

The Responses of Single Units to Simple and Complex Sounds from the Superior Olivary Complex of the Guinea Pig

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Summary

We have recorded the responses of single units in the superior olivary complex (SOC) of the guinea pig to simple and complex stimuli. We can readily identify the responses of the four principal ascending nuclei as described in other species and we are therefore confident that the guinea pig is a suitable model for studying this region. We found single units in the medial superior olive that represent both diotic iterated rippled noise and dichotic repetition pitch in their temporal discharge patterns. Our data demonstrate a use of the SOC beyond sound-source localisation.

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1. Introduction

The superior olivary complex consists of a group of auditory nuclei in the mammalian brainstem. Two of the largest nuclei, the medial superior olive (MSO) and lateral superior olive (LSO), receive bilateral, direct and/or indirect inputs, from the bushy cells of the ventral cochlear nucleus on both sides and are thus major sites of binaural integration. Not surprisingly, previous physiological studies have examined the role of the MSO and LSO in sound localisation. Here we examine, for the first time, the responses of single units in the guinea pig SOC to simple and complex sounds, including stimuli that can evoke a binaural pitch in humans.

Human psychoacoustic studies have demonstrated striking “binaural pitch” phenomena. These pitch percepts are produced by sounds that, presented to either ear on its own, evoked no pitch [1, 2]. One such example is dichotic repetition pitch (DRP), consisting of Gaussian noise with a small inter-aural time difference (ITD) [1]. Neural processing to combine information from the two ears is essential for this aspect of pitch perception. Here, we demonstrate neural correlates of binaural pitch in the temporal discharge patterns of single units in the MSO. The MSO is well known to perform inter-aural computations that represent inter-aural time differences. Analysis of the temporal

discharge patterns of MSO units to diotic iterated rippled noise, and dichotic repetition pitch reveal a neural correlate of the pitch of these stimuli. These findings suggest a role for the MSO in the neural machinery underlying binaural pitch.

2. Methods

Our methods are described in detail elsewhere [3], so only a brief description is given here. Data were obtained from normal-hearing (based on round-window CAP thresholds), anaesthetised and normothermic, pigmented guinea-pigs (*Cavia porcellus*). Experiments were performed in accordance with the Animals (Scientific Procedures) Act 1986 (Amendment Regulations 2012) following ethical review by the University of Cambridge Animal Welfare and Ethical Review Body.

An estimate of inter-aural crosstalk attenuation was obtained from single ventral cochlear nucleus units by measuring the difference between monaurally-evoked spiking responses to BF tones presented ipsi-laterally and contralaterally. Between 0.10- and 2.00-kHz, the attenuation was greater than 50 dB. This, combined with our relatively low signal levels, means that the results are unlikely to be contaminated by inter-aural acoustic crosstalk.

Glass-insulated tungsten microelectrodes were positioned at the surface of the dorsal cochlear nucleus (DCN) under operating-microscope control, and advanced parasagittally through the brainstem at 45° to the horizontal

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plane using a hydraulic microdrive. Signals from the microelectrode were amplified ($\times 1000$) and bandpass filtered (0.3–10 kHz) before online spike discrimination and timing. Spike times were stored for offline analysis (10 μ s resolution). Superior olivary complex units were defined as those found at depths greater than 3.3 mm from the surface of the DCN. The presence of a neurophonic in response to monaural or binaural stimulation with low-frequency pure tones gave an initial indication that the electrode was close to the MSO or the low frequency limb of the LSO. Receptive fields were measured using 50-ms pure tones, gated with 5-ms cos² ramps. For neurons with BFs <5 kHz, the frequency range was 3 octaves below unit BF to 2-octaves above, for units with BFs 5 kHz or above, tone frequencies ranged from 2 octaves below BF to 1 octave above. For binaural neurons, receptive fields were measured to ipsilateral-only, contralateral-only and diotic tone presentations.

We collected spike times in response to several pitch stimuli. These included: diotic iterated rippled noise (Gaussian noise delayed and added back to itself [comb filtering], identical in both ears), and dichotic repetition pitch (Gaussian noise with a small ITD between the two ears).

3. Results

Recordings were made from all main divisions of the SOC: the superior paraolivary nucleus (SPN), the medial nucleus of the trapezoid body (MNTB), the lateral superior olive (LSO) and the medial superior olive (MSO). Physiological response properties of the principal cells of these nuclei have been characterised in other species. However, to our knowledge, responses from such units in the guinea pig SOC have not been previously reported. Responses to pure tones at unit BF, plotted as post-stimulus time histograms (PSTHs), were used to form an initial classification. MNTB units showed a “primary-like” (PL) PSTH shape or a “primary-like with notch” (PN) shape, and the characteristic three-component spike-waveform shape reported in other species (Figure 1A). SPN units showed chopper-like responses at stimulus offset (Figure 1B), and sensitivity to gaps between tones. We also confirmed interaural phase difference (IPD)-sensitivity in low-BF binaurally-responsive cells of the LSO and MSO, using binaural-beat stimuli (Figures 1C and 1D). MSO units responded weakly to monaural stimulation but more strongly to diotic stimulation, with many units showing binaural facilitation. LSO units were sensitive to interaural level differences of BF tones (Figure 1F).

The microelectrode recording of an MSO unit to stimulation with binaural beats is shown in Figure 2A. This shows three clusters of spikes during the stimulus presentation, corresponding to the best IPD in each 1 second beat period. Figure 2B shows an expanded segment of the same recording to show the presence of the driven neurophonic, readily identifiable as the approximately sinusoidal oscillation of the background noise. The oscil-

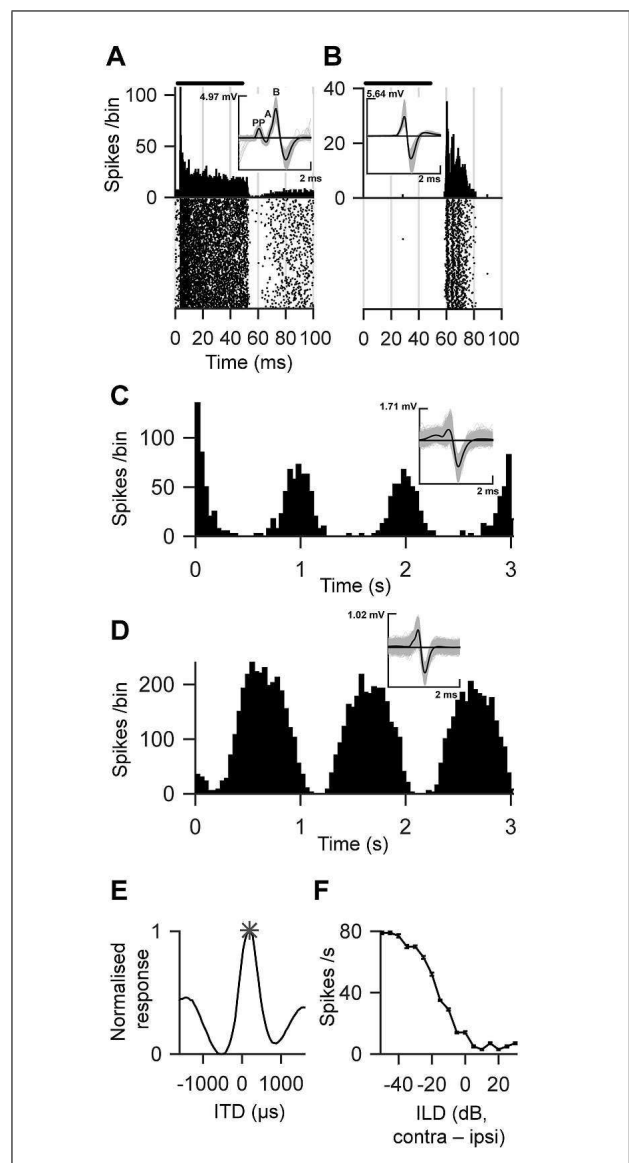


Figure 1. Physiological signatures of the main cell types in the principal nuclei of the superior olivary complex. A & B) post-stimulus time histograms in response to supra-threshold BF tone bursts from the MNTB (BF = 12.5 kHz) and SPN (BF = 15.64 kHz), respectively. Below each histogram is the corresponding dot-raster plot. The horizontal bar above each histogram represents the stimulus duration. C) Response of an MSO unit (BF = 0.13 kHz) to binaural beats at BF and E) an exemplar delay curve. D) Responses of an LSO unit (BF = 0.39 kHz) to binaural beats at BF and F) an exemplar ILD function. Average spike waveform shapes are shown as insets for plots A-D. Note the signature three-component shape for MNTB units (inset in A).

lation frequency was quantified by an FFT of the electrode trace for two time-windows. The first was in the presence of the driven neurophonic and the second was in the later 3 seconds of the recording, when the stimulus was switched off (the spontaneous neurophonic – Figure 2C). Figure 2D shows a clear peak in the spectrum of the waveform around the stimulus frequency of the binaural beat stimulus 333/334 Hz in the driven neurophonic condition

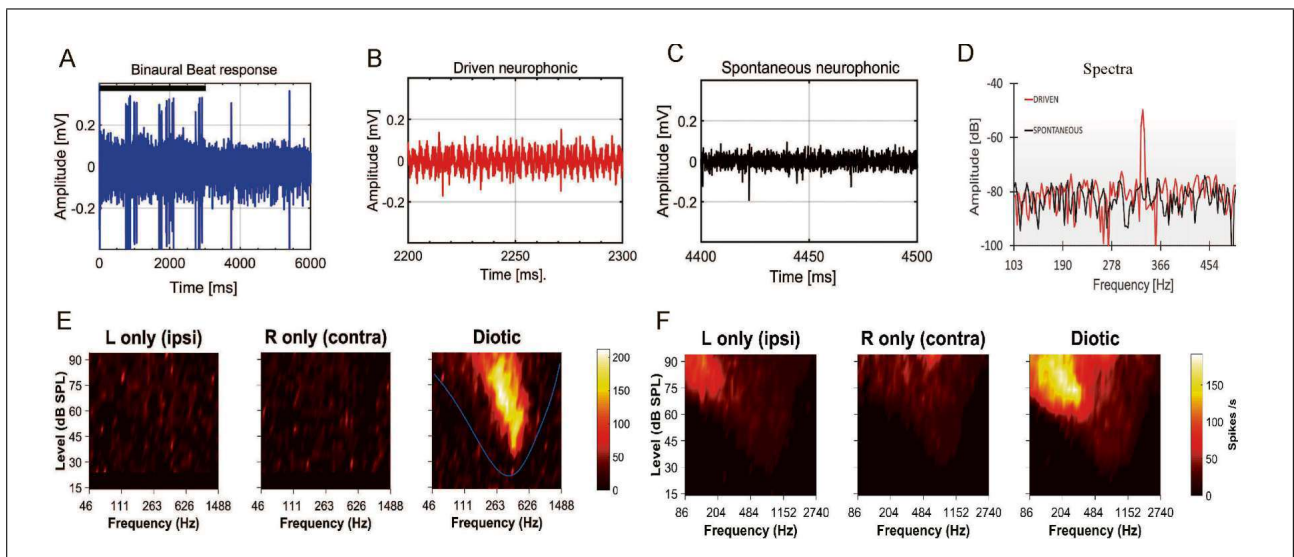


Figure 2. (A) A microelectrode trace showing a single MSO unit responding with a burst of action potentials at the 1s period of a binaural beat stimulus. The duration of the beat stimulus (3 seconds) is shown by the black bar. The driven neurophonic is clearly seen as an amplitude modulation in the second trace [B] which is an expanded section of the waveform in A. The spontaneous neurophonic (in the absence of controlled acoustic stimulation) is shown in C. The frequency of the neurophonic potential is shown in [D] by the peak just below 350 Hz in the spectra of the traces shown in B and C. The carrier frequencies of the binaural beat were 333 and 334 Hz. The spectrum shown by the black line is the electrode noise recorded when the stimulus is off (see scale in A). Facilitation in response to diotic tone bursts for two MSO units is shown in the lower row. In (E) the monaural receptive fields are non-existent while the diotic receptive field (BF = 0.46 kHz) shows conventional tuning. For comparison, the continuous blue line is the frequency-threshold curve of a similar BF filter recorded from a single unit in the ventral cochlear nucleus of the guinea pig. In (F) we show a unit that showed weak excitatory responses in the monaural receptive fields. BF was estimated as 0.74 kHz.

but not in the stimulus-off (spontaneous neurophonic) condition.

The facilitation to diotic tones is illustrated in Figures 2E and F which show ipsi-lateral, contralateral and diotic receptive fields for two MSO units. In the first unit (Figure 2E) the monaural response, both ipsilateral and contralateral, is very weak or non-existent [0, 0] while the diotic response shows a conventional “V” shaped response. This type of response was observed for 29% of our MSO unit population. In contrast, the second unit (Figure 2F) shows a tuned response to monaural stimulation of either ear [E, E], with a stronger response to diotic stimulation. This [E, E] pattern was found for 41% of our MSO units. This percentage is lower than seen in the dog (65%, [3]), cat (58%, [4]) and the gerbil (67% [5]).

Figure 3 shows the responses of a single MSO unit to diotic iterated rippled noise (IRN) and dichotic repetition pitch (DRP). The IRN was generated for one iteration with positive gain at three delays, 8, 16 and 32 ms. There is a clear peak in the all-order inter-spoke interval histogram for each of the delays. It is important to note that the IRN was presented diotically, and the neural representation of the corresponding pitch is available in monaural neural-inputs. In contrast, DRP is generated by presenting broadband noise to one ear and the same noise, delayed by τ ms, to the other ear. DRP is a dichotic pitch, requiring binaural interaction.

Humans do not report the pitch corresponding to $1/\tau$ to be lateralized; it is heard in the centre of the head. If both the delayed and un-delayed noise waveforms are in

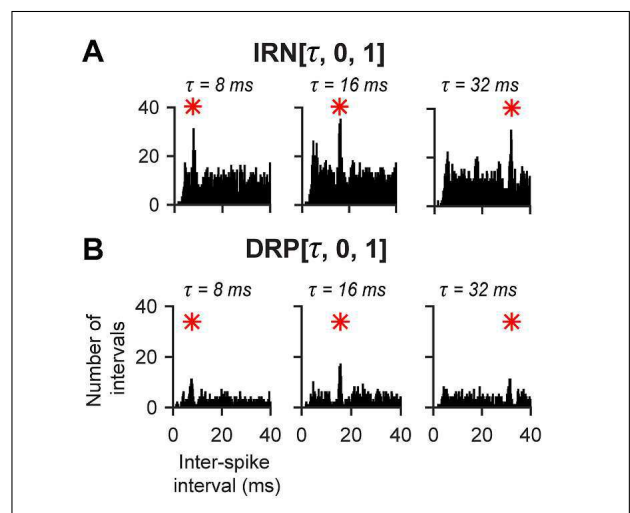


Figure 3. (A) The responses of a single MSO unit (BF = 0.25 kHz) to IRN with 1 iteration presented diotically for three different IRN delays (but zero ITD). In (B), we see the responses of the same unit to DRP with the same three delays presented as ITDs. The all-order interspike interval histograms are plotted with a binwidth of 0.2 ms. The asterisks mark the stimulus delay.

phase (DRP+), the pitch is unambiguous at $1/\tau$. When a broadband phase shift of τ is applied to the delayed noise (DRP-), the DRP is ambiguous, being either $\sim 0.9/\tau$ or $\sim 1.1/\tau$ [6].

This result is very similar to that of the more familiar monaural repetition pitch, that is “[iterated] rippled noise”

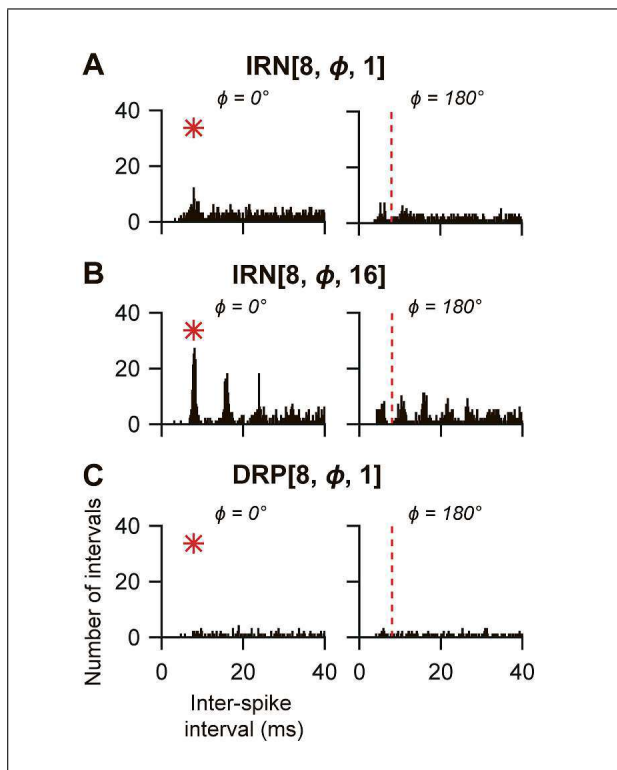


Figure 4. Responses of a single MSO unit (BF = 0.13 kHz) to 1 iteration of diotic iterated ripple noise at a delay of 8ms and either 1 or 16 iterations for both positive and negative gain. The lack of response by the same cell to positive and negative DRP is also shown (C). The all-order interspike interval histograms are plotted with a binwidth of 0.2 ms.

[6]. In Figure 3B, a clear peak can be seen (red asterisks) in the all-order inter-spike interval histograms in response to the same three delays shown in Figure 3A.

It should be noted that only 3 of 11 MSO units in our dataset showed a clear correlate of DRP in their inter-spike interval distributions. In contrast, all of our MSO units showed a clear neural correlate of the pitch of diotic IRN. Figure 4 shows an example of an MSO unit with a clear temporal representation of the pitch of IRN with 16 iterations, but only a weak representation of the pitch of IRN with 1 iteration. This could be interpreted as reflecting the salience of IRN pitch. However, this same MSO unit fails to show responses at the delay in the DRP stimulus (4C).

4. Discussion

We have recorded the responses of single units in the superior olivary complex (SOC) of the guinea pig to simple and complex stimuli. We can readily identify the responses of the four principal ascending nuclei as described in other species and we are therefore confident that the guinea pig is a suitable model for studying this region. We also demonstrated that single units in the MSO can respond to the pitch of diotic IRN, even with a single iteration. Humans only hear a weak pitch with one iteration. A small subset (3/11) of the same units showed a neural correlate to the pitch of DRP. Although DRP produces a rather weak pitch percept, it is currently unknown why only a subset of MSO units responded to DRP. One possibility is a mismatch in best frequency of the ipsilateral and contralateral input filters to the MSO unit. Future studies should consider measuring the responses of single SOC units to sounds which are capable of producing much stronger binaural pitch percepts, such as dichotic complex tones or Huggins pitch.

Acknowledgement

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