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新潟大学脳研究所
「脳神経病理資源活用の疾患病態共同研究拠点」
共同利用・共同研究報告書

知覚判断とアルファ振動の関係を検討する心理実験および脳機能計測

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研究要旨

脳内で生じるリズムは、どのようにして我々の行動に影響しているのだろうか。この心理学および神経科学における難問に対して、近年の研究はリズミカルな注意が知覚判断の成績を予測しうることを示している。本研究の目的は、アルファ波帯域 （8–12 Hz） の脳活動がリズミカルな注意の根底にあり、そのリズムが知覚形成に影響を及ぼすという仮説を検証することである。

1 Methods

1.1 Participants

Twenty-three participants (12 female) between the age of 19 and 52 years (mean age = 28 ± 12 years) took part in the study. All were right-handed, except for one male participant who was left-handed. All participants responded with their right hand. None reported any history of hearing deficits or neurological disorders. Written informed consent was obtained from each participant before the experiment. The study was reviewed and approved by the Ethics Research Committee of Chukyo University (approval no. 22-008).

1.2 Experiment trial and task

In 6 functional runs with a sparse-sampling design (TA = 2 s, TR = 8 s), participants performed a tone target detection task with white noise maskers. Each of these runs consisted of 48 trials, 5 of which were silent trials (i.e., without a noise + tone stimulus) presented at regular intervals (i.e., after every 8th trial). The first 3 trials of every run were dummy trials and thus discarded. The remaining trials all began with a white fixation dot presented at the centre of a gray background (Figure 1A). After 1 s, diotic white noise was delivered to both ears. The noise lasted 800 ms and contained a binaural pure tone of 20 ms duration and 1000 Hz frequency. The target occurred randomly with a stimulus onset asynchrony (SOA) of 266, 300, 333, 366, 400, 433, 466, 500, 533 or 566 ms. The intensity of the tone target was set to -4 dB (*above threshold*), -14 dB (*at threshold*) or -24 dB (*below threshold*) relative to that of the noise mask. Half of the trials contained a target at threshold, while the remaining trials were evenly split between targets above or below threshold. After every stimulus, participants were cued to respond by the display of the same question (“Did you hear the tone?”) and two possible answers (“Yes” or “No”). Participants gave their response via

button press before the subsequent MRI acquisition. The next trial began after a silent interval of 1 s following the acquisition.

1.3 Functional localiser task

To localise the primary auditory cortex (A1), inferior colliculus (IC) and medial geniculate body (MGB) in the individual brain, participants performed a 1-back task on trains of pure tones in 1-2 separate runs with an event-related design (TR = 2 s). The tone trains consisted of 5 pure tones of the same frequency (250, 500, 1000, 2000 or 4000 Hz) but varying lengths (50, 100 or 150 ms) and were interspersed with silent periods of similarly differing lengths. Random combinations of tones and silent periods were generated to produce 1-s tone trains. One run consisted of 120 tone trains and 24 silent trials presented in random order with a SOA of 2.5 s. The stimuli were delivered to either the left or right ear and switched side after every eighth trial. Participants were asked to press a button whenever a tone train of the same frequency was repeated, irrespective of whether the preceding tone train occurred in the same or opposite ear. All participants underwent a short practice session outside the scanner before the experiment to ensure they understood and could perform both experiment and localiser tasks. Four participants did not perform this functional localiser task. Nevertheless, we have included them in the main experiment data analysis, for now.

1.4 MRI acquisition

Images were acquired on a 3.0 Tesla MRI system (GE SIGNATM Architect, GE Medical Systems, Milwaukee, WI, United States) with a 48-channel head coil. Each participant underwent one session of 6 functional runs with a sparse sampling design (see Section 1.2) and 1-2 additional functional runs with an event-related design (see Section 1.3). For the sparse sampling design, a gradient-echo echo-planar imaging (GE EPI) sequence was used with the following parameters: TA/TR/TE = 2/8/30, flip angle = 90°, acquisition matrix = 96 × 96, field of view =192 × 192 mm, reconstruction matrix = 128 × 128, slice thickness = 2 mm, number of slices = 38. For the event-related design, the imaging sequence and parameters were the same as above except for the TR and flip angle, which were 2 s and 80°, respectively. Before the functional runs, a high-resolution and high-contrast structural image was acquired using a T1-weighted gradient echo sequence (GRE) with the following parameters: TR/TE/TI = 6.15/1.93/450 ms, flip angle = 12°, acquisition matrix = 192 × 192, field of view =240 × 240 mm, reconstruction matrix = 512 × 512.

1.5 Data preprocessing

The behavioural and MRI data were processed and analysed in Python version 3.10 (https://www.python.org/). The DICOM files were first converted to NIFTI format using the *dcm2bids* package (Boré et al. 2023) which depends on *dcm2niix* (Li et al. 2016). The NIFTI files were then submitted to a custom pipeline created using the *Nipype* library (Gorgolewski et al. 2011). This library launches commands from various software, including *SPM* (Friston et al. 2013) and *FSL* (Jenkinson et al. 2012). During preprocessing, three dummy scans from each functional volume were first discarded using FSL's *ExtractROI* function, and the remaining scans were corrected for head movements using SPM's *realignment* algorithm. The structural scans were then coregistered to a mean image of all functional runs within each session and submitted to segmentation. From the segmented volumes, we obtained the deformation field for normalising the individual data to the standard *MNI152* space. For coregistration, segmentation and normalisation we used SPM's respective functions. Two participants underwent two structural scans due to a break during the experiment session. We have excluded those two participants from the present analysis, leaving 17 participants in total.

1.6 Statistical analysis

Using *Nilearn*'s library (https://github.com/nilearn/nilearn), we fitted a *General Linear Model (GLM)* to the individual data, with four main predictors obtained by convolving the canonical *Hemodynamic Response Function* (HRF) of SPM with the Dirac impulse functions that corresponded to the presentation time of each trial type (i.e., silence/no stimulus, -24 dB, -14 dB, and -4 dB). In addition, we included the six motion correction parameters from realignment as nuisance variables. To model the temporal structure of the noise, a lag-1 autoregressive model, *ar(1)*, was used. A set of discrete cosine transforms was applied for high pass filtering (cut-off = 160 s), and smoothing was performed with a kernel of 8 mm. To determine the regions that were activated to the auditory stimuli presented, a contrast was computed with all three stimulus conditions added. The resulting maps of z-scores were submitted to a second-level GLM with only an intercept, and the Bonferroni method was used to correct for multiple comparisons across voxels. From the areas that survived this strict correction, we extracted the individual beta weights for each type of trial and submitted them to a repeated measures ANOVA from *statsmodels* (Seabold & Perktold, 2010).

2 Results

2.1 Task performance

Participants (N = 23) detected a brief sine tone (20 ms) masked by white noise (800 ms). The auditory stimuli were delivered diotically, that is, simultaneously to both ears, during the 6-s silent period (blue shaded rectangle in Figure 1A) that always preceded the 2-s period of acquisition (TA, red shaded rectangle). The target could occur with ten possible stimulus onset asynchronies (SOAs) relative to noise onset (red dotted lines). In half of the trials (288 in total), the target's intensity was -14 dB relative to that of the noise. In the other half of the trials, the target intensity could be -4 dB or -14 dB with equal probability. Every eight trials, a "silent" trial occurred where no stimulus was presented but participants still had to give a response (five times in total). As shown in Figure 1B, participants (coloured dots) easily detected *above-threshold* targets (-4 dB), responding on almost all the trials (> 99 %) with 'Yes, I heard the tone'. They showed more inter-individual variance for *at-threshold* targets (-14 dB), with yes-responses ranging between 30-80 % of the trials. Except for four participants (red rectangle), all participants responded on less than 20 % of the trials with 'yes'. As the -24 dB targets are virtually impossible to detect, any "yes" response corresponds to a response bias. Therefore, the four outliers were excluded from subsequent analyses.

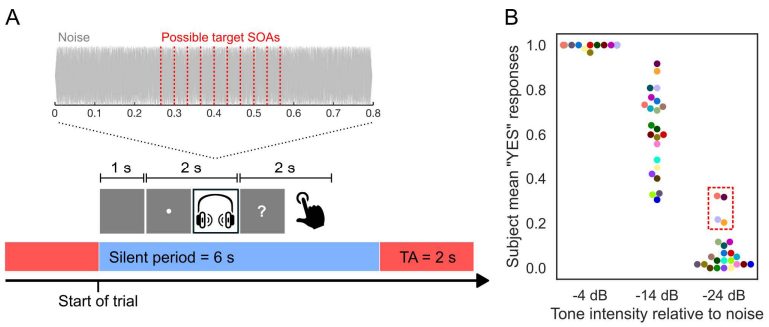

Figure 1: **A** Trial timeline. **B** Performance on detection task.

2.2 BOLD response

To check for auditory activation, we collapsed across the three stimulus conditions, i.e., -4 dB, -14 dB and -24 dB, and computed z-scores, corrected with Bonferroni ($p < 0.05$). Figure 2 shows the significant cortical areas projected onto the MNI glass brain. Even uncorrected, the activations in the subcortical areas were relatively weak and small. A detailed list of all the significant clusters can be found in Table 1. Two large clusters cover the left and right auditory areas from which we extracted the GLM estimates for the three stimulus conditions, along with the silent trials for control. The estimates were entered into a 2-way repeated measures ANOVA with Stimulus (4 levels) and ROI (2 levels: left, right) as within-subject factors. As expected, only Stimulus showed a significant main effect ($F(3, 48) = 100.18$, $p < 0.001$). ROI ($F(1,16) = 3.40$, $p = 0.08$) and the ROI x Stimulus interaction ($F(3,48) = 0.94$, $p = 0.43$) were not significant.

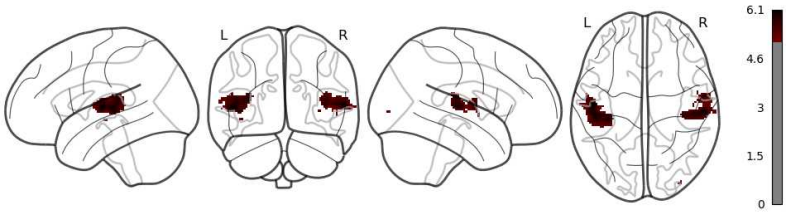

Figure 2: Significant z-scores after Bonferroni correction ($p < 0.05$).

Table 1: Clusters activated to the 3 auditory stimulus conditions (-24 dB, -14 dB, -4 dB)

	Cluster ID	X	Y	Z	Peak Stat	Cluster Size (mm3)
0	1	58.0	-22.0	8.0	6.095271	3552
1	1a	40.0	-24.0	12.0	5.764689	
2	1b	60.0	-6.0	8.0	5.689413	
3	1c	70.0	-20.0	6.0	5.287439	
4	2	-48.0	-16.0	8.0	6.082169	4864
5	2a	-48.0	-24.0	6.0	6.003847	
6	2b	-34.0	-28.0	14.0	5.942451	
7	2c	-42.0	-26.0	2.0	5.875343	
8	3	36.0	-90.0	2.0	5.396077	24
9	4	-42.0	-16.0	-6.0	5.266146	24
10	5	48.0	-16.0	2.0	5.236693	24
11	6	50.0	-12.0	4.0	5.220878	8
12	7	52.0	-2.0	-2.0	5.200550	16
13	8	52.0	-4.0	2.0	5.182157	8
14	9	-60.0	-14.0	4.0	5.176665	8

Figure 3 plots the individual GLM estimates for the 3 stimulus conditions and the silent trials, extracted from the left and right ROIs. Except for one participant (blue dot), auditory activation on silent trials were markedly lower than on trials with auditory stimulation for most participants. This

was confirmed in pairwise comparisons using Tukey's HSD test which showed that auditory activation to "no stimulus" was significantly lower than all three stimulus conditions, i.e., -24 dB, -14 dB and -4 dB (all p's < 0.001). It can be seen from Figure 3 that the individual BOLD response to the three stimulus conditions do not differ from one another, in contrast to the task performance shown in Figure 1. Tukey's HSD test indicated that pairwise comparisons between the three stimulus conditions were non-significant (all p's > 0.05).

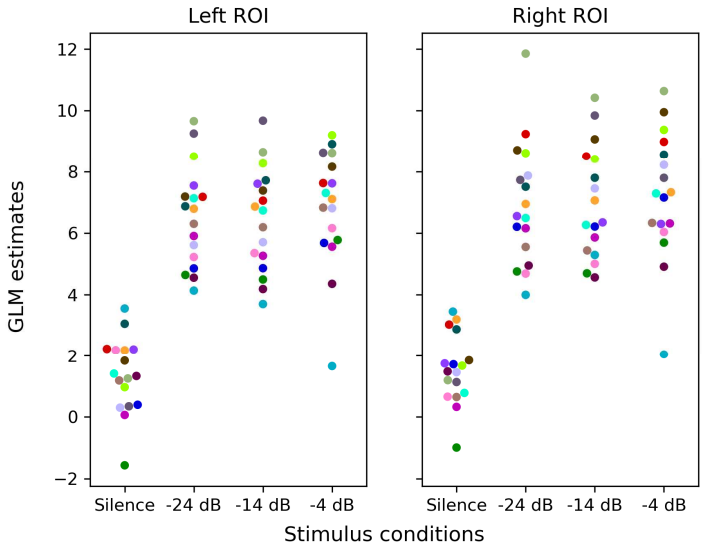

Figure 3: GLM estimates of individual BOLD responses in the 3 stimulus conditions and on the silent trials

3 Discussion

The constant MRI noise during scanning poses a huge problem for auditory fMRI. For that reason, the consistent task performance displayed by most subjects (Figure 1) as well as the robust cortical auditory activations at the group level (Figure 2) are reassuring for future studies with similar low-level auditory stimuli (here, white noise burst + brief sine tone). We did not expect the ROI analysis on the normalised brain to yield large differences in BOLD response between the three tone intensities (Figure 3), as we assume that such differences would be confined to much smaller auditory areas whose locations and other characteristics may vary across subjects. Therefore, in subsequent analyses, we plan to conduct such ROI analyses in individuals' native space, rather than on the normalised brain. To this end, we will use the fMRI data collected during the functional localiser task and try to construct a coarse tonotopic map for each participant.

4 References

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5. 研究発表（上記課題名に関するもの）

1. 論文発表

2023 年度、該当なし

2. 学会発表

2023 年度、該当なし

6. 知的財産権の出願・登録状況（予定を含む）

1. 特許取得

2023 年度、該当なし

2. 実用新案登録

2023 年度、該当なし

3. その他

2022 年度、該当なし