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The occipital place area is recruited for echo-acoustically guided navigation in blind human echolocators

Abbreviated title: Occipital place area and echo-acoustic navigation

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1

23 **Abstract**

24 In the investigation of the brain areas involved in human spatial navigation, the traditional

25 focus has been on visually guided navigation in sighted people. Consequently, it is unclear

26 whether involved areas also support navigational abilities in other modalities. We explored

27 this possibility by testing whether the occipital place area (OPA) – a region associated with

28 visual boundary-based navigation in sighted people – has a similar role in echo-acoustically

29 guided navigation in blind human echolocators. We used fMRI to measure brain activity in

30 six blind echolocation experts (EEs; 5 males, 1 female), twelve blind controls (BCs; 6 males, 6

31 females), and fourteen sighted controls (SCs; 8 males, 6 females) as they listened to pre-

32 recorded echolocation sounds that conveyed either a route taken through one of three maze

33 environments, a scrambled (i.e. spatiotemporally incoherent) control sound, or a no-echo

34 control sound. We found significantly greater activity in the OPA of EEs, but not the control

35 groups, when they listened to the coherent route sounds relative to the scrambled sounds.

36 This provides evidence that the OPA of the human navigation brain network is not strictly tied

37 to the visual modality but can be recruited for non-visual navigation. We also found that EEs,

38 but not BCs or SCs, recruited early visual cortex for processing of echo-acoustic information.

39 This is consistent with the recent notion that the human brain is organised flexibly by task

40 rather than by specific modalities.

41 Keywords: audition, fMRI, route recognition

42

43 Significance statement

44   There has been much research on the brain areas involved in visually guided navigation, but

45   we do not know whether the same or different brain regions are involved when blind people

46   use a sense other than vision to navigate. In this study, we show that one part of the brain

47   (occipital place area) known to play a specific role in visually guided navigation is also active

48   in blind human echolocators when they use reflected sound to navigate their environment.

49   This finding opens up new ways of understanding how people navigate, and informs our

50   ability to provide rehabilitative support to people with vision loss.

51   <u>Introduction</u>

52   Human spatial navigation involves a network of brain areas, reflecting the different

53   components involved in navigation (Ekstrom *et al*, 2017; Kong *et al,* 2017; Boccia *et al*, 2014).

54   What is unclear, however, is whether these areas serve a role that is specific to whichever

55   modality is most dominantly used for navigation (typically vision in humans), or whether they

56   serve a more general role that could accommodate another modality entirely. Indeed, there

57   is an increasing amount of evidence to suggest that the human brain is organised flexibly by

58   task rather than by sensory modality (Amedi *et al*, 2017) – that is, a given brain area can

59   serve the same function across different input modalities.

60   Visual perception has been at the forefront of navigation research in humans due to the

61   uniquely salient role of visual information (Ekstrom *et al*, 2017; Chan *et al*, 2012; Ekstrom

62   2015). That is not to say, however, that non-visual information could also be used. For

63   example, people who are blind are also capable of excellent spatial navigation (Thinus-Blanc

64   & Gaunet, 1997; Loomis *et al*, 2001).   Rather, it is poorly understood whether such non-

65   visual navigational abilities involve the same brain processes as visual-based navigation

66   (Fiehler *et al*, 2015; Kupers *et al*, 2010; Maidenbaum, Chebat & Amedi, 2018).

67 In order to address this, we must identify whether brain areas with specific roles in visual-

68 based navigation have equivalent roles during non-visual navigation. One brain region in

69 particular – the occipital place area (OPA) – is known to provide the perceptual source of

70 environmental boundary information that guides navigation through that environment

71 (Kamps *et al*, 2016; Julian *et al*, 2016). Furthermore, because the OPA it is located near the

72 transverse occipital sulcus, it is assumed that this perceptual representation emerges from

73 visual input. Human echolocation offers a well-suited model in which to test whether the

74 OPA has a similar navigational role in a non-visual modality. Echolocation is the ability to

75 perceive objects and space through sound echoes (Griffin, 1944) and offers the ability to

76 perceive the proximal and distal environment. Some people who are blind use click-based

77 echolocation (i.e. echolocation using mouth-clicks) to perceive an object's position in space

78 as well as its shape, material, and whether it is in motion (for reviews see Kolarik, et al, 2014;

79 Thaler & Goodale, 2016). Furthermore, using echolocation for these purposes is associated

80 with neural activity in areas that are typically associated with perceiving those same

81 properties through vision (Norman & Thaler, 2019; Thaler *et al*, 2011; Arnott *et al*, 2013;

82 Milne *et al*, 2015; Thaler *et al*, 2014).

83

84 We used fMRI to measure brain activity in 6 blind echolocation experts (EEs), 12 blind

85 controls (BCs), and 14 sighted controls (SCs) as they listened to pre-recorded binaural

86 echolocation sounds (i.e. echo-acoustic sound through a first-person perspective) and made

87 perceptual judgments about them. The critical contrast in our analysis was to compare brain

88 activity during coherent route sounds to activity during scrambled (i.e. spatiotemporally

89 incoherent) sounds. This design is an echo-acoustic analogue of one used previously to

90 identify OPA activity during visually guided navigation (Kamps *et al*, 2016).

91 We used a region of interest (ROI) analysis approach, focussing on the OPA in addition to the

92 parahippocampal place area (PHPA) because of its role in the neural representation of places

93 and scenes (Epstein *et al*, 1999), and the superior parietal lobule (SPL) because of its

94 previously identified activation in some non-visual navigation tasks (Kupers *et al*, 2010;

95 Fiehler *et al*, 2015). We also included ROIs for primary visual and auditory areas (V1 and A1,

96 respectively) to analyse activity in low-level sensory processing areas, and also because there

97 is some evidence that V1 is active during non-visual navigation (Maidenbaum *et al*, 2018).   In

98 addition to the ROI analysis, we also ran a whole-brain analysis.

99 Part of the data (behavioural performance outside the scanner for SCs and three EEs) has

100 been reported previously (Dodsworth *et al*, 2020).

101

102 **Materials and Methods**

103 Ethics

104 All Procedures followed the British Psychological Society code of practice and the World

105 Medical Association's Declaration of Helsinki. The experiment had received ethical approval

106 by the Ethics Advisory Sub-Committee in the Department of Psychology at Durham University

107 (Ref 14/13). All participants gave written informed consent to take part in this study.

108 Participants who were sighted and participants who were blind received £6/hr and £10/hr,

109 respectively, to compensate them for their effort and time taking part.

110

111 Participants

112   All participants were recruited through word of mouth and opportunity sampling. Six blind

113   expert echolocators (EEs; 5 males, 1 female) took part (details given in Table 1). Our

114   requirements for classing an individual as an echolocation expert were that they reported

115   using click-based echolocation on a daily basis for more than 10 years. In our sample, five out

116   of the six EEs (EEs) had cause of vision loss present from birth and were diagnosed as legally

117   blind from birth/within the first year of life. The remaining EE (EE4) received an official

118   diagnosis age 12 due to sudden vision loss. Thus, the majority of our echolocation expert

119   participants are classified as early blind.

120

121   <Table 1>

122

123   Twelve blind participants (BCs; 6 males, 6 females) with no prior experience in click-based

124   echolocation took part (details shown in Table 1). In our sample, all BCs had cause of vision

125   loss present from birth. All were diagnosed as legally blind in childhood, with only two official

126   diagnoses at an age that might have coincided with onset of puberty, or may have been after

127   onset of puberty (i.e. 13 yrs and 10 yrs; BC9 and BC2), but again with vision impairment

128   having been present from birth. Thus, the majority of our participants were classified as early

129   blind. All our blind participants were independent travellers, and all had received mobility

130   and orientation training as part of visual impairment (VI) habilitation and VI rehabilitation

131   that is provided to people with VI in the UK. Fourteen sighted participants (SCs; 8 males, 6

132   females) took part (ages: 21, 21, 22, 22, 23, 24, 25, 27, 32, 35, 38, 48, 60, and 71; mean =

133   33.5, SD = 15.8, median = 26). All reported to have normal or corrected to normal vision and

134   no prior echolocation experience (based on self-report).

135

136   All participants had normal hearing appropriate for their age group (ISO 7029:2017) as

137   assessed using pure tone audiometry, with the exception of one blind participant (BC6, aged

138   72 yrs) who wore hearing aids to compensate for age related hearing loss. For purposes of

139   testing, the participant with hearing aids did not wear their aids during any of the

140   experimental testing sessions, as they would not be able to wear these in the MRI scanner.

141   For our statistical analyses that involve comparisons to the BC group, we report the results of

142   those analyses both with and without BC6 included. All participants who had any residual

143   vision were tested under blindfold.

144

145   Experimental design and statistics

146   The design contained a between-subject variable (subject group) and within-subject variable

147   (sound stimulus). Full details of the statistical analyses of the behavioural, ROI, and whole-

148   brain data are given in the relevant sections below. To summarise briefly, behavioural and

149   ROI data was analysed using ANOVAs and Kruskal-Wallis tests and, where appropriate, one-

150   sample t tests and Wilcoxon signed-rank tests. The issue of multiple comparisons was

151   addressed using either Bonferonni correction or the Benjamini-Hochberg method. Whole-

152   brain fMRI data was analysed using ANOVAs and one-sample t tests, with cluster-based

153   thresholding and Gaussian random field correction (Worsley, 2001).

154

155   Echolocation stimuli

156   The stimuli were created from a large set of recordings first described by Dodsworth, Norman

157   & Thaler (2020). For full details of those stimuli, please refer to that report. Briefly, binaural

158 recordings of clicks and click-echoes were made with an anthropometric manikin in physical

159 spaces comprising corridors in specific spatial arrangements (T-mazes, U-mazes, Z-mazes).

160 Details of the manikin have been reported in (Norman & Thaler, 2018). In addition, we also

161 created spatially mirrored versions of these recordings by flipping the left and right channels,

162 giving six maze layouts in total.

163

164 For each of the six mazes, we created two samples by selecting recordings corresponding to a

165 specific sequence of locations and orientations within that maze (see figure 1). This gave a

166 total of 12 sound files that were each 10.53 s in length and contained 18 clicks and echoes,

167 each separated by 600 ms (a rate of 1.71 clicks/s). These 12 sound files were assigned to one

168 of three categories: (1) single-turn route, (2), two-turn route in same direction, (3), two-turn

169 route in different (opposite) directions.

170

171 In addition to these spatially coherent route sounds, we created two types of control sounds:

172 scrambled route sounds and clicks with no echoes. A scrambled route sound was created for

173 each of the original route sounds in order to create sounds that had exactly the same low-

174 level acoustic information (i.e. timing, clicks and echoes), but did not convey spatially

175 coherent information. To do this, the individual click-echo sounds in each route sound file

176 were randomly shuffled and pieced together (maintaining the same click rate) so that there

177 was no coherent route. In order to create a secondary set of control stimuli (i.e. stimuli with

178 clicks but not containing any echoes), a sound recording was used during which the manikin

179 had been placed facing the foam padded wall in the anechoic chamber. The sound was then

180 repeated at the same temporal sequence as that for the 'route' and 'scrambled' sound files.

181

182   <Figure 1>

183

184   In total, five types of sound stimuli were created: single-turn route, two-turns-same route,

185   two-turns-different route, scrambled route, and click only. Example .wav files for each of

186   these stimuli can be found on Open Science Framework: https://osf.io/c5pn2/, but note that

187   playback of these example sounds should be done using a high-spec sound card and

188   headphones, due to the nature of the echolocation sounds.

189

190   Stimuli containing echoes ('route' and 'scrambled' stimuli) were of higher root mean square

191   (RMS) intensity than stimuli not containing echoes ('no echo').   Specifically, T and T-

192   scrambled sounds: −41.4 dB; U and U scrambled sounds: −41.4 dB; Z and Z-scrambled

193   sounds: −40.8 dB; No echo sounds: −44.2 dB). In terms of absolute intensity at which sounds

194   were played, each participant selected a sound intensity that felt comfortable for them to do

195   the task. The same intensity was maintained for that participant throughout testing.

196   Recorded sound files were filtered to achieve frequency response equalisation for playback

197   through the MRI-compatible insert earphones (Model S-14, Sensimetrics, Malden, MA; filters

198   provided by the manufacturer).

199

200   Behavioural paradigm before fMRI scanning

201   On a separate day before fMRI scanning, participants completed two runs of 30 trials. On

202   each trial they heard one of the sound stimuli from one of the five categories (single-turn

203   route, two-turns-same route, two-turns-different route, scrambled, and no echo), with each

204   condition being repeated six times. The order of trials was randomly determined at the start

205   of each run. When the sound finished playing, participants gave a verbal response to indicate

206   which category the sound belonged to.   The experimenter recorded this response and

207   started the next trial. Before participants performed the two runs of 30 trials, they were

208   played two examples for each type of sound to make them familiar with the sounds and the

209   required responses.

210

211   <u>Setup and apparatus before fMRI scanning</u>

212   Participants completed the task in a sound-insulated and echo-acoustic dampened room

213   (approx. 2.9 m × 4.2 m x 4.9 m) lined with foam wedges (cut-off frequency 315 Hz) in the

214   Department of Psychology at Durham University.   Sounds were played through MRI-

215   compatible insert earphones (Model S-14, Sensimetrics, Malden, MA; filters provided by the

216   manufacturer) encased in disposable foam tips (the earphones provided a 20 to 40-dB

217   attenuation level information). These earphones were amplified by a Kramer 900N Stereo

218   Power Amplifier (Kramer Electronics Ltd., Jerusalem, Israel), with input provided by a USB

219   Soundcard (Creative Sound Blaster X-Fi HD Sound Card; Creative Technology Ltd., Creative

220   Labs Ireland, Dublin, Ireland).   The experimenter used a laptop (Dell Latitude E7470; Intel

221   Core i56300U CPU 2.40; 8GB RAM; 64-bit Windows 7 Enterprise) running MATLAB R2018b

222   (The Mathworks, Natick, MA) and modified functions from the Psychtoolbox library (Brainard,

223   1997) to control sound playback and to record participants' responses.

224

225   <u>Behavioural paradigm during fMRI scanning</u>

226   Participants' task inside the scanner was the same as that outside the scanner, with some

227   modifications. Participants gave their response after each stimulus presentation by pressing

228   one of five buttons on an MR compatible response unit (5-Button Fibre Optic Response

229   Button System, Psychology Software Tools, Inc, Pittsburgh, USA). Each finger was assigned a

230   different response (thumb = no echo, index = single-turn, middle = two-turns-same, ring =

231   two-turns-different, pinkie = scrambled). A beep (1.2 kHz, 50 ms) at the end of stimulus

232   presentation prompted participants to respond. In addition to the five stimulus categories, a

233   sixth "silence" category was also used (to allow comparisons to baseline activity in the fMRI

234   data analysis). During these silence trials, no sound was played to participants and no

235   response was required. The order of stimulus presentation was counterbalanced with respect

236   to the three main stimulus conditions (route, scrambled, and no echo). This was achieved by

237   breaking down 36 trials in each run into nine sequential groups of four. The first trial in each

238   group was always a silence trial, and the remaining three were a random order of route,

239   scrambled, and no echo. The order of these three trial types was counterbalanced such that

240   after every two runs, each type was presented equally often in each of the three sequence

241   positions. The same randomised order of sounds was used for all participants.

242

243   <u>Setup and apparatus during fMRI scanning</u>

244   All MR data were acquired at Durham University Centre for Imaging (James Cook University

245   Hospital, Middlesbrough, UK), with a 3-Tesla, whole-body MRI system (Magnetom Tim Trio;

246   Siemens, Erlangen, Germany) and 32-channel head coil. For sound presentation the same

247   equipment as that used before fMRI scanning was used to play sounds, with the exception

248   that a PC (Intel Core i7-6700 CPU 3.40; 8GB RAM; 64-bit Windows 7 Enterprise) was used

249   instead of a laptop. Further, participants gave their response using an MRI-compatible 5-

250   button fibre-optic button response unit (Psychology Software Tools, Inc., Pittsburgh, USA)

251   with their right hand. To minimize background noise, the MRI bore's circulatory air fan was

252   turned off during experimental runs. To minimise interference from light sources, all lights

253   inside the MRI room were turned off and participants who were not totally blind wore a

254   blindfold.

256   <u>fMRI scanning parameters</u>

257   High-resolution structural images for each participant were acquired using a T1-weighted,

258   optimised sequence (MP RAGE), at a resolution of 1 x 1 x 1 mm. Functional images were

259   acquired using a single-shot gradient echo-planar pulse sequence in combination with a

260   sparse sampling design (Hall *et al,* 1999), with a repetition time of 13 seconds (11 seconds of

261   inactivity for stimulus presentation, followed by 2 seconds of volume acquisition). Thus,

262   during stimulus presentation, no functional volumes were acquired. Instead, a single

263   functional volume was acquired in the 2-s period after the end of stimulus presentation. Field

264   of view was 192 mm with a matrix size of 64 x 64, giving an in-slice resolution of 3 mm. 38

265   contiguous axial slices were acquired in ascending order with a slice thickness of 3.5 mm,

266   covering the whole brain. Echo time was 30 ms and flip angle was 90°. For each run, a total

267   of 38 functional volumes were acquired, with each run lasting 8 minutes and 14 seconds.

268   The first and last volume in each run were acquired after silence. A total of six runs were

269   completed per participant, except for one participant (EE2) where only four runs were

270   completed.

272   <u>fMRI data processing</u>

273   FMRI data pre-processing and analysis was carried out using FEAT (FMRI Expert Analysis Tool)

274   Version 6.00, part of FSL (FMRIB's Software Library, www.fmrib.ox.ac.uk/fsl; Woolrich, Ripley,

275   Brady & Smith, 2001; Woolrich, Behrens, Beckmann, Jenkinson, & Smith, 2004).

277   Images were brain-extracted (using BET; Smith, 2002) and within-participant registration of

278   low-resolution functional images to high-resolution structural (T1) images was achieved using

279   FLIRT (6 d.f.; Jenkinson, Bannister, Brady, & Smith, 2002; Jenkinson & Smith, 2001). Further

280   non-linear registration to MNI152 standard space (voxel size of 2 mm) was achieved using

281   FNIRT (Andersson, Jenkinson & Smith, 2020) with a warp resolution of 2 mm. The very first

282   functional volume within each run was discarded, leaving 37 volumes to analyse, the first and

283   last of which were acquired after silence. The following pre-statistic processing was applied

284   to each run of functional data: slice-timing correction using Hanning-windowed sinc

285   interpolation, motion correction using MCFLIRT (Jenkinson *et al,* 2002), high-pass temporal

286   filtering (maximum allowed period = 100 s, or 0.01 Hz), and spatial smoothing (full-width at

287   half maximum Gaussian kernel of 5 mm).

288

289   <u>fMRI modelling and contrasts</u>

290   In the first-level analysis for each run, three explanatory variables (EVs) were modelled using

291   stick function regressors (with no haemodynamic response convolution, due to the sparse

292   sampling design): route stimulus, scrambled stimulus, and no-echo stimulus. The silence trials

293   were used as an implicit baseline. These EVs were then used to define the three contrasts of

294   interest: route vs. scrambled (EV weights: route = +1, scrambled = -1, no echo = 0), echo vs.

295   no echo (EV weights: route = +1, scrambled = +1, no echo = -2), and sound vs. silence (EV

296   weights: route = +1, scrambled =+1, no echo = +1).

297

298   In a second-level analysis stage, single-participant activations across all runs were calculated

299   using a fixed effects model, by forcing the random effects variance to zero in FLAME (FMRIB's

300   Local Analysis of Mixed Effects; Beckmann, Jenkinson & Smith, 2003, Woolrich, *et al* 2004,

301   Woolrich 2008). In a higher-level analysis stage, group-level activations were calculated using

302   a mixed effects model.

303

304   <u>ROI definition and analysis</u>

305   Five regions of interest (ROIs) were defined in standard MNI space (see table 2). Contrasts

306   analysed for each ROI were 1) route vs. scrambled, 2) echo vs. no-echo, and 3) sound vs.

307   silence. FSL's Featquery was used to extract percent signal change (PSC) associated with each

308   of the three contrasts for each ROI for each participant.

309

310   <Table 2>

311

312   <u>Whole Brain Analysis</u>

313   In addition to the ROI analysis, we also ran a series of whole-brain analyses. First, we ran a

314   between-subject ANOVA to identify brain areas in which there was a significant difference

315   between the three groups (i.e. testing whether EE = BC = SC) for each stimulus contrast.

316   Following this, we calculated averages for each group (i.e. one-sample t tests) for each

317   contrast (same as those used in the ROI analysis). Z statistic images (Gaussianised T/F) were

318   thresholded using cluster-based thresholding determined by Z>2.3 and a cluster significance

319   threshold of p=0.05 (corrected using Gaussian Random Field theory; Worsley 2001).

320

321   In order to objectively assign anatomical labels to activation clusters, the coordinates of the

322   peak activity within each cluster were extracted, along with the coordinates of the local

323   maxima within each cluster, and these was used to extract corresponding labels from the

324   Jülich Histological Cyto-Architectonic Atlas (Eickhoff *et al.*, 2007) and MNI structural atlas

325   (Collins *et al*, 1995; Mazziotta *et al*, 2001). Where the atlases returned probabilistic values of

326   at least 25% for a particular anatomical label, this label was then assigned to that cluster.

327

328   <u>Results</u>

329   <u>Behavioural</u>

330   For the data collected prior to MR scanning, we calculated the proportion of correct

331   responses for three different measures of performance: specific route identification, route

332   vs. scrambled identification, and echo identification. One-way ANOVAs (with subject group

333   as the between-subject variable) were used to test for group differences for each of these

334   measures in performance, reported below (in addition to non-parametric Kruskal-Wallis

335   tests). Behavioural performance during fMRI was also analysed in the same way, and the

336   pattern of results was consistent with what we observed prior to scanning. We found the in-

337   scanner measure to be more variable, however, due to participants pressing more than one

338   key accidentally or failing to respond on some trials.

339

340   Specific route identification

341   When considering specific route identification, a response was correct when participants

342   identified the specific route (single-turn; two-turns-same; two-turns-different) when it was

343   presented. Thus, specific route identification measures participants' ability to correctly

344   identify specific echo-acoustic routes. There was a significant group difference in route

345   identification ($F(2,29) = 26.159$, $p < .001$, $\eta^2 = 0.643$; Kruskal-Wallis: $H(2)=13.830$, $p<.001$).

346   EEs (mean = .806) were significantly more accurate than BCs (mean = .475; $p < .001$; and

347    $p<.001$ with BC6 excluded) and SCs (mean = .470; $p < .001$). BCs and SCs were not

348   significantly different to one another ($p = 1.000$). These data are shown in figure 2a.

349

350 Route vs. scrambled identification

351 When considering scrambled vs. route identification, a response was identified as correct

352 when participants gave a 'scrambled' response to a scrambled sound, but also when they

353 gave any of the route responses when any of the route sounds were presented (regardless of

354 whether it was a single turn, two-turn-same or two-turn-different). Thus, scrambled vs. route

355 identification measures participants' ability to distinguish spatially coherent echo-acoustic

356 sounds from spatially incoherent echo-acoustic sounds. There was a significant group

357 difference in this measure ($F(2,29) = 10.681$, $p < .001$, $\eta^2 = 0.424$; Kruskal-Wallis:

358 H(2)=13.719, p<.001). EEs (mean = .962) were significantly more accurate than BCs (mean =

359 .790; p = .001; and p=.002 with BC6 excluded) and SCs (mean = .784; p < .001). BCs and SCs

360 were not significantly different to one another (p = 1.000). These data are shown in figure

361 2b.

362

363

364 Echo vs. no-echo identification

365 When considering echo identification, a response was identified as correct when participants

366 responded with 'no echo' when stimuli containing no echoes were present, and also when

367 participants gave any other response when any of the other stimuli were presented (e.g. if a

368 'single turn' route was labelled as 'scrambled', then this would be classed as correct because

369 the sound contains echoes). Thus, echo identification measures participants' ability to

370 distinguish echo from non-echo sounds. There was no significant group difference in this

371 measure ($F(2,29) = 2.507$, $p = .099$; Kruskal-Wallis: H(2)=3.710, p=.156). This is likely because

372 all groups had very high accuracy (EEs mean = 1.000; BCs mean = .963; SCs mean = .986).

373 This high level of performance in detecting the presence of echoes even for naïve

374 echolocators is consistent with our previously published results (Norman & Thaler, 2020;

375 2021). These data are shown in figure 2c.

376

377 Overall, these results suggest that EEs as a group performed better than both BCs and SCs for

378 those measures where spatial interpretation of echo information was required (i.e. route vs.

379 scrambled and route identification), but not for simple echo detection. Also, BCs and SCs did

380 not perform different from one another on any measure, suggesting that experience with

381 echolocation rather than blindness drives performance in this task.

382

383 <Figure 2>

384

385

386 <u>fMRI – ROI analysis</u>

387 The group means for all contrasts are shown in figure 3 (the individual data for the six EEs are

388 shown in table 3). We tested for group differences in PSC for each ROI and for each contrast

389 using one-way ANOVAs (subject group as the between-subject variable) and non-parametric

390 Kruskall-Wallis tests. Each resulting p value was Bonferroni-corrected by multiplying it by 5

391 (the number of ROIs). Any results in which these corrected p values were less than .05 are

392 reported as significant (thus, the alpha level was effectively .0083). Post-hoc tests were also

393 Bonferroni-corrected by a factor of 3 (the number of multiple comparisons). One-sample t

394 tests and non-parametric Wilcoxon signed-rank tests were also used to test whether PSC in

395 each ROI was significantly different from zero. The issue of multiple comparisons was

396 addressed using the Benjamini-Hochberg method to control false discovery rate (FDR, set at

397 .05; Benjamini & Hochberg, 1995). This was chosen over the highly conservative Bonferroni

398 adjustment due to the large number of tests (15 for each contrast). Briefly, this method

399 involves ranking the observed p values in order of size and calculating a Benjamini-Hochberg

400 critical value for each one (based on the rank number and the FDR). Any p values that are

401 less than the critical value for their rank are considered to be statistically significant. Thus,

402 the p values reported for these tests are not adjusted *per se*, but results are only reported as

403 significant where the p values were less than the Benjamini-Hochberg critical value.

404

405

406 <Figure 3>

407 <Table 3>

408

409 Route vs. scrambled

410 For the route vs. scrambled contrast, a significant group difference was found in the OPA

411 $F(2,29) = 13.344$, $p < .001$, $\eta^2 = .479$; Kruskal-Wallis: $H(2)=12.370$, $p=.010$). The EE group

412 showed significantly greater PSC than the BC ($p = .001$; and $p=.002$ with BC6 excluded) and SC

413 ($p < 0.001$) groups. The BC and SC groups did not differ ($p = .732$; and $p=.657$ with BC6

414 excluded). None of the other ROIs showed a significant difference between groups (A1:

415 $F(2,29) = .266$, $p = 1.000$; Kruskal-Wallis: $H(2)=.401$, $p=1.000$; V1: $F(2,29) = .563$, $p = 1.000$;

416 Kruskal-Wallis: $H(2)=1.167$, $p=1.000$; PHPA: $F(2,29) = .636$, $p = 1.000$; Kruskal-Wallis:

417 $H(2)=1.289$, $p=1.000$; SPL: $F(2,29) = 1.405$, $p=1.000$; Kruskal-Wallis: $H(2)=1.791$, $p=1.000$).

418

419 PSC in the OPA was significantly greater than zero for the EE group (t(5) = 5.591, p = .003;

420 Wilcoxon signed rank: z= 2.201, p=.028). No other tests showed a significant difference from

421 zero.

422

423 Our SCs were, on average, younger than our EEs. To test the possibility that age might be a

424 determining factor in the strength of response in the OPA, we correlated age with the route

425 vs. scrambled response in the OPA in our SC groups and found no significant association

426 (r(12)=.316, p=.272).

427

428

429 Echo vs. no-echo

430 A significant group difference was found in V1 (F(2,29) = 14.837, p < .001, η^2 = .506; Kruskal-

431 Wallis: H(2)=13.479, p=.006). The EE group showed significantly greater PSC than the BC (p <

432 .001; and p = .001 with BC6 excluded) and SC (p < .001) groups. The BC and SC groups did

433 not differ (p = .824). A significant group difference was also found in the OPA F(2,29) =

434 14.979, p < .001, η^2 = .508; Kruskal-Wallis: H(2)=14.779, p=.003). The EE group showed

435 significantly greater PSC than the BC (p = .005; and p = .005 with BC6 excluded) and SC (p <

436 .001) groups. The BC and SC groups did not differ (p = 0.072). None of the other ROIs

437 showed a significant group effect (A1: F(2,29) = 2.443, p = .523; Kruskal-Wallis: H(2)=5.643,

438 p=.298; PHPA: F(2,29) = 4.818, p = .078; Kruskal-Wallis: H(2)=11.388, p=.017; SPL: F(2,29) =

439 1.618, p = 1.000; Kruskal-Wallis: H(2)=3.632, p=.814).

440

441 PSC in V1 was significantly greater than zero for the EE group (t(5) = 4.628, p = .006; Wilcoxon

442 signed rank: z= 2.201, p=.028). PSC in A1 was significantly greater than zero for the SC group

443 (t(13) = 5.641, p < .001; Wilcoxon signed rank: z= 3.233, p=.001). PSC in PHPA was

444 significantly lower than zero for the SC group (t(13) = 5.282, p < .001; Wilcoxon signed rank:

445 z= 2.982, p=.003). No other tests showed a significant difference from zero.

446

447 Sound vs. silence

448 A significant group difference was found in V1 (F(2,29) = 5.872, p = .036, η^2 = .288; but note

449 Kruskal-Wallis was not significant: H(2)=8.228, p=.082). The EE group showed significantly

450 greater PSC than the SC group (p = .006) but not the BC group (p = .050; and p = .086 with

451 BC6 excluded). The BC and SC groups did not differ (p = .180). A significant group difference

452 was also found in the OPA F(2,29) = 9.965, p = .003, η^2 = .407; Kruskal-Wallis: H(2)=11.366,

453 p=.017). The EE group showed significantly greater PSC than the SC group (p < .001) but not

454 the BC group (p = .069; but p=.018 with BC6 excluded). The BC and SC groups did not differ

455 (p = .071). None of the other ROIs showed a significant group effect (A1: F(2,29) = 2.337, p =

456 .573; Kruskal-Wallis: H(2)=5.030, p=.404; PHPA: F(2,29) = 1.224, p = 1.000; Kruskal-Wallis:

457 H(2)=3.331, p=.945; SPL: F(2,29) = .801, p=1.000; Kruskal-Wallis: H(2)=1.152, p=1.000).

458

459 PSC in A1 was significantly greater than zero for the SC group (t(13) = 9.313, p < .001;

460 Wilcoxon signed rank: z= 3.296, p<.001), BC group (t(11) = 3.174, p = .009; Wilcoxon signed

461 rank: z= 2.197, p=.028), and EE group (t(5) = 4.626, p = .006; Wilcoxon signed rank: z= 2.201,

462 p=.028). PSC in V1 was significantly greater than zero for the EE group (t(5) = 4.394, p = .007;

463 Wilcoxon signed rank: z= 2.201, p=.028). PSC in PHPA was significantly lower than zero for

464 the SC group (t(13) = 3.631, p = .003; Wilcoxon signed rank: z= 2.794, p=.005). PSC in the

465 OPA was significantly greater than zero for the EE group (t(5) = 3.495, p = .017; Wilcoxon

466 signed rank: z= 2.201, p=.028). No other tests showed a significant difference from zero.

467

468   Additional ROI analyses: OPA activity and echolocation ability

469   It is possible that the activity observed in the OPA is only driven by high performance on the

470   route vs. scrambled identification task, regardless of participants being EEs, BCs or SCs. In our

471   study, BC and SC groups were, expectedly, less accurate on this task than the EE group. Thus,

472   to address the possibility that OPA activity in EEs is due to their more accurate task

473   performance, we ran two further analyses. First, we reran the route vs. scrambled contrast

474   analysis only using trials in which participants had classified correctly. To avoid differences in

475   statistical power between EEs and controls, we subsampled data from EEs to match number

476   of trials across groups. Analysing PSC in the OPA using only correct trials showed the same

477   pattern of results as we found when using all trials (EEs mean =.26, BCs mean = .10, SCs mean

478   = -.02) and there was a significant difference between groups (F(2,29)=9.562, p=.003,

479   η^2=.397; Kruskal-Wallis: H(2)=12.948, p=.008), with EEs showing a significantly greater

480   response compared to SCs (p<.001) but not BCs (p=.067). BCs and SCs were not significantly

481   different to one another (p=.090). Applying the Benjamini-Hochberg method, only the EE

482   group showed a response in the OPA significantly greater than zero (t(5)=5.604, p=.003;

483   Wilcoxon signed rank: z= 2.201, p=.028). Secondly, to further investigate possible

484   associations between behavioural performance and OPA response (for the route vs.

485   scrambled contrast), we ran a correlation analysis which revealed for EEs a borderline

486   significant correlation between behavioural performance and PSC in the OPA (r(4)=.808,

487   p=.052), but no correlation for BCs (r(10)=.361, p=.249) or SCs (r(12)=-.001, p=.998). Figure 4

488   shows the scatter plot of these data. These results suggest that responses in the OPA are not

489   driven solely by the ability to identify route vs. scrambled sounds, but is likely the result of

490   both long-term echolocation experience and task-specific echolocation ability.

491

492 <Figure 4>

493

494

495

496 Additional ROI analyses: functionally localised OPA ROI

497 In the sighted brain, the location of the OPA is typically defined using a functional localiser

498 with the contrast of static visual scenes > static visual objects (e.g. Sun et al, 2021; Kamps *et*

499 *al*, 2016; Dilks *et al,* 2013). In our study, this region was defined as a single sphere centred on

500 the average MNI coordinates from an independent study that used the functional localiser in

501 17 sighted subjects (Sun *et al*, 2021). To verify that our observed activation in the OPA EEs

502 corresponds to the functionally defined OPA, we carried out an additional analysis using

503 localiser data for 14 sighted adults from a second independent study (Meissner *et al*, 2019).

504 The raw data were obtained through Open Science Framework (https://osf.io/aydqz/) and

505 analysed using FSL's FEAT pre-processing (brain-extraction, non-linear registration at 2-mm

506 resolution, slice-timing correction, motion correction, high-pass temporal filtering at 70 s,

507 and spatial smoothing at 5 mm) and mixed effects statistical model. The group-level

508 statistical map for the contrast scenes > objects was thresholded using clusters determined

509 by Z>4.00 and a (corrected) cluster significance threshold of p=.05, and we used this result to

510 identify two clusters in occipital cortex that were centred at approximately spatially mirrored

511 locations across the left and right hemispheres (left: -36, -74, 26, number of voxels = 153;

512 right: 34, -78, 20, number of voxels = 166). The coordinates of those clusters corresponded

513 well to those from Sun et al (2021; left: -29.4, -83.8, 23.9; right: 35.7, -78.5, 23.7). We then

514 used these cluster masks as ROIs with which to analyse PSC for the route vs. scrambled

515 contrast. Replicating our original finding, EEs showed a significant response for route vs.

516 scrambled in left (t(5)=3.930, p=.011; Wilcoxon signed rank z= 2.201, p=.028) and right

517 hemisphere ROIs (t(5)=5.074, p=.004; Wilcoxon signed rank z= 2.201, p=.028).

518

519 Additional ROI analyses – PSC for individual stimulus conditions

520 Furthermore, in order to determine the nature of the effect(s) underlying the response in the

521 OPA in EEs, we analysed the PSC in this area in response to each of the three individual

522 stimulus conditions (i.e. relative to silence baseline) and compared these to the same values

523 in control regions A1 and V1. These values (and those for all ROIs) are shown in figure 5. In a

524 two-way within-subject ANOVA with the factors ROI (OPA, A1, V1) and stimulus (route,

525 scrambled, no echo), there was a significant interaction (F(4,20)=5.446, p=.004, η_p^2 = .521).

526 This implies a difference in response profiles across the three ROIs to the different stimuli.

527 This was further explored in separate ANOVAs for each ROI. In the OPA there was a

528 significant difference between stimulus conditions (F(2,10)=11.457, p=.003, η_p^2 = .696), with

529 route sounds evoking greater PSC compared to no echo sounds (t(5)=3.674, p=.014) and

530 scrambled sounds (t(5)=5.613, p=.002). Scrambled sounds did not evoke significantly

531 stronger PSC compared to no echo sounds (t(5)=2.479, p=.056). In contrast, in A1 there was

532 no significant difference between stimulus conditions (F(2,10)=.371, p=.699). In V1, there

533 was a significant difference (F(2, 10)=14.725, p=.001, η_p^2 = .747), with route sounds evoking

534 greater PSC compared to no echo sounds (t(5)=4.907, p=.004) but not scrambled sounds

535 (t(5)=1.054, p=.340), although scrambled sounds did evoke greater PSC compared to no echo

536 sounds (t(5)=3.727, p=.014). Furthermore, by considering PSC to the individual stimulus

537 conditions, we were able to validate using one-sample t tests (applying the Benjamini-

538 Hochberg method, as previously described) that in OPA route sounds evoked activity

539 significantly greater than zero (t(5) = 3.988, p = .010; Wilcoxon signed rank z= 2.201, p=.028),

540 whilst neither scrambled (t(5) = 2.889, p = .034; note that this is a non-significant result when

541 p value is compared against the Benjamini-Hochberg critical value of .023; Wilcoxon signed

542 rank z= 2.201, p=.028) nor no-echo sounds (t(5)=.685, p=.524; Wilcoxon signed rank z= .524,

543 p=.600) led to significant activity. All significant one-sample t-tests are displayed on figure 5.

544

545 <Figure 5>

546

547 For BCs, the same analysis did not reveal a significant interaction between stimulus condition

548 and ROI (F(4,44)=.729, p=.577).   For SCs, there was a significant interaction (F(4,52)=11.003,

549 p<.001, η_p^2 = .458).   Further ANOVAs revealed that in the OPA there was a significant

550 difference between stimulus conditions (F(2,10)=3.468, p=.046, η_p^2 = .211), with route

551 sounds evoking *less* PSC compared to no echo sounds (t(5)=2.194 p=.047). There was no

552 difference between scrambled sounds and route sounds (t(5)=.693, p=.500) or between

553 scrambled sounds and no echo sounds (t(5)=1.881, p=.083).   In A1 there was also significant

554 difference between conditions (F(2,26)=24.034, p<.001, η_p^2 = .649), which was driven by click

555 sounds evoking less PSC compared to both scrambled (t(13)=5.109, p<.001) and route sounds

556 (t(13)=5.572, p<.001), but no difference between scrambled and route sounds t(13)=1.273,

557 p=.225).   There was no significant difference between stimulus conditions in V1 (F(2,

558 26)=.344, p=.712).   Neither BCs nor SCs showed significant PSC in the OPA in response to any

559 of the stimulus conditions.

560   Overall, these results show that the OPA in EEs has a unique response profile across the three

561   stimulus conditions compared to the other ROIs and to the other control groups.   This

562   response profile is consistent with its role in processing spatially coherent echo-acoustic

563   sounds for navigation.

564

565

566   <u>fMRI – whole-brain analysis</u>

567

568   Route vs. scrambled

569   Results for the analysis of a group difference for the route vs. scrambled contrast on the

570   whole brain are shown in figure 6. These results reveal significant clusters in and around the

571   OPA ROI and other occipital and parietal regions. Separate whole-brain activation maps for

572   each subject group are shown in figure 7. For this contrast, EEs showed two activation

573   clusters. The largest was centred on the superior parietal lobule (subregion 7P) in the left

574   hemisphere, and the other was centred on the inferior parietal lobule (subregion PGp) in the

575   right hemisphere. Both of these clusters extend into the OPA region, and are therefore

576   consistent with the findings from our ROI analysis. BCs did not show any significant clusters.

577   SCs, however, did show four significant clusters. Three of these covered similar areas

578   identified in EEs (i.e. superior/inferior parietal lobules), in addition to anterior parietal sulcus

579   and some frontal areas (motor cortex and Broca's area). None of the activation clusters for

580   SCs extended into the OPA region. A detailed summary of the activation clusters found for

581   the route vs. scrambled contrast is shown in table 4.

582

583   <Figure 6>

584 <Figure 7>

585 <Table 4>

586

587 We also quantified the degree of spatial overlap between the cluster maps for the EEs' route

588 vs. scrambled contrast and the functionally defined OPA ROI resulting from the analysis of

589 Meissner *et al's* (2019) sighted localiser data (see section 'Additional ROI analyses:

590 functionally localised OPA ROI' for cluster description). In the right hemisphere, the spatial

591 overlap covered 77 voxels (46% of all voxels in the sighted localiser cluster and 25% EEs'

592 route vs. scrambled cluster). In the left hemisphere the spatial overlap covered 32 voxels

593 (21% of voxels in the sighted localizer cluster, and 4%, in EE's route vs. scrambled cluster).

594 The low percentage of overlap in EEs in the left hemisphere is attributable to the fact that

595 this cluster in EEs is comparably larger, extending further into the parietal lobe (compare

596 table 4 and figure 7).

597

598 Echo vs. no-echo

599 Results for the analysis of a group difference for the echo vs. no echo contrast on the whole

600 brain are shown in figure 8. These results reveal large areas of activation in occipital and

601 parietal cortex. Separate whole-brain activation maps for each subject group are shown in

602 figure 9. The pattern of results was similar across BCs and SCs and included primary auditory

603 cortex, premotor cortex, and parietal areas (anterior intraparietal sulcus and superior/inferior

604 parietal lobules). There were also significant activation clusters in Broca's areas in both

605 groups. The pattern of activity observed for the EE group included similar areas that were

606 activated in the BC and SC groups, but additionally included a large activation cluster in early

607 visual cortex. Detailed descriptions of these clusters are shown in table 5.

608

609   <Figure 8>

610   <Figure 9>

611   <Table 5>

612

613   Sound vs. Silence

614   Results for the analysis of a group difference for the sound vs. silence contrast on the whole

615   brain are shown in figure 10. These results reveal similar areas of activation to the echo vs.

616   no echo contrast.   Separate whole-brain activation maps for each subject group are shown

617   in figure 11. All three groups showed significant activation clusters in a number of different

618   brain areas (this is to be expected, based on the non-specific nature of the contrast). Most

619   notably, these activation clusters included primary auditory cortex, motor/premotor cortex,

620   and parietal areas (anterior parietal sulcus and superior/inferior parietal lobules). The EE

621   group was the only group that also showed a significant activation cluster in early visual

622   cortex. Detailed descriptions of these clusters are shown in table 6.

623

624   <Figure 10>

625   <Figure 11>

626   <Table 6>

627

628

629

630   Discussion

631   In the present study, we have shown that the occipital place area (OPA) is recruited in blind

632   echolocation experts (EEs) during traversal of a virtual echo-acoustic space in first-person

633   perspective. This was not found in blind or sighted controls (BCs or SCs, respectively). The

634   task we used can be considered an echo-acoustic analogue of a vision-based task that has

635   previously been found to evoke activation in the OPA in sighted people (Kamps *et al*, 2016).

636   Our study, therefore, provides evidence that the OPA is not uniquely associated with visually

637   guided navigation, but can also be similarly recruited for echo-acoustic navigation.   ROI and

638   whole-brain analyses provided converging evidence for OPA involvement, and our

639   behavioural measures verified that EEs could discriminate coherent route sounds from

640   scrambled sounds. Further, the critical contrast was based on sounds that controlled for

641   spectro-temporal acoustic properties.

642

643   The OPA has been previously identified as an important part of the human navigation brain

644   network, being associated with visual perception of static scenes (Dilks *et al*, 2013) as well as

645   dynamic boundary-based spatial navigation (Kamps *et al*, 2016; Julian *et al*, 2016). Julian and

646   colleagues (2016), for example, used TMS to show that, in sighted people, the OPA is causally

647   involved in the encoding of object locations relative to boundaries in the environment.

648   Specifically, they hypothesise that the OPA serves as the source of the perceptual

649   representation of environmental boundary information, which is then used in the spatial

650   coding of the environment in the larger network of navigation-related brain regions. It is also

651   known that the OPA and PHPA are functionally connected (Baldassano *et al*, 2013), which

652   might mediate input form the OPA to the hippocampal formation (Naber *et al*, 1997). What

653   the present study demonstrates, however, is that the perceptual representation formed in

654   the OPA is not necessarily formed through visual input, and can also be formed in the

655   absence of vision.

656

657   Participants in the BC but not EE group tended to have some residual visual sensitivity. It is

658   thus possible that complete blindness itself, rather than echolocation experience, is sufficient

659   to elicit OPA responses to echo-acoustic sounds. In this context it is important to note that

660   our BCs and SCs were very similar in their brain activations, whilst both groups differed

661   greatly from EEs.   This suggests that long term experience in echolocation rather than

662   blindness *per se* underlies the response in the OPA. Furthermore, our additional analyses

663   also suggested that the activity in the OPA was unique to EEs and not simply driven by

664   participants' accuracy at identifying route vs. scrambled sounds, regardless of them being

665   EEs, BCs or SCs. Specifically, our data suggested that, although OPA activity was significantly

666   higher for EEs compared to the control groups, there was no evidence in the control groups

667   that this activity was predicted by their task performance. In contrast, the pattern of results

668   *within* the six EEs indicated a positive association (though only borderline statistically

669   significant) between task performance and OPA activity. This dual influence of long-term

670   echolocation experience and task specific ability is strikingly similar to our previous finding

671   that both long-term echolocation experience *and* echo-localisation acuity predict the degree

672   of retinotopic-like mapping of sounds in V1 (Norman *et al*, 2019).

673

674   With respect to activations in parietal cortices (in particular SPL), our ROI analysis, which

675   considered SPL as combination of subareas 5Ci, 5L, 5M, 7A, 7M, 7P, did not show any

676   significant involvement for any contrast or participant group. Yet, the whole brain analysis

677 revealed significant clusters of activation for subareas of SPL for different participant groups

678 and contrasts. These activations are generally consistent with those reported in a previous

679 study examining echolocation-based route following (Fiehler *et al,* 2015). The result by

680 Fiehler et al (2015), however, was based on the contrast echo vs. no-echo sounds, but the

681 present results from our route vs. scrambled contrast do suggest that the activation in SPL

682 reflects the processing of the coherent spatiotemporal structure of echolocation navigation

683 sounds. The SPL has also been shown to be active in sighted people whilst solving a vision-

684 based route recognition task, and in blind people solving the same task using a sensory

685 substitution device (Kupers *et al*, 2010). The specific functional role that the SPL might play

686 in navigation remains unclear, but it has previously been associated with the egocentric

687 coding of visual space (Galati *et al*, 2000).

688

689 In addition to SPL, both EEs and SCs showed activation in the inferior parietal lobule (area

690 PGp), with SCs showing additional activation in the anterior intra-parietal sulcus (aIPS).

691 Fiehler *et al* (2015) also found some activation in these areas in SCs, and the aIPS has also

692 previously been associated with egocentric spatial coding (Galati *et al*, 2000). A recent study

693 found activation within the visual dorsal stream (i.e. parietal cortex), including a posterior

694 area close to the occipitoparietal sulcus (V6/V6a complex), in both blind and sighted

695 blindfolded participants when using a visual-to-auditory SSD to navigate a virtual

696 environment (after training; Maidenbaum *et al*, 2018). Together with our results, these

697 findings suggest that there are several areas within parietal cortex that might play a role in

698 navigation (with or without vision). It is important to note, however, that areas of posterior

699 parietal cortex such as aIPS and SPL are more generally also considered to be part of the

700   dorsal frontoparietal attention network (Szczepanski, Pinsk, Douglas, Kastner & Saalmann,

701   2013) – a network that is thought to control top-down attention to environmental objects

702   and tasks (Corbetta *et al,* 2008; Corbetta & Schulman, 2002).   Although this network is

703   typically described with respect to visual processing, effects of spatial attention within the

704   auditory modality have also been observed in posterior parietal cortex (Shomstein & Yantis,

705   2006). Thus, it remains unclear whether the activity in these posterior parietal areas reflects

706   processes specific to navigation, the multimodal perception of space, or the effects of spatial

707   attention. It is, of course, possible that these areas contribute to complex tasks such as the

708   one used here in a number of ways.

709

710   We found no evidence of positive activity in the parahippocampal place area for the contrast

711   route vs. scrambled. The parahippocampal place area is considered to be central to the

712   spatial navigation network in humans (i.e. parahippocampal cortex; Hartley *et al*, 2003;

713   2014). The absence of activity in our paradigm is consistent with studies using a similar

714   paradigm to ours (e.g. Fiehler *et al,* 2015; Kamps *et al*, 2016) and is likely the result of the

715   nature of the task requirements. Specifically, participants were not required to navigate

716   previously learned environments or to match routes to those held in memory, but were

717   instead required to identify the directions of the turns taken along each route. This task

718   design was chosen so we could include a suitable control condition (scrambled sounds) to

719   rule out activity driven by spectro-temporal properties of the stimuli. Kupers and colleagues

720   (2010), in contrast, required participants using a visual-to-tactile SSD to explicitly match one

721   of two sample routes to a previous one and found parahippocampal activity in blind

722   participants. Interestingly, for our echo vs. no-echo and sound vs. silence contrasts we found

723   evidence of negative activity in the parahippocampal place area in SCs. This is similar to the

724　findings of Maidenbaum and colleagues (2018), in which negative activity in the medial

725　temporal lobe was found in blind and sighted participants when navigating using a visual-to-

726　auditory SSD. The implication of this negative activity remains unclear.

727

728　Both ROI and whole brain analysis showed activation in occipital cortex, including early visual

729　cortex, in the EE group for the contrast echo vs. no-echo. This activation was in addition to

730　activity in other areas, including parietal areas, and Broca's areas, which was present in all

731　three groups. The same pattern of results was also observed for the sound vs. silence

732　contrast, for which additional activity was also observed in all three groups' primary auditory

733　areas. This pattern of results strongly suggests that recruitment of V1 for processing of echo-

734　acoustic information is tied to experience with echolocation rather than blindness *per se*. It is

735　by now well-established that the neural correlates of echolocation in EEs include several

736　areas of occipital cortex typically associated with inherently visual functions, including V1

737　(Arnott *et al,* 2013; Fiehler *et al,* 2015; Flanagin et al., 2016; Norman & Thaler, 2019;Milne *et*

738　*al*, 2015; Thaler *et al,* 2011; Thaler *et al,* 2014; Wallmeier et al., 2015). The results of the

739　present study therefore lend further support to the notion that the organization of the

740　human brain is not strictly tied to specific modalities, but organised flexibly according to task

741　demands, and shaped by experience with a specific task or computation (e.g. echolocation),

742　rather than sensory experience per se (e.g. blindness; see Amedi *et al*, 2017).

743

744　In conclusion, the present study found that the OPA – an area previously assumed to be

745　strongly associated with boundary-based visually-guided navigation – is driven in EEs during

746　echo-acoustically guided navigation. This opens up novel ways of understanding the brain

747　areas and networks typically involved in visual spatial navigation.

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879

880   Tables

881

882   Table 1

883   Details of all blind participants, organised by group. EE refers to echolocation expert; BC

884   refers to blind control.

885

Participant	Sex	Age	Degree of vision loss	Cause and age of vision loss	Echolocation use
EE1	M	53	Total blindness	Enucleation due to retinoblastoma at 13 months.	Daily, since early childhood/no exact age remembered
EE2	M	60	Bright light detection both eyes	Retinal detachment; from birth	Daily, since age 6
EE3	M	49	Total blindness	Enucleation due to retinoblastoma at 18 and 30 months.	Daily, since 8 years old
EE4	M	24	Total blindness.	Vision loss suddenly at age 12 due to unknown causes. Enucleation at age 19 to alleviate ocular discomfort.	Daily, since 12 years old

EE5	M	37	Total blindness	Gradual sight loss since birth due to glaucoma.	Daily, since 12 years old
EE6	F	43	Total blindness.	Leber's congenital amaurosis, from birth	Daily, since 31 years old
BC1	F	60	Total blindness in left eye; some peripheral vision in right eye.	Stichler's syndrome. Retinal sciasis, from birth with increasing severity.	Some experience; very little regular use
BC2	M	38	Tunnel vision (<2 deg) and decreased acuity (< 20/200) in both eyes.	Retinitis Pigmentosa and other retinal pathology (unknown). Official diagnosis in early childhood (no exact age remembered but was known when commencing school, i.e. age 5yrs).	None
BC3	M	54	Residual bright light perception	Retinitis pigmentosa. Official diagnosis age 10 yrs. Gradual sight loss from birth.	Some experience; very little regular use
BC4	M	39	Residual bright light perception	Retinitis pigmentosa. Gradual sight loss from	None

				birth. Official diagnosis in early childhood (no exact age remembered but was known when commencing school, i.e. age 5yrs).	
BC5	F	44	Total Blindness right eye; bright light detection left eye.	Micropthalmia and Glaucoma; right eye enucleated aged 39 yrs	None
BC6	F	72	Bright Light detection.	Retinitis Pigmentosa. Gradual sight loss from birth. Official diagnosis in early childhood (no exact age remembered but was known when commencing school, i.e. age 5yrs).	None
BC7	M	46	Total blindness	Ocular albinism. Gradual sight loss from birth.	Some experience; very little regular use
BC8	F	36	Bright Light detection.	Unknown cause, from birth.	None
BC9	M	37	Tunnel vision (<5 deg) and decreased	Retinitis pigmentosa. Gradual sight loss from	None

			acuity (< 20/200) in both eyes.	birth. Official diagnosis age 13yrs.	
BC10	F	27	Left eye ca. 1 deg of foveal vision left with reduced acuity (<20/200); right eye bright light detection	Leber's Amaurosis and Cataracts, from birth.	None
BC11	F	79	Some blurred foveal vision; prone to bleaching	Rod Cone Dystrophy, from birth.	None
BC12	M	48	Total blindness in left eye; residual bright light perception in right eye.	Severe childhood glaucoma, from 3 months old.	None

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887

888   Table 2

889   ROI details. For each named ROI, data were averaged across the left and right hemispheres

890   (unless stated otherwise). Where a probabilistic atlas was used to define the ROI, the

891   classification threshold is given (i.e. only voxels with a probabilistic value above this threshold

892   were included).

893

ROI label	Description
A1	Primary auditory cortex, based on areas TE 1.0, 1.1 and 1.2 in the Jülich histological (cyto- and myelo-architectonic) atlas (threshold > 50%).
V1	Primary visual cortex, based on area 17/V1 in the Jülich histological (cyto- and myelo-architectonic) atlas (threshold > 50%).
OPA	Sphere of 7.5-mm radius at approximate location of the occipital place area (OPA), based on average MNI coordinates (left: -29.4, -83.8, 23.9, right: 35.7, -78.5, 23.7) provided by Sun *et al* (2021). These coordinates were acquired using a scene > objects localiser, averaged across 17 participants.
PHPA	Parahippocampal place area (PHPA), based on probabilistic atlas from Weiner et al (2018), fitted to the MNI standard template.
SPL	Superior parietal lobule (SPL), based on the combination of subareas 5Ci, 5L, 5M, 7A, 7M, 7P, and 7PC in the Jülich histological (cyto- and myelo-architectonic) atlas (threshold > 50%).

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896   Table 3

897   Individual PSC datapoints for the six EEs, organised by contrast and ROI (group means of

898   these data are shown in figure 3).

899

Route vs scrambled	A1	V1	PHPA	OPA	SPL
EE1	0.14	0.27	-0.01	0.23	0.31
EE2	-0.09	-0.24	-0.18	0.24	-0.12
EE3	-0.02	0.05	0.04	0.05	0.06

	A1	V1	PHPA	OPA	SPL
EE4	-0.02	0.10	0.03	0.18	0.18
EE5	-0.14	0.27	0.16	0.33	-0.08
EE6	0.11	0.03	0.07	0.26	0.20
Echo vs no echo	**A1**	**V1**	**PHPA**	**OPA**	**SPL**
EE1	0.19	0.16	0.27	0.06	0.11
EE2	0.02	0.48	0.14	0.20	-0.09
EE3	0.09	0.27	-0.08	0.14	0.14
EE4	0.10	0.32	0.01	0.54	0.31
EE5	-0.11	0.71	0.17	0.82	0.29
EE6	-0.07	0.73	0.33	0.56	0.58
Sound vs silence	**A1**	**V1**	**PHPA**	**OPA**	**SPL**
EE1	0.37	0.27	-0.09	0.24	0.25
EE2	0.30	0.10	0.20	0.10	-0.34
EE3	0.12	0.17	-0.09	0.01	0.01
EE4	0.15	0.27	-0.07	0.49	0.28
EE5	0.16	0.53	0.06	0.47	0.03
EE6	0.11	0.49	0.00	0.41	0.32

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906   Table 4

907   Summary of peak activations within each cluster for the route vs. scrambled contrast.

908

Subject group	Cluster	Region label	MNI coords (mm)			z-stat	Num voxels
			x	y	z		
EEs	1	GM Superior parietal lobule 7P L (continuous with OPA)	-24	-72	28	3.14	899
	2	GM Inferior parietal lobule PGp R (continuous with OPA)	42	-82	20	3.21	325
BCs	n/a	n/a	n/a	n/a	n/a	n/a	n/a
SCs	1	GM Inferior parietal lobule PGp L	-18	-66	62	3.95	1370
		GM Superior parietal lobule 7A L					
		GM Superior parietal lobule 7P L					
	2	GM Broca's area BA44 L	-46	20	16	3.91	790
		GM Broca's area BA45 L					
		GM Premotor cortex BA6 L					
	3	Caudate	14	14	-4	3.85	423
	4	GM Anterior intra-parietal sulcus hIP3 R	28	-58	58	3.42	320
		GM Superior parietal lobule 7A R					
		GM Superior parietal lobule 7P R					

909

910

911   Table 5

912   As table 4, but for the echo vs. no echo contrast.

913

Subject group	Cluster	Region label	MNI coords (mm)			z-stat	Num voxels
			x	y	z		
EEs	1	GM Visual cortex V2 BA18 R	34	-88	22	4.51	11224
		GM Visual cortex V3V R					
	2	GM Premotor cortex BA6 R	40	-2	46	4.51	2163
		GM Anterior intra-parietal sulcus					
	3	hIP3 L	-30	-58	54	4.09	1504
		GM Inferior parietal lobule PFm L					
		GM Inferior parietal lobule Pga L					
		GM Superior parietal lobule 7A L					
	4	GM Broca's area BA44 L	-50	8	28	4.07	1307
		GM Broca's area BA45 L					
	5	GM Premotor cortex BA6 R	-4	18	44	4.27	794
	6	Thalamus	-12	-14	0	3.36	731
	7	Temporal Lobe	-50	-48	12	4.12	622
BCs	1	Cerebellum	52	-62	-12	4.23	6047
		Temporal Lobe					
	2	GM Broca's area BA45 L	-42	52	-4	4.49	3959
		GM Premotor cortex BA6 L					
	3	Frontal Lobe	30	26	0	4.64	3873
	4	GM Anterior intra-parietal sulcus	50	-40	58	4.59	2031

	Region	x	y	z	t	size
	hIP2 R					
	GM Anterior intra-parietal sulcus					
	hIP3 R					
	GM Inferior parietal lobule PF R					
	GM Inferior parietal lobule PFm R					
	GM Superior parietal lobule 7P R					
	GM Anterior intra-parietal sulcus					
5	hIP1 L	-32	-60	44	4.21	1880
	GM Anterior intra-parietal sulcus					
	hIP3 L					
	GM Inferior parietal lobule Pga L					
	GM Primary somatosensory cortex BA2 L					
	GM Superior parietal lobule 7A L					
	GM Superior parietal lobule 7P L					
6	Frontal Lobe	-36	18	-2	4.3	938
	Insula					
	Putamen					
7	GM Inferior parietal lobule PFcm L	-50	-40	20	4.28	925
	GM Primary auditory cortex TE1.1 L					
8	GM Premotor cortex BA6 R	-4	20	44	5.13	791
9	GM Inferior parietal lobule PF R	66	-30	8	3.94	533
	GM Inferior parietal lobule PFcm R					
10	Putamen	20	12	-10	3.42	515
	Thalamus					

		Region	x	y	z		
	11	Inferior Temporal Gyrus, temporooccipital part	-52	-54	8	3.75	308
		Lateral Occipital Cortex, inferior division					
		Middle Temporal Gyrus, temporooccipital part					
SCs	1	GM Broca's area BA44 R	46	8	24	5.96	10360
		GM Broca's area BA45 R					
		GM Anterior intra-parietal sulcus					
	2	hIP1 L	-46	-38	56	5.11	4597
		GM Inferior parietal lobule Pga L					
		GM Insula Id1 L					
		GM Primary somatosensory cortex BA1 L					
		GM Primary somatosensory cortex BA2 L					
		GM Anterior intra-parietal sulcus					
	3	hIP1 R	48	-38	52	5.45	3123
		GM Anterior intra-parietal sulcus hIP2 R					
		GM Anterior intra-parietal sulcus hIP3 R					
		GM Inferior parietal lobule PF R					
		GM Inferior parietal lobule PFm R					
		GM Inferior parietal lobule PFt R					

		Region label	MNI coords			z-stat	Num voxels
			x	y	z		
		GM Primary somatosensory cortex BA1 R					
		GM Primary somatosensory cortex BA2 R					
	4	GM Inferior parietal lobule PF R	50	-32	8	4.73	2951
		GM Primary auditory cortex TE1.1 R					
	5	GM Broca's area BA44 L	-58	6	28	5.31	2785
		GM Premotor cortex BA6 L					
	6	Cerebellum	-10	-82	-30	5.62	1981
	7	Thalamus	12	10	2	4.78	1121
	8	Frontal Orbital Cortex	-36	28	2	4.77	805
		Frontal Pole					
		Insular Cortex					
	9	Cerebellum	14	-78	-46	4.13	440

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917 Table 6

918 As tables 4 and 5, but for the sound vs. silence contrast.

919

Subject group	Cluster	Region label	MNI coords (mm)			z-stat	Num voxels
			x	y	z		
EEs	1	GM Visual cortex V2 BA18 R	36	-90	6	4.2	7745
	2	GM Broca's area BA44 R	42	12	20	4.25	2636

		GM Broca's area BA45 R					
		GM Premotor cortex BA6 R					
		GM Anterior intra-parietal sulcus					
	3	hIP3 L	-34	-58	54	4.08	1987
		GM Superior parietal lobule 7A L					
		GM Superior parietal lobule 7P L					
	4	GM Premotor cortex BA6 R	6	26	42	4.04	728
		GM Inferior parietal lobule PFcm L					
		GM Primary auditory cortex TE1.0 L					
		GM Primary auditory cortex TE1.1 L					
		WM Acoustic radiation L					
	5	GM Inferior parietal lobule PFcm L	-50	-48	8	4.32	628
		GM Primary auditory cortex TE1.0 L					
		GM Primary auditory cortex TE1.1 L					
		WM Acoustic radiation L					
	6	GM Broca's area BA44 L	-58	12	22	3.86	539
		GM Premotor cortex BA6 L					
	7	GM Inferior parietal lobule PF R	62	-36	12	4.19	437
		GM Primary auditory cortex TE1.0 R					
		GM Primary auditory cortex TE1.1 R					
		WM Acoustic radiation R					
		GM Anterior intra-parietal sulcus					
BCs	1	hIP3 L	-42	-36	46	5.24	6653
		GM Primary somatosensory cortex BA1 L					

	GM Primary somatosensory cortex BA2 L					
	GM Primary somatosensory cortex BA3b L					
2	Frontal Lobe	36	22	0	4.83	4237
	Insula					
	GM Anterior intra-parietal sulcus					
3	hIP2 R	42	-42	50	4.34	1370
	GM Anterior intra-parietal sulcus hIP3 R					
	GM Inferior parietal lobule PF R					
	GM Inferior parietal lobule PFm R					
	GM Superior parietal lobule 7A R					
	GM Superior parietal lobule 7P R					
	GM Superior parietal lobule 7PC R					
4	GM Inferior parietal lobule PFcm L	-46	-38	18	4.31	1271
	GM Primary auditory cortex TE1.0 L					
	GM Primary auditory cortex TE1.1 L					
	GM Secondary somatosensory cortex / Parietal operculum OP1 L					
	WM Acoustic radiation L					
5	GM Inferior parietal lobule PF R	62	-34	12	5.15	1021
	GM Primary auditory cortex TE1.1 R					
	GM Secondary somatosensory cortex / Parietal operculum OP1 R					

		GM Secondary somatosensory cortex / Parietal operculum OP4 R					
SCs	1	GM Anterior intra-parietal sulcus hIP1 L	-36	-28	10	6.57	8164
		GM Anterior intra-parietal sulcus hIP3 L					
		GM Inferior parietal lobule PFcm L					
		GM Insula Ig1 L					
		GM Insula Ig2 L					
		GM Primary auditory cortex TE1.1 L					
		GM Primary somatosensory cortex BA2 L					
		WM Acoustic radiation L					
	2	GM Broca's area BA44 R	38	0	50	5.58	7588
	3	GM Primary auditory cortex TE1.0 R	46	-26	8	5.54	2377
		GM Primary auditory cortex TE1.1 R					
		WM Acoustic radiation R					
	4	GM Premotor cortex BA6 R	-2	32	40	5.27	2153
	5	GM Anterior intra-parietal sulcus hIP1 R	38	-54	42	5.83	2123
		GM Anterior intra-parietal sulcus hIP2 R					
		GM Anterior intra-parietal sulcus hIP3 R					
		GM Inferior parietal lobule PFm R					

	GM Inferior parietal lobule Pga R					
6	Frontal Lobe	-34	18	-2	4.94	1047
	Insula					
7	Cerebellum	-12	-78	-22	4.74	806

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940 Figures

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942 **Figure 1**

943 Illustration of spatial arrangements used to construct virtual spaces (T-mazes, U-mazes, Z-

944 mazes) and the pre-specified routes taken through each one. Each route was composed of

945 18 click recordings taken at regularly spaced intervals. Specifically, there was one click for

946 each position along the route (marked by the intersections) and two clicks for each rotation

947 of 90° (in 45° steps).

948

Figure 2

Data from the behavioural task conducted before the fMRI task. Three separate measures of performance are given: ability of participants to identify specific route types (A), to identify coherent route sounds vs. scrambled sounds (B), and to identify the sounds containing echoes from those that do not (C). Error bars show standard error of the mean. Circles illustrate performance of individual EEs. EE – Expert Echolocator; BC – Blind Control; SC – Sighted Control.

959

960 **Figure 3**

961 Results of the ROI analysis for route vs scrambled (A), echo vs no echo (B), and sound vs

962 silence (C) contrasts. In each panel, percent signal change (PSC) is shown for each contrast,

963 ROI and for participant group. Error bars show standard error of the mean. Asterisks

964 indicate where the PSC for that ROI was significantly different from zero, after applying the
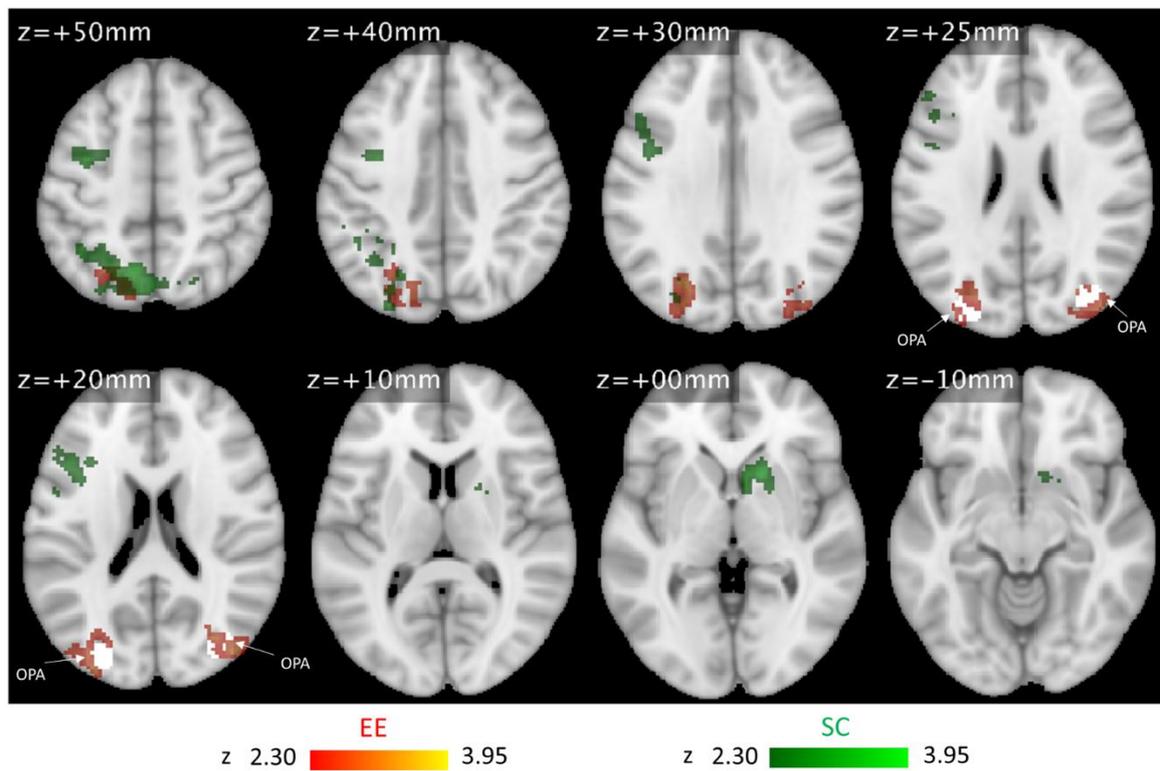
965 Benjamini-Hochberg method. See also table 3 for the individual data for the six EEs.

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Figure 4

The association between the PSC in OPA for the route vs scrambled contrast (y axis) and perceptual identification accuracy of route vs scrambled sounds (x axis). Each point represents an individual subject, with separate groups denoted by different colours. The solid lines show linear model fits.

979

980 **Figure 5**

981 Results of the ROI analysis for the individual stimulus conditions (i.e. EVs relative to silence

982 baseline): route sound (A), scrambled sound (B), and no echo sound (C). In each panel,

983 percent signal change (PSC) is shown for each contrast, ROI and for participant group.

984 Asterisks indicate where the PSC for that ROI was significantly different from zero, after

985 applying the Benjamini-Hochberg method.

986

987

Test of group difference (EE = BC = SC)
z 2.30 ▰ 3.90

Figure 6

Activation maps showing locations of significant group difference for the contrast route vs. scrambled (cluster level threshold of z > 2.3 and p < .05) displayed on the MNI152 standard-space template. The OPA ROI is visible in white in the cross-sectional slices for Z = +20 and +25 mm. Orientation of the images is in neurological convention (i.e. left is left).
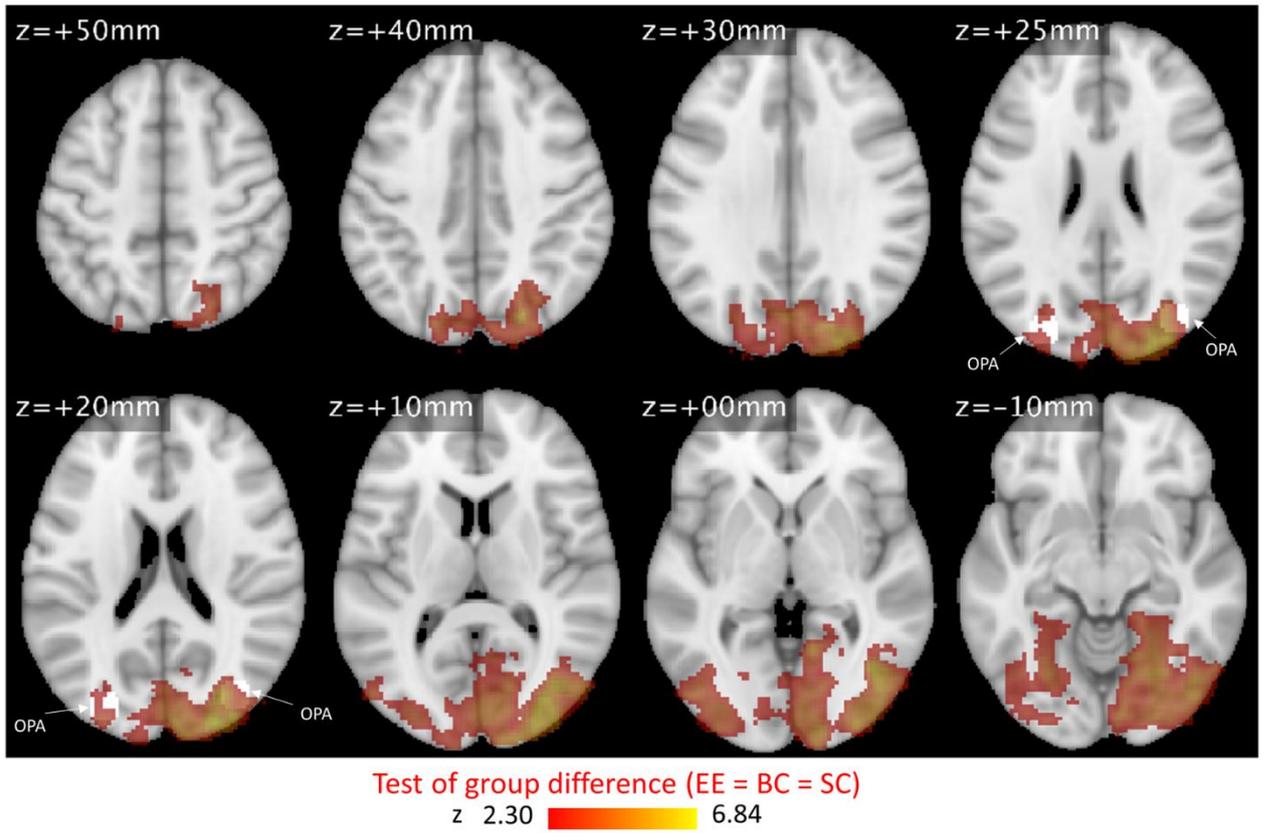
58

Figure 7

Activation maps for the contrast route vs. scrambled (cluster level threshold of z > 2.3 and p < .05) displayed on the MNI152 standard-space template. Separate colour overlays are used to show results from EEs, BCs, and SCs on the (note there were no significant clusters for BCs). The colormap used to display each overlay is scaled such that they all have the same upper bound (determined by the largest z value in all three overlays). The OPA ROI is visible in white in the cross-sectional slices for Z = +20 and +25 mm.   Orientation of the images is in neurological convention (i.e. left is left).

Test of group difference (EE = BC = SC)
z 2.30 6.84

1008

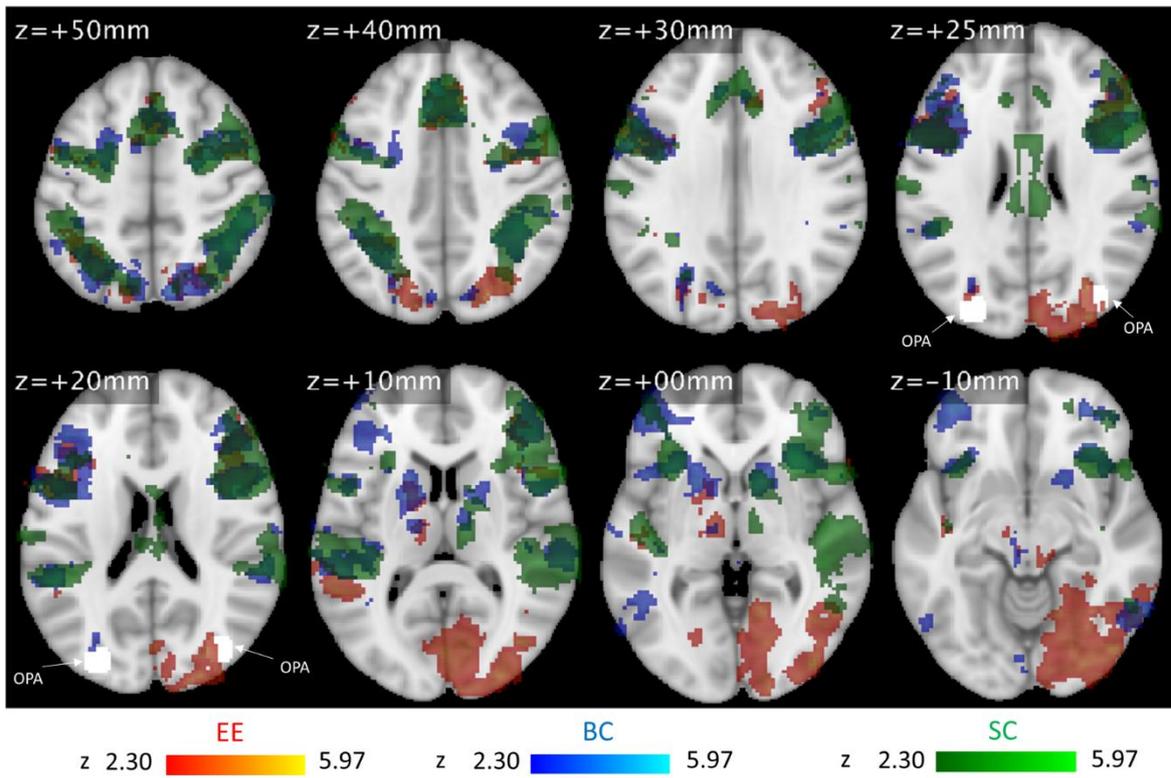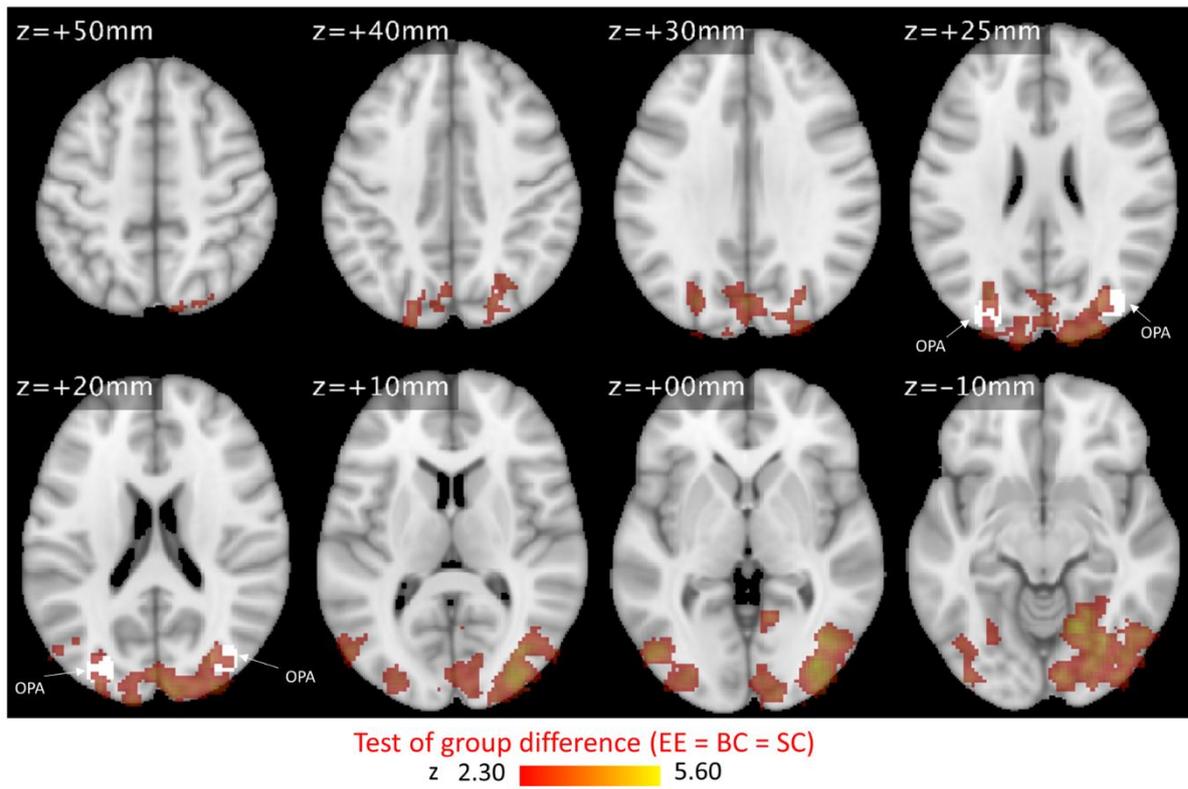1009 **Figure 8**

1010 As figure 6, but for the contrast echo vs. no echo.

1011

1012

1013

Figure 9

As figure 7, but for the contrast echo vs. no echo.

Test of group difference (EE = BC = SC)
z 2.30 ___ 5.60

1020
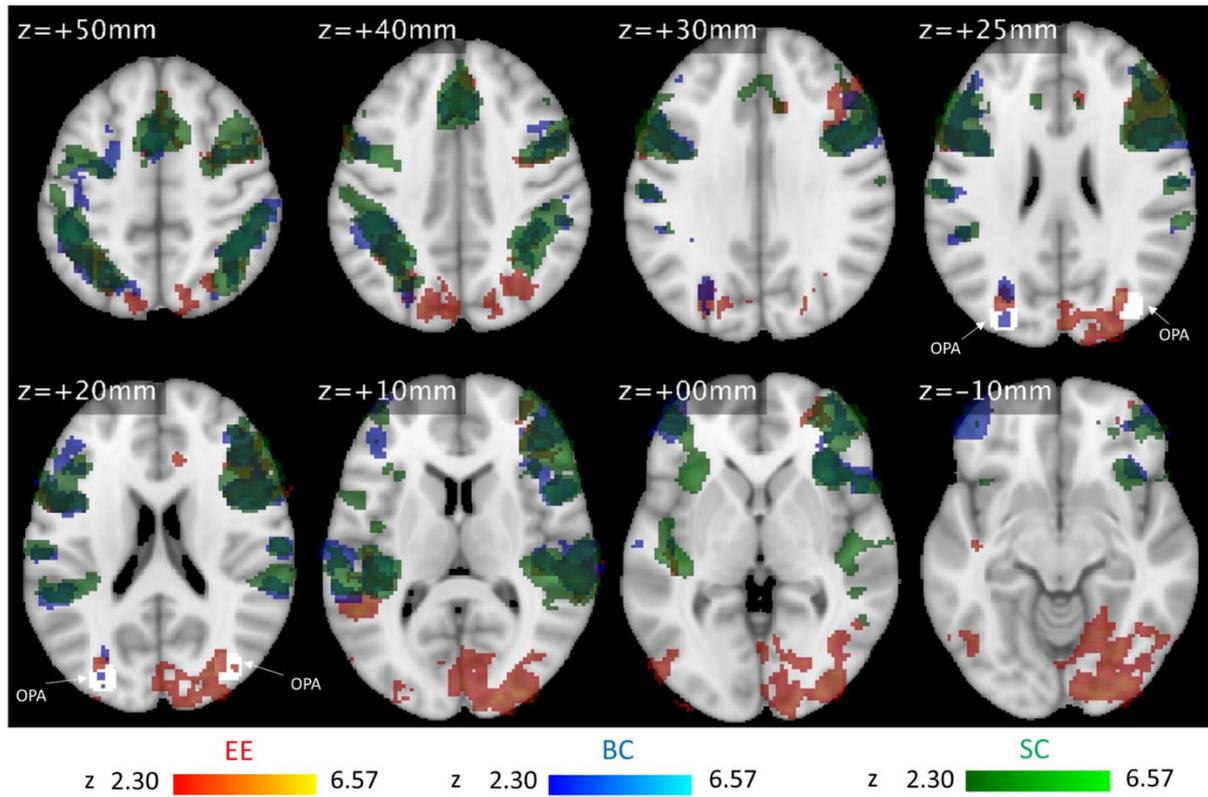
1021 **Figure 10**

1022 As figures 6 and 8, but for the contrast sound vs. silence.

1023

1024

1025

Figure 11

As figures 7 and 9, but for the contrast sound vs. silence.