

Chapter 45

Stimulus-Specific Adaptation Beyond Pure Tones

Israel Nelken, Amit Yaron, Ana Polterovich, and Itai Hershenhoren

Abstract Detecting rare and surprising events is a useful strategy for sensory systems. In the human auditory system, deviance detection is indexed by an important component of the auditory event-related potentials, the mismatch negativity (MMN). Responses of single neurons in the inferior colliculus, medial geniculate body, and auditory cortex of mammals (cats, rats, and mice) show responses that share some properties with MMN: they are evoked by rare events, are preattentive (in as much as they occur in anesthetized animals), and, at least at the level of primary auditory cortex, cannot be accounted for by simple fatigue of the incoming sensory information. Here we extend these results to deviations beyond tone frequency. Recording in rat primary auditory cortex and using oddball sequences consisting of two frozen tokens of broadband noise samples, we found differences between the responses to the same token when used as the common and when used as the deviant, showing an exquisite sensitivity to the small differences between two spectro-temporally similar sounds. Similarly, differential adaptation can be demonstrated when using two word-like stimuli that have been derived from human speech

I. Nelken (✉)

Department of Neurobiology, Silberman Institute of Life Sciences,
Hebrew University, Edmond J. Safra Campus, Givat Ram,
Jerusalem, Israel

Edmond and Lily Safra Center for Brain Sciences,
Hebrew University, Jerusalem, Israel

Interdisciplinary Center for Neural Computation,
Hebrew University, Jerusalem, Israel
e-mail: israel@cc.huji.ac.il

A. Yaron • I. Hershenhoren • A. Polterovich
Department of Neurobiology,
The Silberman Institute of Life Sciences,
The Interdisciplinary Center for Neural Computation,
Hebrew University, Jerusalem, Israel

but adapted to the rat auditory system. Thus, differential adaptation to common and rare sounds is present also with sounds whose complexity mirrors that of natural environments.

1 Introduction

Stimulus-specific adaptation (SSA) is the reduction in the responses to a common sound which does not generalize, or generalizes only partially, to a second, rare sound that is presented in the same sequence. SSA has been recently demonstrated in a number of mammalian and nonmammalian species, including cats (Ulanovsky et al. 2003), rats (Taaseh et al. 2011), mice (Anderson et al. 2009), gerbils (Bauerle et al. 2011), and barn owls (Reches and Gutfreund 2008). SSA at the single-neuron level has been initially described in auditory cortex but has been since demonstrated also in rat inferior colliculus (Malmierca et al. 2009; Zhao et al. 2011), in rat medial geniculate body (Antunes et al. 2010; Bauerle et al. 2011), and in mouse MGB (Anderson et al. 2009).

The mechanisms underlying the generation of SSA have been under intense study recently. While SSA is present at least from the IC and up, it is at best weak in the lemniscal divisions of the IC (the central nucleus, ICc) and the MGB (the ventral division, vMGB). In contrast, in the non-lemniscal divisions of the IC and the MGB, SSA is extremely strong, with some units barely responding to the common sound beyond its first few presentations (Antunes et al. 2010; Bauerle et al. 2011; Perez-Gonzalez et al. 2005). Since on the one hand cooling cortex does not modify SSA in the thalamus (Antunes et al. 2010) but on the other hand SSA in rat auditory cortex tends to increase from the thalamo-recipient layers and out into both the infra- and supra-granular layers (Szymanski et al. 2009), current results suggest that SSA is generated at least twice, once in the non-lemniscal IC and a second time in primary auditory cortex, with a possible third locus in non-lemniscal MGB.

The computations underlying SSA are of great interest as well. Attempts to model SSA to frequency deviants rely on a tonotopic, narrowly tuned input that feeds into a layer of more widely tuned neurons (Mill et al. 2011; Taaseh et al. 2011). This model, in which adaptation occurs within narrow-frequency channels, can be fitted to some of the current results. Furthermore, neurons in non-lemniscal IC and MGB tend to have relatively wide, sometimes badly defined frequency response areas, suggesting the presence of integration across frequency.

In primary auditory cortex (A1), the ability of such a model to account for the full pattern of the published results is less clear. Neurons in A1 tend to have wider tuning width than their MGB input (Miller et al. 2001), suggesting again the presence of integration across frequency that could underlie SSA. However, Taaseh et al. (2011) demonstrated that the responses to a rare tone in the presence of a common one is almost twice as large as that predicted by the model of adaptation in

narrow-frequency channels. Thus, there seems to be additional mechanisms, beyond adaptation in narrow-frequency channels, which enhance the responses to deviant tones in rat A1.

Part of the initial interest in SSA was due to the possibility that it is the neural correlate of mismatch negativity (MMN), an important component of the human event-related potentials (ERPs) which is sensitive to deviance. While a substantial amount of data supports the view that SSA is not MMN (Farley et al. 2010), the fact that SSA and MMN both depend largely in the same way on many stimulus parameters suggests that SSA is upstream of MMN – a hypothesis supported by the recent discovery of deviance sensitivity in midlatency potentials (Grimm and Escera 2012).

The main contribution of this chapter is a demonstration that SSA is more than just “frequency-specific adaptation,” in the sense that SSA can be elicited by stimuli with complex spectral structure, and is present even in the absence of substantial spectral differences between the common and the rare sounds. These findings demonstrate that the mechanisms underlying SSA may be operative in real-world conditions, with complex sounds that include both spectral and temporal variations.

2 Methods

For detailed methods, see Taaseh et al. (2011). We used six adult female Sabra rats weighing 220–250 g. The joint ethics committee (IACUC) of the Hebrew University and Hadassah Medical Center approved the study protocol for animal welfare (protocols NS-06-10041-3, NS-08-11349-3). The Hebrew University is an AAALAC International accredited institute.

Electrophysiological recordings were conducted from the left auditory cortex. A craniotomy was performed over the estimated location of the left auditory cortex. We recorded extracellularly from the auditory cortex using 4–6 glass-coated tungsten electrodes (Alpha-Omega Ltd., Nazareth-Ilit, Israel) with tip separations of ~600 μm . Electrical signals were amplified and filtered between 3 Hz and 8 kHz to obtain both LFP and action potentials. All experiments were conducted in a sound-proof chamber (IAC, Winchester, UK). Sounds were stored as computer files, transduced to voltage signals by a sound card (HDSP9632, RME, Germany), attenuated (PA5, TDT), and played through a sealed speaker (EC1, TDT) into the right ear canal of the rat.

3 Results

The two white noise tokens used here were synthesized in MATLAB using the function `randn`. Ten tokens were generated, and the two tokens with the largest squared difference between their power spectra were selected for use in the oddball

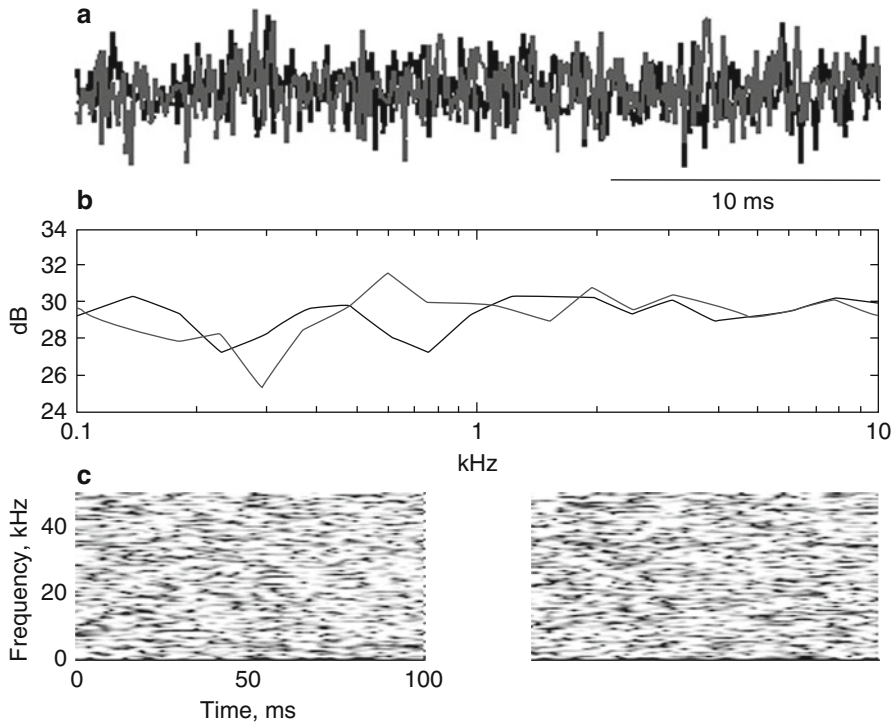


Fig. 45.1 The two noise tokens used in the SSA experiments. (a) Waveforms of the first 30 ms of each of the two tokens. (b) Power spectra of the two tokens, calculated in 1/3 octave bands. (c) Spectrograms of the two tokens

sequences. The two tokens are presented in Fig. 45.1. While their temporal waveforms (Fig. 45.1a), power spectra (Fig. 45.1b), and spectrograms (Fig. 45.1c) are certainly not identical, they are nevertheless very similar to each other.

The two word-like stimuli are presented in Fig. 45.2. They were synthesized using the default settings in the text-to-speech synthesizer, Festival (available in Linux, Fedora 14). The two words have been modified with the help of the vocoder STRAIGHT (Kawahara et al. 2008) using additional processing routines written by us. The frequency content of the two sounds was shifted to above 1 kHz, and the pitch contour was set to a constant 350 Hz. These modifications resulted in sounds that had some features of speech, notably strong spectro-temporal modulations in the speech range. We specifically equalized the peak energy (see Fig. 45.2a) and the overall power spectra (Fig. 45.2b) of the two stimuli. Their spectro-temporal modulations are, however, different (Fig. 45.2c).

The two white noise tokens were used as the common and rare stimuli in oddball sequences. Two sequences were used, with each token playing both roles. The responses of three multiunit clusters to the two tokens are displayed in Fig. 45.3a–c. Figure 45.3a shows the responses of a multiunit cluster that responded essentially

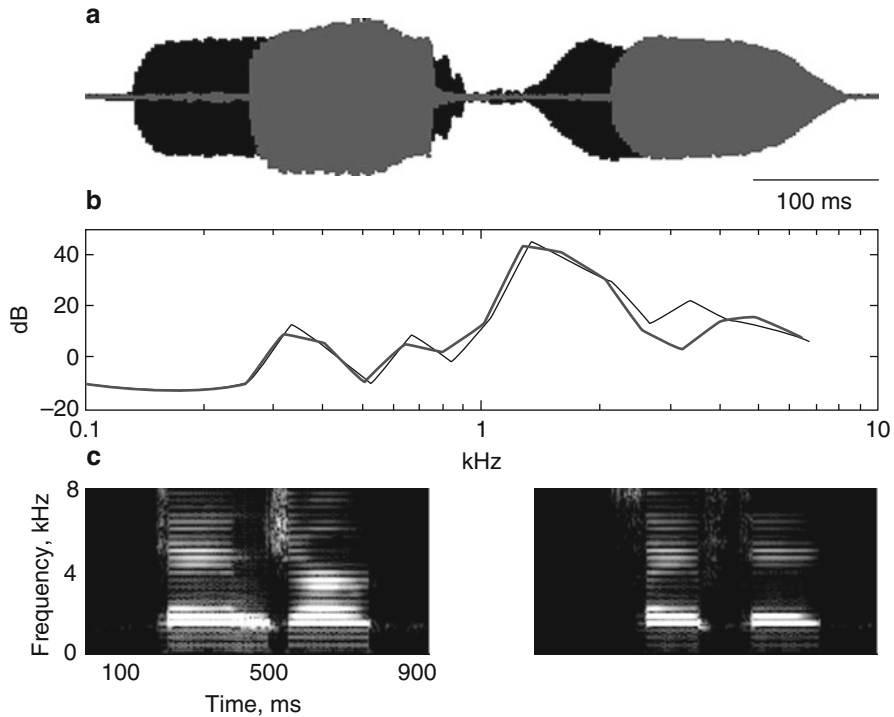


Fig. 45.2 The two word-like stimuli used in the SSA experiments. (a) Waveforms of the two stimuli (*black*: “danger,” *gray*: “safety”). (b) Power spectra of the two stimuli, calculated in 1/3 octave bands (same color convention). (c) Spectrograms of the two stimuli (*left*: “danger,” *right*: “safety”)

identically to the two tokens when common and when rare. Figure 45.3b shows the responses of a multiunit cluster that showed substantial reduction in the response to a token when common, relative to the response to the same token when rare. This is a somewhat extreme example – in most multiunit clusters, the effect was more subtle, as illustrated in Fig. 45.3c. The differences between the responses to a token when common and when rare are significant but small. Note in addition that the enhanced responses to a token when common and when rare had to a large extent the same time course. On the other hand, the responses to the two different tokens could follow quite different time courses (and have quite different overall magnitude).

The word-like stimuli had a longer duration and were presented at a substantially lower rate (ISI of 1,200 ms) than the white noise tokens. Nevertheless, they elicited differential responses when used in oddball sequences, with each of the stimuli tested both as standard and as deviant. Examples of local field potentials recorded in response to the word-like stimuli are shown in Fig. 45.4. The major component of the responses to both words occurred at about the time of the major amplitude transient into the first vowel. The peak-to-peak amplitudes of the responses were

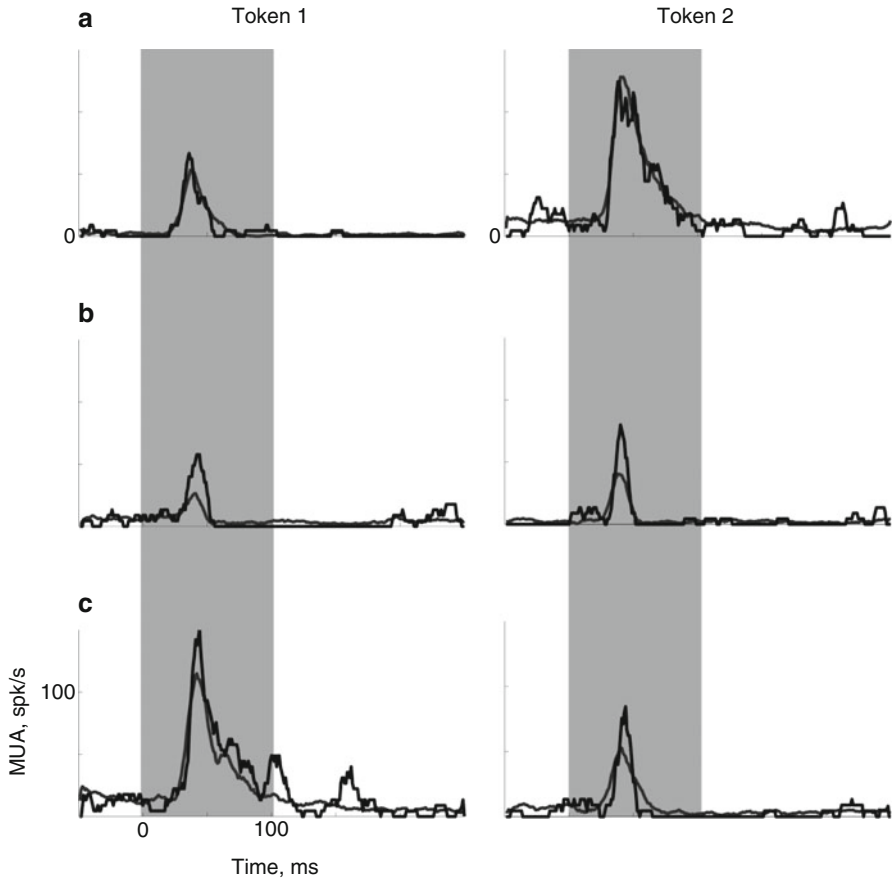


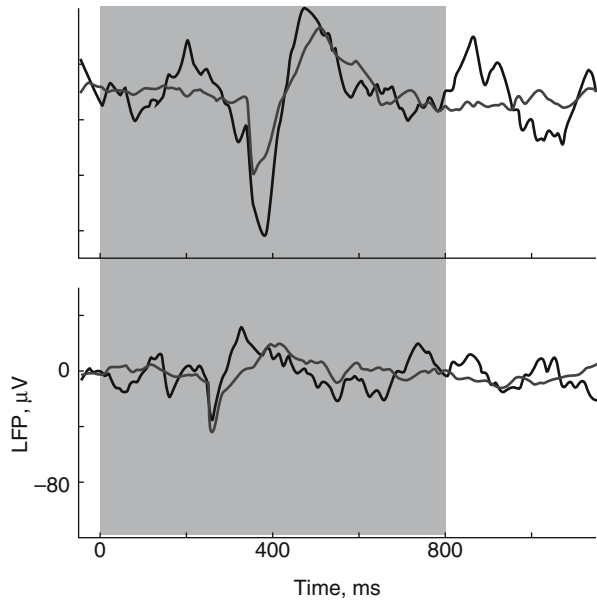
Fig. 45.3 MUA elicited by the two noise tokens when used as common (*gray lines*) and rare (*black lines*) sounds in oddball sequences. (**a–c**) responses at three recording sites

larger when stimuli were rare than when common, although both the response itself and the contrast between common and rare responses were larger for the word-like stimulus derived from “safety” than for the stimulus derived from “danger.” The response to “safety” (top) may have included another response component at offset, although its significance is difficult to establish.

4 Discussion and Conclusions

The single-neuron deviance detection system in A1 has been studied mostly with pure tones and frequency deviants. The differential responses to common and rare sounds demonstrated here suggest that deviance detection in A1 is sensitive to

Fig. 45.4 LFP elicited by the two word-like stimuli (*top*: “safety,” *bottom*: “danger”) when used as standards (*gray lines*) and deviants (*black lines*)



spectro-temporal features as subtle as the differences between two white noise tokens and is capable of distinguishing two word-like stimuli with very similar average spectra (but differing in their spectro-temporal modulations).

While the sensitivity of SSA to subtle spectro-temporal differences is remarkable, the mechanisms that underlie SSA to these complex stimuli may be to a large extent the same mechanisms that underlie SSA to pure tones. For example, while very similar, the two white noise tokens nevertheless differ in their spectral content – some frequencies have average levels that are greater in one than in the other. It could be that these differences in spectro-temporal structure were sufficient to evoke SSA.

To test this hypothesis, we need to know more about the spectro-temporal features of the noise that elicited the responses. Such information can be extracted using an appropriate variant of reverse correlation. Unfortunately, the overall duration of the noise tokens was only 100 ms, and we used only two of them. Thus, we do not have enough information to extract the relevant stimulus features from the responses.

The word-like stimuli illustrated another feature of SSA – the fact that adaptation seems to affect individual temporal components of the responses. This finding extends the observation that SSA occurs close to, or at, response onset. When using word-like stimuli, with relatively long durations and complex spectro-temporal structures, the dominant response components may occur away from stimulus onset. SSA for the word-like stimuli occurred at about the same time as responses to physical events within the sound. This is different from the behavior of MMN, which is locked to the onset of deviance rather than to the time at which a response component occurred.

The findings presented here suggest that SSA in A1 is more than just “frequency-specific adaptation” and that SSA contributes to the detection of small changes in complex, ethologically valid stimuli. At the same time, these findings emphasize the differences between SSA and MMN. Thus, this chapter supports a hierarchical view of deviance detection in which SSA in A1 determines some, but not all, MMN properties (Grimm and Escera 2012).

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