Brain bases for navigating acoustic features

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Abstract

Whether physical navigation shares neural substrates with mental travel in other behaviourally relevant domains is debated. With respect to sound, pure tone working memory in humans elicits hippocampal as well as auditory cortical and inferior frontal activity, and rodent work suggests that hippocampal cells that usually track an animal's physical location can also map to tone frequency when task-relevant. We generated a sound dimension based on the density of random-frequency tones in a stack, resulting in a percept ranging from low- ("beepy") to high-density ("noisy"). We established that unlike tone frequency, which listeners automatically associate with vertical position, this density dimension elicited no consistent spatial mapping. During functional magnetic resonance imaging, human participants (both sexes) held in mind the density of a series of tone stacks and, after a short maintenance period, adjusted further stacks to match the target ("navigation"). Density was represented most strongly in bilateral non-primary auditory cortex, specifically bilateral planum polare. Encoding and maintenance activity in hippocampus, inferior frontal gyrus, planum polare and posterior cingulate was positively associated with subsequent navigation success. Bilateral inferior frontal gyrus and hippocampus were among regions with elevated activity during navigation, compared to a parity-judgment condition with closely matched acoustics and motor demands. Bilateral orbitofrontal cortex was more active when navigation was toward a target density than when participants adjusted density in a control condition with no particular target. We find that self-initiated travel along a non-spatial auditory dimension engages a brain system overlapping with that supporting physical navigation.

Keywords: Auditory memory, working memory, navigation, hippocampus, sound

Significance Statement

Work in rodents suggests that navigation in physical space and the active analysis of sounds share a neural substrate in the hippocampus, supporting the use of common computational mechanisms. We examined the human brain system for navigation through an acoustic environment to a remembered target. In addition to high-level auditory cortex we demonstrate involvement of the hippocampus along with sites in frontal and cingulate cortex that also support physical navigation.

Introduction

Finding our way in the physical world is supported by computations involving hippocampus as well as entorhinal, parietal, cingulate, and prefrontal cortices (O'Keefe and Dostrovsky, 1971; Ekstrom et al., 2003; Hafting et al., 2005; Spiers, 2008; Doeller et al., 2010; Bicanski and Burgess, 2020; Basu et al., 2021). Recent theoretical and empirical work suggests that this neural machinery may operate over more general sensory or knowledge spaces (Tavares et al., 2015; Constantinescu et al., 2016; Aronov et al., 2017; Bao et al., 2019; Whittington et al., 2020). In the auditory world a principal organising dimension is frequency. Linguistic and musical communication often depend on generating and making sense of trajectories in frequency, which is mapped tonotopically at multiple levels of the auditory system from the cochlea to sensory cortex. When tone frequency is controlled by a rat to match a target and obtain a reward, neurons tuned to frequency are also found in hippocampus and entorhinal cortex (Aronov et al., 2017). Many of these neurons also represent individual or geometrically related spatial locations (place and grid cells, respectively) during physical navigation, suggestive of a flexible code for traversing different dimensions of experience. Such a correspondence may arise simply because frequency has a natural mapping to spatial location: higher frequencies are implicitly associated with higher points in physical space (Rusconi et al., 2006). It may also be that ensembles of sequentially firing hippocampal cells map progress toward a goal or reward, rather than encoding the particular dimension along which such progress is made (see Zutshi et al., 2024 for an example using tones).

Navigation involves not only adjusting one's position but also maintaining a representation of the destination. In the spatial domain, target maintenance engages frontal sites including ventromedial prefrontal and orbitofrontal cortex (Spiers, 2008; Basu et al., 2021). Holding a tone frequency in mind over seconds modulates activity in auditory cortex but also inferior frontal gyrus and hippocampus (Zatorre et al., 1994; Kumar et al., 2016; Kumar et al., 2021). The network required to maintain a complex, but non-verbal, auditory target in working memory is less well studied (but see Linke et al., 2015; Pomper et al., 2023; Uluç et al., 2023). We designed a stimulus and task that allowed us to probe the neural substrates of non-spatial navigation toward such targets in humans.

We used successions of tone stacks that varied in the number of concurrently presented tones of random frequency (Figure 1A). This gave rise to a percept varying from sparse ("beepy") to dense ("noisy"). Using objective and subjective behavioural measures we established that this acoustic dimension does not consistently elicit a spatial association. We then had participants undergo functional

magnetic resonance imaging (fMRI) while performing tasks that separately tapped processes of working memory and navigation in this auditory dimension. The main condition of interest involved holding in mind a series of tone stacks of fixed density, then adjusting a new set of stacks to match the target. In order to establish whether any coding for density was distinct from proximity to the target we used different starting and target densities in different trials. In control conditions we removed either (a) the working memory component by having participants randomly adjust tone stacks with no particular target, and/or (b) the navigation component by having participants respond as to whether each in a series of spoken numbers was odd or even while listening passively to the tone stacks. As far as possible we matched the acoustics and number of button presses across conditions.

We established that acoustic spectral density is represented in non-primary auditory cortex. Navigation in density space engaged brain regions including inferior frontal gyrus and hippocampus, with orbitofrontal cortex activated more when navigation was toward a target. Encoding and maintenance activity in areas including hippocampus, inferior frontal gyrus, auditory cortex and cingulate cortex was positively associated with subsequent successful navigation.

Methods and Materials

Stimuli

The main experimental stimuli were 190-ms tone stacks (with 2-ms cosine on- and offset ramps) interspersed with 10 ms of silence. Each stack contained between 2 and 196 pure tones randomly drawn from 400 frequencies logarithmically spaced from 250 to 4000 Hz. Varying the number of concurrent tones in a segment (along a logarithmic scale with 26 levels) gave rise to a “density” percept described to participants as ranging from “beepy” to “noisy” (see Figure 1A). Tone stacks were equated for root-mean-square intensity, which gave a reliable loudness match during piloting. For the fMRI experiment we also created recordings of spoken digits from 1 to 10 using a text-to-speech tool (notevibes.com; voices: Daniel, Gabriela; speed: 1.6). These were trimmed to have duration below 400 ms and normalised for root mean square intensity.

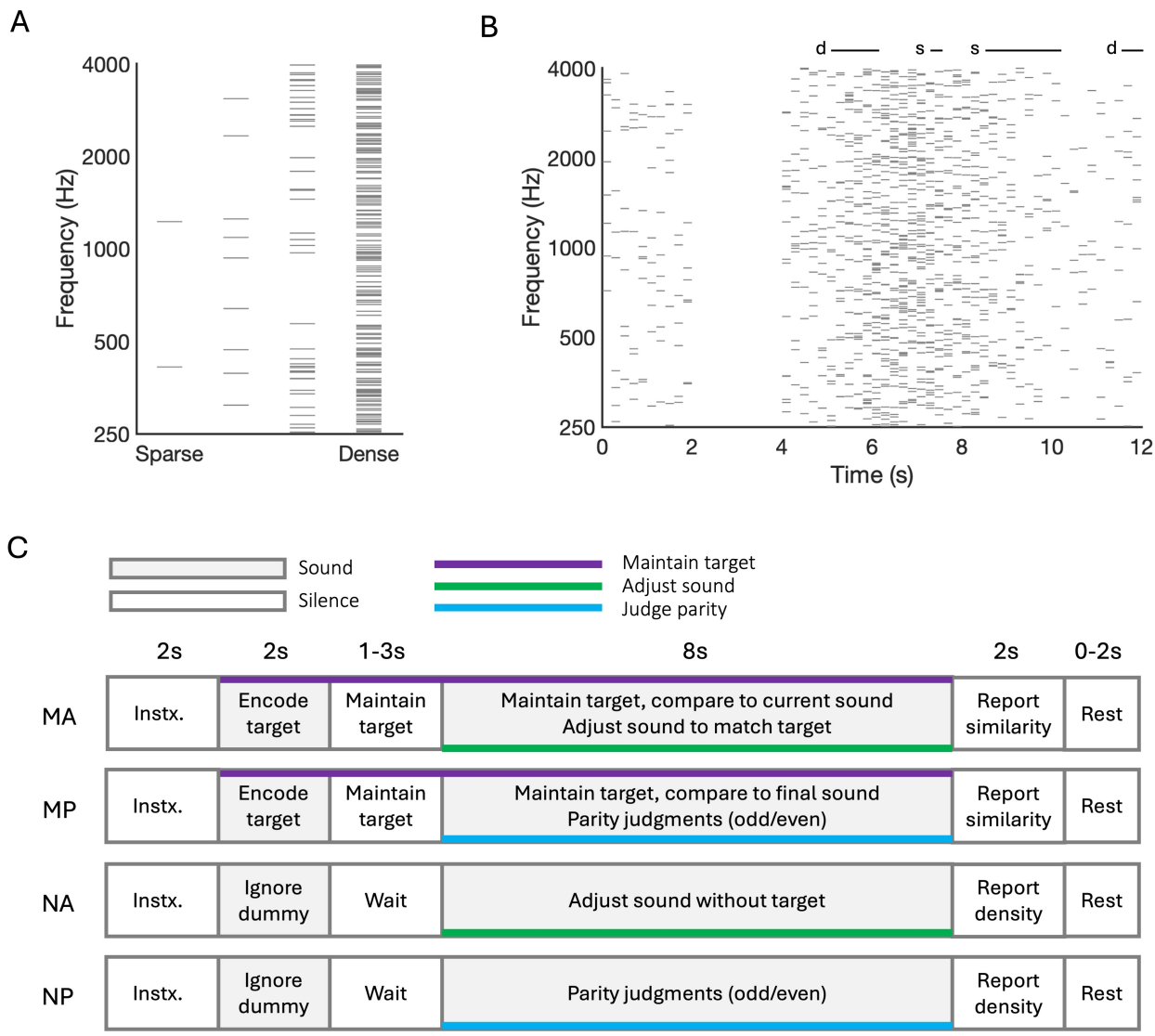

Figure 1: Stimuli and experimental design. A) Four stacks ranging in spectral density from sparse ("beepy", left) to dense ("noisy", right) based on the number of pure tone components. In the initial behavioural experiment participants judged whether the second in a pair of stacks was beepier or noisier than the first. **B)** Example of target sound (starting at 0s), maintenance (starting at 2s), and adjustment period (starting at 4s) in an MA (memory adjust) trial in the fMRI experiment. Button presses (reflecting attempts to match the target density) are shown as 'd' (make denser) and 's' (make sparser). Horizontal lines represent durations of button presses. **C)** Structure of trials in each of the four conditions. Conditions with labels containing 'M' involved maintaining a target density in memory (purple lines) and reporting its similarity to that at the end of a subsequent series of stacks; those containing 'N' did not - instead participants reported how beepy or noisy the sound at the end of the series of stacks was. Conditions with labels containing 'A' (green lines) involved adjusting the ongoing series of stacks (either to match the target density in the MA condition, or at will in the NA condition); those containing 'P' (blue lines) instead required participants to report the parity of each a series of spoken digits (i.e. whether it was odd or even).

Tone stacks and digits were present in all conditions, including when task-irrelevant. Instx. = Instructions, MA = memory adjust, MP = memory parity, NA = no-memory adjust, NP = no-memory parity.

Participants

Ten individuals (aged 21-40 years, median 26.5 years, 4 males, 6 females) with self-reported normal hearing took part in the initial behavioural experiment. A different group of 30 right-handed individuals with no reported neurological or hearing impairment took part in the fMRI experiment. Data from 25 of these (aged 19-40 years, median 24 years, 12 males, 13 females) were included in the analysis. Of the remaining five participants, one did not complete the experiment, two performed more than two standard deviations below the group mean in the adjustment task (see fMRI experiment procedure), and three (including one of the poor performers) moved more than 3 mm (one voxel) in the scanner. Participants were not selected on the basis of musical training in either experiment. The study was approved by the University College London Research Ethics Committee. Informed consent was obtained from all participants, who were compensated for their time and travel.

Behavioural experimental procedure

The purpose of the behavioural experiment was to establish how well participants could discriminate different levels of tone stack density and whether reaction times were affected by the physical layout of response keys. After familiarisation with the density feature and instruction that avoided language relating to space, participants heard pairs of 200-ms tone stacks separated by 1s of silence. Participants had to respond whether the second stack was “beepier” or “noisier” than the first, as quickly and accurately as possible. Different pairs of keys were mapped to “beepier” and “noisier” responses in eight blocks. In two blocks the “down” arrow was used for a “beepier” response and the “up” arrow for a “noisier” response; in another two blocks this was reversed; in two further blocks the “left” arrow key was assigned to “beepier” and the “right” arrow to “noisier”; in a final two blocks this was reversed. Block order was counterbalanced over participants. The density difference between the first and second stack in a trial was adaptively tracked using a two-down, one-up staircase procedure converging on the participant’s 70.7% correct threshold (averaging over the final two of six reversals, step size 1/3 until second reversal then 1/6). Two adaptive tracks were run in parallel in each of the eight blocks, resulting in sixteen tracks. Feedback was provided after each response.

Online training for fMRI participants

To ensure that participants were proficient at the tasks before scanning, we provided an online version of the main experiment (presented in Gorilla with custom JavaScript code) for training at home during the preceding week. Participants were familiarised with the density manipulation and then practised each element of each task (described in the next section) with feedback, building up to performing several trials of the full experiment. Several further training trials were administered immediately prior to scanning.

fMRI experimental procedure

Participants took part in four experimental runs in the scanner, each lasting 8.5 minutes and comprising 28 trials. Each run contained seven trials of each of four conditions, which separately manipulated the presence of memory and adjustment task components while balancing acoustics and button presses. Figure 1C illustrates the trial structure for each condition. In both the “Memory Adjust” (MA) and "Memory Parity" (MP) conditions, participants held in mind the density of a target sound over a maintenance period. The target consisted of ten stacks, all having the same density but containing different randomly selected frequencies. In the MA condition participants then adjusted the density of a series of stacks (with starting density chosen randomly) to match the target density (Figure 1B). At the end of the trial, they rated how close in density the final sound was to the target. In the MP condition after hearing the target they performed an “odd/even” task on a series of spoken digits. They then turned their attention to the end of an ongoing series of tone stacks and rated its similarity to the initial target. The “No-Memory Adjust” (NA) and "No-Memory Parity" (NP) conditions did not include a target. In the NA condition, after hearing a series of stacks of mixed density, participants adjusted a new series of stacks at will, i.e. not toward any target. They then rated how “beepy” or “noisy” the final adjusted stack was. The NP condition also began with a series of stacks of mixed density, was followed by the “odd/even” task on spoken digits and ended with a rating of how “beepy” or “noisy” the final stack of an ongoing series was. Trials began with two seconds of silence while instructions were displayed on screen. These varied with condition, included a reminder of the available response options, were shown in black text on a light grey background, and covered all three phases of the trial (see Table 1).

Table 1. Participant instructions for each condition

Condition code	Condition description	Phase 1 instructions	Phase 2 instructions	Phase 3 instructions
MA	Memory, Adjust	Store	Adjust	Compare
MP	Memory, Parity	Store	Odd/Even	Compare
NA	Non-memory, Adjust	Ignore	Adjust	Beepy/Noisy
NP	Non-memory, Parity	Ignore	Odd/Even	Beepy/Noisy

Once the sounds started, the instructions for the relevant phase were highlighted in white. The initial sound in all conditions was a series of ten 190-ms stacks, each followed by 10 ms of silence. In the MA and MP conditions the density of these stacks was set to a fixed target value, the specific frequencies varying from stack to stack over the resulting 2-s target. In the NA and NP conditions these initial stacks instead alternated between the lowest- and highest-density values. This was to emphasise that they formed a "dummy" sound that was to be ignored, while matching the average spectrum and density across conditions. In all conditions, the 2-s sound was followed by 1-3 s of silence, sampled from a rectangular distribution – in the MA and MP conditions this silence acted as a working memory maintenance phase. Over the next 8 s two simultaneous sound streams were heard: (1) a series of 40 stacks (each lasting 190 ms and followed by 10 ms of silence) and (2) between one and six spoken digits. The value of each digit was randomly selected between 1 and 10 and spoken by either a male or female voice, also randomly selected. Digits could appear in slots beginning at one-second intervals from second two of the eight-second phase. This left the first and final second free of digits, such that only the tone stacks were audible. In the MA and NA (adjustment) conditions participants ignored the digits and directed attention to the tone stacks throughout. They held down one right-hand button to increase the density of the subsequent tone stacks, and another right-hand button to reduce it. In the MA condition they were instructed to try to match the target as closely as possible, using as much of the eight seconds as needed to make multiple adjustments. In the NA condition they adjusted the sounds at will and were asked to use a similar number of presses as in the MA trials. When no button was pressed, the density remained fixed from stack to stack although the specific frequency components changed.

In the MP and NP (parity) conditions, participants attended to spoken digits and responded via one of two right-hand buttons as to whether each digit was odd or even (a similar task has served as an appropriate baseline for hippocampal studies in the visual domain; Stark and Squire, 2001). To try to match the number of button presses across conditions we set the number of digits presented in each trial to the number of button presses during the previous MA or NA trial plus the mean number of digits for which no response was made across all previous MP and NP trials (or 0.5 when no such trials were available at the start of a block), rounded up or down (at random) to the nearest integer. For the last

second of this 8-s section of MP and NP trials, participants redirected their attention to the final few tone stacks. To match acoustics across conditions, in these MP and NP trials the densities of the ongoing tone stacks matched those generated in the most recent MA or NA trial respectively. Identity, speaker, and timing of (ignored) digits in the MA and NA trials were identical to those in the most recent MP or NP trials respectively (or, when no previous trials were available at the start of a block, to those in a randomly generated dummy trial). In the MA and MP conditions, the target density and starting density of the 8-s tone series of stacks for each trial were randomly drawn from a predetermined set of 28 pairs that would generate a range of expected trajectories spanning the density space with equal sampling of high- and low-density sounds. In the NA and NP conditions the starting density of the 8-s series of tone stacks for each trial was drawn from the same set of 28 pairs (with the target density disregarded).

The final phase of each trial required a judgment of either how different the density of the final tone stack was to that of the target (MA and MP trials; response options: "Very similar", "Somewhat similar", "Somewhat different", "Very different") or how beepy/noisy the final tone stack was (NA and NP trials; response options: "Very beepy", "Somewhat beepy", "Somewhat noisy", "Very noisy"). Participants had three seconds to respond using one of four left-hand buttons. After a pause of between 0 and 2 seconds (sampled from a rectangular distribution) the next trial began. No feedback was provided. The 28 trials in a block were grouped into seven sets of four (not made explicit to participants), each set containing one trial of each condition. Ordering within each set was pseudo-randomised, with the constraint that the MA trial appeared earlier than the NA trial, and the MP trial appeared earlier than the NP trial. This ensured that the 8-s series of tone stacks in the NA and NP trials could be matched to those in the previous MA or NA trials, while preventing two trials of the same condition occurring in succession.

The first two experimental blocks were separated by a break of up to two minutes. These were followed by field mapping and anatomical scans (apart from for one participant whose anatomical scan was obtained at the start of the session), lasting a total of around ten minutes. The final two experimental blocks followed and were also separated by a break of up to two minutes. Sounds were presented through an Edirol UA-4FX (Roland Corporation, Shuzuoka) USB soundcard and Ear-Tone Etymotics tube earphones (Etymotic Research, Inc.) with foam tips. Levels were tested and adjusted at the start of the session to ensure that both the tone stacks and spoken digits were audible over the scanner noise. Instructions were displayed via an Epson EB-L1100U projector and viewed with a head-coil-mounted mirror. The experiment was controlled using Psychtoolbox and custom MATLAB code.

261 ***MRI data acquisition***

262 Data were collected using a 3-Tesla Siemens MAGNETOM Prisma MR scanner (Siemens Healthcare)
263 with a 32-channel receive head coil at the Wellcome Centre for Human Neuroimaging (London, UK).
264 Whole-brain $T2^*$-weighted functional images were acquired using 3D echo-planar imaging with field of
265 view 192 x 192 x 144 mm, voxel size 3 mm isotropic, 48 transverse slices, 3D acceleration factor 2,
266 repetition time (TR) 0.044 s, volume acquisition time 1.056 s, anterior-to-posterior phase encoding, and
267 bandwidth 2298 Hz/Px. The accelerated functional images were reconstructed using a motion-robust
268 higher-order sensitivity encoding approach (https://github.com/fil-physics/gadgetron-
269 matlab/tree/master/FIL-recon). Respiratory signals were obtained with a breathing belt. Field maps
270 (short echo time (TE) = 10.00 ms, long TE = 12.46 ms) and a whole-brain T1-weighted anatomical
271 image (MPRAGE, field of view 256 x 256 x 176 mm, voxel size 1 mm isotropic, 176 transverse slices,
272 GRAPPA acceleration factor 2, TR = 2530 ms, TE = 3.34 ms) were acquired during the same scanning
273 session.

274 ***MRI preprocessing***

275 MRI data were processed in SPM12 (Wellcome Centre for Human Neuroimaging). Each participant's
276 functional images were unwarped using their field map and realigned to the first volume. Functional and
277 anatomical images were coregistered to the mean functional image. For the univariate analyses, the
278 coregistered images were normalised to the SPM12 template (avg305T1) in MNI space and the
279 functional images were spatially smoothed using a Gaussian kernel with 6 mm full-width at half-
280 maximum.

281 ***Behavioural data analysis***

282 For the behavioural experiment, participants' just-noticeable-differences (JNDs) were obtained as a
283 function of density. Reaction times were log-transformed and analysed as a function of button mapping
284 using a repeated-measures 4-way ANOVA. For the fMRI experiment, navigation success was scored
285 using the absolute number of steps in density space between the final adjusted sound and the target.
286 Parity judgments were scored by dividing the number of matches by the larger of two values: the number
287 of digits presented or the number of responses made. When determining matches, the series of responses
288 in a trial was allowed to be dislocated by an extra or missing response. Accuracy of responses to the final
289 question in each trial was assessed by calculating the Spearman's rank correlation of the responses (1-4)
290 with the true values (closeness in density for MA and MP conditions; actual density for NA and NP

conditions), after replacing missing responses with a value of 2.5 (the midpoint of both rating scales). Proportions were compared following arcsine square root transformation, and correlation coefficients following the Fisher *z*-transformation.

Univariate fMRI analyses

In a first level analysis a General Linear Model (GLM) was created for each participant's fMRI time series data. Regressors of no interest were included for motion and respiration. Task phases of interest were modelled as boxcar functions and convolved with the canonical haemodynamic response function. A high pass filter of 1/128 Hz (corresponding to twice the longest interval between trials of the same condition) was applied to remove low frequency noise, and SPM12's "FAST" option (appropriate for rapid imaging sequences; Corbin et al., 2018) was used to model temporal correlations. To distinguish activity relating to the different task components we first modelled the whole trial period and tested for main effects of memory [contrast: (MA+MP)-(NA+NP)] and adjustment [contrast: (MA+NA)-(MP+NP)], and for their interaction [contrast: (MA-MP)-(NA-NP)]. In a control analysis we modelled these effects only during the portion of the MA trials during which adjustment responses were made (and matching portions of trials in other conditions). Effects of density (all trials), distance from target (MA trials), time in trial (MA trials), and performance in adjustment (MA trials) and parity judgment (MP trials) tasks were examined by entering centered and orthogonalised linear parametric modulators into the GLM over the relevant time intervals.

For each comparison of interest, participants' contrast images were entered into a second level analysis, with one-sample *t*-tests conducted at the group level. Statistical parametric maps were obtained and thresholded using a family-wise error- (FWE-) corrected *p*-value of .05, and a minimum cluster size matching the "expected voxels per cluster" value in SPM for the corresponding height threshold. Additional tests with small volume corrections were conducted in three a priori regions of interest, namely bilateral auditory cortex (voxels assigned at least 20% probability of lying in Heschl's gyrus, planum polare, planum temporale, or superior temporal gyrus in the Harvard-Oxford Cortical Structural Atlas), bilateral inferior frontal gyrus pars opercularis and pars triangularis (voxels assigned at least 20% probability of lying in one of these two regions in the Harvard-Oxford Cortical Structural Atlas), and bilateral hippocampus (based on segmentation of the average T1w image across participants using the Automatic Segmentation of Hippocampal Subfields (ASHS) software package, Yushkevich et al., 2014).

Multivariate fMRI analyses

The unsmoothed, unnormalised functional images were entered into two further GLMs. One contained regressors for lower- versus higher-density sounds (splitting the 26 density levels into two groups) and used trials of all conditions. The other contained regressors for navigation in the direction of decreasing versus increasing density and used MA and NA trials. In both models these binary labels were applied to each stack during the adjustment period and could therefore change within a trial. In both GLMs the same regressors of no interest were entered as described in Univariate fMRI analyses above. Multivariate analysis was performed using The Decoding Toolbox (Hebart et al., 2015) to obtain cross-validated whitened Euclidean ("crossnobis") distances between neural representations corresponding to the two category labels in a given model. Further analyses used the same approach to find distances between representations of lower- versus higher-density targets, either during the encoding and maintenance period only, or with inclusion of the adjustment period (in MA and MP conditions). Neural representations were beta weights scaled for each run separately using residuals from the GLM with the "Ledoit-Wolf retain variances" option selected. A spherical volumetric searchlight with 4mm radius was used over the whole brain. Leave-one-run-out cross-validation was applied and the lower diagonal values of the dissimilarity matrices averaged over cross-validation iterations. Each participant's resulting distance image was normalised to the SPM12 template (avg305T1) in MNI space and spatially smoothed using a Gaussian kernel with 6 mm full-width at half-maximum. These were entered into a second level analysis, which proceeded as described in Univariate fMRI analyses.

Code availability

All custom code is available on request.

Results

Tone stack density: discrimination and associations with physical space

In the initial behavioural experiment, just-noticeable differences for density increased with density [$t(9) = 13.717$, $p < .001$, $d = 4.338$; Figure 2A]. For this reason, density values in the fMRI experiment were logarithmically spaced to ensure steps along the density scale were similarly discriminable. Reaction times when comparing the density of two tone stacks was not affected by the spatial mapping of response keys [$F(3, 27) = 0.549$, $p = .653$, $\eta^2_p = .057$; Figure 2B]. When prompted, fewer than half of the

participants in the fMRI experiment reported forming a spatial association with the stimuli (nine associated beepier sounds with "left", one with "right", and two with "up"). To confirm that the group neural results were not driven by this spatial association we also report the relevant analyses by excluding the corresponding participants, obtaining qualitatively similar results.

Behavioural performance in the scanner

In the MA (memory adjustment) condition of the main experiment, participants finished closer to the target than they started in 94% of trials on average (range: 82-100%; Figure 2C), with a mean final distance of 16% of the density scale (range: 9-33%). Participants tended to undershoot the target, that is to remain on the same side of the target on the density scale as they began; on average this occurred in 70% of trials (range: 32-86%; Supplementary Figure S1). Performance did not differ between participants who reported forming spatial associations and those did not who [$t(23) = 0.503$, $p = .620$, $d = .100$]. Parity judgment performance did not differ between the memory and non-memory conditions [MP and NP; $t(24) = 1.132$, $p = .269$, $d = 0.227$; Figure 2D], with an average score of 89% (range: 59-98%). Accuracy in comparing the target density to the final density did not differ significantly between the MA and MP conditions [$t(24) = 1.475$, $p = .139$, $d = 0.298$; Figure 2E], while accuracy in reporting the final density was significantly greater in the NA than the NP condition [$t(24) = 2.441$, $p = .022$, $d = 0.584$].

Matching of motor activity across conditions

There was a significant effect of condition on the number of presses despite our attempt to eliminate this potential confound [$F(3, 72) = 10.256$, $p < .001$, $\eta^2_p = .299$]. Although the majority of participants were well matched (on average a difference of less than one press per trial between pairs of conditions of interest, namely MA versus NA, and MP versus NP), eight participants had more than one extra press on average in adjustment trials (MA, NA) compared to parity trials (MP, NP), and six participants had more than one extra press on average in non-memory trials (NA, NP) compared to memory trials (MA, MP). Eleven participants met both criteria. To confirm that the group neural results were not confounded by activity relating to motor preparation or execution we also report the relevant analyses excluding the corresponding participants, obtaining qualitatively similar results.

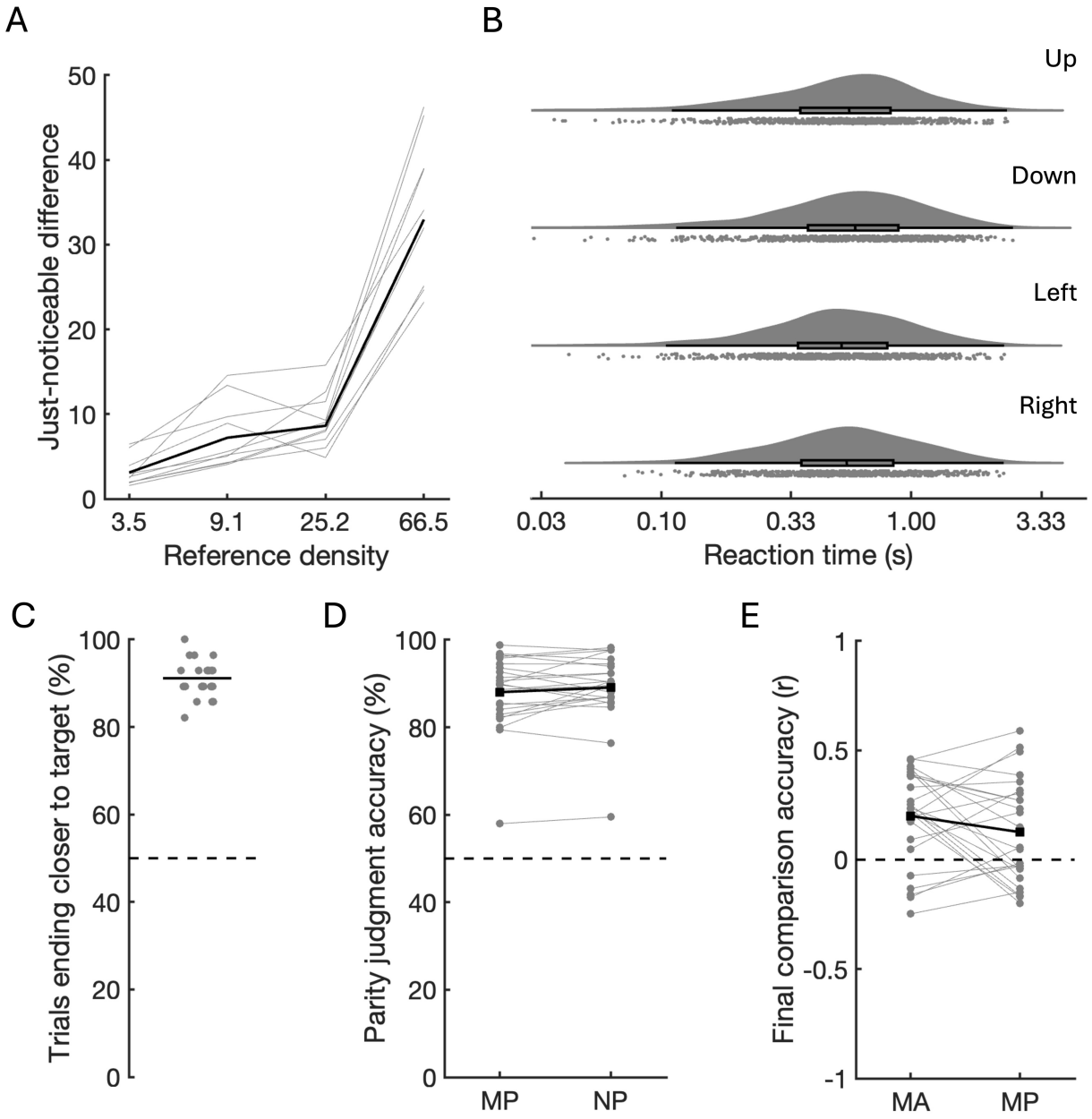

Figure 2: Behavioural results. A) Just-noticeable differences in density increase as a function of density. Grey lines: individual participants in the initial behavioural experiment. Black line: group mean. **B)** Raincloud and box-and-whisker plots of reaction times for correct trials in the initial behavioural experiment. Each plot corresponds to a different button mapping (the arrow key that was mapped to "beepier" responses is shown; the opposite arrow key was mapped to "noisier" responses). Distributions did not differ by condition. **C)** Percentage of MA trials in main experiment in which participants (grey dots) adjusted the ongoing density to be closer to the target than before adjustment. Black line represents mean performance and dotted line represents 50% chance performance. **D)** Percentage accuracy of parity judgments, which did not differ significantly between MP (left) and NP (right) conditions. Joined grey dots represent individual participants. Joined black squares represent group mean performance and dotted line represents 50% chance performance. **E)** Correlation between actual and reported target-versus-final density similarity, which did not differ significantly between MA (left) and MP (right)

conditions. Joined grey dots represent individual participants. Joined black squares represent group mean performance and dotted line represents chance performance.

Neural responses to sound and representation of tone stack density

Sites that were more active during sound compared to silence were bilateral auditory cortices in Heschl's gyrus, planum temporale, and posterior superior temporal gyrus, along with parietal, somatomotor, frontal, parietal and cerebellar areas (see Table 2). This contrast did not reflect purely sensory processes since cognitive and motor demands also differed when sound was presented compared to when it was not. During the adjustment phase (or equivalent period in the parity judgment task), activity in a more restricted set of brain regions, shown in Figure 3A and Supplementary Table S1, was parametrically modulated by the density of the tone stacks. Activity was greater for the sparser (less noise-like) tone stacks - particularly in bilateral planum polare but also in Heschl's gyrus and along the temporal convexity. During the same phase, multivoxel patterns for sparser versus denser sounds were also most distinct at these sites (Figure 3B, Table 3). After small volume correction, a significant representation of density was also found in right inferior frontal gyrus (pars opercularis and triangularis; Supplementary Table S2), but not hippocampus.

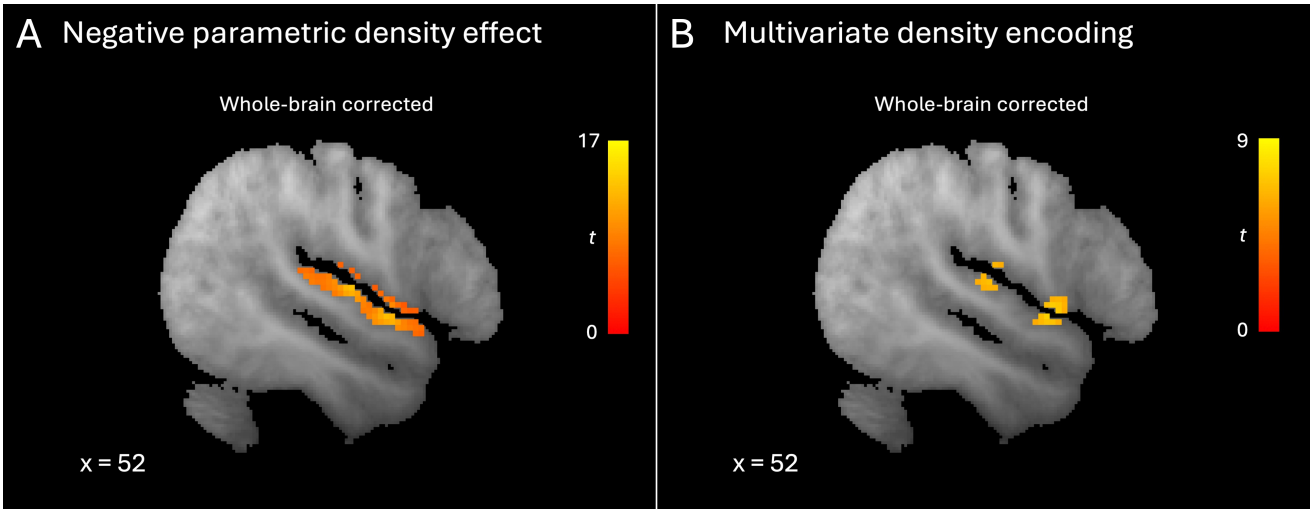

Figure 3: Representation of tone stack density. A) Sagittal slice showing negative parametric effect of density in auditory cortex, i.e. a lower univariate response to progressively denser tone stacks. **B)** Sagittal slice showing accuracy (transformed to *t*-score) of multivariate decoding of density in auditory cortex. All clusters significant at $p < .05$ (familywise error-corrected, whole brain).

412 **Table 2. Clusters more active during sound presentation than silence**

Regions	Voxels	Peak MNI coordinates			Peak *t*-value
Right planum temporale, Heschl's gyrus, superior temporal gyrus (posterior)	407	56	-14	6	10.29
Left planum temporale, Heschl's gyrus, superior temporal gyrus (posterior)	333	-54	-28	10	9.65
Left supplementary motor area, superior frontal gyrus	131	-6	8	54	9.45
Left precentral gyrus, postcentral gyrus	174	-40	18	60	8.89
Right superior frontal gyrus, supplementary motor area	108	6	10	58	8.11
Left supramarginal gyrus (anterior)	72	-52	-32	50	7.79
Left precentral gyrus	16	-56	6	18	7.55
Right inferior frontal gyrus (pars opercularis)	14	52	10	10	6.85
Left precentral gyrus	7	-28	-6	62	6.49
Right cerebellum (lobe V)	5	20	-52	-24	6.19

Clusters significant at $p < .05$ (FWE-corrected), minimum cluster size: 5 voxels

413

414 **Table 3. Clusters with multivoxel representation of density**

Regions	Voxels	Peak MNI coordinates			Peak *t*-value
Right planum polare	63	54	6	-4	8.37
Right planum temporale	125	64	-20	10	7.80
Left planum polare	23	-50	-8	-2	7.71
Left Heschl's gyrus, planum temporale	100	-48	-20	10	7.04
Left central opercular cortex	11	-58	-18	16	6.74
Left superior temporal gyrus (posterior)	6	-52	-16	-4	6.61

Clusters significant at $p < .05$ (FWE-corrected), minimum cluster size: 5 voxels

415

416 ***Memory-related neural activity***

417 Next we contrasted activity in the two conditions in which participants held a target density in mind (MA
418 and MP) versus those with no such target (NA and NP), considering activity throughout the trial. This
419 revealed memory-related activity in bilateral anterior insula, as well as frontal pole, middle frontal gyrus,
420 and cerebellum (Figure 4 middle, right; Table 4). After small volume correction, memory-related activity
421 was also found in bilateral inferior frontal gyrus (pars opercularis and pars triangularis, Figure 4 (left),
422 Supplementary Table S3), but not hippocampus. No regions exhibited a multivoxel representation of the
423 target density in the MA and MP trials, whether considering just the encoding and maintenance periods
424 or the whole trial. Note that target sounds were only physically present for a quarter of the amount of
425 time as the adjustment sounds that could be decoded in auditory cortex (previous section).

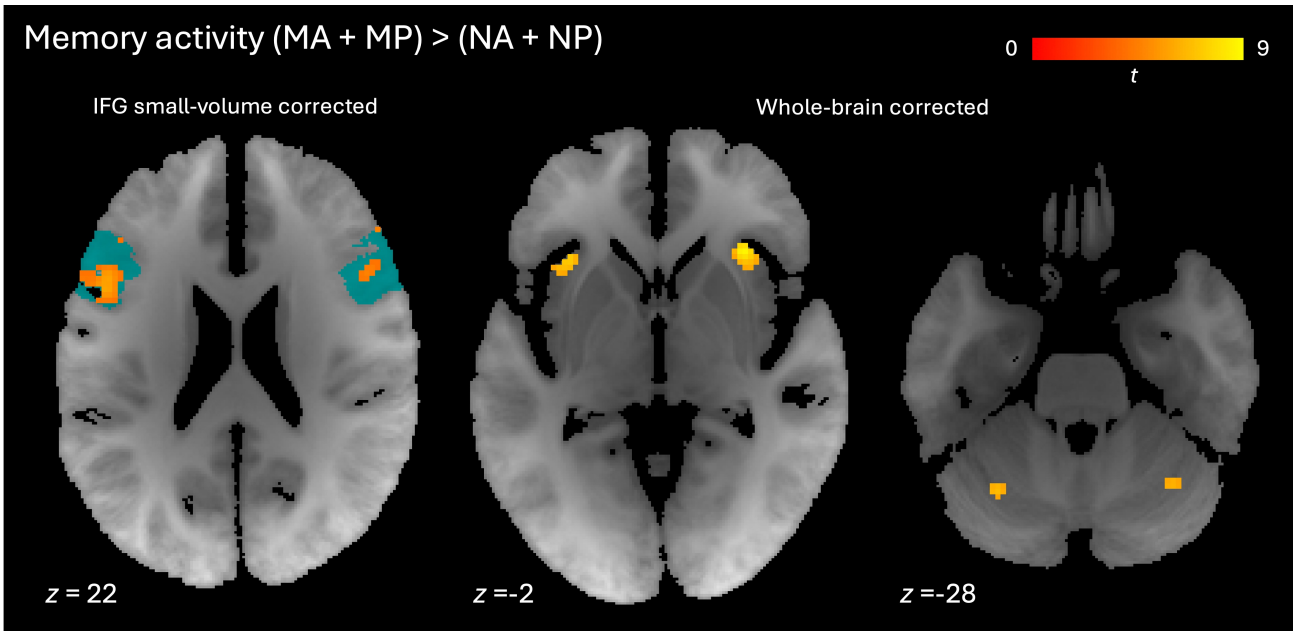

Figure 4: Activity associated with target memory. Axial slices showing clusters with greater activity for MA and MP conditions than NA and NP conditions. **Left**: Inferior frontal gyrus clusters significant at $p < .05$ (familywise error-corrected, small volume for bilateral inferior frontal gyrus). **Middle**: Anterior insular clusters significant at $p < .05$ (familywise error-corrected, whole brain). **Right**: Cerebellar clusters significant at $p < .05$ (familywise error-corrected, whole brain). Red-yellow gradient represents *t*-score. Blue indicates regions of interest for small volume corrections. IFG = Inferior frontal gyrus.

Table 4. Clusters more active during memory than non-memory conditions

Regions	Voxels	Peak MNI coordinates			Peak *t*-value
Right insular cortex	58	30	24	0	8.92
Right frontal pole	30	46	40	28	8.23
Left insular cortex	43	-32	20	-4	7.50
Left middle frontal gyrus	6	-44	2	54	6.90
Left cerebellum (lobe VI)	13	-30	-64	-28	6.76
Right cerebellum (crus I)	11	34	-62	-28	6.46

Clusters significant at $p < .05$ (FWE-corrected), minimum cluster size: 5 voxels

Adjustment-related neural activity

The contrast of adjustment conditions (MA + NA) minus non-adjustment conditions (MP + NP) revealed activity in our regions of interest of hippocampus and inferior frontal gyrus after small volume correction (Figure 5; Supplementary Table S4). The corresponding clusters remained significant when excluding participants who reported noticing a spatial mapping of density (Supplementary Table S5) or for whom button presses were not well matched across conditions (Supplementary Table S6). We also considered

the fact that even when button presses were comparable across conditions, subjects could choose to stop adjusting before the end of an adjustment trial whereas they needed to remain alert throughout parity judgment trials, even if they made no further presses. It is therefore possible that some differences were driven by task-negative (e.g. mind-wandering) activity toward the end of adjustment trials. In an analysis including only the interval in a given MA or NA trial during which adjustments actually occurred and using the same intervals in matching MP and NP trials, the more anterior of the hippocampal clusters in Figure 5 was no longer significant (Supplementary Table S7). At the whole brain level, additional frontal, parietal, insular, cingulate and cerebellar sites also showed adjustment-related activity (Table 5, Figure 6).

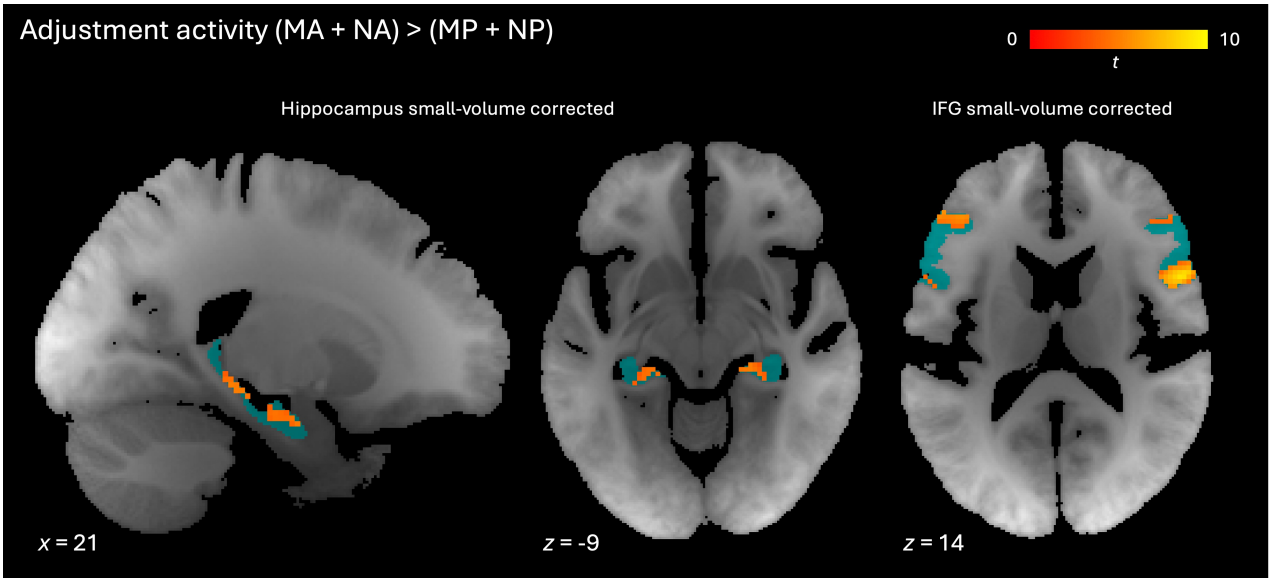

Figure 5: Activity associated with density adjustment in regions of interest. Clusters showing greater activity for MA and NA conditions than MP and NP conditions. **Left**: Sagittal slice with hippocampal clusters significant at $p < .05$ (familywise error-corrected, small volume for bilateral hippocampus). **Middle**: Axial slice with hippocampal clusters significant at $p < .05$ (familywise error-corrected, small volume for bilateral hippocampus). **Right**: Axial slice with inferior frontal gyrus clusters significant at $p < .05$ (familywise error-corrected, small volume for bilateral inferior frontal gyrus). Red-yellow gradient represents *t*-score. Blue indicates regions of interest for small volume corrections. IFG = Inferior frontal gyrus.

Table 5. Clusters more active during adjustment than parity conditions

Regions	Voxels	Peak MNI coordinates			Peak *t*-value
Right frontal pole	471	44	42	6	13.32
Left cerebellum (crus I, crus II, lobe VI)	945	-28	-72	-28	12.39
Right supramarginal gyrus (posterior, anterior)	618	56	-40	48	10.45
Right precentral gyrus, inferior frontal gyrus (pars opercularis/triangularis)	201	54	10	14	9.02
Left supramarginal gyrus (anterior), angular gyrus	315	-58	-34	44	8.66
Left insular cortex	67	-40	-4	6	8.58
Right frontal pole	59	40	48	22	8.37
Right insular cortex	65	40	0	4	8.34
Left frontal pole	264	-42	52	4	8.27
Right cerebellum (crus II)	280	38	-70	-42	8.07
Right inferior temporal gyrus (posterior)	11	56	-24	-22	7.85
Left frontal pole	10	-26	44	-14	7.32
Left lateral occipital cortex (superior)	54	-44	-64	42	7.25
Right supplementary motor area	16	4	26	42	7.03
Right cingulate gyrus (posterior)	45	6	-34	44	7.02
Right frontal pole	11	16	60	-6	6.82
Right central opercular cortex	7	46	-2	8	6.69
Right superior frontal gyrus	9	22	12	64	6.61
Left middle frontal gyrus	17	-36	30	44	6.48
Left insular cortex	6	-38	-16	-2	6.45
Right middle frontal gyrus	6	44	26	44	6.43
Left frontal pole	7	-42	42	26	6.38

Clusters significant at $p < .05$ (FWE-corrected), minimum cluster size: 6 voxels

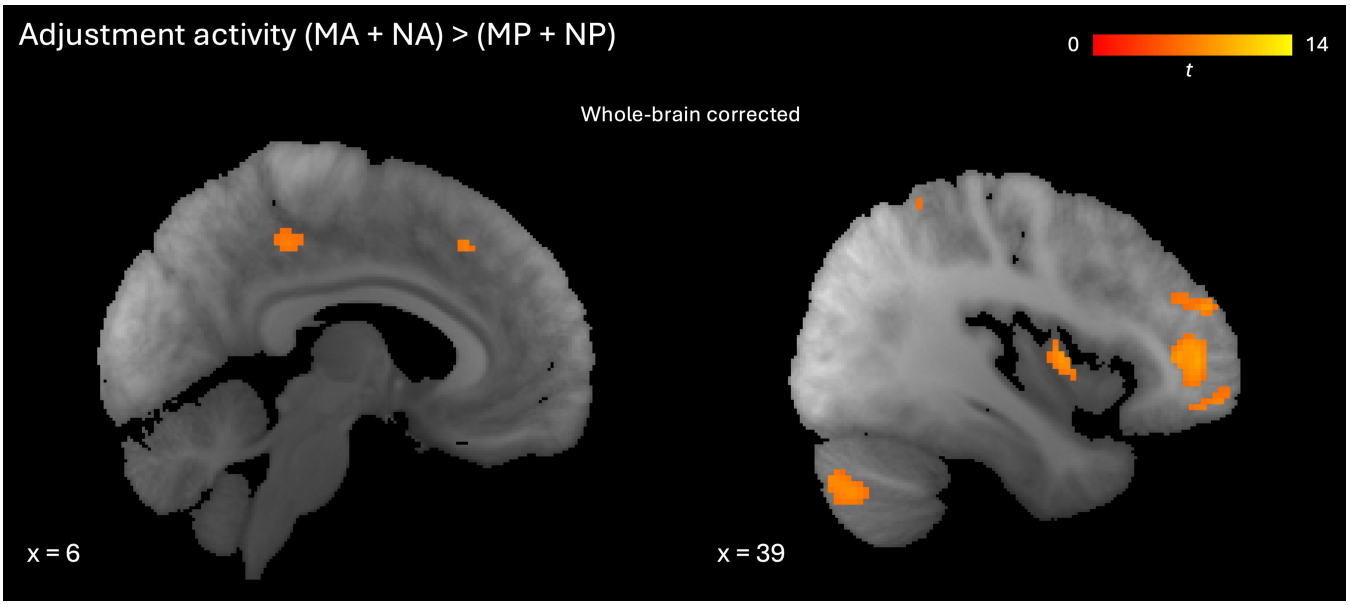

Figure 6: Activity associated with density adjustment in other regions. Clusters showing greater activity for MA and NA conditions than MP and NP conditions significant at $p < .05$ (familywise error-corrected, whole brain). **Left**: Sagittal slice with clusters in posterior cingulate cortex and supplementary motor area. **Right**: Sagittal slice with clusters in frontal pole, insula, and cerebellum. Red-yellow gradient represents *t*-score.

Navigation toward a target

We next looked for sites that showed an interaction between memory and adjustment, i.e. for which adjustment-related activity was greatest when there was a target to be navigated toward. No regions survived a family-wise error correction at $p < .05$, however at a more liberal threshold ($p < .001$ uncorrected), bilateral orbitofrontal cortex was more active for navigation toward a target than for aimless navigation (Figure 7A; Supplementary Table S8). This result was qualitatively unaffected by the exclusion of subjects reporting spatial associations (Supplementary Table S9). There was no interaction effect in any of our regions of interest.

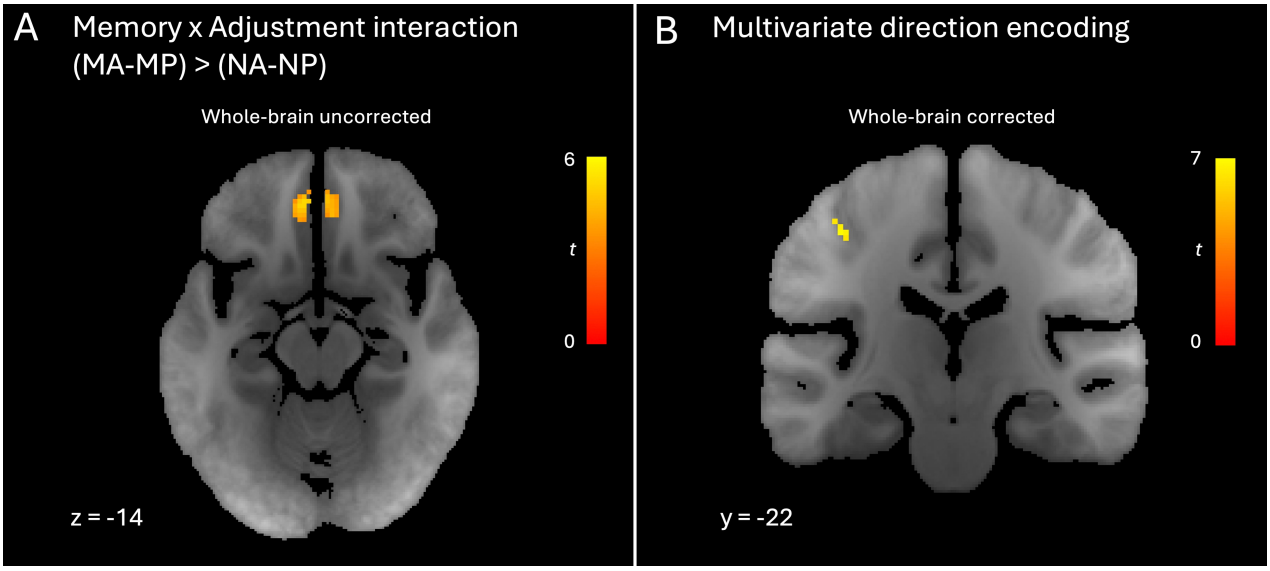

Figure 7: Adjustment activity relating to target presence and direction. A) Axial slice showing interaction between memory and adjustment in orbitofrontal cortex. Clusters significant at $p < .001$ (uncorrected). **B)** Coronal slice showing accuracy (transformed to *t*-score) of multivariate decoding of navigation direction in left postcentral gyrus. Cluster significant at $p < .05$ (familywise error-corrected, whole brain).

Direction and distance from target

The only areas encoding adjustment direction in MA and NA trials were left postcentral gyrus (Figure 7B) and right intracalcarine sulcus (Supplementary Table S10). The former may relate to the specific fingers used to adjust sounds to become sparser or denser. To investigate correlates of distance from target, we had to account for its negative correlation with time in trial. We assessed the unique contribution of distance from target in an analysis in which elapsed time during the adjustment period was entered as an initial regressor, and distance from target as a second orthogonal regressor. This

analysis included only the interval in each MA or NA trial during which adjustments actually occurred, along with matching intervals in the corresponding MP and NP trials. No clusters showed effects of distance at the corrected whole brain level, nor did our regions of interest after small volume correction. There were significant clusters at the $p < .001$ uncorrected level in frontal and parietal cortex (Table 6), with the largest cluster in left postcentral gyrus likely reflecting a greater likelihood of button pressing when participants were more distant from the target; this peak was close to that shown in Figure 7B at which adjustment direction was encoded. Effects of elapsed time can be found in Supplementary Tables S11 and S12.

Table 6. Clusters with adjustment activity modulated by distance from target (uncorrected)

Modulation direction	Regions	Voxels	Peak MNI coordinates			Peak *t*-value
Positive	Left postcentral gyrus	251	-50	-22	50	4.64
Negative	Right supramarginal gyrus	69	60	-32	46	4.38
	Right frontal pole	45	46	48	8	4.29
	Right postcentral gyrus, precentral gyrus	48	40	-26	60	4.18

Clusters significant at $p < .001$ (uncorrected), minimum cluster size: 31 voxels

Navigation performance as a function of encoding and maintenance activity

Navigation to an auditory target requires that the target is first adequately encoded. In a final analysis we looked for brain areas in which encoding and maintenance activity was parametrically associated with performance in the MA trials (i.e. negatively related to the final distance from the target; see Table 7, Figure 8). Two peaks in right auditory cortex were well aligned with those from which density could be decoded (Figure 8 bottom left, compare Figure 3B). Other sites with activity associated with subsequent performance were posterior cingulate gyrus (Figure 8 bottom right) and, after small-volume corrections, hippocampus and inferior frontal gyrus (Figure 8 top, Supplementary Table S13). These effects were specific to the adjustment task: none of these clusters' encoding/maintenance activity was modulated by performance in the parity task in the MP trials.

Table 7. Clusters with encoding/maintenance activity positively modulated by adjustment performance

Regions	Voxels	Peak MNI coordinates			Peak *t*-value
Right middle frontal gyrus	17	-32	12	60	9.26
Right Heschl's gyrus	43	54	-14	4	7.32
Right planum temporale	12	62	-26	12	7.12
Left cingulate gyrus (posterior)	16	-2	-32	30	7.03
Right planum polare	5	52	-2	-6	7.02
Right cingulate gyrus (posterior)	19	2	-34	30	6.96
Left occipital pole	7	-18	-100	10	6.55

Clusters significant at $p < .05$ (FWE-corrected), minimum cluster size: 5 voxels

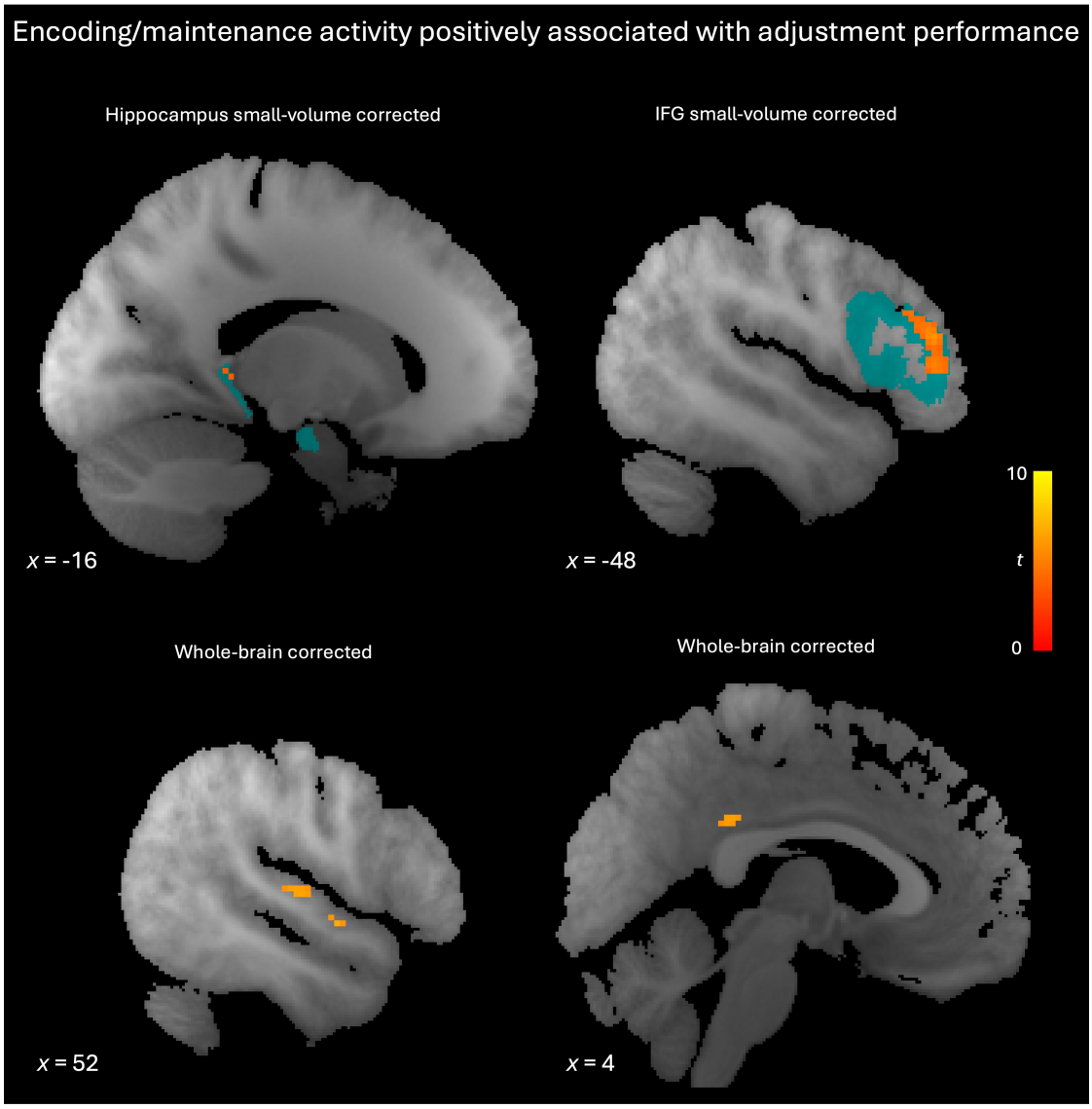

Figure 8: Encoding and maintenance activity positively associated with navigation performance. Top left: Sagittal slice with hippocampal cluster significant at $p < .05$ (familywise error-corrected, small volume for

bilateral hippocampus). **Top right:** Sagittal slice with inferior frontal gyrus clusters significant at $p < .05$ (familywise error-corrected, small volume for bilateral inferior frontal gyrus). **Bottom left:** Sagittal slice with clusters in auditory cortex (familywise error-corrected, whole brain). **Bottom right:** Sagittal slice with cluster in posterior cingulate cortex (familywise error-corrected, whole brain). Red-yellow gradient represents *t*-score. Blue indicates regions of interest for small volume corrections. IFG = Inferior frontal gyrus.

Discussion

We studied the neural basis for perceiving, storing, and "navigating" toward an auditory target, defined by the density of its acoustic spectrum, a parameter that participants did not consistently map to any physical spatial dimension. It was represented most strongly in non-primary auditory cortex, and adjusting it engaged a broad network including inferior frontal gyrus and hippocampus. Orbitofrontal cortex was differentially activated when adjustments were made to match a target sound, compared to aimless navigation. The level of activity in auditory cortex, inferior frontal gyrus, hippocampus, and posterior cingulate during target encoding and maintenance was positively associated with navigation performance.

Our study was partly motivated by suggestions that hippocampus and neighbouring entorhinal cortex, known to be involved in mapping physical space, can also represent task-relevant sensory spaces (Killian et al., 2012; Aronov et al., 2017; Bao et al., 2019). The adjustment-related activity we observed in hippocampus and elsewhere was not driven by "low-level" stimulus features (which were matched across conditions), nor by motor demands or direct spatial associations (which control analyses accounted for). An anterior hippocampal cluster dominated by activity after adjustments finished may reflect greater mind-wandering toward the end of these trials (Zeidman et al., 2016). Posterior hippocampus showed more robust activation; it is involved in retrieving sounds from working memory (Kumar et al., 2016) and in spatial navigation (Kühn and Gallinat, 2014) - for example this region shows experience-dependent structural changes in taxi drivers (Maguire et al., 2000). Previous work also demonstrated structural changes in hippocampus (although more anteriorly) associated with a form of navigation through an auditory space in highly trained piano tuners (Teki et al., 2012). Our study supports hippocampal activation during acoustic navigation in novice participants.

Although the above suggests parallels in the neural basis for spatial and auditory navigation, hippocampal activity patterns did not distinguish sparser from denser sounds. Aronov et al. (2017) found individual hippocampal neurons that tiled frequency space when relevant to a rat engaged in a related adjustment task. We may not have had a strong enough hippocampal signal for any spectral density

coding to be identified with the low temporal resolution of fMRI; other techniques such as single neuron recordings from patients may prove fruitful. An alternative explanation is that hippocampus only represents dimensions readily mapped to physical space, such as frequency. Rusconi et al. (2006) showed that mapping sounds that were higher or lower in frequency or pitch to keys positioned higher or lower on a computer keyboard, respectively, led to quicker responses than under the reverse mapping - even when the task was unrelated to frequency. Under this explanation, spatially tuned machinery in rat hippocampus would have been readily co-opted by space-associated sounds in Aronov et al. (2017). We found no such consistent "dimensional overlap" for our stimulus, although a subset of participants reported spatial associations. Another possibility is that neurons in Aronov et al. (2017) were tracking progress toward a goal. Frequencies were always presented in the same order, although their rate of change varied. The observed tuning could in fact reflect firing of hippocampal "time cells" that adapt their temporal tuning scale in accordance with task demands (Macdonald et al., 2011, Shimbo et al., 2021). This argument is reinforced by recent findings that apparent frequency-specific firing in hippocampus or entorhinal cortex is absent in trials in which animals fail to stop at the target sound (Nguyen et al., 2024; Zutshi et al., 2024). We deliberately chose trial-specific target and start densities, such that participants' trajectories varied over trials, with a view to identifying tuning specific to the acoustic feature. Density tuning was most robust in planum polare and also present in planum temporale and anterior parts of Heschl's gyrus. It was driven by stronger responses to sparser sounds (chords with individually identifiable frequency components) than denser (more noise-like) ones. This difference might be due in part to greater adaptation within frequency channels for denser tone stacks. Planum polare is also known to reflect higher-order acoustic features, such as pitch change (Warren and Griffiths, 2003) and spectrotemporal correlation (Overath et al., 2008), and to respond to music over scrambled musical sounds (Angulo-Perkins and Concha, 2019).

Although previous work found changes in activity relating to working memory for sound in auditory cortex (Kumar et al., 2016; Linke et al., 2015; Kumar et al., 2021), our contrast comparing memory to non-memory conditions did not. Our silent maintenance period was much shorter (1-3 s) than in other fMRI studies and not designed to be distinguished from the remainder of the trial. Instead, our analysis encompassed the whole trial, which was dominated by periods of auditory stimulation. Any memory-related activity in auditory cortex may have been swamped by responses to the input, present in both memory and no-memory conditions. We did however find memory-related activity in anterior

insula, cerebellum and frontal sites including inferior frontal gyrus, consistent with previous work (Zatorre et al., 1994; Kurth et al., 2010; Kumar et al., 2016; Brissenden et al., 2021; Llorens et al., 2023).

The role of hippocampus during working memory maintenance has been hard to pin down (Axmacher et al., 2007; Jenseon and Squire, 2011; Stretton et al., 2012). Recent studies have described both elevated firing during working memory maintenance in hippocampal cells selective for particular concepts (Daume et al., 2024) and reduced broadband high frequency power at hippocampal sites at which spectrotemporal ripples held in working memory can nonetheless be decoded (Uluç et al., 2023). It has been argued that not only persistent firing (Fuster and Alexander, 1971) but also "activity-silent" mechanisms involving changes in synaptic weights (Mongillo et al., 2008; Miller et al., 2018) can support working memory maintenance. Holding a target sound in mind may therefore not require increases in the ensemble activity observed indirectly in the BOLD signal. We did however find a link between the level of posterior hippocampal activity and subsequent success in the auditory navigation task. This contrasts with the finding of Kumar et al. (2016) where participants with better tone working memory showed a reduced hippocampal signal during maintenance (although activity was elevated above baseline at the group level). It is possible that our behavioural effect was dominated by activity during target presentation, rather than in the subsequent short silent maintenance period.

This link between auditory navigation success and encoding/maintenance activity, together with the navigation-related activity, add to growing evidence for a role of the hippocampus in auditory cognition (Billig et al., 2022), disruption of which may mediate links between hearing loss and dementia (Griffiths et al., 2020). A highly connected structure, in our task the hippocampus likely formed part of a functional network with areas including non-primary auditory cortex where spectral density was encoded. The posterior cingulate was also more active during encoding and maintenance for trials in which participants were subsequently more successful in reaching the target. Changes in posterior cingulate structure and function have been associated with impaired working memory performance in healthy ageing, schizophrenia, and attention deficit hyperactivity disorder (Leech and Sharp, 2014). In our task this region was also more active during adjustment than parity-judgment trials. Reduced connectivity between posterior cingulate and entorhinal cortex is associated with impaired navigation, and six-fold rotational symmetry in the blood-oxygen-level-dependent (BOLD) response has been detected there during navigation in virtual and abstract spaces, suggestive of the presence of grid cell populations (Doeller et al., 2010; Constantinescu et al., 2016). Regions of medial frontal cortex appear to be essential when rats (Basu et al., 2021) or humans (Ciaramelli, 2008; Spiers, 2008) maintain a goal

in physical space. We found clusters in bilateral orbitofrontal cortex that may serve the same purpose during auditory navigation, showing a greater memory effect during the adjustment than the non-adjustment task. Effective connectivity has been demonstrated in humans between auditory cortex and hippocampus on the one hand and orbitofrontal cortex on the other (Rolls et al., 2023). It is another site at which grid-like navigation signals have been detected in the BOLD signal (Constantinescu et al., 2016). A fuller understanding of the network supporting auditory navigation - both holding targets in mind and making adjustments in auditory space to reach them - will require experiments teasing apart contributions of these areas and others in which we observed related activity, such as cerebellum, insula, and multiple frontoparietal sites (Tables 4 and 5), some of which may be domain general (Nozari and Martin, 2024).

Distinguishing activity relating to adjustment and working memory processes required a complex design. The baseline conditions for the adjustment comparison employed a parity-judgment task that minimised hippocampal activity. It required participants to redirect attention between the tone stacks and spoken digits within a trial. This had no significant impact on working memory performance (participants stored the target density similarly well in MA and MP trials) but the "adjustment" effects reported should be interpreted with the nature of the baseline task in mind.

Overall, we find that self-initiated travel in humans along a non-spatial auditory dimension - here acoustic spectral density - engages a brain system overlapping that supporting physical navigation.

Author contributions

Alexander Billig: Conceptualization, Methodology, Software, Formal Analysis, Investigation, Data Curation, Writing - Original Draft, Writing - Review & Editing, Visualization, Project Administration. **William Sedley**: Conceptualization, Methodology, Software, Writing - Review & Editing. **Phillip Gander**: Methodology, Writing - Review & Editing. **Sukhbinder Kumar**: Methodology, Writing - Review & Editing. **Meher Lad**: Methodology, Writing - Review & Editing. **Maria Chait**: Methodology, Writing - Review & Editing. **Yousef Mohammadi**: Methodology, Writing - Review & Editing. **Joel Berger**: Writing - Review & Editing. **Timothy Griffiths**: Conceptualization, Methodology, Writing - Review & Editing, Supervision, Funding Acquisition.

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