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On sound and silence

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Chapter 3

Effects of acoustic trauma on envelope coding in the inferior colliculus of the guinea pig

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Abstract

The temporal fluctuations of a sound, as reflected by its envelope, are encoded in central auditory neurons to represent complex sounds, such as speech. Sensorineural hearing loss affects envelope coding at the level of the auditory nerve. The current study investigated the effects of acoustic trauma on envelope coding in the inferior colliculus. We found that envelope coding was enhanced immediately after acoustic trauma in neurons with a characteristic frequency below the trauma frequency, specifically in response to amplitude modulations ≤ 256 Hz. The observed changes in the auditory midbrain may relate to the problems that hearing-impaired people encounter while listening in noisy environments.

Keywords: envelope coding; inferior colliculus; acoustic trauma; guinea pig; amplitude modulation

Abbreviations: AM, amplitude modulated; AN, auditory nerve; CF, characteristic frequency; IC, inferior colliculus; MTF, modulation transfer function; PSTH, post-stimulus time histogram; SI, synchronization index; SPL, sound pressure level

1. Introduction

Natural sounds carry an important part of their information in the slow fluctuations of their amplitude. These envelope fluctuations support the perceptual separation of different sound sources (Grimault et al., 2002). Furthermore, a degraded speech signal, with only the envelope preserved, remains intelligible, demonstrating the importance of the envelope in speech understanding (Shannon et al., 1995). Thus, the envelope is involved in processing speech and separating it from other, less relevant, sound sources.

Hearing-impaired listeners often encounter problems with speech perception in noisy environments, in particular when one attempts to understand one target talker out of a number of competing talkers (Bronkhorst and Plomp, 1992). Remarkably, it has been shown that patients with sensorineural hearing loss have normal to better-than-normal envelope detection thresholds (Moore and Glasberg, 2001; Füllgrabe et al., 2003). Furthermore, in laboratory animals, noise-induced hearing loss results in enhanced envelope coding by the auditory nerve (AN). Especially AN fibers with high thresholds and steep rate-level functions have an enhanced response to amplitude-modulated (AM) sounds (Kale and Heinz, 2010). Coding of envelope information is also enhanced in the auditory-evoked potentials of chinchillas with noise-induced hearing loss (Zhong et al., 2014). These results suggest that hearing-impaired listeners might benefit from enhanced envelope coding, e.g. in understanding speech. However, the enhanced coding also applies to the background noise. Consequently, enhanced envelope coding may not help to improve the signal-to-noise ratio in a speech-in-noise communication (Kale and Heinz, 2010).

The current study aimed at identifying the effects of sound exposure on envelope coding at the level of the auditory midbrain. Spike trains of responses to AM noise were recorded in the inferior colliculus (IC) of the anesthetized guinea pig, before and immediately after bilateral exposure to a 124 dB SPL pure tone. Because the envelope coding is enhanced in the periphery, we hypothesized to see that reflected in the responses of more central neurons. This study provides results about the alterations in central processing caused by acoustic trauma and might give additional insight into the mechanisms involved in the problems encountered by hearing-impaired people during listening in a fluctuating background noise.

2. Methods

2.1 Animals

Six normal-hearing male albino guinea pigs (Dunkin Hartley; Harlan Laboratories, Horst, the Netherlands) were used for this study. Animals were anesthetized with a mixture of 70 mg/kg ketamine (10% Ketamine, Alfasan, Woerden-Holland) and 6 mg/kg xylazine (2% Rompun, Bayer-Healthcare; i.m.). Half the original dose was administered every hour to maintain a deep level of anesthesia. Body temperature was kept constant at 38 °C by a homeothermic heating pad (Harvard Apparatus), and heart rate and blood oxygen saturation were closely

monitored. A tracheotomy allowed for artificial respiration. The head of the animal was fixated by a skull screw. The right IC was surgically approached by a craniotomy and a subsequent careful ablation of the overlying cortical tissue. A linear 16-channel microelectrode array (A1x16-10mm-100-413-A16; NeuroNexus) was inserted in a dorsal-lateral to ventral-medial direction into the visualized IC. Online inspection of neural activity during the presentation of 100-ms noise bursts allowed for the optimal placement of the electrode in the IC. Neural spike trains were recorded before and immediately after a one-hour bilateral acoustic trauma. The acoustic trauma was an 11-kHz pure tone of 124 dB SPL, presented by two free-field Piezo tweeters (PH8; Velleman) that were positioned approximately 5 cm from each ear, respectively. The electrode remained inserted in the IC during exposure. The experiment was conducted in an anechoic sound-attenuating booth. The study was approved by the Animal Experiment Committee of the University of Groningen (DEC # 6068D) and was in compliance with Dutch and European law and regulations.

2.2 Acoustic stimuli

Acoustic stimuli were designed by custom-made MatLab programs (R2010b, Mathworks), generated using TDT hardware (RP2.1, PA5, and ED1), and presented by a free-field electrostatic speaker (ES1; TDT Inc.) positioned at ± 5 cm from the left ear, contralateral to the exposed IC. Pure tones (duration 300 ms, 10-ms cosine ramp) were presented to obtain receptive fields. The frequency of the pure tones ranged between 2 and 40 kHz (25 frequencies, logarithmically spaced steps) and the intensity ranged between 20 and 80 dB SPL (15 intensities, linearly spaced steps); each frequency-level combination was presented once. In order to study envelope coding, AM broadband noise was presented (duration 400 ms, 10-ms cosine gate, 300 repetitions, 70 dB SPL). The carrier noise had a spectrum that was flat within 1 dB between 2 and 40 kHz (butterworth filter) and was an unfrozen noise, i.e. for every repetition the carrier noise was newly regenerated. The amplitude of the carrier noise was modulated by multiplying the signal with

$$E(t) = 1 - \left(m\cos\left(2\pi ft\right)\right), \qquad \{1\}$$

where m is the modulation depth, fixed at 50% ($m = 0.5$), and f is the modulation frequency, with a value between 8 and 1024 Hz in logarithmically spaced steps. All stimuli, including the trauma stimulus, were calibrated with a B&K microphone and amplifier (type 2670 and type 2610, respectively) positioned at the entrance of the ear canal.

2.3 Data analysis

The neural signal was amplified (RA16PA; Tucker Davis Technologies [TDT] Inc.), recorded (RX5; TDT Inc.), and stored on a PC using custom-made MatLab programs (digitized with

a sampling rate of 24,414 Hz). Next, signals were filtered (300-3000 Hz) and spikes were defined by the instants when the signal exceeded the threshold of 2.6 times the root-mean-square level of the signal. Responses to pure tones revealed the unit's receptive field, which was defined by the range of pure tones that elicited a significant increase in firing rate. The receptive field was contoured by the tuning curve; the lowest tip of the tuning curve defined a unit's characteristic frequency (CF) and corresponding threshold. Post-stimulus time histograms (PSTHs) were plotted from the neural responses to the AM stimuli. The tendency of a spike train to phase lock to the amplitude modulation of the stimulus was expressed by the synchronization index (SI), which was calculated by

$$SI = \frac{1}{N}\left|\sum_{j=1}^{N} e^{i\varphi(j)}\right|, \qquad \{2\}$$

where N is the number of spikes, i refers to $\sqrt{(-1)}$, and $\phi(j)$ is the phase of the j-th spike relative to the sinusoidal amplitude modulation ($E(t)$) of the acoustic stimulus (Eq. 1). Only the spikes that occurred during the presentation of the noise stimulus were taken into account. To eliminate the effect of response latency and the on-response, spikes occurring during an additional 25 ms relative to the start of the stimulus were not taken into account either. The modulation depth of the PSTH in percentage was calculated by multiplying the synchronization index with 200 (Rees and Palmer, 1989). The modulation response gain (G; in dB) was computed by

$$G = 20 \times \log_{10}\left(\frac{\%\text{ modulation depth of PSTH}}{\%\text{ modulation depth of stimulus}}\right), \qquad \{3\}$$

and represents the degree of neural synchrony relative to the modulation of the stimulus. A modulation response gain of 0 dB indicates that the neural modulation coding in the PSTH follows the modulation of the stimulus. If the response gain is higher than 0 dB, the auditory system has amplified the modulation. A modulation transfer function (MTF) is obtained by plotting the response gain (G in Eq. 3) against the modulation frequency of the stimulus (f in Eq. 1). The maximum response gain of the MTF was considered as a measure for envelope coding. All analyses were executed using custom-made MatLab software.

Paired-sample T-tests and Student's T-tests were used for statistical analyses, as appropriate (IBM SPSS Statistics; Version 22). P-values were Bonferroni corrected for multiple testing.

3. Results

Before acoustic trauma, IC multi units (n = 69) had a CF between 2.0 kHz and 35.3 kHz, with a corresponding threshold that ranged from 20 dB SPL to 74 dB SPL (Figure 3.1A). After a 1-h exposure to an 11-kHz pure tone of 124 dB SPL, CFs ranged from 2.0 kHz to 10.1 kHz (Figure 3.1B). The electrode remained in the IC during acoustic trauma, implying that the neural signal recorded from the units without a receptive field after exposure (n = 30, markers with arrows at the top of the panel in Figure 3.1B) derived from auditory units of the IC as well. Therefore, these units remained included in further AM analyses. Multi units that remained sensitive to pure tones after trauma (n = 39) had an average threshold shift of 14 dB (± 3.1 standard-error of the mean).

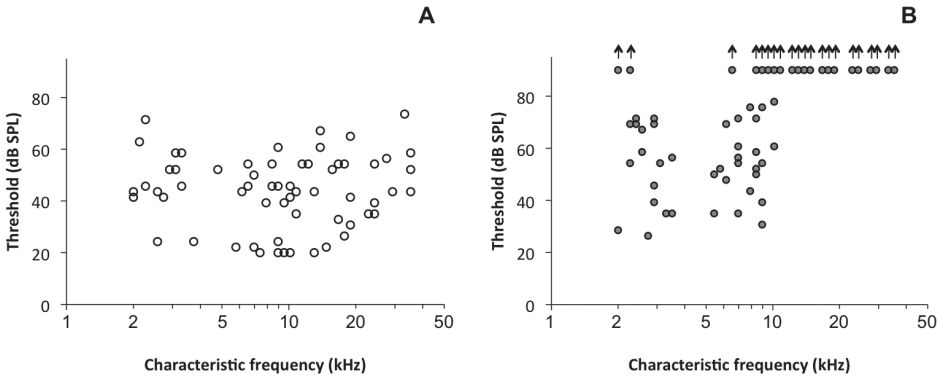

Figure 3.1 Characteristic frequency and thresholds of IC multi units. **A)** The CF and corresponding threshold of the IC units before acoustic trauma. **B)** The CF and corresponding threshold of the IC units immediately after acoustic trauma. Markers with upward arrows represent units that were included in the analyses, but did not have distinguishable receptive fields immediately after acoustic trauma. The location of these markers on the x-axis indicate the CF of these units before trauma.

Figure 3.2A shows a representative example of the MTF of an IC multi unit with a CF below the trauma frequency (CF = 4.8 kHz). Before exposure, this IC unit had a best modulation frequency of 256 Hz, at which the response gain was 1.68 dB (open markers). After exposure (filled markers), the highest response gain in the MTF increased to 6.36 dB in response to a 128 Hz amplitude modulation. In general, this unit showed an increased response gain for low modulation frequencies (f = 8 – 256 Hz) and a decreased response gain for high modulation frequencies (f = 512 – 1024 Hz). For a high-CF unit, that had a CF before acoustic trauma of 16.7 kHz, a similar clockwise 'tilting' of the shape occurred following acoustic trauma (Figure 3.2B). Response gain increased for the lower modulation frequencies (8 – 64 Hz, except for f = 32 Hz in which response gain was unchanged) and decreased for the higher modulation frequencies (f = 128 – 1024 Hz). Before acoustic trauma, the IC unit responded best to a

modulation frequency of 256 Hz with a response gain of 2.91 dB. After exposure, 256 Hz was still the best modulation frequency, but the unit coded less well for it, with a response gain of -2.41 dB.

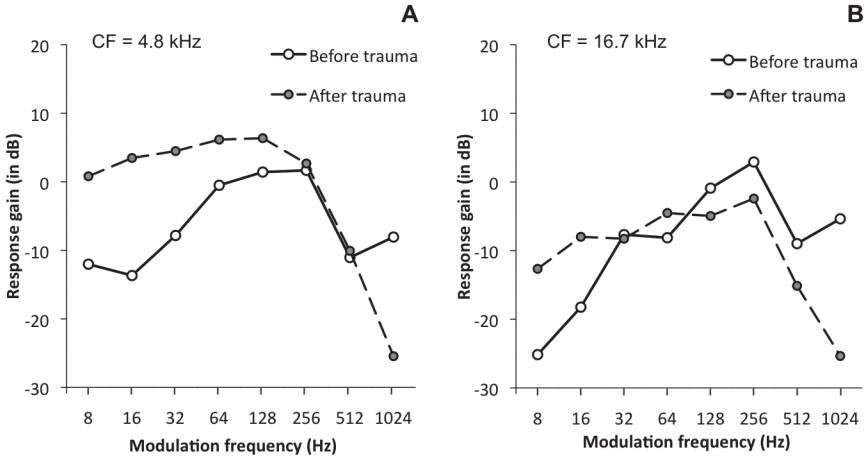

Figure 3.2 Modulation transfer functions. **A)** A representative example of the MTF of a low-CF unit (CF = 4.8 kHz). **B)** A representative example of the MTF of a high-CF unit (CF = 16.7 kHz). Open markers represent the MTF before exposure, filled markers represent the MTF immediately after exposure.

Figure 3.3A shows the average difference (± 95% confidence interval) between the response gain before and after acoustic trauma per modulation frequency. A positive difference indicates an increase in response gain following trauma. In low-CF units (CF < 11 kHz; closed markers), response gains to low modulation frequencies (f = 8 – 128 Hz) increased following exposure (difference > 0 dB), whereas response gains to modulation frequencies between 256 and 1024 Hz typically decreased (Figure 3.3A). High-CF units (CF > 11 kHz *before* exposure; open markers) showed a similar pattern, but with a general downward shift. For these units, the response gain remained unchanged (f = 16 Hz) or decreased (f = 8, 32 – 1024 Hz) following acoustic trauma. This decrease was larger for the high modulation frequencies.

The maximum response gain of the MTF was taken as a measure for envelope coding. For low-CF units (CF < 11 kHz), envelope coding was significantly increased following acoustic trauma (paired-sample T-test $T(43) = -9.300$, $p < 0.001$). For high-CF units (CF > 11 kHz), envelope coding was significantly decreased (Figure 3.3B; paired-sample T-test: $T(24) = 4.224$, $p < 0.001$). Envelope coding of units before exposure were more or less similar across the tonotopic map of the IC (Figure 3.3C) and did not significantly differ between low- and high-CF units (Figure 3.3B; Student's T-test: $T(67) = -2.000$, $p = 0.050$).

Acoustic trauma resulted in a significant difference in envelope coding between low- and high-CF units, in which low-CF units had higher maximum response gains (better envelope coding) than high-CF units (Figure 3.3D; Student's T-test: $T(29.710) = 7.976$, $p < 0.001$, degrees of freedom corrected for unequal variances).

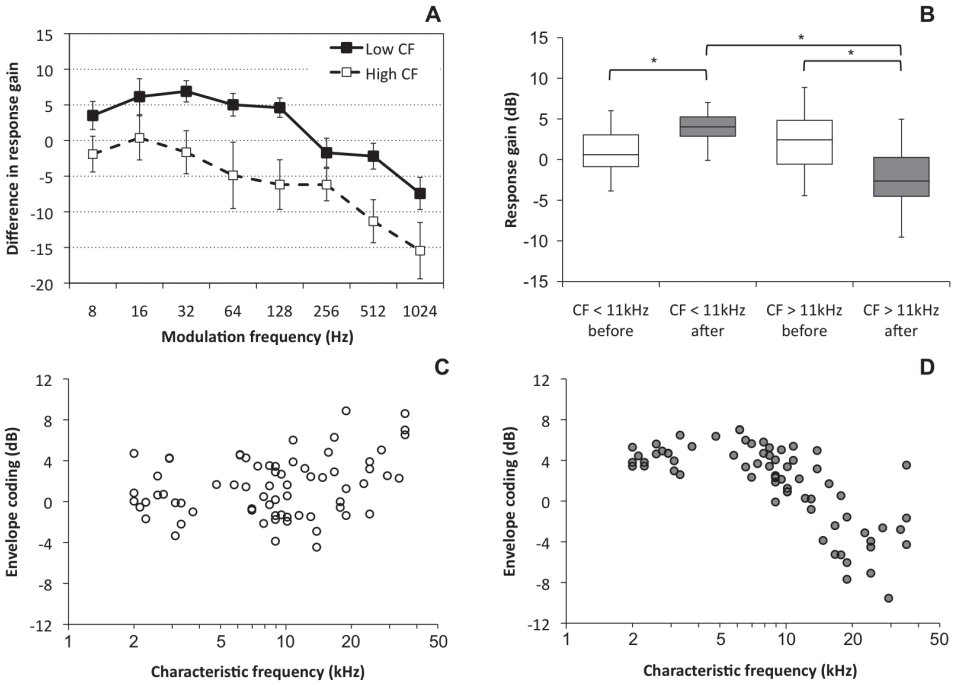

Figure 3.3 Envelope coding. **A)** The mean difference in response gain (± 95% confidence interval) induced by acoustic trauma. A positive difference in response gain (> 0 dB) indicates that the response gain increased as a result of acoustic trauma. Closed markers represent the IC units with a low CF (< 11 kHz), open markers represent IC units with a high CF (> 11 kHz). **B)** Box plots representing the minimum, 25% quartile, median, 75% quartile, and maximum of the response gains of IC units before (open boxplots) and after (filled boxplots) acoustic trauma. A distinction was made between units with a low CF (< 11 kHz) and units with a high CF (> 11 kHz). * represents a significant difference ($p < 0.05$ Bonferroni corrected). **C)** Envelope coding before acoustic trauma plotted as a function of the CF. **D)** Envelope coding measured immediately after acoustic trauma, plotted as a function of the CF that was determined before trauma.

4. Discussion

With the current study, we showed that immediate acoustic trauma resulted in enhanced envelope coding in multi units of the IC with a CF below the trauma frequency (< 11 kHz). In particular, response gains for the low modulation frequencies were enhanced.

Following acoustic trauma, there were no units with a CF of 11 kHz or higher, indicating that afferent input carrying high frequency information was impaired. Obviously, this input innervates mainly the high-CF units. Thus, the high-CF units were deprived from their main input, which presumably explains why these units showed reduced envelope coding after exposure (Figure 3.3B). At first sight, these findings appear inconsistent with the results of Kale and Heinz (2010), who showed in the AN that noise-induced threshold shifts are positively correlated with response gain. However, the authors corrected for threshold shifts by presenting the AM stimuli at the fiber's best-modulation level, which was approximately 20 dB louder for the AN fibers of hearing-impaired animals compared to control animals (Kale and Heinz, 2010; Fig. 7). In the current study, all AM stimuli were presented at the same level, both before and after sound exposure. Thus, our results demonstrated that enhanced envelope coding in the auditory midbrain was apparent even when threshold shifts were not corrected for.

To date, the neurophysiological mechanisms that are responsible for enhanced envelope coding observed after noise-induced hearing loss are not entirely known. Previous studies showed that enhanced envelope coding in chinchillas is present between 27 and 40 days after exposure (Kale and Heinz, 2010; Zhong et al., 2014). The current study showed that this effect was already apparent immediately following overexposure in the IC. This suggests that mechanisms involved in enhanced envelope coding were unmasked immediately after acoustic trauma and are likely to persist over time. In contrast to the results reported here, it has been shown that age-related hearing loss impairs auditory temporal-processing abilities in the IC (Walton et al., 1998). Thus, the effect of hearing loss on envelope coding differs between age-related and noise-induced hearing loss.

Enhanced envelope coding induced by acoustic trauma can be explained by a steepening of the rate-level function due to noise exposure (Kale and Heinz, 2010; Niu et al., 2013). In addition, there appears to be a second mechanism acting on the specific modulation frequencies after exposure. This mechanism seems to filter envelope coding at about -2 to -3 dB/oct and is effective for both low- and high-CF fibers (Figure 3.3A). This low-pass filter possibly suggests a reduced timing accuracy of auditory neurons, which would affect the response gain at high modulation frequencies more than at low modulation frequencies. Thus, the fact that modulation frequencies were not affected equally by the acoustic trauma resulted in an abnormal balance in the envelope information coded by the IC. Potentially, this mechanism may contribute to the difficulties hearing-impaired people encounter with auditory stream segregation.

In conclusion, the current study showed that envelope coding was enhanced in low-CF units of the IC immediately after acoustic trauma. Specifically, modulation gains in

response to low modulation frequencies ($f \leq 128$ Hz) were enhanced. Our results are consistent with responses in the auditory nerve and in auditory-evoked potentials after noise-induced hearing loss (Kale and Heinz, 2010; Zhong et al., 2014), but had not been shown before in the IC. The observed changes in envelope coding after acoustic trauma might be associated with the problems that hearing-impaired people encounter with listening to competing talkers (Bronkhorst and Plomp, 1992). An unnatural amplification of a specific range of modulation frequencies might affect the complex neural processes involved in auditory stream segregation (Grimault et al., 2002). Enhanced envelope coding after acoustic trauma may also be involved in the normal to better-than-normal envelope detection thresholds observed in patients with sensorineural hearing loss (Moore and Glasberg, 2001; Füllgrabe et al., 2003).

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