at home for 5 minutes each day. Active exercises included: clicking towards and away from a corner, detecting the presence of a wall without touching it and identifying an open doorway to the left or right whilst walking along a corridor. During these tasks, participants were encouraged to walk and move their head. As sessions advanced, participants were asked to complete these exercises without the physical guidance of an experimenter, increasing the complexity of the task. Whilst participants performed this task during each of their 20 visits, and as homework exercise, there was no formal assessment.

3. Results

3.1. Virtual Navigation Task

We first examined how performance changed across 18 training sessions when multiple mazes were repeatedly presented to sighted participants. We measured the time taken to complete each maze, the number of errors made, i.e. bumping into walls, and the proportion of mazes successfully completed in each of the 18 training sessions. We then examined how performance changed upon presentation of 'old' (previously navigated) and 'new' (novel) mazes in sessions 19 and 20. The logic here was to determine if people had learned a 'stereotyped' response or if their skill in navigating using echo-acoustic information generalised to novel virtual spaces. Again, we measured the time taken to complete each maze, the number of errors made and the proportion of mazes successfully completed.

3.1.1. Performance Across Repeated Training Sessions

To investigate navigational abilities in sighted participants, we ran six repeated measures ANOVAs to examine the effect of sessions 1-14 and sessions 15-18 on the time taken to navigate, number of errors made, and proportion of routes successfully completed. This subdivision is because in session 15, participants had been introduced to more difficult starting positions and a 15s time-out when an error was made. We also ran a paired sample t-test to compare performance in sessions 14 and 15 for the time taken, number of errors made and the proportion of routes successfully completed.

3.1.1.1. Time Taken to Complete Maze

We found a significant effect of session ($F_{GG(3.005,39.066)}$ = 20.926, p <.001, η^2 = .617), along with a significant linear trend ($F_{(1,13)}$ = 41.189, p <.001, η^2 = .760). Taken with figure 6, this shows that the average time taken to navigate significantly decreased as sessions progressed from 1 to 14. When examining the performance between sessions 14 and 15, we found a significant difference ($t_{(13)}$ = -5.789, p <.001), with participants completing mazes significantly faster in session 14 (M = 40.866), compared to session

15 (M = 90.329). However, no significant difference ($F_{(3,39)}$ = 1.820, p = .160, η² = .123) was found for the time taken to complete the mazes in sessions 15-18.

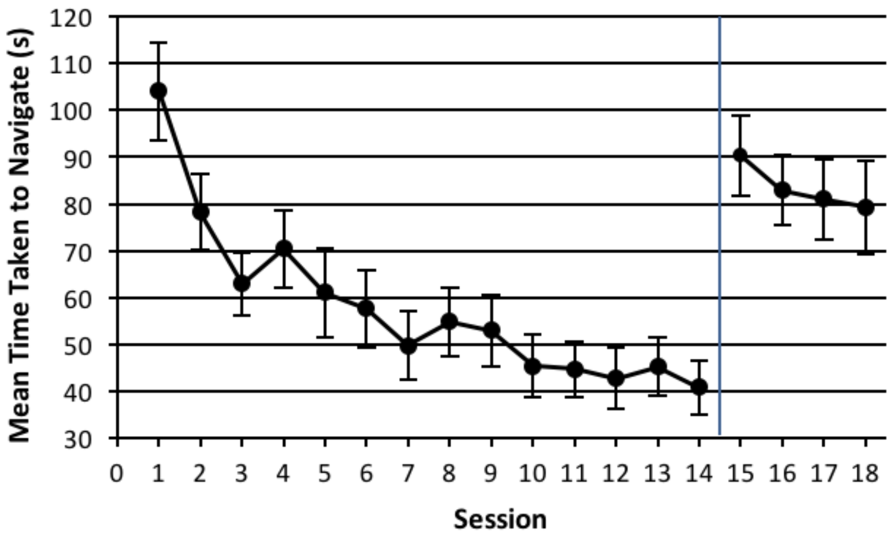

Figure 6. The mean time taken (seconds) to complete various mazes in sessions 1-18. In session 15 the computer program changed, and as a result multiple starting positions were introduced, along with a 15s time-out when a collision occurred. This change in computer program is represented by the solid blue line. Error bars represent the standard error mean.

3.1.1.2. Number of Errors Made

A significant effect of session ($F_{GG(2.512,32.657)}$ = 5.779, p = .004, η² = .308), and a significant linear trend ($F_{(1,13)}$ = 27.848, p <.001, η² = .682) were found when looking at the number of errors made in sessions 1-14. When taken with figure 7, this shows that the number of errors decreased as sessions progressed. Upon comparison of the number of errors made in sessions 14 and 15, no significant difference was found ($t_{(13)}$ = .144, p = .888), with an average of 2.044 errors being made in session 14, and an average of 1.972 errors in session 15. Again, no significant difference ($F_{(3,39)}$ = 2.336, p = .0.89, η² = .152) in the number of errors made was found in sessions 15-18. This is shown in figure 7. The results suggest that the increase in time taken to complete the mazes from sessions 14 to 15 (see figure 6) is largely due to the time-out that was imposed for errors.

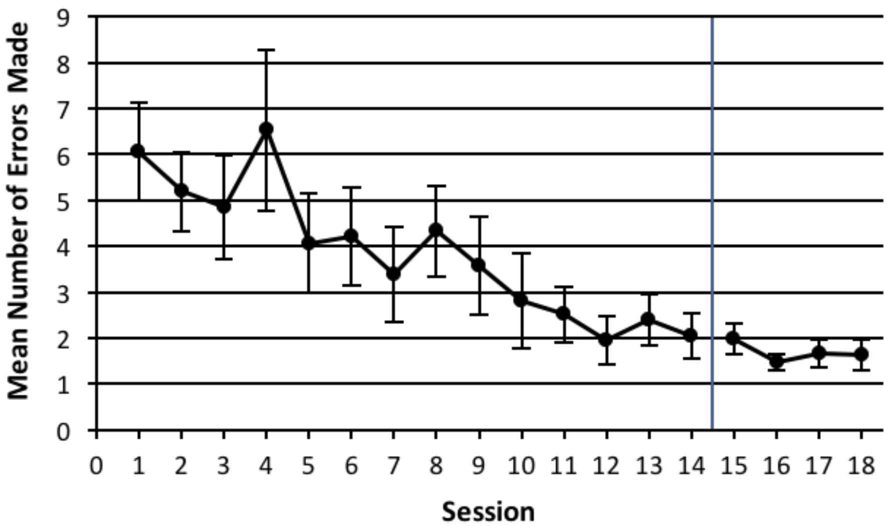

Figure 7. The mean number of errors made in sessions 1-18. In session 15 the computer program changed, and as a result multiple starting positions were introduced, along with a 15s time-out when a collision occurred. This change in computer program is represented by the solid blue line. Error bars represent the standard error mean.

3.1.1.3. Proportion of Mazes Successfully Completed

When looking at the proportion of mazes successfully completed, we found a significant effect ($F_{G(2.578,33.517)}$ = 6.995, p = .001, η^2 = .350) of session, along with a significant linear trend ($F_{1,13)}$ = 14.377, p = .002, η^2 = .525). As figure 8 shows, participants became increasingly successful at navigating as sessions progressed from 1-14. We also found a significant difference in performance between sessions 14 and 15 ($t_{(13)}$ = 3.381, p = .005), with a greater proportion of mazes successfully completed in session 14 (M = .9802), compared to session 15 (M = .8413). This is likely because of the additional time-out and more difficult starts from session 15 onwards, which made it harder to complete the maze within the time limit. Despite this, no significant difference ($F_{GG(1.853,\ 24.087)}$ =.995, p =. 406, η^2 = .071) in the proportion of mazes successfully completed was found in sessions 15-18.

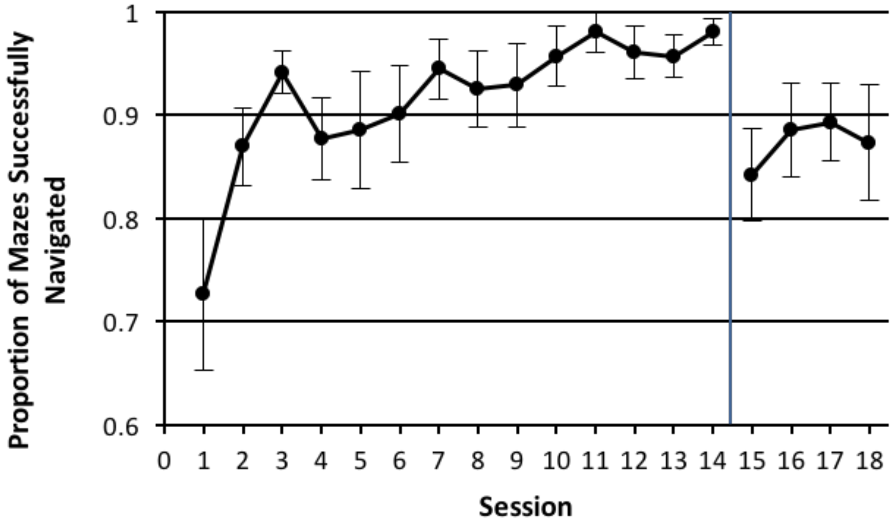

Figure 8. The proportion of mazes successfully navigated in sessions 1-18. In session 15 the computer program changed, and as a result multiple starting positions were introduced, along with a 15s time-out when a collision occurred. This change in computer program is represented by the solid blue line. Error bars represent the standard error mean.

3.1.2. Performance for 'Old' and 'New' Mazes

A paired sample t-test was used to compare performance for 'old' (previously navigated) and 'new' (untrained) mazes in sessions 19 and 20. We did this for the time taken to navigate, the number of errors made, i.e. bumping into a wall, and the proportion of mazes successfully completed.

Overall, we found no significant differences between performance for 'old' mazes compared to 'new' mazes in sessions 19 and 20. This is illustrated in figure 9. Specifically, we found no significant difference ($t_{(13)}$ = -.068, p = .351) between the time taken to navigate 'old' (M = 75.313) and 'new' (M = 77.750) mazes. There was no significant difference ($t_{(13)}$ = -1.020, p = .326) in the number of errors made when navigating 'old' (M = 1.591) and 'new' (M = 1.670) mazes. Similarly, no significant difference, ($t_{(13)}$ = .327, p = .749), was present for the proportion of mazes successfully completed for 'old' (M=.889) and 'new' (M=.882). Essentially, participants performed just as well with the new, as they did with the old mazes, suggesting that what they had learned did generalise to novel virtual spaces.

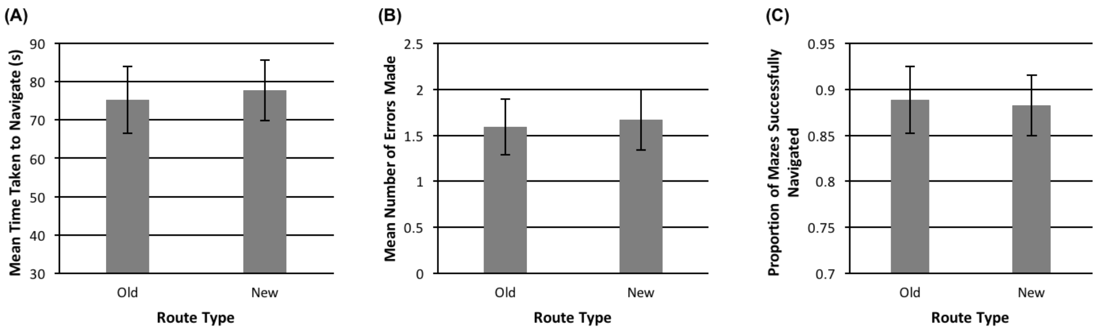

Figure 9. **(A).** Mean time taken (seconds) to navigate old and new mazes. **(B).** Mean number of errors made when navigating old and new mazes. **(C).** Proportion of old and new mazes successfully navigated. Error bars represent the standard error mean.

3.1.3. Virtual Navigation Task – Pre fMRI

To examine the effect of 'session', the proportion of correct responses given for echo identification, scrambled vs. route identification and route type identification were calculated.

When considering echo identification, a response was identified as correct when participants' responded with 'no echo' when stimuli containing no echoes were presented, along with anything else otherwise, i.e. this would also be correct if a 'single turn' was labeled 'scrambled'. When looking at scrambled vs. route identification, a 'scrambled' response was correct when a scrambled route was presented. Identification of a route sound, regardless of whether it was a single turn, two-turns-same, two-turns-different was also identified as a correct response. When examining route type identification, a response was identified as correct when participants correctly identified each stimulus type (single turn, two-turns-same, two-turns-different, scrambled and no echo) when it was presented.

We ran thee paired sample t-tests to investigate the difference in performance between pre-training and post-training sessions in sighted participants. These results, which are shown in figure 10, are displayed alongside the results obtained from expert echolocators.

A significant effect of session ($t_{(13)}$ = -2.370, p = .034) was found when looking at the proportion of correct responses given for echo identification. Participants were more successful in correctly identifying stimuli containing echoes in the post-training session (M=1.00), compared to the pre-training session (M=.9841). Furthermore, we found a significant difference ($t_{(13)}$ = -5.704, p <.001) for scrambled vs. route identification. Specifically, we found participants were better able to discriminate between scrambled and coherent routes in the post-training session (M=.8971), compared to the pre-training session (M= 7693). We also observed a significant effect of session ($t_{(13)}$ = -6.411, p <.001) when considering route type identification. A greater proportion of routes were correctly identified in the post-training session (M=.7136), than in the pre-training session (M=.5321). Overall, participants performed significantly better in all tasks, after echolocation training.

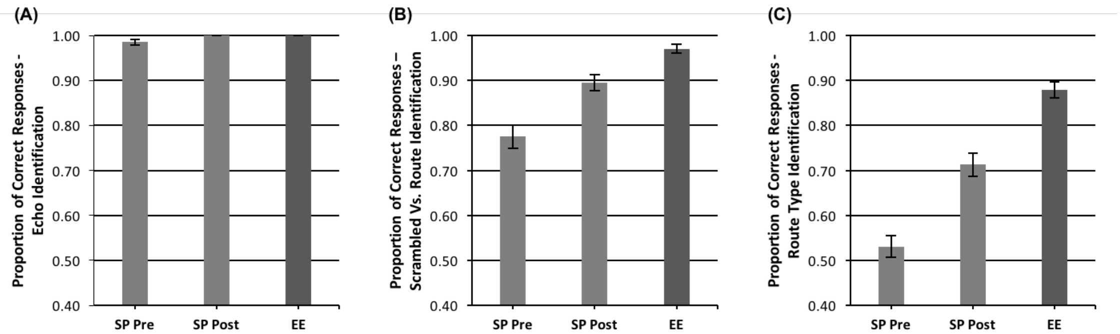

Figure 10. The proportion of correct responses given for **(A)** echo identification, **(B)** scrambled vs. route identification, and **(C)** route type identification. Sighted participants completed pre-training (SP Pre) and post-training (SP Post) sessions. Expert echolocators (EE) completed a single session. Error bars represent the standard error mean.

3.1.4. Virtual Navigation Task – During fMRI

To examine the effect of 'session', we calculated the proportion of correct responses given for echo identification, scrambled vs. route identification and route type identification during the pre and post-training fMRI. The data were analysed in the same way as for the pre fMRI data (3.1.3). The results of the analyses are shown in figure 11, and are displayed alongside data from expert echolocators.

No significant differences in performance ($t_{(13)}$ = -1.500, p =.157) were found when considering echo identification in the pre-training (M=.9794) and post-training (M=.9926) fMRI. However, when examining the proportion of correct responses for scrambled vs. route identification we did find a significant effect of session ($t_{(13)}$ = -4.951, p <.001). Participants were able to correctly discriminate between scrambled routes and coherent routes at a higher accuracy in the post-training fMRI (M=.8319) than the pre-training fMRI (M=.7473). Similarly, a significant difference ($t_{(13)}$ = -4.115, p =.001) was found for route type identification, with participants correctly identifying a greater proportion of routes in the post-training fMRI (M=.6931), compared to the pre-training fMRI (M=.6155).

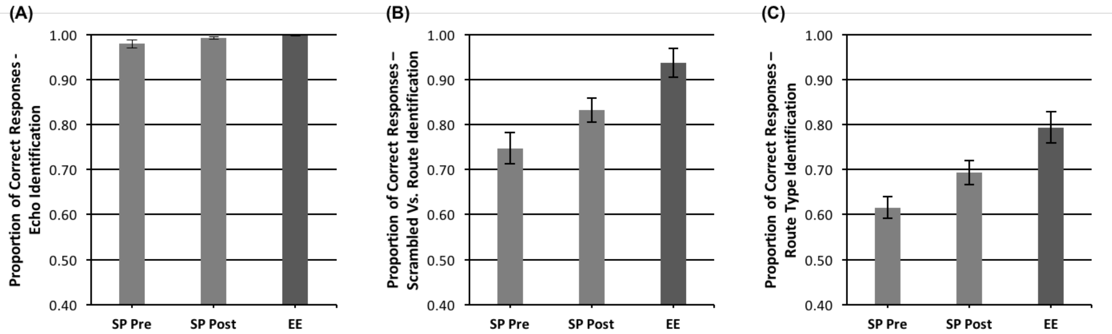

Figure 11. The proportion of correct responses given for **(A)** echo identification, **(B)** route vs scrambled identification and **(C)** route type identification. Sighted participants completed pre-training (SP Pre) and post-training (SP Post) fMRI scans. Expert echolocators (EE) completed a single session. Error bars represent the standard error mean.

3.2. fMRI: Whole Brain Analysis

We measured BOLD activity associated with a navigational task in sighed participants and expert echolocators. We ran an RFX group analysis on data collected from sighted participants (n=14) to compare BOLD activity in a post-training scan to activity in a pre-training scan. We also ran an RFX group analysis to data collected from expert echolocators (n=5) in a single scanning session. An average brain (n=19) was created in Talairach space and volume maps obtained from group analyses of sighted and expert echolocator data were overlaid. Data are shown at p <.05, with a cluster size threshold of 31 for sighted participants and 102 for expert echolocators. Sighted participants' data are shown in blue, expert echolocators data are shown in purple.

3.2.1. BOLD Activity Related to Processing of Echolocation Stimuli Compared to Silence: Sound > Silence

BOLD activity associated with the processing of echolocation stimuli, compared to silence, in sighted participants (post–pre) and expert echolocators (single session) is shown in figure 12. All activation clusters are listed in table 2.

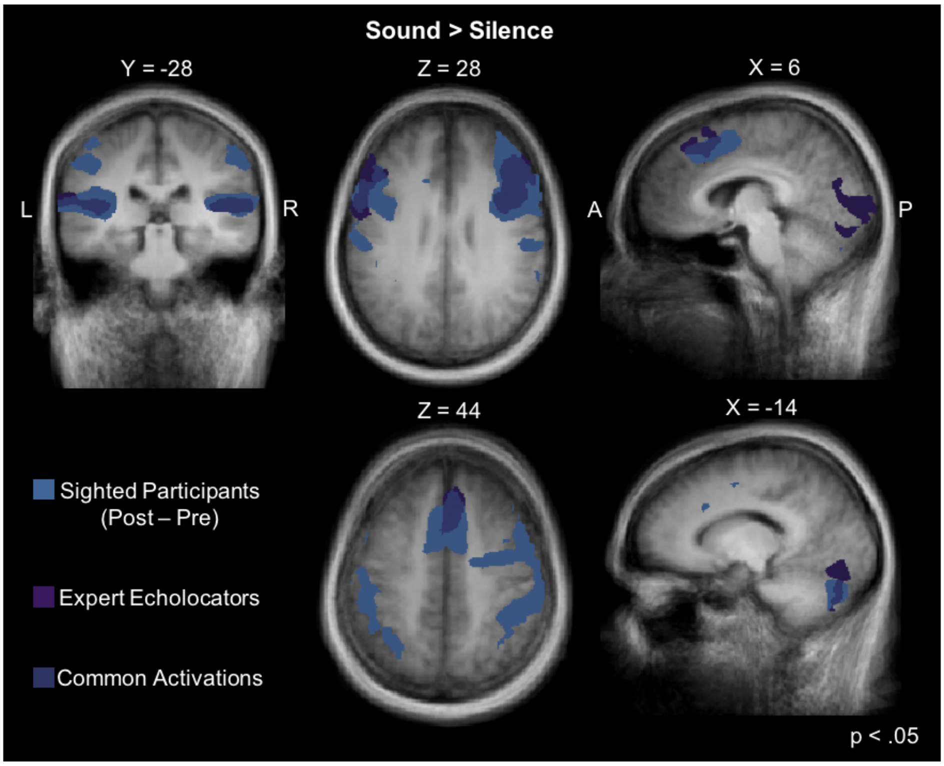

Figure 12. BOLD activity associated with the processing of echolocation stimuli, compared to silence in sighted participants (post-pre) and expert echolocators (single session). Common activations (CA) are also shown. Average data (n=19) are shown in Talairach space and smoothed @6mm.

When comparing the two groups, overlapping activations were observed bilaterally in the superior temporal gyri, i.e. primary auditory cortex. These activations were expected based on previous research measuring BOLD activity in response to the presentation of sound compared to silence in sighted participants and expert echolocators (Arnott et al., 2013; Fiehler, Schütz, Meller & Thaler, 2015; Milne et al., 2015; Thaler et al., 2011). Further overlapping activations were found in the frontal lobe for both groups. Specifically, middle and inferior frontal gyri activations were found bilaterally in sighted participants, and in the right lobe for expert echolocators, along with the left inferior frontal gyrus in expert echolocators. Additional bilateral activity was found in the medial frontal gyri for sighted participants, but this was limited to the right medial frontal gyrus in expert echolocators.

Despite common activations in sighted participants and expert echolocators throughout the auditory and frontal cortices, we also found regions of activity in both groups which did not show any overlap. Significant BOLD activity was found in bilateral regions of the occipital cortex in expert echolocators. This included the lingual gyrus and BA18 in the left lobe, and calcarine cortex (i.e. primary 'visual' cortex or BA17) and BA18 in the right lobe. Again, this activation was expected based on previous research investigating the presentation of sound, compared to silence in expert echolocators (Thaler et al., 2011). This occipital cortex activity was absent in sighted participants, however, BOLD activations were found in the left precentral gyrus and bilaterally in the postcentral gyri. These activations were not present in expert echolocators.

In sum, BOLD activations appear to somewhat overlap across the two groups, particularly in the auditory and frontal cortices, suggesting these areas are recruited for the processing of sound, compared to silence, in both groups. Despite this, there are large differences in activation patterns in the occipital and parietal cortices, with expert echolocators displaying activity in the occipital cortex, whilst sighted participants exhibit activity in the parietal cortex. This may indicate that different neural networks were being recruited by each group when listening to sounds.

Table 2. *Activations found for the Sound > Silence contrast in sighted participants (SP) (post – pre) and expert echolocators (EE) (single session) in Talairach space. The co-ordinates given indicate the center of gravity for each cluster.*

			Sound > Silence			
Subj. Group	Hemi.	Location	X	Y	Z	No. of Voxels
SP (Post – Pre)	L&R	Medial Frontal Gyri, Middle & Inferior Frontal Gyrus (R only) and Orbito-Frontal Cortex (R only)	33.27	19.37	25.38	64763
SP (Post – Pre)	L	Precentral Gyrus, Postcentral Gyrus, and Superior Temporal Gyrus	-44.89	-29.07	22.37	27051
SP (Post – Pre)	R	Postcentral gyrus and Superior Temporal Gyrus	45.99	-30.81	22.81	24347
SP (Post – Pre)	L	Middle and Inferior Frontal Gyri	-45.72	6.42	23.52	12595
SP (Post – Pre)	L	Cerebellum	-15.57	-68.90	-28.21	5891
SP (Post – Pre)	L	Inferior Frontal Gyrus	-31.06	19.20	8.85	4506
SP (Post – Pre)	L	Middle Frontal Gyrus	-39.21	45.75	11.70	4386
EE	R	Calcarine Cortex, BA18 & Lingual Gyrus	23.78	-74.75	-3.10	21768
EE	R	Middle & Inferior Frontal Gyri	40.17	25.59	23.37	13635
EE	L	Lingual Gyrus & BA18	-28.28	-74.04	-9.25	13528
EE	L	Inferior Frontal Gyrus	-49.64	24.50	20.89	6713
EE	L	Superior Temporal Gyrus	-48.49	-30.56	10.71	5975
EE	R	Superior Temporal Gyrus	52.66	-31.75	9.40	5754
EE	R	Medial Frontal Gyrus	3.52	21.63	46.80	3105

3.2.2. BOLD Activity Related to Processing of Echoes Compared to No Echoes: Echo > No Echo

We examined BOLD activity related to the processing echoes, compared to stimuli without echoes, in sighted participants (post-pre) and expert echolocators (single session). Figure 13 shows key activations in both groups, whilst table 3 lists all activation clusters.

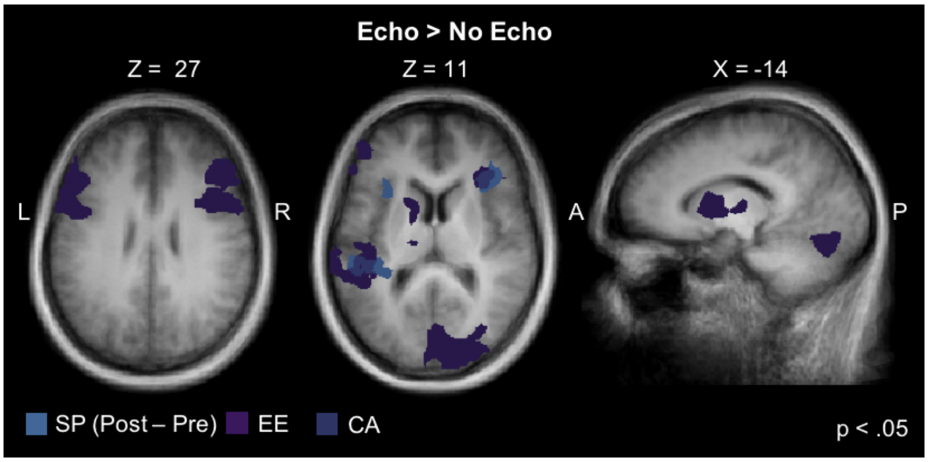

Figure 13. BOLD activity associated with the processing of echolocation stimuli containing echoes, compared to stimuli with the echoes removed in sighted participants (post-pre) and expert echolocators (single session). Common activations (CA) are also shown. Average data (n=19) are shown in Talairach space and smoothed @6mm.

Common regions of BOLD activity, exhibited by sighted participants and expert echolocators, were found in the left superior temporal gyri, i.e. primary auditory cortex. Similar activations in sighted participants and expert echolocators were also found bilaterally in the inferior frontal gyri. Despite this similarity, the number of active voxels were much greater in expert echolocators, with the activation cluster extending to the middle frontal gyrus.

Again, the results are quite different when comparing BOLD activity in the occipital cortex in sighted participants and expert echolocators. Extensive activation was found throughout the right occipital lobe, including calcarine cortex (i.e. primary visual cortex or BA17), BA18 and lingual gyrus. Smaller activation clusters were also found in the left lobe, including the lateral occipital and lingual gyri. Sighted participants did not display any BOLD activity in the occipital cortex. This is in line with previous research, (Thaler et al., 2011; Wallmeier et al., 2015), however it was hypothesised that activity shown in the post-training fMRI, compared to the pre-training fMRI in sighted participants would match the BOLD activity displayed by expert echolocators completing the task. As this is not the case, it may be that the neural networks underlying the processing of echoes are different in sighted participants, even after training.

Table 3. *Activations found for the Echo > No Echo contrast in sighted participants (SP) (post – pre) and expert echolocators (EE) (single session) in Talairach space. The co-ordinates given indicate the center of gravity for each cluster.*

			Echo > No Echo			
Subj. Group	Hemi.	Location	X	Y	Z	No. of Voxels
SP (Post – Pre)	L	Superior Temporal Gyrus & Lateral Ventricle	-36.87	-33.58	8.12	3401
SP (Post – Pre)	R	Inferior Frontal Gyrus	33.73	23.83	6.65	3097
SP (Post – Pre)	L	Inferior Frontal Gyrus	-31.80	20.45	5.97	1378
EE	R	Calcarine Cortex BA18 & Lingual Gyrus, leading to Parahippocampus	18.91	-73.71	-2.97	45706
EE	R	Cerebellum	17.81	-57.92	-36.65	3853
EE	R	Middle & Inferior Frontal Gyri	41.59	21.19	24.06	13373
EE	L	Middle & Inferior Frontal Gyri	-49.49	19.45	23.03	9240
EE	L	Superior Temporal Gyrus	-49.52	-28.92	9.22	5878
EE	L	Lateral Occipital Gyrus, leading to Parahippocampus	-39.31	-68.84	-8.16	5663
EE	L	Lingual Gyrus leading to Cerebellum	-13.09	-72.25	-16.80	3210
EE	L	Caudate leading to Thalamus	-14.42	-0.61	6.84	2922

3.2.3. BOLD Activity Related to Processing of Routes Compared to Scrambled Routes: Route > Scrambled

Figure 14, shows BOLD activity related to the processing of routes, compared to scrambled routes in sighted participants (post-pre) and expert echolocators (single session). All activation clusters are listed in table 4.

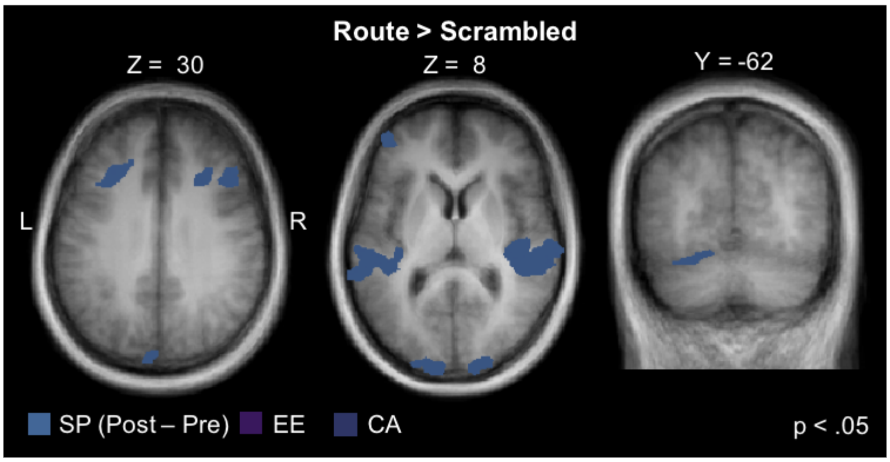

Figure 14. BOLD activity associated with the processing of routes, compared to scrambled routes in sighted participants (post-pre) and expert echolocators (single session). Common

activations (CA) are also shown. Average data (n=19) are shown in Talairach space and smoothed @6mm.

Large differences in BOLD activations were found between the two groups. Bilateral activity was observed in the superior temporal gyri of sighted participants, i.e. primary auditory cortex. This was unexpected because the acoustic properties of route and scrambled route sounds had been exactly matched, and suggests that training influenced how these two types of sounds were processed in primary auditory cortex. BOLD activations were also found bilaterally in the middle frontal gyri, along with the left inferior frontal gyrus in sighted participants. Significant BOLD activity was also displayed within the occipital cortex of sighted participants. This includes bilateral activations of the cuneus, calcarine cortex (BA17) and BA18, along with the left medial occipito-temporal gyrus and leading to the parahippocampus. These activations were expected based on previous research investigating navigational abilities in an alternative modality in people with vision loss (Kupers et al., 2010). However, it was surprising to find BOLD activity for expert echolocators was completely absent at this cluster size threshold. Due to the large differences in observed BOLD activation patterns, it seems to suggest that different cortical networks may be recruited by sighted participants, in the post-training MRI, compared to the pre-training MRI, and expert echolocators when completing a navigational task.

Table 4. *Activations found for the Route > Scrambled contrast in sighted participants (SP) (post – pre) and expert echolocators (EE) (single session) in Talairach space. The co-ordinates given indicate the center of gravity for each cluster.*

			Route > Scrambled			
Subj. Group	Hemi.	Location	X	Y	Z	No. of Voxels
SP (Post – Pre)	R	Superior Temporal Gyrus	49.48	-24.89	9.19	7954
SP (Post – Pre)	L	Superior Temporal Gyrus	-47.49	-30.29	11.55	5805
SP (Post – Pre)	L	Middle & Inferior Frontal Gyri	-37.32	12.87	23.02	5163
SP (Post – Pre)	L	Middle Frontal Gyrus	-38.18	47.28	10.63	3708
SP (Post – Pre)	L	Cuneus, BA17 & 18	-11.88	-91.22	15.33	2858
SP (Post – Pre)	R	Middle Frontal Gyrus	33.78	28.93	25.01	2584
SP (Post – Pre)	L	Medial Occipito-Temporal Gyrus, leading to parahippocampus	-17.53	-70.85	-19.39	1914
SP (Post – Pre)	R	Cuneus, BA17 & 18	15.72	-93.56	8.77	843

3.3. fMRI: Additional Results from Exploratory Data Analyses

We then examined BOLD activity elicited by sighted participants (post-pre) and expert echolocators (single session) when completing the same navigational task. The same analyses were undertaken as the whole brain analysis (3.2), and data are presented at p <.05, but cluster size thresholds were removed.

3.3.1. BOLD Activity Related to Processing of Echolocation Stimuli Compared to Silence: Sound > Silence

Common regions of activity were found within the cortex of sighted participants (post-pre) and expert echolocators (single session) in response to the processing of sound, compared to silence. These regions are shown in figure 15, and all activation clusters are listed in appendix G.

Upon removal of the cluster size threshold, expert echolocators displayed activity in the left middle frontal gyrus; a similar pattern to that shown by sighted participants. This result is in line with our expectation that sighted participants, in the post-training fMRI, compared to the pre-training fMRI could show similar activation patterns to expert echolocators. The postcentral gyrus of expert echolocators was also found to be active, following the removal of the cluster size thresholds. This activation was located bilaterally and are similar to activations initially found in sighted participants. This means that when the cluster size threshold was removed, bilateral activations were present in the postcentral gyri for sighted participants and expert echolocators. This postcentral gyri activation extended to the right precuneus of expert echolocators, an area also found to be active in sighted participants, without the cluster size threshold. This may suggest that the parietal lobe may be involved in the processing of sound, compared to silence in both expert echolocators and sighted participants.

Widespread activations were found within the right occipital cortex of expert echolocators, including calcarine cortex, lingual gyrus and BA18, but were limited to the lingual gyrus and BA18 in the left lobe when the cluster size threshold was applied. However, when this was removed, additional activations were found within the left occipital lobe, including the middle occipital gyrus. Sighted participants did not show any occipital cortex activation when processing sounds, compared to silence. These results are in line with previous research (Thaler et al., 2011), however, seems to suggest that different networks may be recruited by each group for the processing of sound, compared to silence.

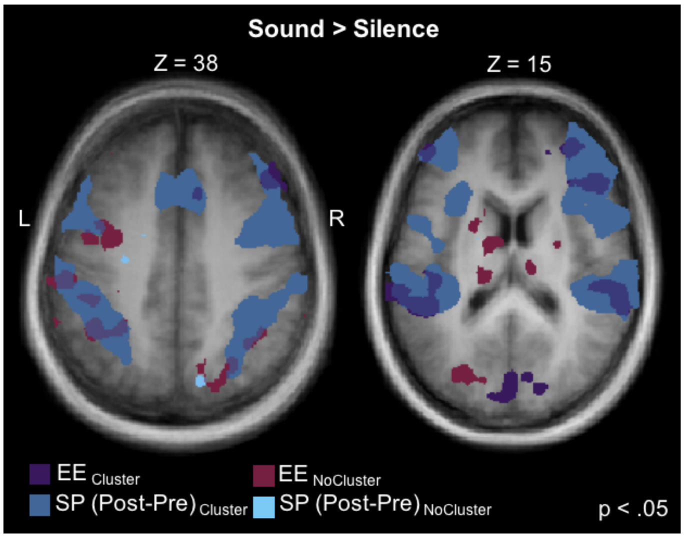

Figure 15. BOLD activity associated with the processing of sound, compared to silence, in sighted participants (post-pre) and expert echolocators (single session). Average data (n=19) are shown in Talairach space and smoothed @6mm. Data are shown with and without cluster level thresholds applied.

3.3.2. BOLD Activity Related to Processing of Echoes Compared to No Echoes: Echo > No Echo

We examined BOLD activity related to echolocation stimuli that contained echoes, compared to the stimuli with the echoes removed, in sighted participants (post-pre) and expert echolocators (single session). The resulting activations are shown in figure 16, and activation clusters can be found in appendix H.

Initial results, using a cluster threshold, show that both groups display activity within the left superior temporal gyrus when presented with echoic stimuli. When this cluster threshold was removed, activity was also found within the right superior temporal gyrus, resulting in bilateral activation of the auditory cortices in both groups. Initial analyses revealed significant BOLD activity within the right occipital cortex, including calcarine cortex (BA17), lingual gyrus and BA18. In addition, smaller regions of activation were present in the left lateral occipital and lingual gyri. When the cluster size threshold was removed, further activations were found within the left cuneus of expert echolocators. This occipital cortex activity was absent in sighted participants. Despite an increase in regions of overlapping BOLD activations due to the removal of the cluster size threshold in sighted participants and expert echolocators; occipital cortex activity was still absent in sighted participants. This seems to show that expert echolocators make use of the occipital cortex for the processing of echoes, whereas sighted people do not seem to do this, even after training in echolocation. This may indicate that different cortical networks are being recruited by sighted participants.

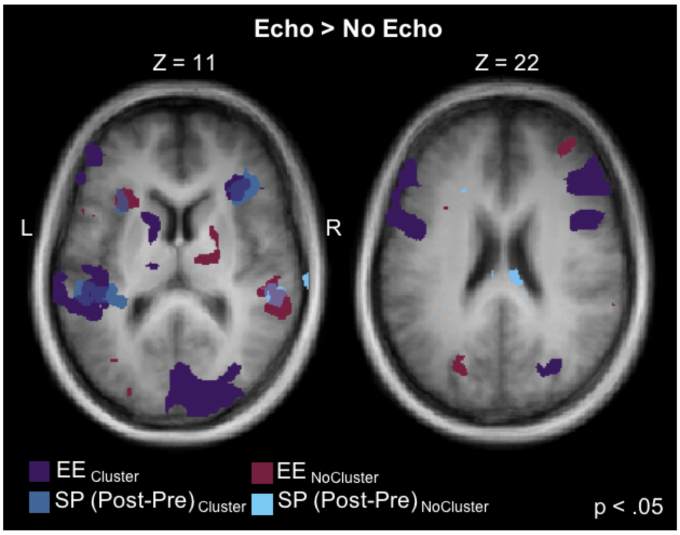

Figure 16. BOLD activity associated with the processing of stimuli containing echoes, compared to stimuli with the echoes removed in sighted participants (post-pre) and expert echolocators (single session). Average data (n=19) are shown in Talairach space and smoothed @6mm. Data are shown with and without cluster level thresholds applied.

3.3.3. BOLD Activity Related to Processing of Routes Compared to Scrambled Routes: Route > Scrambled

Figure 17 highlights BOLD activations related to the processing of routes, compared to scrambled routes in sighted participants (post-pre) and expert echolocators (single session), when the cluster size threshold was applied and removed. All activation clusters are presented in appendix I.

Initial analyses, shown in figure 14, highlight activation within the left parahippocampus of sighted participants. When the cluster threshold was removed, a small region of parahippocampal activation was also found in expert echolocators.

Upon removal of the cluster threshold, activation of the right middle occipital gyrus and cuneus of expert echolocators was also observed. Sighted participants also displayed additional areas of activation within the occipital cortex; the left and right cuneus. Despite this similarity, the differences between activations in the two groups remain large, which could suggest that each group recruit different brain regions for the processing of routes, compared to scrambled routes.

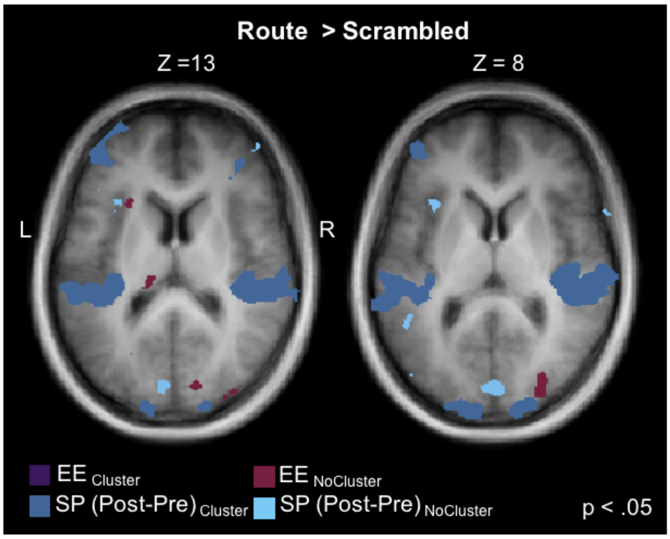

Figure 17. BOLD activity associated with the processing of routes, compared to scrambled routes, in sighted participants (post-pre) and expert echolocators (single session). Average data (n=19) are shown in Talairach space and smoothed @6mm. Data are shown with and without cluster level thresholds applied.

3.4. Active Echolocation Tasks

Data for sighted participants were analysed using repeated measures ANOVA. To test for sphericity, we used Mauchly’s test. When Sphericity could not be assumed the degrees of freedom were adjusted in accordance with the Greenhouse-Geisser correction.

3.4.1. Size Discrimination Task

All sighted participants and three expert echolocators completed this task. The other two echolocators did not take part in this task because of time constraints. To examine the accuracy of responses given, a two-way repeated measures ANOVA was carried out, with within factors of 'session' (1-20) and 'sound (no click or click).

We found a significant effect of session ($F_{(19,247)}$ = 6.824, p<.001, η² = .344) and of sound ($F_{(1,13)}$ = 161.351, p = .000, η² = .925) on accuracy of response made. Most importantly, the interaction between session and sound was found to be significant ($F_{(19,247)}$ = 5.417, p = <.001, η² = .294). Thus, we ran two repeated measures ANOVAs to investigate the impact of 'session' on accuracy of response made, when no clicks were made and when clicks were made. For 'no click' conditions, the effect of session was non-significant ($F_{(19,247)}$ = .762, p = .750, η² = .055), indicating that the accuracy of responses remained the same across sessions when no clicks were made. In contrast, for 'click' conditions, the effect of session was significant ($F_{(19,247)}$ = 8.447,p <.001, η² = .394) and so was the linear trend ($F_{(1,13)}$= 34.045, p < .001, η² = .724). This, along with figure 18, suggests that the accuracy of responses improved as training sessions progressed when clicks were made.

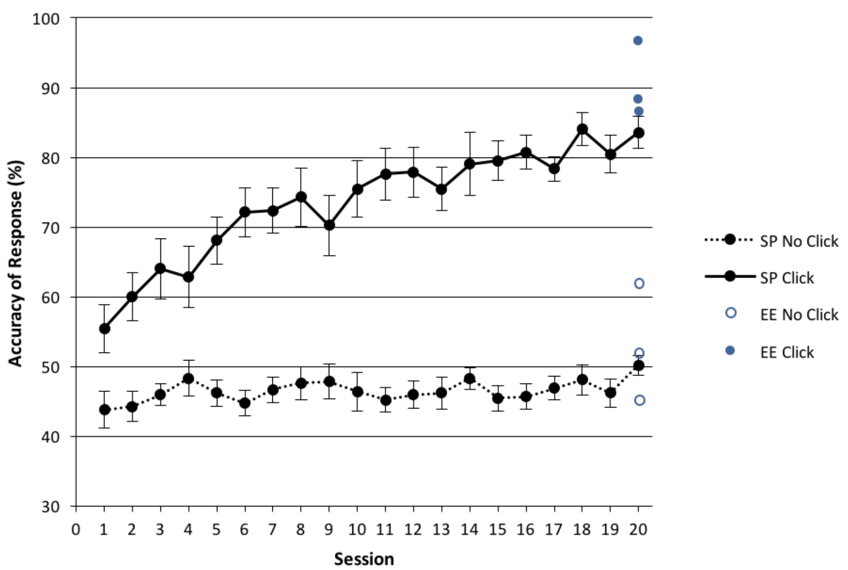

Figure 18. The accuracy of response (% correct) given, by sighted participants, for each training session (1-20), when no clicks (SP No Click) were made and when clicks (SP Click) were made. Data from three expert echolocators (EE), who completed a single session, are also shown. Error bars represent the standard error mean.

3.4.2. Orientation Discrimination Task

All sighted participants and five expert echolocators completed this task. A repeated measures ANOVA was undertaken, with a within factor of 'session' (1-20) for the mean accuracy of response given by sighted participants. The effect of session was significant ($F_{(19,247)} = 8.487$, $p <.001$, $\eta^2 = .395$) and so was the linear trend ($F_{(1,13)} = 29.167$, $p < .001$, $\eta^2 = .692$). Along with figure 19, this shows that participants became more accurate as sessions progressed.

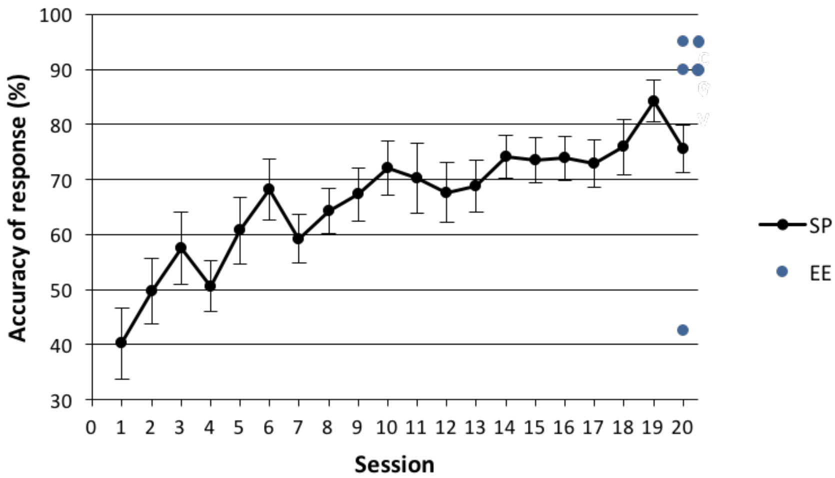

Figure 19. The accuracy of response (% correct) given by sighted participants (SP) for each training session (1-20). The accuracy of response given by five expert echolocators (EE), who completed one session, is also shown. Error bars represent the standard error mean.

4. Discussion

The functional organisation of the brain is yet to be fully understood. Traditionally, sensory areas within the brain were thought to be driven by modality, but an emerging view suggests that the brain is organised in a more flexible way, and is driven by task. For example, blind individuals have shown activity within the 'visual' cortex in response to processing olfactory and syntactic information (Finney, Fine & Dobkins, 2001; Kupers et al., 2011), and deaf individuals have displayed activity within the 'auditory' cortex in response to visual stimuli (Lane, Kanjilla, Omaki & Bedny, 2015). Here, we used echolocation to investigate to what degree the brain is organised by sensory modality or by task.

Our results, from active echolocation tasks, confirm previous findings that sighted people can successfully learn to echolocate (Ekkel et al., 2017; Hausfeld et al., 1982; Schenkman & Nilsson, 2010; Teng et al., 2012; Tonelli et al., 2016). We found that over a 10-week training period the accuracy of responses in size and orientation discrimination tasks increased as training sessions progressed, with performance in the final sessions rivalling performance of expert echolocators.

Furthermore, we found improvements in echolocation ability in a virtual navigation task. As a result of training, sighted participants became faster, made fewer errors and successfully completed more mazes. On changing the computer program in session 15 (i.e. time-out after collision and more difficult starting positions), we discovered an increase in the time taken to navigate the mazes and a lower completion rate. It is likely that this reduction in performance is due to the time-out enforced upon collision with a wall, i.e. making an error. Overall, our results from the virtual navigation task show that sighted people are able to learn to use echo-acoustic cues to successfully navigate various virtual mazes. Importantly, the level of performance remained stable when 'new' (untrained) mazes were introduced in sessions 19 and 20. This confirms previous research (Kupers et al., 2010; Levy-Tzedek et al., 2016), which demonstrate that non-visual modalities can be used by sighted people to navigate. Importantly, our results extend those previous findings, in which skills were not tested in new environments. Training and assessing abilities within the same environments does not rule out the possibility that participants may have acquired a set of 'automated responses' which would allow them to successfully complete the task. However, our comparison of performance when navigating 'old' (previously navigated) and 'new' (untrained) mazes, shows that sighted participants were able to learn to utilise echo-acoustic cues to successfully navigate even in new environments, thus ruling out stereotypical behaviour.

Further support for sighted people's ability to interpret echo-acoustic information is shown in results from our passive navigation, i.e. route recognition tasks. All participants improved in their ability to detect the presence of echoes, discriminate between scrambled and coherent routes, and identify specific routes, with performance after training approaching that of expert echolocators. The only comparison that was not statistically significant was the comparison between pre and post-training echo identification during fMRI, whilst everything else was significant (i.e. all pre-fMRI comparisons, as well as route vs. scrambled and route type identification during fMRI). However, participants were able to identify echoes with a high degree of accuracy (98%) in the pre-training MRI, so this might reflect a ceiling effect. Our results highlight the ability of sighted participants to learn about specific features of echo stimuli, and identify stimuli at a higher accuracy after training. Furthermore, the behavioural data obtained during fMRI show that participants were engaged with the passive task, before and after training. The responses given in all conditions were above chance, and show reduced accuracy as the task demands became more specific. This indicates that BOLD activations obtained during fMRI were task related.

Upon examining BOLD activity associated with the processing of sounds, compared to silence, we observed activity within the primary auditory cortex of expert echolocators. A result which is well supported by previous research (Arnott et al., 2013; Milne et al., 2015; Thaler et al., 2011). With training, sighted participants also exhibited activity within the primary auditory cortex in response to processing sounds, compared to silence. It is likely that these patterns of activation, displayed by both groups, are due to the acoustic differences between 'sound' and 'silence' conditions, with sound intensity differences driving activity in the primary auditory cortex (Jäncke, Shah, Posse, Grosse-Ryuken & Müller-Gärtner, 1998; Lasota, Ulmer, Firszt, Biswal, Daniels & Prost, 2003).

Furthermore, expert echolocators also recruited the primary 'visual' cortex (BA17), along with surrounding regions of the occipital cortex for the processing of sounds compared to silence, whereas activity within the occipital cortex of sighted participants was absent, even after training. Previous research has also found that the occipital cortex of congenitally blind individuals is active when listening to sound (Weeks et al., 2000; Campus, Sandini, Concetta Morrone & Gori, 2017), and it is likely that this recruitment is due to long term neuroplastic changes caused by blindness (Amedi, Lofti, Merabet, Bermpohl & Pascual-Leone, 2005; Cecchetti, Kupers, Ptito, Pietrini, Ricciardi, 2016; Kupers & Ptito, 2014; Merabet & Pascual-Leone, 2010), resulting in the recruitment of 'visual' areas for the processing of sound.

When we isolated the processing of echoes, we found activity within the primary auditory cortices of both expert echolocators and sighted participants after training. Again, it is likely that this activation is due to the acoustic differences present between 'echo' stimuli and 'no echo' stimuli, with echoic stimuli being louder and thus driving activity within the primary auditory cortex (Jäncke et al., 1998; Lasota et al., 2003). An increase in activation of the primary auditory cortex in response to stimuli containing echoes has previously been reported (Fiehler et al., 2015), and in a similar way to the current study, echoic stimuli were also louder than sounds with the echoes removed, supporting the idea that the acoustic differences between stimuli were responsible for the recruitment of the primary auditory cortex. Expert echolocators also displayed bilateral BOLD activations within the calcarine cortex, and surrounding regions of the occipital cortex, in response to echoic stimuli; a similar result to that previously found (Arnott et al., Milne et al., 2015; Thaler et al., 2011). Due to 'echo' stimuli being louder than 'no echo' stimuli, it is possible that this acoustic difference is also the driving force behind the activity observed in the occipital cortex of expert echolocators. This co-activation of the primary auditory and 'visual' cortices may be due to cross-modal plasticity as a result of blindness (Amedi et al., 2005; Cecchetti et al., 2016; Kupers &

Ptito, 2014; Merabet & Pascual-Leone, 2010). In contrast, sighted participants did not display any activation within the occipital cortex, even after training. This may suggest that the sighted brain is organised in a modality specific way, with activation of the auditory cortex in response to processing stimuli containing echoes, which were louder than stimuli with the echoes removed.

When considering the neural underpinnings of navigation using click-based echolocation, little is known. To investigate the neural correlates of navigation using echolocation, we isolated the processing of coherent spatial information. ‘Route’ stimuli contained spatially coherent information, whereas ‘scrambled’ stimuli did not provide a coherent route through a maze, and thus did not contain coherent or useful spatial information. This isolation of meaningful spatial information in the absence of any acoustic differences was achieved by using the same sounds in ‘route’ and ‘scrambled’ conditions, with the only difference being the order in which the clicks and echoes had been presented.

As a result of training, we found bilateral activation within the primary auditory cortex of sighted participants. The cause of this activation is unlikely due to any acoustic differences between stimuli, as the only difference was the presence or absence of coherent spatial information. Therefore, this activation of the primary auditory cortex seems to suggest that training influences the way in which ‘route’ and ‘scrambled’ stimuli are processed by sighted participants. We then examined BOLD activations within the occipital cortex, of expert echolocators and sighted participants after training in response to the processing of routes, compared to scrambled routes. Expert echolocators displayed activity within the middle occipital gyrus, an area previously found to be involved in the spatial processing of auditory and tactile stimuli in blind people (Collignon et al., 2011; Renier et al., 2010). Again, expert echolocators seem to be demonstrating cross-modal plasticity by recruiting the occipital cortex for the processing of spatial information, conveyed by sound. This suggests that the brains of expert echolocators may be organised in a flexible way (Murphy, Nau, Fisher, Kim, Schuman & Chan, 2016), with ‘visual’ areas being driven by the task. Contrary to previous contrasts (Sound > Silence; Echo > No Echo), we also found bilateral activation of the calcarine cortex, along with surrounding regions of the occipital cortex in sighted participants after training in echolocation. It has previously been suggested that activity within the calcarine cortex may be a result of the processing of spatial information provided by echoes (Milne et al., 2015; Thaler et al., 2011). Thus, it may be that the coherent spatial information contained within 'route' stimuli may be driving activity within the calcarine cortex of sighted participants after training. Therefore, the sighted brain may also be organised in a flexible way (Draganski & May, 2008; Herholz & Zattore, 2012; Power & Schlaggar, 2016), with the occipital cortex, a region typically devoted to the processing of visual information, possibly processing spatial information present in echoic stimuli after training.

Previous research has found that blind individuals show BOLD activations within the parahippocampus when using the TDU to navigate (Kupers et al., 2010). Similarly, sighted people also recruit the same region when navigating using vision (Aguirre, Detre, Alsop, & D'Esposito, 1996; Boccia, Nemmi & Guariglia, 2014; Weniger et al., 2010). We found a similar pattern, with small regions of activity within the parahippocampus of expert echolocators and sighted participants after training. This suggests that the parahippocampus is also recruited by expert echolocators and sighted participants when performing a click based echolocation navigation task. A possible explanation for the small amount of activity observed in expert echolocators and sighted participants could reflect the use of a tactile-to-visual SSD (Kupers et al., 2010), compared to the use of click-based echolocation in the current study. Echolocation relies on the interpretation of a weak echo, whereas TDU users were receiving constant tactile stimulation to the tongue, which could result in the acquisition of more spatial information. Therefore, the difference in the level of BOLD activity could reflect the different methods of conveying spatial information for navigation. Another plausible, and possibly more likely explanation for the limited parahippocampal activation displayed by expert echolocators and sighted participants after training might be due to the use of a sparse sampling design. The use of sparse sampling in the current experiment was necessary to allow for the presentation of auditory stimuli, without any interference from scanner noise (Hall et al., 1999; Perrachione & Ghosh, 2013). However, the use of sparse sampling results in reduced acquisition of data compared to traditional MRI methods. For example, in the current experiment we acquired 38 volumes per run, compared to 282 volumes acquired during continuous scanning by Kupers et al. (2010). This results in a large power difference, which could potentially account for the small regions of parahippocampal activity observed.

A further limitation lies in the brain normalisation technique used. Transforming a brain into Talairach space (Talairach & Tournoux, 1988) produces a set of 3-dimensional coordinates which should correspond to the same anatomical area across subjects. However, this can be problematic, as the same coordinate can often refer to a different anatomical area (Frost & Goebel, 2012) and previous research has found the discrepancy between anatomical areas could be as large as 10mm (Van Essen & Dury, 1997). This possible misalignment of anatomical regions can cause problems when trying to identify small clusters of common activations across subjects. To improve, it would be beneficial if future research were to employ a curvature driven cortex based alignment (Frost & Goebel, 2012; Goebel et al., 2006), in which sulci and gyri are aligned. This could reduce variability between subjects, and simultaneously increase statistical power, allowing a more accurate group analysis to be undertaken.

Future research would also include a group of blind subjects, who have been trained to echolocate. The comparison of brain activity in echolocation experts, blind trained and sighted trained participants may allow us to determine if the brain is organised by sensory modality or by task, in which case we may expect all three groups to show overlapping regions of BOLD activation.

In sum, our results show that activations of the primary auditory and ‘visual’ cortices in expert echolocators are largely due to the acoustic differences between ‘sound’ stimuli and ‘silence’, along with ‘echo’ and ‘no echo’ stimuli, with louder stimuli driving activity within the auditory and ‘visual’ cortices. This demonstration of cross-modal plasticity by expert echolocators suggests the brain is organised in a flexible way, with areas which are typically devoted to processing visual information recruited for the processing of sound, in blind people. With training, sighted participants also displayed activity within the primary auditory cortex in response to the acoustic differences present between stimuli. However, the lack of activity observed within the occipital cortex of sighted participants may suggest that the brain is organised in a modality specific way. Despite this, it seems the occipital cortex may be adept at processing spatial information, conveyed by sound, in expert echolocators and sighted participants after training.

Overall, our results support the idea that those with vision loss demonstrate cross-modal plasticity (Amedi et al., 2005; Cecchetti et al., 2016; Kupers & Ptito, 2014; Merabet & Pascual-Leone, 2010), and thus show a flexible organisation of the brain, with sensory areas such as the occipital cortex recruited for the processing of sound. Furthermore, the involvement of the calcarine cortex, in sighted participants after training, for processing stimuli containing coherent spatial information may hint at the possibility that the sighted brain is also organised in a flexible way (Draganski & May, 2008; Herholz & Zattore, 2012; Power & Schlaggar, 2016), with occipital cortex activations being driven by the processing of spatial information conveyed by sound.

Appendix A: Information Sheet

Participant Information Sheet
Project title: The Neural Basis of Echolocation: an fMRI Investigation

Researcher(s): Caitlin Dodsworth (caitlin.dodsworth@durham.ac.uk)
Department: Psychology
Supervisor name: Lore Thaler (lore.thaler@durham.ac.uk)

You are invited to take part in a research study concerning human echolocation. This study has received ethical approval from the Psychology Ethics Committee of Durham University. Before you decide whether to agree to take part, it is important for you to understand the purpose of the research and what is involved as a participant. Please read the following information carefully and feel free to get in contact if you have any questions or would like more information.

What is the purpose of the study?
Echolocation was initially studied in bats (Griffin, 1944) and dolphins (Au & Benoit-Bird, 2003), but humans can also echolocate, for example using mouth clicks (Kolarik et al, 2014; Thaler & Goodale, 2016). Echolocation can be learnt by blind and sighted individuals (Kolarik et al, 2014; Thaler & Goodale, 2016), and is an important tool for spatial navigation in people with vision loss (Thaler, 2013). In terms of brain activity, echolocation experts show activation in visual cortical areas but sighted people who do not echolocate, do not show this activity (Thaler, Arnott & Goodale, 2011). The purpose of the study is to discover whether echolocation training will elicit functional changes in brain activity, over a 10-week period, in sighted individuals. Furthermore, we aim to determine whether people's age will affect their ability to learn and also how their brain changes as a result of learning. This will reveal the extent to which early sensory areas, such as the primary visual and auditory cortices, are able to re-organise and adapt in response to learning.

The study will be completed by December 2018.

What you will need to do:
You will participate for ~ 10 weeks. Training sessions will occur twice per week and will involve practicing echolocation for 1-2 hours. You will listen to pre-recorded sounds of clicks and echoes and navigate a virtual route on a computer. You will be blindfolded and wearing headphones whilst completing this task. You will also be asked to make mouth clicks to perform size and angular discrimination tasks, along with walking on level flooring. Echolocation tasks, such as making mouth clicks to walk along a corridor and make a turn, will also need to be practiced at home.

You will also attend two fMRI scanning sessions, taking place at Durham University Neuroimaging Centre in Middlesbrough. The first session will be at the beginning of the study, and the second will be after 10 weeks of training. During each fMRI session, you will be listening to pre-recorded echo-acoustic sounds while blindfolded and wearing headphones. Transport can be provided if needed, and each session will last ~2 hours.
At the end of the study, you will be asked to complete a questionnaire providing general feedback, such as enjoyment of participation. There is no requirement to answer all questions.

Reimbursement will be offered for participating in this study in the form of £6/hr for training and £10/hr for fMRI scans, or participant pool credit for Psychology students. The difference in reimbursement for the training and scanning sessions reflects the increased inconvenience and consumption of your time in travelling to the 3T facility in Middlesbrough.

Why have I been invited to take part?
You have been invited because you fall into our age categories, are right-handed, have normal hearing, no neurological conditions and have normal/corrected to normal vision.

Do I have to take part?
Your participation is voluntary and you do not have to take part. If you do agree to take part, you can withdraw at any time, without providing a reason. Your rights in relation to withdrawing any data that is identifiable to you are explained in the accompanying Privacy Notice.

Are there any potential risks involved?
Potential risks are related to fMRI hazards, such as the presence of ferromagnetic material in the body or on the person, this is because the strong magnetic field will attract such objects, causing them to move towards the magnet with great force. However, a screening process will take place before this to ensure you do not have any objects which could be hazardous in or on your person, and before taking part in the fMRI session, you will be asked to complete an fMRI questionnaire to ensure it is safe for you to enter the scanner. Researchers have also participated in fMRI safety training to minimize any risks.

You may experience slight discomfort when in the fMRI scanner due to having to remain still for an extended period of time. If you anticipate you will be uncomfortable inside of the scanner, you are advised not to take part in this study.

Benefits include learning to echolocate! You should see substantial improvements in this ability after 10 weeks of training and very few individuals have this skill.

Will my data be kept confidential?
All information obtained during the study will be kept confidential using anonymous codes and stored on a password protected computer. Published data will not be identifiable as your own. Data will be destroyed after 10 years. Full details are included in the accompanying privacy notice.

What will happen to the results of the project?
Anonymised data may be used in publications, reports, presentations, web pages and other research outputs. At the end of the project, anonymised data may be archived and shared with others for legitimate research purposes.

Who do I contact if I have any questions or concerns about this study?
If you have any further questions or concerns, please speak to the researcher or their supervisor. If you remain unhappy or wish to make a formal complaint, please submit a complaint via the University's Complaints Process.
https://www.dur.ac.uk/resources/academicsupport.office/150818ComplaintFormAG2015-V2.pdf

Thank you for reading this information and considering taking part in this study.

Caitlin Dodsworth (caitlin.dodsworth@durham.ac.uk)
Supervisor: Lore Thaler (lore.thaler@durham.ac.uk)

Appendix B: Privacy Notice

PART 1 – GENERIC PRIVACY NOTICE

Durham University's responsibilities under data protection legislation include the duty to ensure that we provide individuals with information about how we process personal data. We do this in a number of ways, one of which is the publication of privacy notices. Our privacy notices comprise two parts – a generic part and a part tailored to the specific processing activity being undertaken.

Data Controller
The Data Controller is Durham University. If you would like more information about how the University uses your personal data, please see the University's Information Governance webpages or contact:

Information Governance Unit
Telephone: (0191 33) 46246 or 46103
E-mail: info.access@durham.ac.uk

Data Protection Officer
The Data Protection Officer is responsible for advising the University on compliance with Data Protection legislation and monitoring its performance against it. If you have any concerns regarding the way in which the University is processing your personal data, please contact the Data Protection Officer:

Jennifer Sewel
University Secretary
Telephone: (0191 33) 46144
E-mail: jennifer.sewel@durham.ac.uk

Retention
The University keeps personal data for as long as it is needed for the purpose for which it was originally collected. Most of these time periods are set out in the University Records Retention Schedule.

Your rights in relation to your personal data

Privacy notices and/or consent
You have the right to be provided with information about how and why we process your personal data. Where you have the choice to determine how your personal data will be used, we will ask you for consent. Where you do not have a choice (for example, where we have a legal obligation to process the personal data), we will provide you with a privacy notice. A privacy notice is a verbal or written statement that explains how we use personal data.

Whenever you give your consent for the processing of your personal data, you receive the right to withdraw that consent at any time. Where withdrawal of consent will have an impact on the services we are able to provide, this will be explained to you, so that you can determine whether it is the right decision for you.

Accessing your personal data

You have the right to be told whether we are processing your personal data and, if so, to be given a copy of it. This is known as the right of subject access. You can find out more about this right on the University's Subject Access Requests webpage.

Right to rectification
If you believe that personal data we hold about you is inaccurate, please contact us and we will investigate. You can also request that we complete any incomplete data.
Once we have determined what we are going to do, we will contact you to let you know.

Right to erasure
You can ask us to erase your personal data in any of the following circumstances
We no longer need the personal data for the purpose it was originally collected
You withdraw your consent and there is no other legal basis for the processing
You object to the processing and there are no overriding legitimate grounds for the processing
The personal data have been unlawfully processed
The personal data have to be erased for compliance with a legal obligation
The personal data have been collected in relation to the offer of information society services (information society services are online services such as banking or social media sites).
Once we have determined whether we will erase the personal data, we will contact you to let you know.

Right to restriction of processing
You can ask us to restrict the processing of your personal data in the following circumstances:
You believe that the data is inaccurate and you want us to restrict processing until we determine whether it is indeed inaccurate
The processing is unlawful and you want us to restrict processing rather than erase it
We no longer need the data for the purpose we originally collected it but you need it in order to establish, exercise or defend a legal claim and
You have objected to the processing and you want us to restrict processing until we determine whether our legitimate interests in processing the data override your objection.
Once we have determined how we propose to restrict processing of the data, we will contact you to discuss and, where possible, agree this with you.

Making a complaint
If you are unsatisfied with the way in which we process your personal data, we ask that you let us know so that we can try and put things right. If we are not able to resolve issues to your satisfaction, you can refer the matter to the Information Commissioner's Office (ICO). The ICO can be contacted at:

Information Commissioner's Office
Wycliffe House
Water Lane
Wilmslow
Cheshire
SK9 5AF
Telephone: 0303 123 1113
Website: Information Commissioner's Office

PART 2 – TAILORED PRIVACY NOTICE

This section of the Privacy Notice provides you with the privacy information that you need to know before you provide personal data to the University for the particular purpose(s) stated below.

Type(s) of personal data collected and held by the Department and method of collection:
All individuals who are scanned are asked to complete and sign a Durham-University-MRI-Facility-consent-form and a Durham University consent form that allows imaging and behavioural data to be used for research purposes only.

For each fMRI study we will ask you to provide the following personal information:
Year of birth
Contact Info (e-mail)
Gender
Hand preference
Colour Vision (intact/altered)
Visual acuity (normal/corrected)
Native Language

We will also ask you to complete and sign a fMRI screening form in which you will be asked about whether you suffer from various medical or neurological conditions. In addition to this, we will acquire images of your brain activity when you are doing a task in the scanner. We will additionally collect behavioural responses during scanning.

During training sessions, we will collect data from a virtual computer based navigation task and active size and orientation tasks. Data will include: time taken, errors made, response made and overall accuracy. We will also make a short audio-recording of your mouth clicks at the start of each session.

How personal data is stored by the Department:
Your data will be treated with full confidentiality and if published will not be identifiable as yours. Your data will be securely stored in a password- protected file on a password protected computer and anonymous coding of the experimental data will be employed and information that identifies you will be kept separate from the anonymised data. A key to this coding will be held securely by the principal investigator. Your consent form and questionnaires will be retained in their original form and stored in a locked filing cabinet and only available to the principal investigator. They will be securely stored for a period of 10 years after which they will be destroyed.

The brain images are stored in a password-protected database of the South Tees hospital Trust for 6 months, after which they will be destroyed. After this, the brain images will be stored on password-protected Durham University computers for 50 years after which they will be destroyed. Fully anonymised data (i.e., results from statistical analyses and data which are not identifiable) may be kept longer for use in future studies.

How personal data is processed by the Department:
The University's core purpose includes undertaking research in the public interest. Processing of your data is carried out as part of this core purpose.

The signed consent form provides evidence of your consent to take part in this study which is an ethical requirement. The fMRI screening form assesses your suitability for neuroimaging before the first scanning session. The fMRI data collected will allow us to analyse your brain activity and behavioural responses to echolocation stimuli, before and after learning to

echolocate. Behavioural data, acquired in training sessions, will be used to analyse performance over a 10-week training period. Information will be entered into a database for analysis. After six months the data will be completely anonymised and the original records, including any information which can identify you personally will be destroyed.
We keep a record of the anonymous code that has been assigned to you to provide you with the opportunity to withdraw your data from the study. Please note however that you will not be able to withdraw your data when it has been fully anonymised.

Who the Department shares personal data with:
None of the personal data that you have provided on the consent form or questionnaires will be shared. However, anonymised (i.e. not identifiable) data may be used in publications, reports, presentations, web pages and other research outputs. At the end of the project, anonymised data may be archived and shared with others for legitimate research purposes. In addition, brain scans may be archived and shared with others for legitimate research purposes. Brain scans are not strictly anonymous, because individual brains are unique (a bit like a fingerprint), but they will be processed to decrease the likelihood of identifying an individual. No personal information such as names or birth dates will be attached to the brain scans.

Durham University staff are not authorised to release any information direct to individuals/third parties or to discuss anything relating to the images obtained during the scan with individuals/third parties, except in the case of a suspected anomaly, in which case the scans will be made available to the participant's General Practitioner.

How to object to the Department processing your personal data:
If you have any concerns regarding the processing of your personal data, or you wish to withdraw your data from the project, contact Caitlin Dodsworth (caitlin.dodsworth@durham.ac.uk)

For further information, please contact: Lore Thaler (lore.thaler@durham.ac.uk)

Appendix C: Consent Form

Consent Form
Project title: The Neural Basis of Echolocation: an fMRI Investigation

Researcher(s): Caitlin Dodsworth
Department: Psychology
Contact details: caitlin.dodsworth@durham.ac.uk
Supervisor name: Lore Thaler
Supervisor contact details: lore.thaler@durham.ac.uk

This form is to confirm that you understand what the purposes of the project, what is involved and that you are happy to take part. Please initial each box to indicate your agreement:

I confirm that I have read and understand the information sheet dated ________ for the above project.	
I have had sufficient time to consider the information and ask any questions I might have, and I am satisfied with the answers I have been given.	
I understand who will have access to personal data provided, how the data will be stored and what will happen to the data at the end of the project.	
I agree to take part in the above project.	
I understand that my participation is voluntary and that I am free to withdraw at any time without giving a reason.	
I consent to being audio recorded, and understand how recordings will be used in research outputs.	
I understand that anonymised (i.e. not identifiable) versions of my data may be archived and shared with others for legitimate research purposes.	
I understand that brain scans without any other personal information attached may be archived and shared with others for legitimate research purposes.	

Participant's Signature_____________________________________ Date_______________

(NAME IN BLOCK LETTERS)____

Researcher's Signature____________________________ Date_______________

(NAME IN BLOCK LETTERS)____

Appendix D: fMRI Consent Form

fMRI consent form: South Tees Hospital NHS Trust and Durham University MRI Facility
General Consent Form

Project Title: The Neural Basis of Echolocation: an fMRI Investigation
Principal Investigator: Lore Thaler

I consent to taking part in the present study that has been approved by the South Tees Hospital NHS Trust and Durham University MRI Facility and confirm that I have been fully informed about the nature of the procedures and have completed the safety questionnaires: **YES NO**

I consent to the use of my MRI scans in the present study: **YES NO**

I consent to the use of my MRI scans in future studies that have been approved by the South Tees Hospital NHS Trust and Durham University MRI Facility on the understanding that my brain scans will be passed on without any personal information attached by the Principal Investigator of the present study (see the attached privacy notice for more information about data management) **YES NO**

You may withdraw yourself from the study without giving a reason at any stage of the experiment and you can withdraw your data up until 3 months after you have participated.
The South Tees Hospital NHS Trust and Durham University MRI Facility is not a clinical diagnostic facility and as such does not routinely inspect all scans for anomalies. However, from time to time an anomaly is observed on MRI scan. South Tees Hospital NHS Trust and Durham University MRI Facility can only indicate that further advice might be sought. The presence or absence of an anomalous scan is not an indication of the presence or absence of pathology.

If an anomalous observation were made South Tees Hospital NHS Trust and Durham University MRI Facility **must** inform your General Practitioner.

Please note: If you prefer not to have your General Practitioner's practice informed South Tees Hospital NHS Trust and Durham University MRI Facility will regrettably be unable to scan you. If you are not currently registered with a UK General Practitioner or do not know the contact address of your current General Practitioner South Tees Hospital NHS Trust and Durham University MRI Facility will be unable to scan you.

I consent to my General Practitioner's practice being contacted if an anomaly is observed and I understand that the South Tees Hospital NHS Trust and Durham University MRI Facility is not offering diagnostic advice and that no clinical advice will be offered.

Please Tick One: **YES NO**
Participant Name: ……………………………………………………………………………………
Telephone number: ………………………………………….. E-mail: ………………………………
Signature: …………………………………………………. Date: ………………………………..
General Practitioner's Practice Address:
……
……
………

Appendix E: fMRI Screening Form

South Tees Hospital NHS Trust and Durham University MRI Facility: SCREENING FORM

So that we can safely proceed with the examination, we need to check that there are no factors that would prevent you from having an MRI scan. Please complete this questionnaire and bring it with you. A member of staff will check through it with you when you arrive

QUESTION	YES	NO	COMMENTS
Do you have a cardiac pacemaker or an implanted cardioverter defibrillator?			
Do you have an artificial heart valve?			
Do you have severe heart disease (including susceptibility to arrhythmias)?			
Do you have an intracranial aneurysm clip?			
Do you have a programmable intracranial shunt?			
Do you have Meniere's disease?			
Do you have epilepsy or diabetes or a thermoregulatory condition?			
Do you have a cochlear implant, other type of hearing aid or false teeth?			
Do you have an implanted neurostimulator or medicine delivery pump?			
Have you ever been injured by a metallic foreign body which was not removed (e.g., bullet, BB, shrapnel)?			
Have you had any surgery on your head, spine or chest?			
Are you wearing an artificial limb?			
Do you wear a medicine patch (e.g. nicotine, contraceptive, or angina)?			
Have you ever had any operations which may have involved the use of metallic pins, plates, screws, artificial limbs or ocular implants?			
Do you have dental work other than fillings?			
To the best of your knowledge, do you have impaired renal function or are you awaiting a liver transplant?			
Have you ever worked with metal (grinding, fabricating, welding, etc.) or ever had an injury to the eye involving a metallic object (e.g., metallic slivers, shavings)?			
Do you have any tattoos or permanent eyeliner?			
Do you have any body piercings that cannot be removed?			
Female patients:			
Is there any possibility that you may be pregnant?			
Are you currently breast feeding?			
Do you have an contraceptive intrauterine device (IUD)?			

Due to the strong magnetic field, watches, jewellery, body piercings, hearing aids, credits cards, mobile phones, belts with metal buckles, and pagers are not permitted in the scanner. Neither are loose metallic objects such as pens, coins, hair clips, cigarette lighters, metallic denture plates. Please empty your pockets.

I have removed the following items from my body (Items will be kept securely in the Control room):	
Any jewellery, wrist watch or belts	
Any body piercings	
Any hairpins or clips	
Wallet and credit cards	
Coins, pens and cigarette lighter	
Anything else from any of your pockets	
Female participants:	
Underwire bra	

Signed …………………………………………………. Date……………….
Print Name ………………………………………………….

Witnessed By (Member of staff) …………………………………………………. Date…………….
Print name …………………………………………………

Appendix F: Debrief sheet

Debriefing Sheet
The Neural Basis of Echolocation: an fMRI Investigation

Thank you for taking part in this research project. Please find further information below about the purpose of the project and expected findings.

Echolocation was initially studied in bats (Griffin, 1944) and dolphins (Au & Benoit-Bird, 2003), but people can echolocate also, for example using mouth clicks (Kolarik et al, 2014; Thaler & Goodale, 2016). Echolocation can be learnt by blind and sighted individuals (Kolarik et al, 2014; Thaler & Goodale, 2016), and it is an important tool for spatial navigation in people with vision loss (Thaler, 2013).

In terms of brain activity, echolocation experts show activation in visual cortical areas but sighted people who do not echolocate, do not show this activity (Thaler, Arnott & Goodale, 2011). It is not clear, therefore, if echolocation related activity is due to blindness or skill in echolocation. There is also no literature to explore the impact of training on the neural correlates of echolocation

The aim of the study you took part in is to discover whether echolocation training will elicit functional changes in brain activity, over a 10-week period, in sighted individuals. Furthermore, we aim to determine whether people's age will affect their ability to learn and also how their brain changes as a result of learning.

It is expected that all participants will show an improvement in echolocation ability, shown by behavioural performance, after the 10-week training period. In terms of brain activity, an increase in echo-acoustic related activity in visual and auditory cortices is expected. A comparison of age will reveal whether age impacts the degree to which people can learn to echolocate and how the brain adapts to learning with age.

Personal information will remain confidential and anonymous, and data will only be accessed by the research team. If you would like further information about the study or results, please contact myself or Lore Thaler (my supervisor), using the contact information below. We cannot however provide you with your individual results. If you wish to withdraw your data, this is possible if you make contact within one week of participation, or alternatively contact the psychology office on 0191 334 3240, and cite your anonymous code. No reason for withdrawal is required.

If you have any questions or queries, please contact either myself or Lore Thaler (my supervisor), using the contact details below.

Thank you again for your participation.

Caitlin Dodsworth (caitlin.dodsworth@durham.ac.uk)
Lore Thaler (lore.thaler@durham.ac.uk)

Appendix G: fMRI Additional Exploratory Analyses: Sound > Silence

Additional *activations found, upon removal of cluster size threshold, for the Sound > Silence contrast in sighted participants (SP) (post – pre) and expert echolocators (EE) (single session) in Talairach space. The co-ordinates given indicate the center of gravity for each cluster.*

			Sound > Silence			
Subj. Group	Hemi.	Location	X	Y	Z	No. of Voxels
SP (Post – Pre)	L&R	Medial Frontal Gyri, Middle & Inferior Frontal Gyrus (R only) and Orbito-Frontal Cortex (R only)	33.27	19.37	25.38	64763
SP (Post – Pre)	L	Precentral Gyrus, Postcentral Gyrus, and Superior Temporal Gyrus	-44.89	-29.07	22.37	27051
SP (Post – Pre)	R	Postcentral gyrus and Superior Temporal Gyrus	45.99	-30.81	22.81	24347
SP (Post – Pre)	L	Middle and Inferior Frontal Gyri	-45.72	6.42	23.52	12595
SP (Post – Pre)	L	Cerebellum	-15.57	-68.90	-28.21	5891
SP (Post – Pre)	L	Inferior Frontal Gyrus	-31.06	19.20	8.85	4506
SP (Post – Pre)	L	Middle Frontal Gyrus	-39.21	45.75	11.70	4386
SP (Post – Pre)	R	Precuneus	9.84	-71.33	41.40	565
SP (Post – Pre)	L	Middle Frontal Gyrus	-25.59	-9.71	53.84	560
SP (Post – Pre)	L	Oribito-Frontal Cortex	-17.24	48.26	-2.85	325
SP (Post – Pre)	L	Cerebellum	-37.16	-66.58	-40.36	216
SP (Post – Pre)	L	Caudate	-20.60	-0.01	11.47	106
SP (Post – Pre)	L	Frontal Lobe, Sub Gyral	-26.69	-12.87	38.41	39
SP (Post – Pre)	R	Occipito-Temporal Sulcus	27.15	-54.12	-19.97	34
SP (Post – Pre)	L	Frontal Lobe, Sub Gyral	-18.38	-0.77	35.92	26
SP (Post – Pre)	L	BA17	-14.32	-100.32	-8.32	19
SP (Post – Pre)	L	Precentral Gyrus	-42.22	-15.89	52.44	9
SP (Post – Pre)	R	Postcentral Gyrus	21.00	-42.78	67.33	9
SP (Post – Pre)	R	Postcentral Gyrus	36.00	-34.33	53.17	6
SP (Post – Pre)	L	Cingulate Gyrus	-18.20	-33.60	22.00	5
SP (Post – Pre)	L	Frontal Lobe, Sub Gyral	-25.00	-25.00	40.00	5
SP (Post – Pre)	R	Lateral Ventricle	3.33	13.67	13.00	3
EE	R	Calcarine Cortex (BA17), BA18 & Lingual Gyrus	23.78	-74.75	-3.10	21768
EE	R	Middle & Inferior Frontal Gyrus	40.17	25.59	23.37	13635
EE	L	Lingual Gyrus & BA18	-28.28	-74.04	-9.25	13528
EE	L	Inferior Frontal Gyrus	-49.64	24.50	20.89	6713
EE	L	Superior Temporal Gyrus	-48.49	-30.56	10.71	5975
EE	R	Superior Temporal Gyrus	52.66	-31.75	9.40	5754
EE	R	Medial Frontal Gyrus	3.52	21.63	46.80	3105

EE	L	Middle Frontal Gyrus	-36.80	-3.77	41.80	2403
EE	L	Caudate	-13.39	4.30	9.71	2243
EE	L	Postcentral Gyrus	-53.05	-25.88	34.56	1953
EE	R	Precuneus leading to Parieto-Occipital Junction & Cuneus	17.18	-74.23	33.41	1790
EE	L	Postcentral Gyrus	-37.01	-47.13	40.48	1289
EE	L	Middle Occipital Gyrus	-25.42	-74.63	14.40	1263
EE	R	Postcentral Gyrus	34.98	-49.65	33.93	574
EE	R	Medial Frontal Gyrus	9.06	1.95	51.76	458
EE	L	Thalamus	-15.02	-21.15	13.01	420
EE	R	Middle Frontal Gyrus	29.96	-4.09	58.82	407
EE	L	Frontal Lobe, Sub-Lobar	-28.46	19.29	7.45	260
EE	R	Frontal Lobe, Sub-Gyral	18.38	38.25	-7.51	253
EE	R	Thalamus	9.34	-16.13	13.88	238
EE	L	Inferior Parietal Lobule	-59.55	-43.36	34.77	211
EE	L	Occipito-Temporal Junction, leading to Parahippocampus	-28.08	-51.16	-13.41	189
EE	L	Paracentral Lobule	-13.99	-40.81	55.33	172
EE	L	Inferior Temporal Gyrus	-46.40	-43.06	-18.34	163
EE	L	Precentral Gyrus	-38.32	-25.40	51.05	123
EE	R	Precuneus	25.97	-66.14	25.19	121
EE	R	Caudate	23.08	-5.29	15.46	103
EE	R	Postcentral Gyrus	17.80	-42.02	61.63	102
EE	R	Medial Frontal Gyrus	6.55	27.40	29.17	78
EE	R	Postcentral Gyrus	33.56	-46.79	55.08	72
EE	L	Middle Frontal Gyrus	-23.78	-8.47	57.17	59
EE	R	Inferior Parietal Lobule	61.15	-41.15	33.42	53
EE	L	Postcentral Gyrus	-21.77	-53.54	40.90	48
EE	L	Parietal Lobe, Sub-Gyral	-33.85	-42.46	30.10	39
EE	L	Cuneus	-11.28	-67.49	10.64	39
EE	L	Precuneus	-17.60	-74.83	33.77	35
EE	R	Cerebellum	14.13	-73.26	-31.97	31
EE	L	Inferior Frontal Gyrus	-49.61	13.64	4.18	28
EE	L	Precuneus	-18.63	-60.74	45.81	27
EE		Corpus Callosum	0.30	-27.96	25.04	23
EE	L	Cerebellum	-34.53	-63.73	-25.73	15
EE	R	Cingulate Gyrus	3.00	-8.36	33.86	14
EE	L	Cerebellum	-12.17	-64.67	-41.50	12
EE	L	Superior Frontal Gyrus	-12.00	62.12	6.88	8

Appendix H: fMRI Additional Exploratory Analyses: Echo > No Echo

Additional *activations found, upon removal of cluster size threshold, for the Echo > No Echo contrast in sighted participants (SP) (post – pre) and expert echolocators (EE) (single session) in Talairach space. The co-ordinates given indicate the center of gravity for each cluster.*

			Echo > No Echo			
Subj. Group	Hemi.	Location	X	Y	Z	No. of Voxels
SP (Post – Pre)	L	Superior Temporal Gyrus & Lateral Ventricle	-36.87	-33.58	8.12	3401
SP (Post – Pre)	R	Inferior Frontal Gyrus	33.73	23.83	6.65	3097
SP (Post – Pre)	L	Inferior Frontal Gyrus	-31.80	20.45	5.97	1378
SP (Post – Pre)	R	Superior Temporal Gyrus	51.05	-30.61	9.79	758
SP (Post – Pre)	R	Cingulate Gyrus & Lateral Ventricle	10.24	-19.26	26.43	589
SP (Post – Pre)	R	Middle Frontal Gyrus	30.98	0.03	33.58	129
SP (Post – Pre)	R	Superior Temporal Gyrus	44.20	-10.48	0.49	107
SP (Post – Pre)	R	Inferior Frontal Gyrus	41.97	49.04	2.80	98
SP (Post – Pre)		Brainstem	-7.99	-26.19	-41.10	79
SP (Post – Pre)	R	Precentral Gyrus	26.60	-28.85	50.47	68
SP (Post – Pre)	L	Postcentral Gyrus	-34.65	-29.23	28.00	62
SP (Post – Pre)	R	Orbito-Frontal Cortex	20.44	49.70	-4.80	54
SP (Post – Pre)	R	Inferior Frontal Gyrus	48.86	7.39	16.63	49
SP (Post – Pre)	R	Inferior Frontal Gyrus	45.13	35.97	0.87	31
SP (Post – Pre)	L	Precentral Gyrus	-48.77	-21.23	30.23	31
SP (Post – Pre)	R	Sub-Lobar	20.14	-41.62	25.81	21
SP (Post – Pre)	R	Orbito-Frontal Cortex	30.44	41.78	-7.06	18
SP (Post – Pre)	L	Cingulate Gyrus	-9.00	-18.17	26.67	12
SP (Post – Pre)	L	Precentral Gyrus	-15.33	-19.56	54.44	9
SP (Post – Pre)	R	Middle Frontal Gyrus	42.38	1.88	25.50	8
SP (Post – Pre)	L	Frontal Lobe, Sub Gyral	-20.88	23.12	22.38	8
SP (Post – Pre)	L	Sub-Lobar	-21.00	-45.00	25.00	3
EE	R	Calcarine Cortex (BA17), BA18 & Lingual Gyrus, leading to Parahippocampus	18.91	-73.71	-2.97	45706
EE	R	Middle & Inferior Frontal Gyri	41.59	21.19	24.06	13373
EE	L	Middle & Inferior Frontal Gyri	-49.49	19.45	23.03	9240
EE	L	Superior Temporal Gyrus	-49.52	-28.92	9.22	5878
EE	L	Lateral Occipital Gyri, leading to Parahippocampus	-39.31	-68.84	-8.16	5663
EE	R	Cerebellum	17.81	-57.92	-36.65	3853
EE	L	Lingual Gyrus & Calcarine Cortex (BA17), leading to cerebellum	-15.01	-71.72	-17.94	3163
EE	L	Caudate leading to Thalamus	-14.42	-0.61	6.84	2922
EE	L	Cerebellum	-15.28	-56.23	-37.65	2490
EE	R	Thalamus leading to Midbrain	10.15	-16.90	-0.30	2480

EE	L	Inferior Frontal Gyrus	-28.88	18.55	9.62	1837
EE	R	Superior Temporal Gyrus	53.48	-34.63	12.19	1823
EE	L	Brainstem	-2.52	-31.80	-28.04	1477
EE	R	Middle Frontal Gyrus	33.74	46.89	18.40	1308
EE	R	Superior and Middle Frontal Gyri	18.68	-2.88	47.51	1109
EE	L	Cuneus	-26.70	-69.78	17.69	857
EE	L	Middle Frontal Gyrus	-33.29	-6.01	40.47	555
EE	R	Medial Frontal Gyrus	5.55	27.23	47.28	484
EE	L	Cerebellum	-28.30	-56.27	-27.67	372
EE	R	Precuneus	17.84	-61.72	33.95	306
EE	L	Inferior Temporal Gyrus	-42.90	-41.13	-19.13	293
EE	R	Precuneus	28.80	-51.38	40.23	249
EE		Corpus Callosum	0.45	-29.58	25.11	171
EE	L	Middle Occipital Gyrus	-27.88	-83.30	8.68	139
EE	L	Postcentral Gyrus	-57.10	-27.72	32.09	132
EE	L	Precuneus	-22.15	-53.17	39.77	120
EE	L	Precentral Gyrus	-41.11	-26.28	51.53	109
EE	L	Postcentral Gyrus	-40.21	-35.78	40.11	100
EE		Corpus Callosum	1.40	-2.95	30.91	58
EE	R	Cerebellum	33.34	-40.68	-38.32	50
EE	L	Frontal Lobe, Sub Gyral	-27.33	-27.84	37.29	45
EE	R	Postcentral Gyrus	14.48	-40.19	61.40	42
EE	L	Postcentral Gyrus	-35.26	-47.32	39.00	34
EE	R	Inferior Temporal Gyrus	55.37	-46.44	-12.15	27
EE	R	Cingulate Gyrus	7.65	4.95	27.95	20
EE	R	Middle Frontal Gyrus	27.00	-13.00	61.00	3

Appendix I: fMRI Additional Exploratory Analyses: Route > Scrambled

Additional *activations found, upon removal of cluster size threshold, for the Route > Scrambled contrast in sighted participants (SP) (post – pre) and expert echolocators (EE) (single session) in Talairach space. The co-ordinates given indicate the center of gravity for each cluster.*

			Route > Scrambled			
Subj. Group	Hemi.	Location	X	Y	Z	No. of Voxels
SP (Post – Pre)	R	Superior Temporal Gyrus	49.48	-24.89	9.19	7954
SP (Post – Pre)	L	Superior Temporal Gyrus	-47.49	-30.29	11.55	5805
SP (Post – Pre)	L	Middle & Inferior Frontal Gyri	-37.32	12.87	23.02	5163
SP (Post – Pre)	L	Middle Frontal Gyrus	-38.18	47.28	10.63	3708
SP (Post – Pre)	L	Cuneus, BA17 & 18	-11.88	-91.22	15.33	2858
SP (Post – Pre)	R	Middle Frontal Gyrus	33.78	28.93	25.01	2584
SP (Post – Pre)	L	Medial Occipito-Temporal Gyrus, leading to parahippocampus	-17.53	-70.85	-19.39	1914
SP (Post – Pre)	R	Cuneus, BA17 & 18	15.72	-93.56	8.77	843
SP (Post – Pre)	R	Orbito-Frontal Cortex	30.67	41.80	-0.49	822
SP (Post – Pre)	L&R	Cuneus	-1.83	-82.62	9.68	656
SP (Post – Pre)	L	Caudate	-17.35	6.60	1.77	594
SP (Post – Pre)	R	Medial Frontal Gyrus	14.51	16.65	45.46	403
SP (Post – Pre)	L	Postcentral Gyrus	-52.78	-16.93	25.53	379
SP (Post – Pre)	R	Caudate	21.00	0.02	24.13	244
SP (Post – Pre)		Corpus Callosum	1.52	-5.52	22.53	240
SP (Post – Pre)	L	Insula	-32.61	17.36	9.91	235
SP (Post – Pre)	L	Cerebellum	-42.70	-57.09	-30.58	234
SP (Post – Pre)	R	Caudate	29.56	-10.90	19.98	221
SP (Post – Pre)	L	Frontal Lobe, Sub Gyral	-30.52	27.82	-1.51	196
SP (Post – Pre)	L	Middle Temporal Gyrus	-47.39	-46.73	8.44	153
SP (Post – Pre)	R	Cerebellum	42.96	-40.59	-27.95	98
SP (Post – Pre)	R	Inferior Parietal Lobule	51.73	-51.42	39.22	97
SP (Post – Pre)	R	Occipito-Temporal Junction, leading to Parahippocampus	24.41	-57.67	-21.02	94
SP (Post – Pre)	L	Middle Frontal Gyrus	-41.71	28.34	30.62	85
SP (Post – Pre)	L	Postcentral Gyrus	-46.13	-28.79	36.96	70
SP (Post – Pre)	R	Cerebellum	28.00	-41.10	-26.19	69
SP (Post – Pre)	L	Postcentral Gyrus	-22.62	-26.90	45.41	68
SP (Post – Pre)	R	Middle Temporal Gyrus	60.05	-47.95	-3.25	56
SP (Post – Pre)	L	Superior Temporal Gyrus	-43.79	-12.06	1.27	48
SP (Post – Pre)	R	Insula	42.28	-19.23	21.13	39
SP (Post – Pre)	L	Precentral Sulcus	-49.49	-9.49	42.49	39
SP (Post – Pre)	R	Frontal Lobe, Sub Lobar	26.28	22.97	1.90	39
SP (Post – Pre)		Interhemispheric	-0.68	31.16	31.49	37
SP (Post – Pre)	R	Postcentral Gyrus	42.31	-28.69	45.19	36

SP (Post – Pre)	L	Postcentral Gyrus	-21.69	-40.69	44.36	36
SP (Post – Pre)	L	Middle Occipital Gyrus	-45.50	-77.56	9.47	34
SP (Post – Pre)	R	Lingual Gyrus	2.84	-71.36	-17.96	25
SP (Post – Pre)	R	Precuneus	20.44	-52.08	41.88	25
SP (Post – Pre)	R	Caudate	15.45	11.05	4.35	20
SP (Post – Pre)	R	Internal Capsule	27.55	18.60	10.10	20
SP (Post – Pre)		Corpus Callosum	6.00	6.83	24.39	18
SP (Post – Pre)		Brainstem	-3.29	-9.71	-31.41	17
SP (Post – Pre)	R	Frontal Lobe, Sub Gyral	26.24	41.35	9.71	17
SP (Post – Pre)	L	Cingulate Gyrus	-15.38	-17.94	40.94	16
SP (Post – Pre)	L	Precentral Gyrus	-54.81	-7.38	30.00	16
SP (Post – Pre)	R	Occipito-Temporal Junction, leading to Parahippocampus	15.50	-61.33	-17.00	6
SP (Post – Pre)	R	Inferior Temporal Gyrus	48.20	-28.00	-14.20	5
SP (Post – Pre)	R	Lingual Gyrus	11.67	-72.67	-14.00	3
EE	R	Middle Occipital Gyrus	26.19	-81.49	5.47	925
EE	L	Precentral Sulcus	-35.18	-14.25	52.07	346
EE	L	Caudate	-15.24	9.74	1.46	200
EE	R	Cuneus	10.67	-82.23	14.05	120
EE	L	Inferior Frontal Gyrus	-42.47	-1.45	32.97	117
EE	R	Inferior Occipital Gyrus	33.77	-85.83	-1.66	96
EE	R	Precuneus	23.33	-67.42	23.80	84
EE	L	Medial Frontal Gyrus	-12.92	1.73	54.99	79
EE	L	Thalamus	-13.74	-24.52	13.88	66
EE	L	Insula	-24.74	12.48	18.33	54
EE	L	Cerebellar Tentorium	-36.21	-63.87	-10.43	53
EE	L	Paracentral Lobule	-10.53	-41.80	54.90	49
EE	R	Superior Frontal Gyrus	3.24	18.53	54.55	38
EE	R	Middle Frontal Gyrus	24.29	2.35	57.62	34
EE	L	Caudate	-20.35	5.78	10.17	23
EE	L	Middle Frontal Gyrus	-32.09	-19.64	60.73	22
EE	L	Inferior Frontal Gyrus	-50.40	4.55	33.70	20
EE	R	Medial Frontal Gyrus	1.93	-7.29	55.00	14
EE	L	Occipitotemporal Gyrus	-39.21	-49.14	-10.36	14
EE	L	Cerebellum	-27.38	-55.23	-26.23	13
EE	L	Postcentral Gyrus	-21.00	-48.85	64.08	13
EE	L	Parahippocampus	-24.20	-44.20	-11.00	5

References

Aguirre, GK., Detre, JA., Alsop, DC., & D'Esposito, M. (1996). The Parahippocampus Subserved Topographical Learning in Man. *Cerebral Cortex, 6*(6), 823-829.

Amedi, A., Hofstetter, S., Maidenbaum, S., & Heimler, B. (2017). Task Selectivity as a Comprehensive Principle for Brain Organisation. *Trends in cognitive Science, 21,* 307-310.

Amedi, A., Lofti, B., Merabet, LB., Bermpohl, F., & Pascual-Leone, A. (2005). The Occipital Cortex in the Blind: Lessons About Plasticity and Vision. *Current Directions in Psychological Science, 14*(6), 306-311.

Amedi, A., Stern, W., Camprodon, J., Bermpohl, F., Merabet, L., Rotman, S., Hemond, C., Meijer, P., & Pascual-Leone, A. (2007). Shape Conveyed by Visual-to-Auditory Sensory Substitution Activates the Lateral Occipital Complex. *Nature Neuroscience, 10*, 687–689.

Arnott, SR., Thaler, L., Milne, JL., Kish, D, & Goodale, MA. (2013). Shape-Specific Activation of Occipital Cortex in an Early Blind Echolocation Expert. *Neuropsychologia, 51,* 938-949.

Boccia, M., Nemmi, F., & Guariglia, C. (2014). Neuropsychology of Environmental Navigation in Humans: Review and Meta-Analysis of fMRI Studies in Healthy Participants. *Neuropsychology Review, 24*(2), 236-251.

Brainard, DH. (1997). The Psychophysics Toolbox. *Spatial Vision, 10,* 433-436.

Campus, C., Sandini, G., Concetta Morrone, M., & Gori, M. (2017). Spatial Localization of Sound Elicits Early Responses from Occipital Visual Cortex in Humans. *Scientific Reports, 7,* 1-12.

Cecchetti, L., Kupers,R., Ptito, M., Pietrini, P., Ricciardi, E. (2016). Are Supramodality and Cross-Modal Plasticity the Tin and Yang of Brain Development? From Blindness to Rehabilitation. *Frontiers in Systems Neuroscience, 10*(89), 1-8.

Collignon, O., Vandewalle, G., Voss, P., Albouy, G., Charbonneau, G., Lassonde, M., & Lepore, F. (2011). Functional Specialization for Auditory-Spatial Processing in the Occipital Cortex of Congenitally Blind Humans. *PNAS, 108*(11), 4435-4440.

Draganski, B., & May, A. (2008). Training-Induced Structural Changes in the Adult Human Brain. *Behavioural Brain Research, 192*, 137-142.

Ekkel, MR., van Lier, R., & Steenbergen, B. (2017). Learning to Echolocate in Sighted People: A Correlational Study on Attention, Working Memory and Spatial Abilities. *Experimental Brain Research, 235*(3), 809-818.

Fiehler, K., Schütz, Meller, T., & Thaler, L. (2015). Neural Correlates of Human Echolocation of Path Direction During Walking. *Multisensory Research, 28,* 195-226.

Finney, EM., Fine, I., & Dobkins, KR. (2001). Visual Stimuli Activate Auditory Cortex in the Deaf. *Nature Neuroscience, 4,* 1171-1173.

Forman, SD., Cohen, JD., Fitzgerald, M., Eddy, WF., Mintun, MA., & Noll, DC. (1995). Improved Assessment of Significant Activation in Functional Magnetic Resonance Imaging (fMRI): Use of a Cluster-Size Threshold. *Magnetic Resonance in Medicine, 33*(5), 636-647.

Frost, MA., & Goebel, R. (2012). Measuring Structural-Functional Correspondence: Spatial Variability of Specialised Brain Regions after Macro-Anatomical Alignment. *Neuroimage, 59*(2), 1369-1381.

Goebel, R., Espodito, R., & Formisano, E. (2006). Analysis of Functional Image Analysis Contest (FIAC) Data with Brain Voyager QX: From Single-Subject to Cortically Aligned Group General Linear Model Analysis and Self-Organizing Group Independent Component Analysis. *Human Brain Mapping, 27,* 392-401.

Griffin, DR. (1944). Echolocation by Blind Men, Bats and Radar. *Science 100*(2609), 589-590.

Hall, DA., Haggard, MP., Akeroyd, MA., Palmer, AR., Summerfield, AQ., Elliott, MR., Gurney, EM., & Bowtell, RW. (1999). “Sparse” Temporal Sampling in Auditory fMRI. *Human Brain Mapping, 7,* 213-223.

Hausfeld, S., Power, RP., Gorta, A., & Harris, P. (1982). Echo Perception of Shape and Texture by Sighted Subjects. *Perceptual and Motor Skills, 55*(2), 623-632.

Herholz, SC., & Zatorre, RJ. (2012). Musical Training as a Framework for Brain Plasticity: Behaviour, Function, and Structure. *Neuron, 76*(3), 486-502.

Hildreth, EC., Beusmans, JMH., Boer, ER., Royden, CS. (2000). From Vision to Action: Experiments and Models of Steering Control During Driving. *Journal of Experimental Psychology: Human Perception and Performance, 26*(3), 1106-1132.

Jäncke, L.,Shah, NJ., Posse, S., Grosse-Ryuken, M., & Müller-Gärtner, HW. (1998). Intensity Coding of Auditory Stimuli: an fMRI Study. *Neuropsychologia, 36*(9), 875-883.

Jones, G. (2005). Echolocation. *Current Biology, 13*(15), 484-488.

Kolarik, AJ,. Cirstea, S., Pardhan, S., & Moore, BCJ. (2014). A Summary of Research Investigating Echolocation Abilities of Blind and Sighted Humans. *Hearing Research, 310,* 60-68.

Kupers, R., Beaulieu-Lefebvre, M., Schneider, FC., Kassuba, T., Paulson, OB., Siebner, HR., Ptito, M. (2011). Neural Correlates of Olfactory Processing in Congenital Blindness. *Neuropsychologia, 49*(7), 2037-2044.

Kupers, R., Chebat, DR., Madsen, KH., Paulson, OB., & Ptito, M. (2010). Neural Correlates of Virtual Route Recognition in Congenital Blindness. *PNAS, 107*(28), 12716-12721.

Kupers, R., & Ptito, M. (2014). Compensatory Plasticity and Cross-Modal Reorganization Following Early Visual Deprivation. *Neuroscience & Biobehavioural Reviews, 41,* 36-52.

Lane, C., Kanjilla, S., Omaki, A., & Bedny, M. (2015). “Visual” Cortex of Congenitally Blind Adults Responds to Syntactic Movement. *The Journal of Neuroscience, 35*(37), 12859-12868.

Lasota, K., Ulmer, J., Firszt, J., Biswal, B., Daniels, D., & Prost, R. (2003). Intensity-Dependent Activation of the Primary Auditory Cortex in Functional Magnetic Resonance Imaging. *Journal of Computer Assisted Tomography, 27*(2), 213-218.

Levy-Tzedek, S., Maidenbaum, S., Amedi, A., & Lackner, J. (2016). Aging and Sensory Substitution in a Virtual Navigation Task. *PLoS ONE, 11*(3), 1-17.

Lomber, S., Meredith, M., & Kral, A. (2010) Cross-modal Plasticity in Specific Auditory Cortices Underlies Visual Compensation in the Deaf. *Nature Neuroscience, 13,* 1421-1427.

Maidenbaum, S., Abboud, S., & Amedi, A. (2014). Sensory Substitution: Closing the Gap Between Basic Research and Widespread Practical Visual Rehabilitation. *Neuroscience and Biobehavioural Reviews, 41,* 3-15.

Merabet, LB., & Pascual-Leone, A. (2010). Neural Reorganisation Following Sensory Loss: The Opportunity of Change. *Nature Reviews Neurosciene, 11*(1), 44-52.

Milne, JL., Arnott, SR., Kish, D., Goodale, MA., & Thaler L. (2015). Parahippocampal Cortex is Involved in Material Processing via Echoes in Blind Echolocation Experts. *Vision Research, 109,* 139-148.

Murphy, MC., Nau, AC., Fisher, C., Kim, SG., Schuman, JS., & Chan, KC. (2016). Top-Down Influence on the Visual Cortex of the Blind During Sensory Substitution. *NeuroImage, 125,* 932-940.

Norman, LJ., & Thaler, L. (2018). Human Echolocation for Target Detection is More Accurate with Emissions Containing Higher Spectral Frequencies, and this is Explained by Echo Intensity. *i-Perception, 9*(3), 1-18.

Pascual-Leone, A., Amedi, A., Fregni, F., & Merabet, L. (2005). The Plastic Human Brain Cortex. *Annual Review of Neuroscience*, *28,* 377-401.

Perrachione, TK., & Ghosh SS. (2013). Optimized Design and Analysis of Sparse-Sampling fMRI Experiments. *Frontiers in Neuroscience, 7*(55), 1-18.

Power, JD., & Schlaggar, BL. (2016). Neural Plasticity Across the Lifespan. *WIREs Developmental Biology 6*(1), 1-9.

Renier, LA., Anurova, I., De Volder AG., Carlson, S., VanMeter, J., & Rauschecker, JP. (2010). Preserved Functional Specialization for Spatial Processing in the Middle Occipital Gyrus of the Early Blind. *Neuron, 68*(1), 138-148.

Schenkman, BN., & Nilsson, ME. (2010). Human Echolocation: Blind and Sighted Persons' Ability to Detect Sounds Recorded in the Presence of a Reflecting Object. *Perception, 39,* 483-501.

Spriggs, MJ., Kirk, IJ., & Skelton, RW. (2018). Hex Maze: A New Virtual Maze Able to Track Acquisition and Usage of Three Navigation Strategies. *Behavioural Brain Research, 339,* 195-206.

Striem-Amit, E., Cohen, L., Dehaene, S., & Amedi, A. (2012). Reading with Sounds: Sensory Substitution Selectively Activates the Visual Word Form Area in the Blind. *Neuron, 76,* 640-652.

Talairach, J., & Tournoux, P. (1988). *Co-planar stereotaxic atlas of the human brain.* New York: Thieme.

Teng, S., Puri, A., & Whitney, D. (2012). Ultrafine Spatial Acuity of Blind Expert Human Echolocators. *Experimental Brain Research, 216*(4), 483-488.

Thaler, L., Arnott, SR., & Goodale, MA. (2011). Neural Correlates of Natural Human Echolocation in Early and Late Blind Echolocation Experts. *PLoS ONE, 6*(5), 1-16.

Thaler, L., & Goodale, MA. (2016). Echolocation in Humans: An Overview. *WIREs Cognitive Science, 7*(6), 382-393.

Thorndyke, PW., & Hayes-Roth, B. (1982). Differences in Spatial Knowledge Acquired from Maps and Navigation. *Cognitive Psychology, 14*(4), 560-589.

Tonelli, A., Brayda, L., & Gori, M. (2016). Depth Echolocation Learnt by Novice Sighted People. *PLoS ONE, 11*(6), 1-14.

Van Essen, DC., & Dury, HA. (1997). Structural and Functional Analyses of Human Cerebral Cortex Using a Surface-Based Atlas. *Journal of Neuroscience, 11*(6), 1123-1130.

Wallmeier, L., Kish, D., Wiegrebe, L., Flanagin, L. (2015). Aural Localization of Silent Objects by Active Human Biosonar: Neural Representations of Virtual Echo-Acoustic Space. *European Journal of Neuroscience, 41,* 533-545.

Weeks, R., Horwitz, B., Aziz-Sultan, A., Tian, B., Wessinger, CM., Cohen, LG., Hallett, M., Rauschecker, JP. (2000). A Positron Emission Tomographic Study of Auditory Localization in the Congenitally Blind. *The Journal of Neuroscience, 20*(7), 2664-2672.

Weniger, G., Siemerkus, J., Schmidt-Samoa, C., Mehlitz, M., Baudewig, J., Dechent, P., & Irle, E. (2010). The Human Parahippocampal Cortex Subserves Egocentric Spatial Learning During Navigation in a Virtual Maze. *Neurobiology of Learning and Memory, 93*(1), 46-55.