**Asymmetries in the representation of space in human auditory cortex depend on the global stimulus context**

Running title: Cortical asymmetries in representing space

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**Abstract**

Studies on humans and other mammals have provided evidence for a two- or three-channel representation of horizontal space in the auditory system, with one channel maximally responsive to each of the left hemispace, right hemispace and, possibly, the midline. Mammalian studies suggest that the contralateral channel is larger in each cortex, but human studies have found this contralateral preference in only one of the cortices. However, human studies conflict as to whether the contralateral preference is in left or right auditory cortex, and there are a number of methodological differences that this conflict could be attributed to. A key difference between studies is the duration of the silent interval preceding each stimulus and any perception of sound-source movement that the absence of a silent interval creates. We presented auditory noises that alternated between -90° (left) and +90° (right), and recorded neural responses (event-related potentials) using electroencephalography. We randomly varied the duration of the silent interval preceding each stimulus to create a condition with an immediate (local) stimulus context similar to that used in a study reporting contralateral preference in left auditory cortex, a condition with local context similar to a study reporting contralateral preference in right auditory cortex, and an intermediate condition. Surprisingly, we found that both auditory cortices exhibited a similarly-strong contralateral preference in all conditions, with responses 27% greater, on average, to contralateral, than ipsilateral, space. This suggests that both cortices can exhibit a contralateral preference, but whether these preferences manifest depends on the global, rather than local, stimulus context.

**Key words:** auditory cortex, cerebral dominance, event-related potentials, human auditory system, lateralization, spatial processing

**Introduction**

Physiological studies on non-human mammals have suggested that auditory cortex represents horizontal (azimuthal) space by the balance of activity in two or three broadly-tuned channels, one maximally responsive to each of the left hemispace (-90°), right hemispace (+90°), and possibly the midline (0°) [1-4]. This theory has recently received support from physiological [5-9] and psychophysical [10-14] studies on humans. The mammalian studies further suggest that both cortices contain each channel, but that the size (number of neurons) of the channel tuned to the contralateral hemispace is larger in each cortex. Physiological studies in humans, however, have found that this contralateral preference is mainly restricted to one cortex, the other showing little such preference [8, 15-21]. This asymmetry is consistent with the finding that patients with injury to the right cortex exhibit sound localisation deficits across azimuthal space, whilst patients with left cortical lesions primarily exhibit deficits in contralateral space [22, 23].

The nature of the human cortical asymmetry in hemifield preference is disputed, with some studies showing a stronger contralateral preference in left auditory cortex [8, 15-17] and others showing a stronger contralateral preference in right auditory cortex [18-21]. Salminen et al.[21], who found the latter pattern, proposed two main reasons for the discrepancy between studies: (1) studies finding stronger contralateral preference in left auditory cortex have typically cued stimulus location using interaural time or level differences alone, whilst studies finding stronger contralateral preference in right auditory cortex have typically presented stimuli containing the full range of cues to stimulus location; (2) studies showing stronger contralateral preference in left auditory cortex have typically presented location changes in an ongoing sound, eliciting a percept of stimulus movement, whereas studies showing stronger contralateral preference in right auditory cortex have typically presented static stimuli separated by silent intervals (800-ms in Salminen et al.’s own study).

Recently, we conducted a study using electroencephalography (EEG) that incorporated a test of the hemifield preferences of left and right auditory cortex [8]. Our study used sound-field stimulus presentation, so incorporated the full range of location cues. There were no spatial transitions within stimuli, but stimuli with different locations were presented back-to-back without silent intervals. We found that left auditory cortex preferred contralateral space whilst right auditory cortex was indifferent. This argues against the first reason Salminen et al. proposed for the discrepancy between studies, i.e. differences in the spatial cues used. It remains possible, however, that our stimuli, presented back-to-back, elicited a motion percept and thus that the silent interval between static stimuli is important in determining the hemifield preferences of the auditory cortices. If this were so, the critical manipulation to move from hemifield preference in left auditory cortex (our own finding) to hemifield preference in right auditory cortex (Salminen et al.’s finding) would be to vary the silent interval between adjacent, static stimuli from small (as in our own study) to large (as in Salminen et al.’s study).

Accordingly, in the current study, we presented stimuli that alternated between the left (-90°) and right (+90°) hemifields, with a new stimulus occurring every second. Stimulus duration was varied randomly from stimulus-to-stimulus, being either 300 ms, 650 ms, or 1000 ms. Thus, a given stimulus could be preceded by a 700-ms silent interval (similar to Salminen et al.), a 350-ms silent interval, or a 0-ms silent interval (similar to Briley et al.). Neural responses to each stimulus were recorded as a function of the hemifield that the stimulus was presented in and the size of the preceding silent interval. If this manipulation (and any consequent presence or absence of a motion percept) can explain the cortical asymmetry, then right auditory cortex should show a strong hemifield preference with the 700-ms preceding silent interval, whilst left auditory cortex should show a strong hemifield preference with the 0-ms preceding silent interval.

**Methods**

Seventeen right-handed participants, with no history of audiological or neurological disease, participated (mean age ± SD, 22.9 ± 2.8 years; 9 females). All had pure-tone hearing thresholds at, or more favourable than, 20 dB HL at octave frequencies between 250 and 4,000 Hz, inclusive. Participants provided written informed consent. The study was approved by the Research Ethics Committee of the Department of Psychology of the University of York. The authors report no conflicts of interest.

Experiments were conducted in a single-walled audiology test room, located in a larger sound-treated enclosure. Participants sat on a chair in the centre of a circular stage with radius 1.5 m, facing an arc of loudspeakers positioned at approximately head height (1.1 m). A noise stimulus was presented every one second, alternating between the leftmost (-90°) and rightmost (+90°) loudspeaker. The stimulus had equal power per octave (so-called “pink” noise) and contained frequency components between 100 and 5,000 Hz. Stimulus duration varied randomly from stimulus-to-stimulus, being 300 ms, 650 ms or 1000 ms. Stimuli were gated on and off with 10-ms raised cosine ramps; the off ramp of each 1000 ms stimulus and the on ramp of the following stimulus overlapped to give a constant amplitude envelope. Throughout the experiment, participants watched a subtitled film of their choice displayed on a screen directly in front of them (0°). 1200 stimuli were presented in total, and the experiment lasted 20 minutes. An average of 200 stimuli were presented for each combination of stimulus location and preceding silent interval.

Neural responses were recorded using 64 Ag/AgCl electrodes, arranged according to the 5% electrode scheme, in an elasticated cap (ANT WaveGuard system, Enschede, Netherlands). During recording, signals were referenced to the mean across channels, and signals were amplified and low-pass-filtered at 500 Hz, then sampled at 1000 Hz. Recordings were processed offline with the EEGLAB toolbox [24] for Matlab (The Mathworks, Natick, MA). They were first bandpass-filtered (0.1 – 35 Hz) and down-sampled to 250 samples/s, before being split into epochs ranging from 100-ms prior to stimulus onset to 500-ms after stimulus onset, and baseline corrected to the 100-ms pre-stimulus interval. Data from all runs were concatenated and epochs containing extreme values (joint probability limits of ±3 SD) were removed. Stereotyped artefacts (eye blinks and lateral eye movements) were removed by manual inspection following statistical decomposition of the data into maximally-independent components. Epochs were then averaged according to stimulus location and preceding silent interval.

The responses from left and right auditory cortex were extracted using an equivalent current dipole source model, with one dipole located at the centroid of primary auditory area TE1.0 in each hemisphere. The orientations of the two dipoles were fitted simultaneously within a 40-ms window centred on the P2 peak of the grand-average stimulus response. Fits were made to the P2 due to its prominence in the neural responses, though fits to the N1 gave similar (albeit noisier) results. Subsequently, for each combination of participant, cortex, stimulus location and preceding silent interval, the sizes of the N1 and P2 peaks were identified as the most negative (N1) and most positive (P2) responses in 40-ms windows centred on the time points corresponding to these peaks in the grand-average response. The N1 and P2 components have overlapping time but opposite polarities, so partially cancel; therefore, as in our previous work [8, 9], we quantified neural response sizes using the peak-to-peak distance between the N1 and the P2.

**Results**

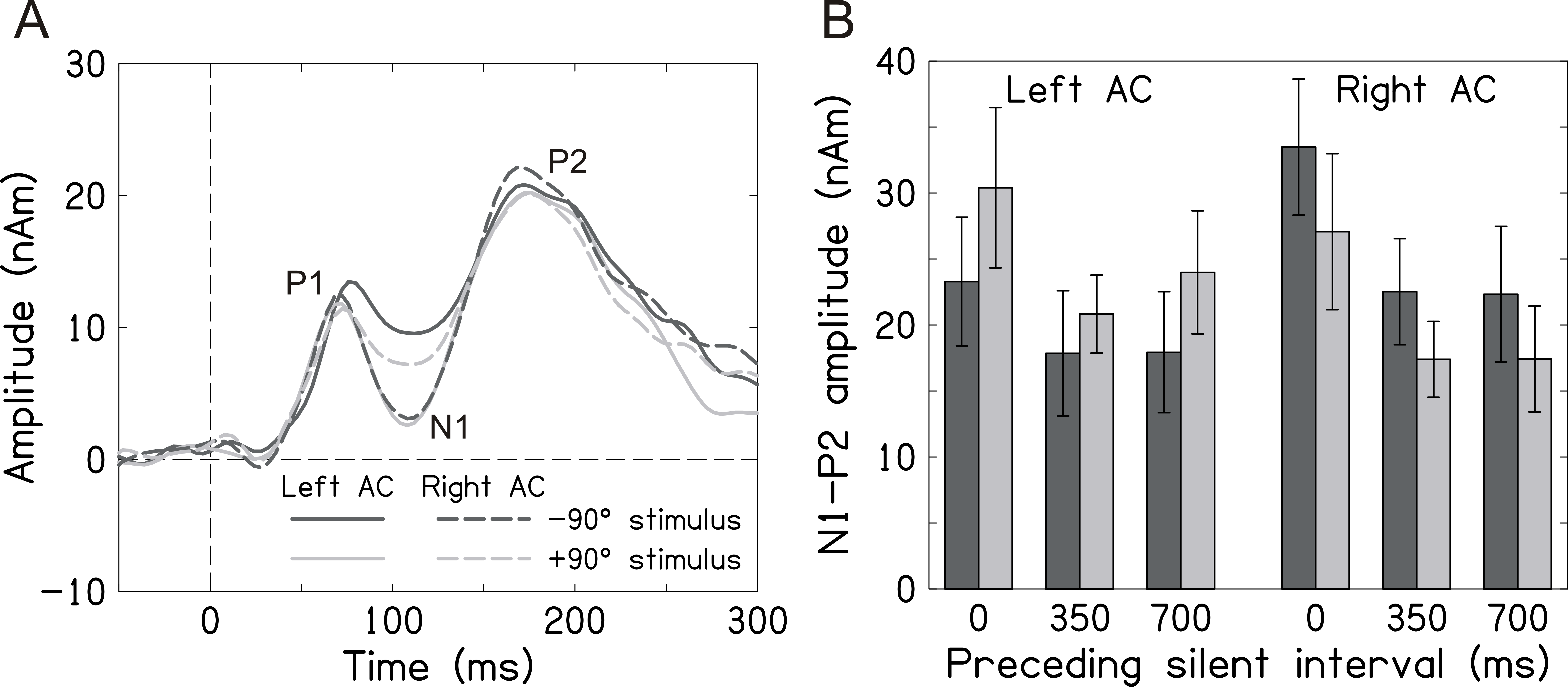


Figure 1. A: Mean responses from the left and right auditory cortices to the -90° and +90° stimulus locations (collapsed across preceding silent intervals). B: Mean N1-P2 peak-to-peak amplitudes for each combination of stimulus location (dark grey: -90°, light grey: +90°), auditory cortex and preceding silent interval. Error bars are 95% within-subjects confidence intervals.

Stimuli elicited triphasic responses corresponding to the P1, N1 and P2 components of the auditory event-related potential (Fig. 1A). Responses were quantified as the peak-to-peak distance from the N1 to the P2, in line with our previous studies (Fig. 1B; see Methods). For all preceding silent intervals and for both auditory cortices, responses were larger when stimuli occurred in the contralateral, than ipsilateral, hemifield. That is, responses from left auditory cortex were larger to stimuli in the right hemifield (+90°) and responses from right auditory cortex were larger to stimuli in the left hemifield (-90°). Responses were also larger when the preceding silent interval was 0 ms (i.e., the preceding and current stimuli occurred back-to-back) than when it was 350 ms or 700 ms.

A linear mixed model (LMM) analysis of response size was conducted, with preceding silent interval (0 ms, 350 ms, 700 ms), stimulus location (-90°, +90°) and auditory cortex (left, right) as fixed factors and participants as a random factor. The three-way interaction was non-significant [*F*(2,176) = 0.375, *p* = 0.688], so was removed from the model. The main effect of preceding silent interval was significant [*F*(2,178) = 20.136, *p* < 0.001], with larger responses when the interval was 0 ms than when it was 350 ms or 700 ms (both *p* < 0.001, 350 ms versus 700 ms was *p* = 0.624). The interaction of stimulus location and cortex was also significant [*F*(1,178) = 18.260, *p* < 0.001]. For both auditory cortices, responses were significantly larger to the contralateral, than ipsilateral, stimulus location (*p* = 0.003).

The interaction of auditory cortex and stimulus location reflects the finding that the cortices responded maximally to different stimulus hemifields. To test whether, in addition, the cortices differed in the sizes of their preference for contralateral stimuli, we conducted another LMM analysis, recoding the stimulus location factor as ipsilateral/contralateral. The three-way interaction was again non-significant [*F*(2,176) = 0.163, *p* = 0.850] so was removed from the model. The main effect of preceding silent interval was significant as before [*F*(2,176) = 19.995, *p* < 0.001]. However, the interaction of stimulus location (ipsilateral/contralateral) with preceding silent interval was non-significant [*F*(1,176) = 0.002, *p* = 0.969]. Instead, there was a main effect of stimulus location [*F*(1,176) = 18.132, *p* < 0.001], with responses being larger to contralateral, than ipsilateral, stimulus locations.

**Discussion**

In the current experiment, each auditory cortex responded more strongly to stimuli in the contralateral, than ipsilateral, hemifield. This contralateral bias was similar between the cortices. It was also unaffected by the duration of the preceding silent interval, and thus whether the immediate (local) stimulus context resembled that of Salminen et al. [21] or Briley et al. [8]. Salminen et al. found a significant contralateral preference in right, but not left, auditory cortex, whilst Briley et al. [8] found a significant contralateral preference only in left auditory cortex. Our current result demonstrates that both auditory cortices can exhibit similarly strong preferences for the contralateral hemispace. Across the different silent intervals, left auditory cortex produced a 27.3% greater response to right, than left, auditory space, whilst right auditory cortex produced a 26.6% greater response to left auditory space. This contralateral preference is somewhat greater than that obtained by Werner-Reiss and Groh [3], who estimated 8-15% greater population activity to contralateral, than ipsilateral, space, from single-unit recordings in rhesus monkeys.

Briley et al. [8] found a 19% greater response to the contralateral hemispace in left auditory cortex but only a 2% greater response in right auditory cortex. There are three key differences between their study and the current study: (1) In the current study, the location of each stimulus was entirely predictable, alternating between -90º and +90º, whereas stimulus locations in Briley et al. varied randomly between five possible locations (0º, ±30º and ±60º); (2) The current study measured hemifield preferences at the extremes of azimuthal space (±90º), whereas Briley et al. measured hemifield preferences at ±60º and ±30º; (3) The current study had a variable silent interval between stimuli, whereas in Briley et al. all stimuli were presented back-to-back.

Salminen et al. [21] used a different paradigm based on stimulus-specific adaptation. They measured responses to a probe stimulus at 0º in four conditions presented in different blocks – the probe stimulus presented alone (maximum response, referred to as 100% response), alternated with adapter stimuli also at 0º (minimum response, referred to as 0%), alternated with adapter stimuli at -45º, or alternated with adapter stimuli at +45º. Using white-noise stimuli, in right auditory cortex, adapters at -45º gave probe responses of 11% (i.e., still a substantial adaptation from contralateral adapters), whilst +45º adapters gave probe responses of 58% (i.e., considerably less adaptation from ipsilateral adapters and thus a contralateral preference). In left auditory cortex, adapters at -45º and +45º gave probe responses of 22% and 16% respectively, indicating a much smaller contralateral preference. The presence of variable silent intervals and the use of stimuli at the extremes of azimuthal space also distinguish the current study from that of Salminen et al.

Surprisingly, in seeking to identify the causes of two differing results (contralateral preference in only left or right auditory cortex), we have discovered a third result different from the others (similar contralateral preferences in both cortices). Our two extreme preceding silent intervals (0 ms and 700 ms) were similar to the local context in which stimuli were presented by Briley et al. and Salminen et al., respectively. As neither Briley et al.’s, nor Salminen et al.’s, result appeared in these extreme conditions, our findings suggest that the *global* context is important in determining the hemifield preferences of the auditory cortices. This conclusion is supported by the results of an fMRI study by Schönwiesner at al. [25], who found contralateral preference in both auditory cortices and auditory subcortical structures when stimuli were presented monaurally. However, when monaural stimuli were interspersed with blocks of binaural stimuli the contralateral preference disappeared in right auditory cortex but remained in left auditory cortex. The functional relevance of this malleability remains to be explored, and our understanding of it will likely depend on elucidating the precise stimulation parameters that determine the different patterns of cortical hemifield preference.

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**Conflicts of interest**

There are no conflicts of interest.

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