

Learning-induced changes of auditory receptive fields

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Classical conditioning specifically modifies receptive fields in primary and secondary auditory cortical areas to favor the frequency of a tone signal over other frequencies, including tuning shifts toward, or to, this frequency. This plasticity of receptive fields is associative and highly specific, can develop very rapidly, can be expressed under anesthesia and can be maintained indefinitely. Muscarinic receptors in the cortex may be involved. Non-lemniscal thalamic nuclei also develop receptive field plasticity that may contribute to cortical plasticity.

Current Opinion in Neurobiology 1993, 3:570–577

Introduction

Receptive field (RF) plasticity is well established for sensory deprivation in the developing visual and adult somatosensory cortices. Learning has long been studied in the adult auditory cortex. Responses to an acoustic conditioned stimulus (CS) that is followed by an unconditioned stimulus (US), such as food or shock (a 'training trial'), are generally enhanced when repeated CS–US pairing (classical conditioning) produces behavioral evidence of learning [1]. Further investigation of RF plasticity was recently initiated to clarify how the processing of an acoustic CS is modified when it acquires behavioral significance.

Enhanced responses to the CS could reflect either a general increase in neuronal excitability or a specific enhancement in the processing of a behaviorally significant stimulus. Comparison of RFs determined before and after training can distinguish between these alternatives [2•]. If the facilitation is caused by a general increase in neural excitability, then responses to other (non-CS) frequencies should also be increased. In contrast, if the increased response reflects a specific modification in the processing of information about the acquired relationship between the CS and the US, then responses to other frequencies would not be increased to the same extent, and might exhibit no change or even decreased responses. This brief article reviews recent work on learning-induced modifications of RFs in the auditory system. Response modifications during training trials themselves are beyond the scope of this review.

Learning-induced receptive field plasticity in the auditory cortex

The auditory cortex consists of multiple fields, some of which have a spatially organized frequency map that reflects the organization of the cochlea ('primary' or 'tonotopic' fields), while others lack this organization ('secondary' or 'non-tonotopic fields') [3]. RF analysis was first used in work on secondary fields in the cat [4]. RFs were determined in infragranular cells before and after three types of training: sensitization (CS/US unpaired), conditioning (CS/US paired) and extinction (CS alone). Behaviorally, classical conditioning, but not sensitization, caused pupillary dilation conditioned responses (CR), which verified the establishment of a CS–US association. Conditioning, but not sensitization training, modified RFs. RF plasticity was usually highly specific to the frequency of the CS and was maintained unless the animal subsequently underwent extinction training, in which case the modifications were diminished or abolished.

Analysis of pupillary behavior during RF determination compared with acquired pupillary dilation during training trials, produced no evidence that arousal was elicited by the CS frequency or other tones. This was attributed to the very different types of acoustic context between training (single tone, 1.3 min^{-1}) and RF determination (16–30 frequencies, 30–60 per minute) [5]. Overall, these findings indicate that associative learning produces CS-specific modification of receptive fields.

Traditionally, learning and memory have been attributed to secondary sensory cortex and association cortex but

Abbreviations

ACh—acetylcholine; **BF**—best frequency; **CR**—conditioned responses; **CS**—conditioned stimulus; **MGd**—dorsal medial geniculate nucleus; **MGM**—magnocellular medial geniculate nucleus; **MGv**—ventral medial geniculate nucleus; **NB**—nucleus basalis; **RF**—receptive field; **US**—unconditioned stimulus.

not to primary sensory cortex. Thus it may not be surprising that learning-induced RF plasticity develops in secondary auditory cortical fields. To clarify this issue, RFs were obtained from infragranular cells in primary tonotopic fields in the guinea pig [6]. The CS frequency was never the best frequency (BF) — the frequency that is the peak of the pre-training tuning curve — to enable determination of the extent to which conditioning shifts frequency tuning. Conditioning (one session consisting of 30 trials) produced behavioral CR in 4–5 trials, typical for aversive, or 'fear', conditioning [7]. Highly specific modifications of RFs developed immediately after training and were maintained at a 24 hour retention test in most cases. Typically, responses to the CS frequency increased, and responses to the BF and many other frequencies decreased or showed little change, shifting tuning toward, or to, the CS frequency which became the new BF. The RF plasticity was highly specific to the frequency of the CS (Figs. 1a(i–iii) and Fig. 1b(i)).

The absence of these modifications in subjects trained in a sensitization control paradigm (CS and US unpaired) indicated that the RF plasticity is associative. It is interesting to note that sensitization training increased responses in general, across the RF (Fig. 1b(ii)). Putative differential arousal effects during RF determination could not account for the detailed findings and in any event were not observed [6]. Further investigation revealed that these general increases are independent of the CS modality. Visual sensitization training (light/shock unpaired) produces the same effects on acoustic RFs as does auditory sensitization training (tone/shock unpaired) (Fig. 1b(ii)) [8].

Specific RF plasticity also develops in habituation. Following response decrements to the repetition of a single tone for several hundred trials, post-repetition, RFs showed an enduring highly specific decreased response to the habituated frequency relative to other frequencies (Fig. 1b(iii)) [9].

Highly specific RF plasticity also develops in primary auditory cortex in two-tone — CS⁺ (reinforced), CS⁻ (not reinforced) — discrimination training. Responses to the CS⁺ frequency increased whereas responses to the frequency of the CS⁻, the pretraining BF and other non-CS⁺ frequencies generally decreased, both in an easy task and in a more difficult task. Tuning shifts were retained or stronger at a 1 hour retention test. In contrast, good behavioral discrimination (cardiac CR) developed only for the easy task [10]. Thus, RF plasticity neither depends upon nor guarantees the behavioral expression of learning. (For concordant discrimination findings using partial RFs, see [11].)

That RF plasticity includes increased response to the CS(+) frequency and decreased response to the BF and other frequencies, raises the question of whether the modifications are sequential or simultaneous, i.e., are they 'cooperative'? A time-sampling study, with RFs determined after 5, 15 and 30 trials of conditioning and at a retention period of 1 hour indicated that these opposite changes at the CS frequency and the BF develop simultaneously. It is interesting to note that RF plasticity was present after only 5 trials of training; if not fully

developed at this time, it continued to develop with additional conditioning trials and was maintained at the 1 hour retention test [12••].

Long term retention and the ability of learning-induced RF plasticity to be expressed under anesthesia were assessed by conditioning guinea pigs in the waking state (30 trials given in a single session) but the RFs were determined while they were deeply anesthetized (pentobarbital or ketamine), on the day before training and from 1 hour to 8 weeks after training [13••]. CS-specific RF plasticity was present at the first post-training retention period and for as long as 8 weeks following training, the longest period tested. That RF plasticity is expressed in the anesthetized state provides yet another indication that it is not the result of arousal to the CS frequency during RF determination [13••].

The rules governing tuning shifts have not yet been completely delineated. It appears, however, that there must be some pre-training excitatory response to the CS frequency and that the shifts to the CS frequency can be as great as 1 octave ([4,13••]; NM Weinberger, unpublished data).

A very recent study using a novel paradigm for discrimination conditioning reports opposite effects on RFs in the primary auditory cortex of the gerbil. Responses to the CS⁺ were decreased relative to responses to CS⁻ frequencies (all other frequencies including the BF), so that the CS frequency lies at a local minimum of the post-training RF ([14••]; F Ohl, C Simonis, H Scheich, *Soc Neurosci Abst* 1992, 18:841; F Ohl, H Scheich, unpublished data). The authors point out that this effect provides for 'lateral contrast enhancement' (Fig. 2).

There are striking differences between the training methods of this study and previous studies that might be responsible for the different findings. In the example above, discrimination conditioning and RF determination were highly similar: one of the several frequencies used to obtain the RF was paired with shock; also brief tones were presented repeatedly at rates greatly exceeding those used in standard training situations. An advantage of this novel procedure is that it minimizes contextual differences between training and RF determination [5] while a possible disadvantage is that subjects may not acquire frequency discriminations under these conditions. No behavioral data were reported, precluding inferences about what the subjects learned. The authors point out that previous RF studies measured the tuning only to 'onset' responses whereas they analyzed discharges during the entire 250 ms duration of the tones. Therefore, to some extent, RF plasticity could consist of facilitated responses to short-latency discharges followed by relative suppression of longer latency discharges at the frequency of the CS.

Implications for frequency maps

Frequency-specific RF plasticity has implications for the representation of frequency across primary auditory cor-

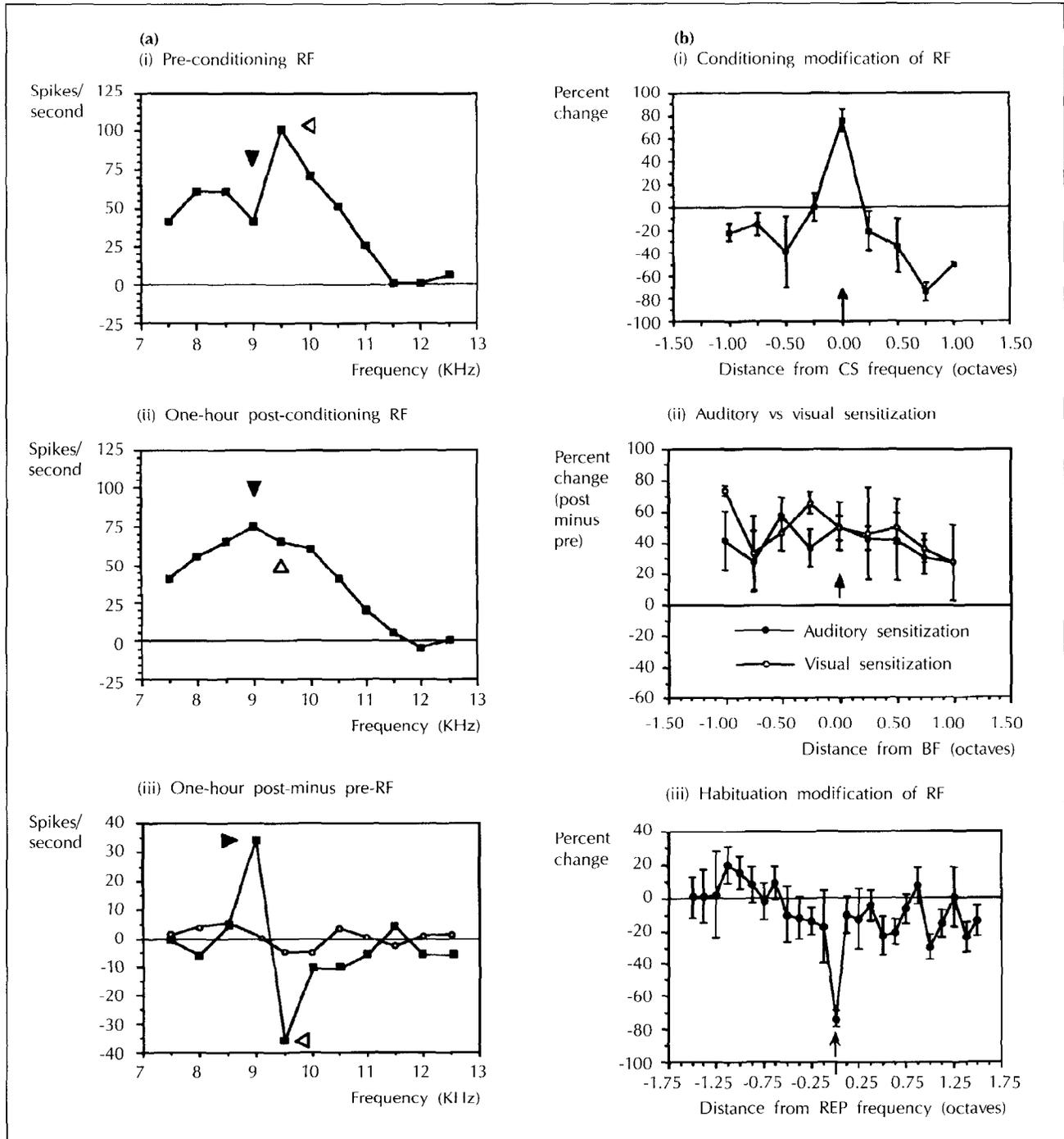


Fig. 1. The effects of learning upon receptive fields in the primary auditory cortex of the waking guinea pig. **(a)** An example of CS-specific receptive field modification produced by classical conditioning. In the case illustrated, the CS frequency became the best frequency (BF). (i) Pre-conditioning the BF was 9.5 kHz (open arrowhead) and the CS was selected to be 9.0 kHz (closed arrowhead) for conditioning, which produced behavioral conditioned responses to this frequency (not shown). (ii) One hour post-conditioning, the CS frequency became the BF due to increased response to this frequency and decreased response to the pre-conditioning BF and other frequencies. (iii) The receptive field difference function (post- minus pre-RFs) shows that conditioning produces the maximal increase at the CS frequency and maximal decrease at the pre-training best frequency. Open circles show no systematic effect on spontaneous activity. Modified from [6]. **(b)** Group receptive field mean (\pm standard error) difference functions (treatment minus control) for three types of training. (i) Conditioning produces increased response at the frequency of the conditioned stimulus and decreases at most other frequencies starting at 0.25 octaves from the CS frequency ('side-band suppression'). (ii) Sensitization training produces a broad, non-specific increase in response across the auditory receptive field, both for auditory and visual sensitization training. Modified from [8]. (iii) Habituation produces a frequency-specific decrease for a frequency which developed a decrement in response due to repeated presentation alone. Note the high degree of specificity; frequencies 0.125 octaves from the repeated frequency were little affected. Modified from [9].

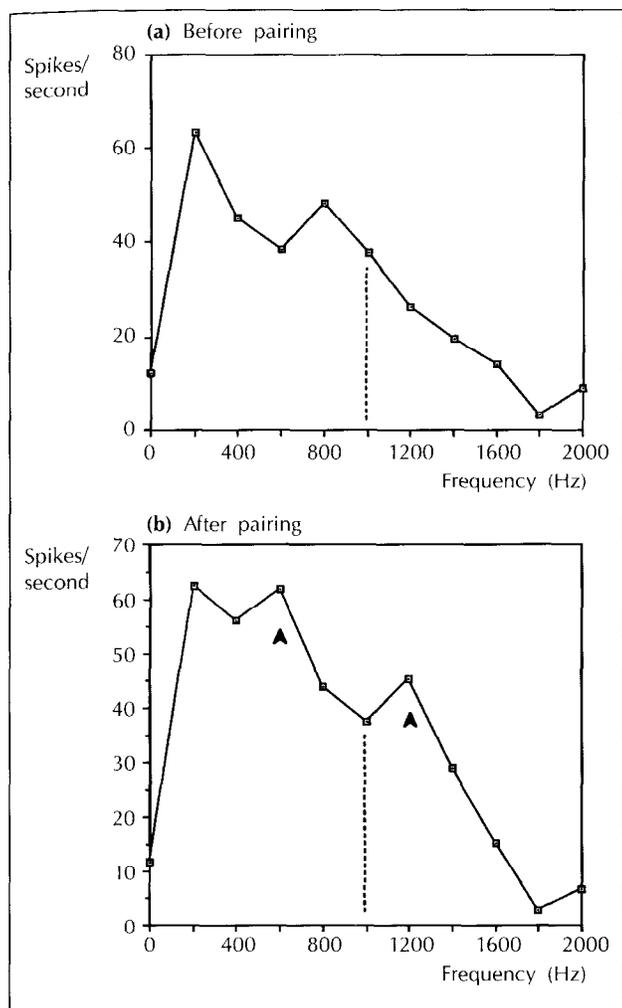


Fig. 2. An example of the effects of discrimination training on frequency receptive fields (FRF) from a unit in primary auditory cortex of the gerbil. **(a)** Before and **(b)** after pairing of 1 kHz tones repeatedly (30 times) with a mild electrocutaneous tail stimulus. Arrows denote increased responses to frequencies lower and higher than the CS frequency. On-responses (stimulus duration 250 ms) to tone bursts of 70–75 db SPL were integrated over 10 repetitions. There is no change of response to the BF nor to the conditioned frequency but to frequencies neighboring the conditioned frequency on the slope of the FRF. In other units this 'sideband effect' was seen as well as a general drop of response to all frequencies. Redrawn with permission of the authors from [14••].

tex. Specifically, it had been hypothesized that the representation of a learned behaviorally significant frequency should increase [15]. A recent study supports the general conception. Owl monkeys trained over several months in a difficult frequency discrimination task for a food reward show increased representation for the frequency band within which discriminations were made [16••].

Measures of metabolic activity that provide the spatial distribution of learning effects during training trials, also reveal specific learning-induced effects in frequency representation (for review see [17]). Rats trained with tone followed by aversive stimulation of the midbrain reticular formation exhibit increased uptake of 2-deoxyglucose in the parts of the auditory cortex representative

of the CS frequencies [18]. These effects are compatible with the idea that RF plasticity favors processing of the CS (F Gonzalez-Lima, personal communication). Also, there are preliminary reports of CS-specific modifications of metabolic activity in the auditory cortex for discriminated appetitive [19••] and aversive conditioning and instrumental avoidance training ([14••]; H Scheich, C Simon, *Soc Neurosci Abst* 1991, 17:451). CS-specific increased metabolic activity has also been reported for an appetitively rewarded acoustic localization task in layer IV of the auditory cortex of the rat [20].

Receptive field plasticity in the medial geniculate nucleus

RF plasticity in learning has also been studied in the medial geniculate nucleus, which consists of three major nuclei that project to auditory cortical fields. The ventral medial geniculate nucleus (MGv) is the lemniscal thalamic auditory nucleus, containing narrowly-tuned cells and providing tonotopically-organized input to the middle layers of primary tonotopic fields of the auditory cortex. During classical conditioning, its neurons do not develop changed responses to the CS [21–24]. Receptive fields obtained from the MGv before and after cardiac conditioning in the guinea pig revealed only restricted, highly transient modifications of RFs [25].

The magnocellular medial geniculate nucleus (MGm) is the non-lemniscal auditory input, containing broadly tuned cells and providing non-tonotopic input to the upper layers of all auditory cortical fields, primary and non-primary. During classical conditioning, its neurons very quickly develop increased responses to the CS [21–24,26]. Following classical conditioning, but not sensitization training, RFs in the MGm are modified to favor the CS frequency; this retuning is highly specific, associative and not transient [11,24,27••]. In fact, RF plasticity in the MGm is present after a 45 day retention interval [28]. This plasticity can also be expressed with animals under general anesthesia [29]. Because their RFs are tuned much more broadly than are those of auditory cortical cells, it seems unlikely that the cortical RF plasticity is simply 'projected' from the MGm. Further detailed experiments are required to elucidate the functional relationships between the MGm and the auditory cortex.

The dorsal medial geniculate nucleus (MGd) projects to secondary cortical fields. It has been little studied during conditioning, but there is some evidence of conditioning and discrimination effects in this nucleus [24]. During conditioning, frequency-specific RF plasticity develops, is associative and is retained in the MGd of the guinea pig [30]. Its relation to RF plasticity in secondary auditory cortex has not been studied.

Frequency specific metabolic changes have also been found for conditioning [20,31–34] and habituation [35] throughout the subcortical auditory system. These findings contrast with the lack of neurophysiological plasticity during training [21–24] and also minimal and transient

plasticity of RFs [25] in the MGv, which might be expected to reflect the plasticity of lower auditory structures. However, many metabolic studies use hundreds of training trials. If RF plasticity develops rapidly in the auditory cortex but more slowly in the subcortical lemniscal auditory system, then this plasticity would not be detected in the MGv during the smaller number of trials used in neurophysiological studies [21–25]. Understanding the relationships between metabolic effects and neurophysiological findings of RF plasticity will benefit from greater similarity of experimental paradigms.

Possible role of cholinergic mechanisms in learning-induced RF plasticity in the auditory cortex

Studies of acetylcholine (ACh) support the notion that it has a role in learning-induced RF plasticity in the auditory cortex. Iontophoretic application of muscarinic agonists produces atropine-sensitive modification of tuning of RFs that endures well beyond the period of ACh application [36]. Similar effects are found for the application of anticholinesterases, indicating that endogenous ACh can modify frequency receptive fields [37]. Pairing one tone with iontophoretic application of muscarinic ago-

nists produces pairing-specific tuning shifts of RFs and these are blocked by atropine [38].

Stimulation of the nucleus basalis (NB), the major source of neocortical acetylcholine, can modulate various evoked responses in the auditory cortex that endure after cessation of application and are blocked by atropine. These include facilitation of field potentials, cellular discharges and excitatory postsynaptic potentials (EPSPs) elicited by medial geniculate stimulation [39,40••], and specific facilitation of neuronal discharges to paired tones in anesthetized and in waking rats ([41•]; E Hennevin, J-M Edeline, B Hars, C Maho, abstract 40, Fifth Conference on the Neurobiology of Learning and Memory, Irvine, October 1992; J-M Edeline, B Hars, C Maho, E Hennevin, unpublished data).

A model of learning-induced receptive field plasticity

A model, consistent with many findings reviewed here and elsewhere, suggests that CS-specific receptive field plasticity is produced by the convergence of three systems in the auditory cortex: auditory lemniscal, from the MGv; auditory non-lemniscal from the MGm; and cholinergic from the NB. The three systems interact during con-

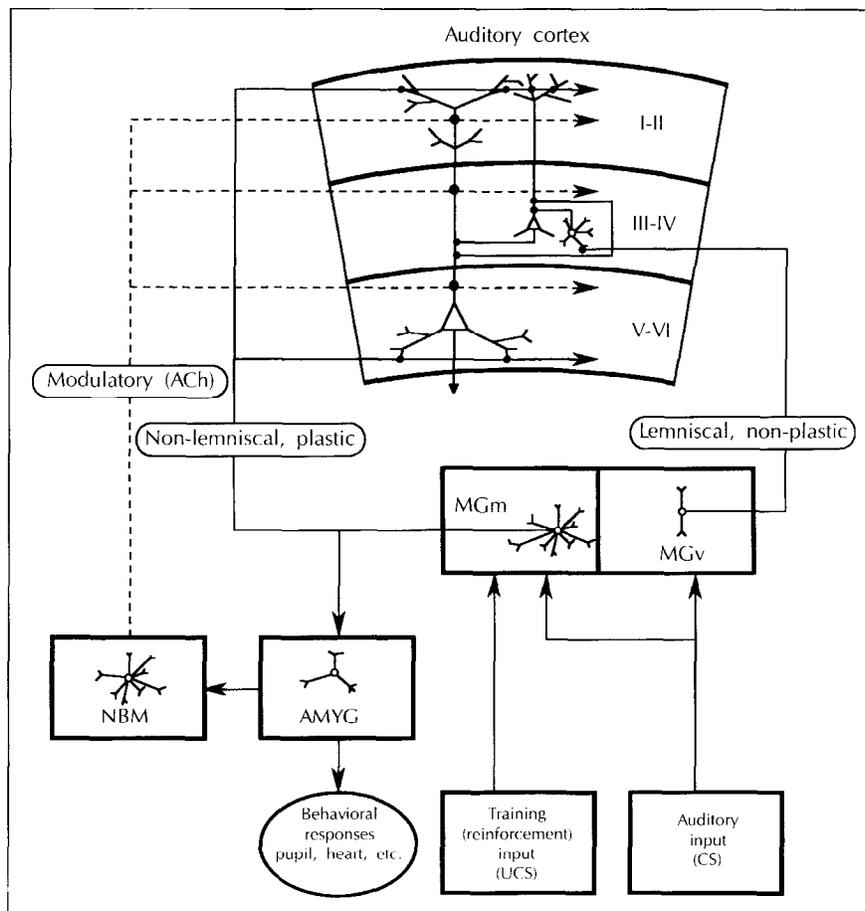


Fig. 3. Diagram showing the major components of a model of conditioning-induced receptive field plasticity in the auditory cortex and initiation of behavioral conditioned responses. The mechanisms for associative CS-specific receptive field plasticity in the auditory cortex are based on the convergence of three subcortical systems at the auditory cortex, which provide detailed frequency information ('lemniscal, non-plastic'), indicate the behavioral significance of a current acoustic stimulus ('non-lemniscal, plastic') and exemplify ACh neuromodulation of pyramidal cells based on the importance of the current auditory stimulus ('modulatory'). See text for explanation. AMYG: amygdala; IC: inferior colliculus; NBM: nucleus basalis of Meynert. Roman numerals refer to cortical laminar zones. Modified from [15].

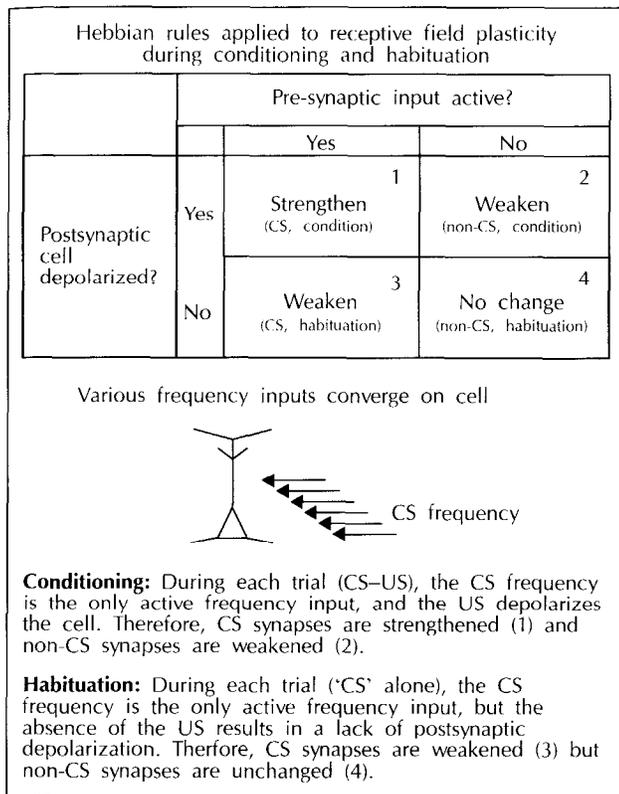


Fig. 4. Application of extended Hebbian Rules to RF plasticity for classical conditioning and habituation. Simple combinations of presynaptic and postsynaptic elements, each of which can be in an active or non-active state might account for the effects of conditioning on CS and non-CS synaptic strengths and for the effects of habituation on the repeated and non-repeated stimuli.

ditioning trials in the following way: the MGv provides unaltered frequency input to the middle layers; the MGm input to the upper layers is increased due to CS-US convergence in this nucleus with subsequent development of increased responses to the CS; and the MGm projection to the amygdala elicits autonomic and somatic behavioral conditioned responses and also causes the ultimate widespread release of ACh via projections from the amygdala to the NB [15] (Fig. 3). ACh acting at muscarinic receptors on the apical dendrites of pyramidal cells is thought to amplify the excitatory input from the MGm by increasing membrane resistance, thus increasing postsynaptic depolarization. Extended Hebbian rules suggest that there is a strengthening of synapses for the CS frequency because this frequency is the only one present during training trials thus effecting a correlation of presynaptic and postsynaptic depolarization. Synapses for non-CS frequencies would be weakened because these frequencies are not present during training trials, resulting in a disconnection with the depolarized postsynaptic pyramidal cells. Habituation effects on receptive fields also could be accounted for in this model (Fig. 4).

Conclusion

Recent receptive field studies reveal that classical conditioning produces associative, rapidly developing (minutes), enduring (8 weeks) and highly specific modification of the representation of spectral information in the primary auditory cortex. Cooperativity of facilitation of discharges to a signal frequency and decreased responses to other frequencies is suggested by their simultaneous and very rapid development. Muscarinic and non-lemniscal auditory thalamic processes may be involved. RF plasticity may underlie learning-induced modifications of spatial frequency maps. The occurrence of representational plasticity during learning in the adult challenges pure feature-detection views of primary sensory cortex. Expanded investigation of learning-induced RF plasticity should promote a better understanding of the relationships among sensory, perceptual, learning and memory functions of the auditory cortex in particular, and perhaps of sensory cortex in general [42••].

Acknowledgments

Preparation of this review and research was supported by Office of Naval research grant N00014-91-J-1193 and by an unrestricted grant from the Monsanto Company. I wish to thank H Scheich and F Ohl for providing recent findings and data for Fig. 2, F Gonzalez Lima for helpful discussions and J Weinberger for preparation of the manuscript.

References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:

- of special interest
 - of outstanding interest
1. WEINBERGER NM, DIAMOND DM: **Physiological Plasticity in Auditory Cortex: Rapid Induction by Learning.** *Prog Neurobiol* 1987, 29:1-55.
 2. WEINBERGER NM: **Beyond Neuronal Excitability: Receptive Field Analysis Reveals That Association Specifically Modifies the Representation of Auditory Information.** In *Neuropsychology of Memory* 2nd Edition. Edited by Squire LR, Butters N. New York:Guilford Press; 1992:496-510.
- Explains logic and need for receptive field analyses of learning effects, in the absence of which fallacious conclusions are that associative conditioning and sensitization training produce the same changes in auditory cortex.
3. WOOLSEY CN: *Cortical Sensory Organization: Multiple Auditory Areas.* New Jersey: Humana Press; 1982.
 4. DIAMOND DM, WEINBERGER NM: **Classical Conditioning Rapidly Induces Specific Changes in Frequency Receptive Fields of Single Neurons in Secondary and Ventral Ectosylvian Auditory Cortical Fields.** *Brain Res* 1986, 372:357-360.
 5. DIAMOND DM, WEINBERGER NM: **Role of Context in the Expression of Learning-Induced Plasticity of Single Neurons in Auditory Cortex.** *Behav Neurosci* 1989, 103:471-494.

6. BAKIN JS, WEINBERGER NM: Classical Conditioning Induces CS-Specific Receptive Field Plasticity in the Auditory Cortex of the Guinea Pig. *Brain Res* 1990, 536:271-286.
 7. LENNARTZ RC, WEINBERGER NM: Analysis of Response Systems in Pavlovian Conditioning Reveals Rapidly vs Slowly Acquired Conditioned Responses: Support for Two-Factors and Implications for Neurobiology. *Psychobiology* 1992, 20:93-119.
 8. BAKIN JS, LEPAN B, WEINBERGER NM: Sensitization Induced Receptive Field Plasticity in the Auditory Cortex is Independent of CS-Modality. *Brain Res* 1992, 577:226-235.
 9. CONDON CD, WEINBERGER NM: Habituation Produces Frequency-Specific Plasticity of Receptive Fields in the Auditory Cortex. *Behav Neurosci* 1991, 105:416-430.
 10. EDELINE J-M, WEINBERGER NM: Receptive Field Plasticity in the Auditory Cortex During Frequency Discrimination Training: Selective Retuning Independent of Task Difficulty. *Behav Neurosci* 1993, 107:82-103.
- Demonstration that discrimination training produces specific RF plasticity. Shows that RF plasticity develops even when task difficulty results in poor behavioral discrimination.
11. EDELINE J-M, NEUENSCHWANDER-EL MASSIOUT N, DUTRIEUX G: Frequency-Specific Cellular Changes in the Auditory System During Acquisition and Reversal of Discriminative Conditioning. *Psychobiology* 1990, 18:382-393.
 12. EDELINE J-M, PHAM P, WEINBERGER NM: Rapid Development of Learning-Induced Receptive Field Plasticity in the Auditory Cortex. *Behav Neurosci* 1993, in press.
- Time series study in which RF plasticity is evident after only five training trials. Shows simultaneous opposite development of increased responses to CS, decreased responses to best frequency, suggesting that cooperative processes may be responsible for learning induced tuning changes.
13. WEINBERGER NM, JAVID R, LEPAN B: Long-Term Retention of Learning-Induced Receptive Field Plasticity in the Auditory Cortex. *Proc Natl Acad Sci USA* 1993, 90:2394-2398.
- An extensive study of retention of learning-induced RF plasticity. Shows indefinite retention up to eight weeks and expression of RF plasticity under general anesthesia; this suggests that studies of auditory cortex in anesthetized subjects may reflect prior learning experiences. For a related rare study of retention of learning-induced plasticity see [28].
14. SCHEICH H, SIMONS C, OHL F, THOMAS H, TILLEN J: Learning-Related Plasticity of Gerbil Auditory Cortex: Feature Maps Versus Meaning Maps. In *Advances in Metabolic Mapping Techniques for Brain Imaging of Behavioral and Learning Functions*. Edited by Gonzalez-Lima F, Finkenstadt T, Scheich H. Netherlands: Kluwer Academic Publishers; 1992:447-474.
- An important empirical and conceptual paper which reviews both metabolic and recent neurophysiological findings of effects of learning. Demonstrates that auditory cortex contains both feature maps and maps that reflect learning.
15. WEINBERGER NM, ASHF JH, DIAMOND DM, METHERATE R, MCKENNA TM, BAKIN J: Retuning Auditory Cortex by Learning: a Preliminary Model of Receptive Field Plasticity. *Concepts Neurosci* 1990, 1:91-132.
 16. RECANZONE GH, SCHREINER CE, MERZENICH MM: Plasticity in the Frequency Representation of Primary Auditory Cortex Following Discrimination Training in Adult Owl Monkeys. *J Neurosci* 1993, 13:87-103.
- First neurophysiological analysis of frequency map subsequent to learning, in owl monkey. Reports increased representation for frequency band used in difficult two-tone discrimination training.
17. SCHEICH H: Auditory Cortex: Comparative Aspects of Maps and Plasticity. *Curr Opin Neurobiol* 1991, 1:236-247.
 18. GONZALEZ-LIMA F, SCHEICH H: Neural Substrates for Tone-Conditioned Bradycardia Demonstration With 2 Deoxyglucose, II. Auditory Cortex Plasticity. *Behav Brain Res* 1986, 20:281-293.
 19. GONZALEZ-LIMA F: Brain Imaging of Auditory Learning Functions in Rats: Studies With Fluorodeoxyglucose Autoradiography and Cytochrome Oxidase Histochemistry. In *Advances in Metabolic Mapping Techniques for Brain Imaging of Behavioral and Learning Functions*. Edited by Gonzalez-Lima F, Finkenstadt T, Scheich H. Netherlands: Kluwer Academic Publishers; 1992:39-109.
- A comprehensive review which explains the technical aspects of the use of metabolic approaches to learning in the auditory system and summarizes findings for several learning paradigms and levels of the auditory system. This work derives from seminal studies, such as that represented by [18], noted both for CS specific increase in metabolic activity and the distinctive use of novel control groups.
20. CARRASCAL E, ORTIN A, COLLIS F, AREVALO M: Metabolic Activity Changes in Auditory System of the Rat During Associative Learning. *New Trends in Exp and Clin Psychia* 1990, 6:53-63.
 21. GABRIEL M, SALTWICK SE, MILLER JD: Conditioning and Reversal of Short-Latency Multiple-Unit Responses in the Rabbit Medial Geniculate Nucleus. *Science* 1975, 189:1108-1109.
 22. RYUGO DK, WEINBERGER NM: Differential Plasticity of Morphologically Distinct Neuron Populations in the Medial Geniculate Body of the Cat During Classical Conditioning. *Behav Neural Biol* 1978, 22:275-301.
 23. BIRT D, OLDS M: Associative Response Changes in Lateral Midbrain Tegmentum and Medial Geniculate During Differential Appetitive Conditioning. *J Neurophysiol* 1981, 46:1039-1055.
 24. EDELINE J-M: Frequency-Specific Plasticity of Single Unit Discharges in the Rat Medial Geniculate Body. *Brain Res* 1990, 529:109-119.
 25. EDELINE J-M, WEINBERGER NM: Thalamic Short Term Plasticity in the Auditory System: Associative Retuning of Receptive Fields in the Ventral Medial Geniculate Body. *Behav Neurosci* 1991, 105:618-639.
 26. EDELINE J-M, DUTRIEUX G, NEUENSCHWANDER-EL MASSIOUT N: Multiunit Changes in Hippocampus and Medial Geniculate Body in Free-Behaving Rats During Acquisition and Retention of a Conditioned Response to a Tone. *Behav Neural Biol* 1988, 50:61-79.
 27. EDELINE J-M, WEINBERGER NM: Associative Retuning in the Thalamic Source of Input to the Amygdala and Auditory Cortex: Receptive Field Plasticity in the Medial Division of the Medial Geniculate Body. *Behav Neurosci* 1992, 106:81-105.
- Shows that very broad receptive fields develop CS-specific plasticity in this non-laminar auditory nucleus that projects to upper lamina of all auditory cortical fields. These findings contrast with the very limited and transient receptive field plasticity in the laminar ventral medial geniculate body which projects topographically to granular layers of tonotopic cortical fields (see [25]).
28. EDELINE J-M, NEUENSCHWANDER-EL MASSIOUT N, DUTRIEUX G: Discriminative Long-Term Retention of Rapidly Induced Multiunit Changes in the Hippocampus, Medial Geniculate and Auditory Cortex. *Behav Brain Res* 1990, 39:145-155.
 29. LENNARTZ RC, WEINBERGER NM: Frequency-Specific Receptive Field Plasticity in the Medial Geniculate Body Induced by Pavlovian Fear Conditioning is Expressed in the Anesthetized Brain. *Behav Neurosci* 1992, 106:484-497.
 30. EDELINE J-M, WEINBERGER N: Subcortical Adaptive Filtering in the Auditory System: Associative Receptive Field Plasticity in the Dorsal Medial Geniculate Body. *Behav Neurosci* 1991, 105:154-175.
 31. GONZALEZ-LIMA F, SCHEICH H: Classical Conditioning Enhances Auditory 2-Deoxyglucose Patterns in the Inferior Colliculus. *Neurosci Lett* 1984, 51:79-85.
 32. GONZALEZ-LIMA F, SCHEICH H: Neural Substrates for Tone-Conditioned Bradycardia Demonstrated with 2-Deoxyglucose.

- cose, I. Activation of Auditory Nuclei. *Behav Brain Res* 1984, 14:213-233.
33. HARVEY JA, WINSKY L, SCHINDLER CW, MCMASTER SE, WELSH JP: Asymmetric Uptake of 2-Deoxy-D-[¹⁴C] Glucose in the Dorsal Cochlear Nucleus During Pavlovian Conditioning in the Rabbit. *Brain Res* 1988, 449:213-224.
34. GONZALEZ-LIMA F, AGUDO J: Functional Reorganization of Neural Auditory Maps by Differential Learning. *Neuroreport* 1990, 1:161-164.
35. GONZALEZ-LIMA F, FINKENSTADT T, EWERT J-P: Learning-Related Activation in the Auditory System of the Rat Produced by Long-Term Habituation: A 2-Deoxyglucose Study. *Brain Res* 1989, 489:67-79.
36. MCKENNA TM, ASHE JH, WEINBERGER NM: Cholinergic Modulation of Frequency Receptive Fields in Auditory Cortex: I. Frequency-Specific Effects of Muscarinic Agonists. *Synapse* 1989, 4:30-43.
37. ASHE JH, MCKENNA TM, WEINBERGER NM: Cholinergic Modulation of Frequency Receptive Fields in Auditory Cortex: II. Frequency-Specific Effects of Anticholinesterases Provide Evidence for a Modulatory Action of Endogenous ACh. *Synapse* 1989, 4:11-51.
38. METHERATE R, WEINBERGER NM: Cholinergic Modulation of Responses to Single Tones Produces Tone Specific Receptive Field Alterations in Cat Auditory Cortex. *Synapse* 1990, 6:133-145.
39. METHERATE R, ASHE JH: Basal Forebrain Stimulation Modifies Auditory Cortex Responsiveness by an Action at Muscarinic Receptors. *Brain Res* 1991, 559:163-167.
40. METHERATE R, ASHE JH: Nucleus Basalis Stimulation Facilitates •• Thalamocortical Synaptic Transmission in Rat Auditory Cortex. *Synapse* 1993, in press.

Tests and supports the hypothesis that ACh acting at muscarinic receptors in the auditory cortex can produce facilitation of auditory input from the medial geniculate, at the level of field potentials, cellular discharges and excitatory postsynaptic potentials. This work follows logically from early findings that endogenous ACh, acting at muscarinic receptors in the auditory cortex, can produce retuning of frequency receptive fields [37] and that pairing cortical application of ACh with a single tone produces frequency specific modifications of receptive fields [38].

41. HARS B, MAHO C, EDELINE J-M, HENNEVIN E: Basal Forebrain • Stimulation Facilitates Tone-Evoked Responses in the Auditory Cortex of Awake Rat. *Neuroscience* 1993, in press.

Reports atropine-sensitive specific facilitation of neuronal responses to tone by activation of source of cholinergic input to cortex. Effects were not long lasting, due perhaps to insufficient exploration of stimulus parametric space.

42. WEINBERGER NM, ASHE JH, EDELINE J-M: Learning-Induced Re- •• ceptive Field Plasticity in the Auditory Cortex: Specificity of Information Storage. In *Neural Bases of Learning and Memory*: Edited by Delacour J. Singapore: World Scientific Publishing; 1993, in press.

An overview of the use of receptive field analysis in learning. Includes both a review of empirical work, based on initial findings in the cat (see [4]) and subsequent studies in the guinea pig, for both classical conditioning (see [6]) and habituation (see [9]) and also a detailed extension of the original model of learning-induced receptive field plasticity (see [15]). For additional important aspects of RF plasticity not covered in this recent citation see [5], which shows that RF plasticity transcends the state in which learning occurs and presents the 'functional mosaic' hypothesis that cells have multiple receptive fields, only one of which is expressed in a given situation.

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