

Plasticity in the Primary Auditory Cortex: Substrate of Specific Long-Term Memory Traces

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Glossary

Best frequency (BF) – The frequency that produces the best cellular response to a frequency at a given sound-level intensity.

Conditioned response (CR) – A behavioral response that is elicited by a conditioned stimulus as a result of classical or instrumental conditioning.

Conditioned stimulus (CS) – An initially neutral stimulus that elicits a behavioral response after it has been associated with an unconditioned stimulus.

Frequency receptive field (frequency RF) – The portion of the acoustic spectrum to which a cell in the auditory system is sensitive. Frequency RFs are often called ‘tuning curves.’

Local field potentials (LFPs) – Responses of sensory (auditory) cortex to sensory (acoustic) stimuli, which are comprised of evoked voltage changes in the low-frequency range (1–300 Hz). They generally index excitatory postsynaptic potentials recorded in extracellular space with a large electrode on the surface or in the depths of the cortex.

Tonotopic map – The progressive distribution of best frequencies across primary auditory cortex. The posterior-to-anterior axis has a systematic range of BFs, from lower to higher, respectively.

Unconditioned response (UR) – An innate behavioral response that is elicited by a stimulus in the absence of conditioning.

Unconditioned stimulus (US) – A stimulus that elicits a UR.

Introduction

The search for the neural substrates of learning and memory has been extremely biased in at least two dimensions: brain structures under investigation and aspects of memory under consideration. With regard to functional anatomy, most attention has been focused on structures such as the hippocampus, amygdala, striatum, cerebellum, frontal, and the so-called association fields of the cerebral cortex. In contrast, the sensory systems have been relatively ignored. Concerning memory itself, interest has been focused on the processes that enable memory storage while inquiry into how the contents of memory are

represented and stored has languished. The two domains of neglect are related, because sensory systems, particularly sensory cortex, appear to be sites of the specific storage of experiences. They are not the only sites of storage, but they provide a particularly advantageous means of locating storage sites and they have now been successfully exploited. The primary auditory cortex (A1) is perhaps that sensory region for which research has yielded the greatest dividends.

This article concerning learning-based plasticity in A1. It will summarize the evidence for specific long-term memory traces. But in so doing, it will more broadly examine the usually implicit assumptions about brain–behavior organization, concluding that the schema, which has served behavioral neuroscience since its inception, is no longer valid.

The Dominant Model of Brain–Behavior Relationships

Scientific study of brain–behavior relationships may be traced back to a sensory–motor conception of the nervous system in the early nineteenth century. Bell and Magendie separately discovered (*c.* 1812–30) that the dorsal roots of the spinal cord are sensory, while the ventral roots are motor. These seminal findings provided the first brain–behavior, structural–functional organizational principle. Much of the research program for the rest of the century concerned the extent to which the entire neuraxis was organized on sensory–motor principles. The last 30 years of the nineteenth century witnessed the discovery of the motor cortex, and the approximate delineation of sensory cortices based on modality-specific sensory deficits following cortical ablations.

Still, sensory and motor areas did not comprise the entire neocortex. Could an overarching principle of cortical organization be discovered? In 1901, Fleshsig reported that sensory and motor cortices exhibited myelination at birth, while other areas could require as long as one postnatal month to myelinate. Further, his observations of fibers in the internal capsule led him to the erroneous conclusion that only the sensory and motor cortices received subcortical projections; the association areas were thought to receive inputs only from other cortical regions. Thus, Fleshsig provided an anatomical

basis for the distinction between lower (i.e., sensory–motor) and higher psychological functions.

It remained only to specify in greater detail the nature of these lower and higher functions. This was supplied in the anatomical studies of AW Campbell. Purely on the basis of cytoarchitectonics (i.e., study of the fine structure of the cortex), Campbell divided sensory cortical fields into two types, such as primary visual cortex (V1) ‘visual sensory’, and nearby regions (e.g., areas 17 and 18) ‘visual psychic’. Similarly, the region now known as A1 was termed ‘auditory sensory’ while adjacent areas, in modern parlance, auditory belt areas, were ‘auditory psychic.’ In so doing, Campbell executed an almost metaphysical leap that has plagued brain–behavior research to the present day, because he cleaved sensory processes from cognition. Subsequent neurophysiological studies of sensory cortices operated within this conceptual constraint, so that the analysis of sounds, sights, and touches was assumed to occur in the primary sensory fields, while interpretation of the behavioral meaning or comprehension of the external world was assigned to nonprimary sensory areas, that is, to the psychic regions. A major implication of this schema was removing learning and memory from primary sensory cortices.

Once learning, memory, and other cognitive processes were removed from the primary sensory regions, without any experimental support, the dominant brain–behavior paradigm was essentially in place. So imbued into neuroscience as to have gone largely unquestioned, it holds a three-stage processing chain: sensory–association–motor. In short, primary sensory cortex analyzes stimuli, association and related cortex comprehend the stimuli, in large part based on past experiences, and send the results to the motor cortex which is responsible for actual behavior.

Note that this S–A–R theory comprises a reflex model of brain–behavior substrates. In reality, this is an extended model of the functional operation of the spinal cord. As this model still dominates neuroscientific thinking, it would seem that we have not achieved fundamental conceptual advances. This would not be a problem if the S–A–R model was adequate. That it cannot account for the role of A1 in learning and memory will soon become apparent.

In closing this section, we would do well to not look at Pavlovian conditioning as a willing accomplice of this reflex-based model. Pavlov himself emphasized the association between two stimuli, for example, the conditioned and unconditioned stimuli (CS and US, respectively). Such CS–US learning (i.e., stimulus–stimulus, S–S) contrasts with stimulus–response learning (S–R) that has come to dominate much thinking. S–R conditioning is, of course S–A–R in reality, for no one holds that Pavlovian conditioning consists of a monosynaptic connection between the CS and the conditioned response (CR). While both S–S and S–R learning certainly occur,

the former appears to develop within a few trials, before the appearance of specific motor CRs. Indeed, conditioning seems to be at least a two-stage process, in which CS–US (S–S) associations first enable animals to predict the future, followed by the formation of CS–CR (S–R) links that enable an animal to take overt behavioral action based on this knowledge. Certainly, S–R conditioning is of great importance and its circuitry has been well delineated, to an extent unmatched for other forms of learning. However, S–S conditioning remains of central importance. Contemporary understanding of Pavlovian conditioning views it as a general process for determining the ‘causal fabric’ of the environment, a general-purpose mechanism for making the best possible predictions in the service of adaptive behavior. Only when Pavlovian conditioning is narrowly construed as S–R, and labeled ‘procedural learning’ in contradistinction to ‘declarative learning’, can one conclude that it supports the S–A–R model. Unfortunately, such a construal is all too popular and grows more so as workers minimally versed in these matters attack the neurobiology of learning and memory.

Learning, Memory, Plasticity, and the Auditory Cortex: The Foundational Period

Introduction

Vast majority of investigations into the neurophysiology of learning and memory and A1 have studied associative learning, in the form of either Pavlovian (classical conditioning) or instrumental conditioning. This is not a constraint because the formation of associations is so fundamental. Associative processes can account for a surprisingly wide range of learning, memory, and other cognitive processes, far transcending traditional narrow construes of conditioning. Studies during the foundational period, roughly 1956–85, focused on the question of whether associative learning involved (e.g., was accompanied by) associative plasticity in A1.

Conditioning

Galambos and colleagues published the first Western study on Pavlovian conditioning and plasticity in A1. Cats received an auditory (click) CS paired with an immediately following puff of air to the face (US), resulting in significantly larger local field potentials (LFPs) to the CS click. The authors validated learning by noting the development of behavioral CRs. Furthermore, they also controlled for CS constancy at the ear by obtaining the same findings with subjects under neuromuscular blockade, thus preventing head and pinna movements and possible contractions of the middle ear muscles that can alter effective sound levels at the tympanic membrane. Interestingly, the authors failed to include a

nonassociative control, such as a group that received the CS and US unpaired. However, subsequent investigations did include proper controls, confirming the associative nature of increased response magnitude of LFPs in A1. LFP research was extended to different conditioning tasks and Pavlovian processes, with essentially the same findings of enhanced responses to sounds that became behaviorally important. Similar results were obtained for instrumental avoidance learning.

In addition to the use of LFPs, workers began recording cellular discharges in A1. Most studies recorded from clusters of cells (multiple-unit activity). The results generally were the same, that is, increased discharges to an acoustic CS as animals formed CRs. This increase in response was fairly consistent, both in simple (one-tone) conditioning and in two-tone discrimination training. Reversal was also obtained when the CS⁺ and CS⁻ acoustic stimuli were interchanged after initial learning. Moreover, acoustic CS⁺ stimuli acquired the ability to elicit responses in the sensory cortex of the shock US, that is, primary somatosensory cortex.

Such cluster recordings have the advantage over single-unit recordings of yielding good data over many hours or days. They have the disadvantage of being unable to determine if single cells develop different directions of plasticity, that is, either increased or decreased responses. In other words, if associative processes produce both increased and decreased responses to the CS, but increased responses dominate, then the decreased responses would not be detected.

Study of single units in auditory cortex during learning also found plasticity. However, as suspected, despite the detection of many cells that developed increased responses to the CS, a substantial number developed decreased responses, and yet others exhibited no change. Similar heterogeneity of unit discharge plasticity was also found in secondary auditory cortex (A2). Such divergent results were not attributable to inadvertent changes in effective acoustic stimulus level in the auditory periphery, undetected movements, muscle contractions, or feedback from muscle spindles, because the same results were obtained when animals were trained while under neuromuscular blockade.

Although single-unit plasticity was shown to be associative, the findings of opposite sign made little functional sense. Thus, while recording in A1 during training trials had provided fundamental information, this approach appeared to be yielding diminishing returns after almost 30 years of research. Nonetheless, research during the foundational period had sufficiently answered the original question in the affirmative: "Yes, associative learning does involve associative plasticity in the primary auditory cortex." Thus, a major crack in the foundation of the S-A-R model was found. Primary sensory (auditory) cortex does not only analyze stimuli but also changes its response to

the same physical stimuli when they acquire behavioral importance. That is, the responses of the same cells in A1 are governed by at least two factors: physical acoustic parameters of sounds and their acquired meaning. Campbell would not have approved.

Contemporary Approaches: A Synthesis of Two Disciplines

Introduction: Toward Specificity of Plasticity, Memory Content and Memory Codes

The contemporary era may be considered to have been initiated in the 1980s when a new question was posed. Instead of asking whether A1 is involved in learning and memory, focus shifted to the functional significance of associative plasticity. For example, do associative processes change the large-scale functional organization of the auditory cortex? If so, then sensory analysis and learning-induced plasticity do not merely coexist, but rather sensory analysis is shaped by learning processes. Moreover, if learning shapes sensory representations of experience in primary sensory cortex, then it may also store them in primary sensory cortex.

In addressing this previously ignored issue, inquiry transcended associativity to reach the domain of specificity of neuronal plasticity, which is necessary to understand how the brain represents and stores the details of experience, that is, the actual contents of memories. While much research has been devoted to the processes that enable memory and to demonstrations of plasticity in learning, there had been virtually no focus on the information itself that is stored or on the memory codes that transform neural activity into an accurate neural representation of a memory.

For example, learning and memory could have caused increased responses to CS frequencies in either of two ways: first, they could have increased responses not only to the CS but also to most other frequencies; or second, they could have specifically increased responses to CS frequencies but had no effect or even decreased responses to other frequencies. In the latter case, learning could have shifted the tuning of cells to the CS frequency, hence revealing that associative processes actually shape sensory analysis within primary sensory cortex. These alternatives cannot be resolved during training trials because the other test tones either would have to be followed, or not followed, by the US. Both situations would constitute new learning tasks so that one could never find out what happens in simple associative learning. The solution was to determine frequency tuning before and after conditioning. To accomplish this goal, it was necessary to combine two fields that had developed along parallel, seldom-intersecting trajectories, auditory neurophysiology and the neurobiology of learning and memory ([Figure 1](#)).

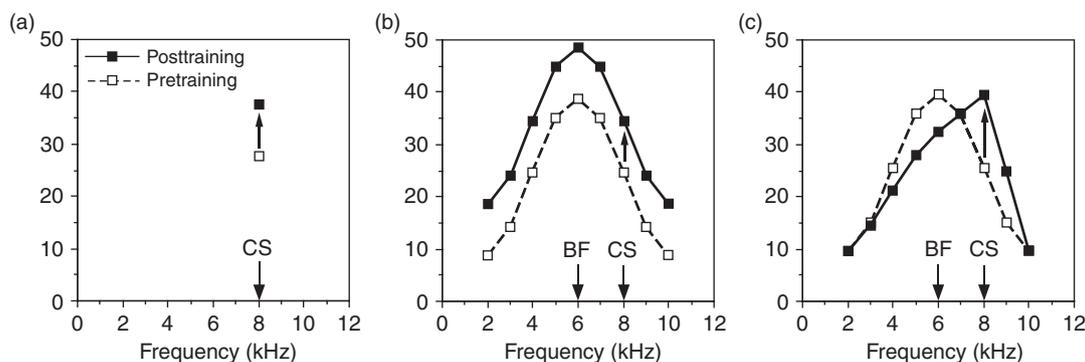


Figure 1 Receptive field analysis reveals whether learning-induced plasticity is general to the dimension of a CS or specific to the value of the CS. (a) During training trials, one can determine whether or not responses to the CS changed; in this case, they increased. However, both general and specific plasticity could produce this result. (b) A general change revealed by receptive field analysis before and after conditioning. (c) A CS-specific instance of associative representational plasticity, in which responses to many non-CS frequencies are reduced, producing a shift in tuning to the frequency of the CS.

Conditioning

Gonzalez-Lima and Scheich used a variant of the new approach. They trained gerbils (tone and aversive stimulation of the mesencephalic reticular formation) and later determined the metabolic response (uptake of 2-deoxyglucose, 2-DG) of the auditory cortex to the CS frequency. Paired animals developed both the behavioral index of learning, that is, conditioned bradycardia, and an increase in the area of A1 with metabolic response to the CS frequency. The absence of similar effects in control groups (CS-US unpaired, CS alone, and US alone) showed that the CS-specific plasticity was associative. These findings indicate that associative processes can enlarge CS-response areas and strongly imply that the underlying neurons have shifted their tuning toward or to the CS frequency within the tonotopic map.

At about the same time, direct evidence of receptive field plasticity was found by obtaining RFs before and after learning. Cats received a single session of tone-shock pairing and behavioral learning was validated by the formation of the pupillary dilation CR. The tuning of single units in two nonprimary auditory fields, A2, and ventral ectosylvian (VE) cortices developed CS-specific plasticity in the paired group but not a control group. Extinction (tone alone) produced a reversal of the RF plasticity, indicating that A1 plasticity reflects the current state of behavioral salience of sound.

Studies then focused on A1 of the guinea pig, with behavioral validation of associative learning, for example, conditioned bradycardia. Following determination of frequency receptive fields, the frequency to be used as the CS was then selected to not be the best frequency (peak of the tuning curve), in order to determine if conditioning caused tuning shifts within the tonotopic map. Animals then received a single session of tone paired with shock. A comparison of posttraining with pretraining RFs revealed increased responses to the CS frequency accompanied by

decreased responses to the pretraining best frequency and many other frequencies. These opposing changes were often sufficiently large to produce frank shifts of tuning toward, and even to, the frequency of the CS, which could become the new best frequency (Figure 2(a)). RF plasticity was found to be associative, as it required stimulus pairing; sensitization training produces only a general increase in response to all frequencies across the RF.

CS-specific shaping of frequency tuning also can develop when receptive fields are complex and even nonexistent (i.e., below threshold). Figure 2(b) shows an example of a pretraining double-peaked frequency RF. The CS frequency was selected to be in the valley between the peaks. For posttraining, the maximum change was an increase in response at the CS frequency. Figure 2(c) illustrates a case in which there was no response to any frequency before conditioning. Nonetheless, postconditioning observations revealed a clear excitatory response to the previously ineffective CS frequency, alone.

Several other attributes of RF plasticity make it an attractive candidate for a process that operates in normal concert with sensory coding processes to subserve the storage of behaviorally relevant auditory information. First, RF plasticity is highly specific to the CS frequency; responses to frequencies a small fraction of an octave away are attenuated. Second, it exhibits generality across different types of training, for example, instrumental avoidance conditioning, two-tone classical discrimination training (i.e., increased responses to the CS⁺ frequency but decreased responses to the CS⁻, BF, and other frequencies), and discriminative instrumental avoidance conditioning. Third, RF plasticity develops very rapidly, after only five training trials, as rapidly as the first behavioral (e.g., cardiac) signs of association. Fourth, RF plasticity exhibits consolidation, that is, continues to develop increased responses to the frequency of the CS

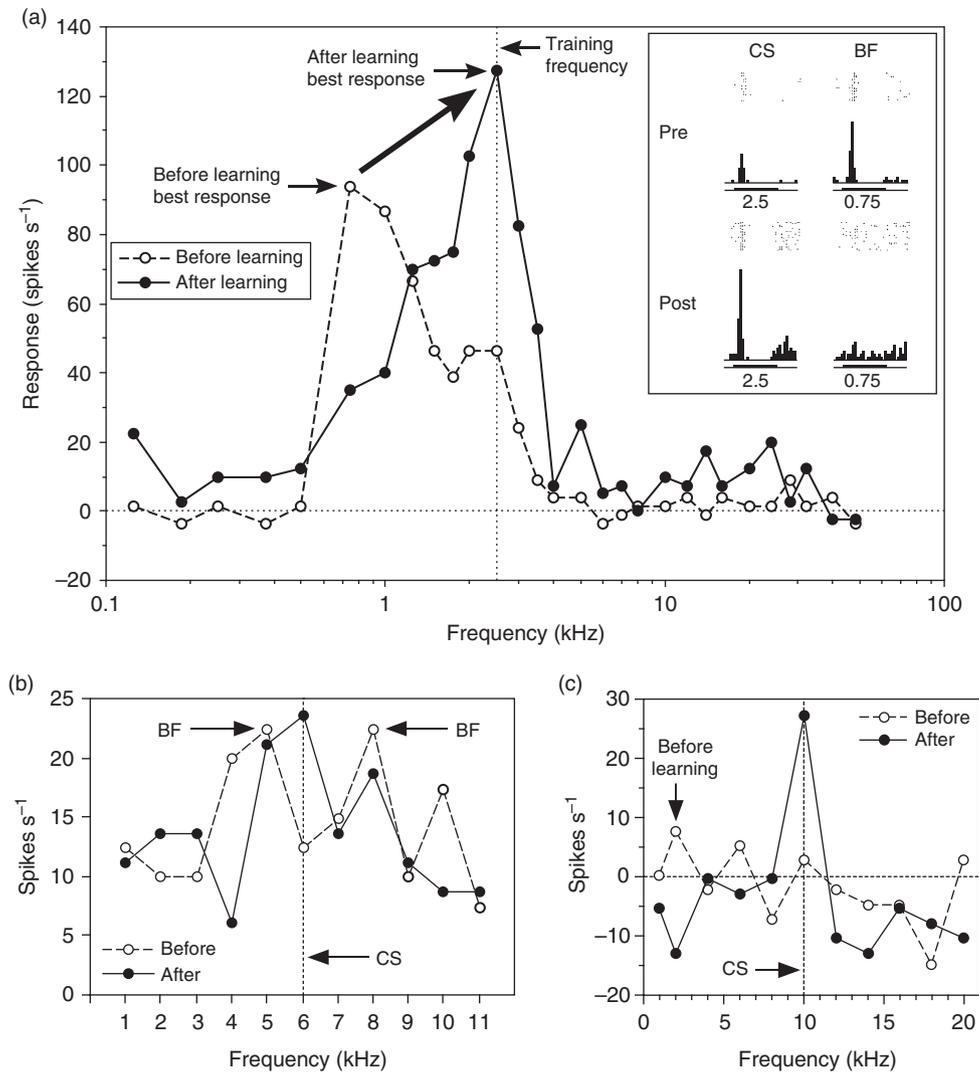


Figure 2 Classical conditioning produces CS-specific facilitation and tuning shifts. (a) An example of a complete shift of frequency tuning of a single cell in A1 of the guinea pig, from a pretraining best frequency (BF) of 0.75 kHz to the CS frequency of 2.5 kHz after 30 trials of conditioning. Inset shows pre- and posttraining poststimulus time histograms (PSTHs) for the pretraining BF and the CS frequencies. (b) Double-peaked tuning, with pretraining BFs at 5.0 and 8.0 kHz. The CS was selected to be 6.0 kHz, a low point. After conditioning (30 trials), responses to the CS frequency increased to become the peak of tuning. (c) A cell that exhibited minimal or no response to tones before tuning developed tuning specifically to the CS frequency after conditioning (30 trials).

versus decreased responses to other frequencies in the absence of further training over hours and days. Fifth, RF plasticity exhibits long-term retention, enduring for the longest periods tested, up to 8 weeks after a single 30-trial conditioning session.

Specific associative RF plasticity is not an artifact of spontaneous changes in tuning because tuning is stable prior to conditioning and shifts are CS directed. Neither is it an artifact of state. Whereas animals exhibit arousal and related responses to sustained (e.g., 2–5 s) CS frequencies during training trials, they do not exhibit any behavioral (e.g., cardiac) responses to the frequency of the CS when it is presented as one of a number of rapidly presented, brief (e.g., 200 ms) sequential tone pips during

RF determination. Moreover, animals trained in the waking state exhibit RF plasticity when tested under deep general anesthesia.

CS-specific associative tuning shifts develop in the A1 of all species studied to date: guinea pig (*Cavia porcellus*), echolocating big brown bat (*Eptesicus fuscus*), cat (*Felis catus*), and rat (*Rattus rattus*). Additionally, CS-directed tuning shifts should increase the representational area of CS frequencies in the tonotopic map of A1. This has been found in instrumental learning in both the owl monkey (*Aotus trivirgatus boliviensis*) and the rat.

Learning-induced tuning plasticity is not limited to animals. The same paradigm of classical conditioning (tone paired with a mildly noxious stimulus) produces

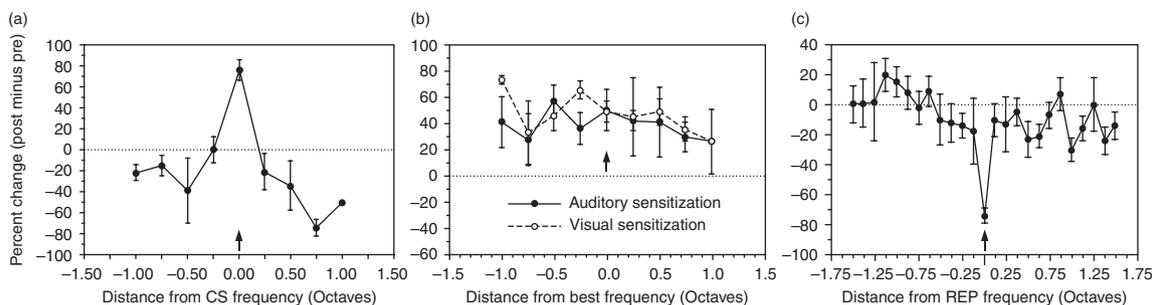


Figure 3 Summary of the effects of (a) conditioning, (b) sensitization, and (c) habituation on frequency receptive fields in the primary auditory cortex (A1) of the guinea pig. Data are normalized to octave distance from (a) the CS frequency, (b) the presensitization best frequency, or (c) the repeated frequency. Note that conditioning produces a CS-specific increased response whereas sensitization (tone–shock or light–shock unpaired) produces general increases across the spectrum. Habituation produces a frequency-specific decreased response.

concordant CS-specific associative changes in A1 of humans (*Homo sapiens*).

In summary, CS-specific RF plasticity has major characteristics of associative memory. It is not only associative, but is also highly specific, discriminative, rapidly acquired, develops consolidation over hours and days, is retained at least for many weeks, and exhibits generality across training tasks, types of motivation, and species. Additionally, when the same tone is repeatedly presented without reinforcement, subjects habituate, that is, learn that the tone does not signal reward or punishment. Habituation produces the opposite effect of associative learning, that is, a frequency-specific decrease in the response of A1 to the repeated sound. **Figure 3** summarizes changes in tuning for conditioning, sensitization, and habituation.

Beyond Specific Plasticity of Acoustic Frequency

Although the plasticity of acoustic frequency has been most extensively studied, specific associative changes in the processing of sound are not confined to this feature of sound. For example, rats were trained in a sound maze in which food reward was contingent upon successful navigation using only auditory cues. In this task, the repetition rate of noise pulses increased as the distance between the rat and target location decreased. After subjects had learned this maze, A1 cells exhibited enhanced responses to high-rate noise pulses and stronger phase locking of responses to the stimuli. In other words, learning produced a shift in tuning to high-repetition rates, that is, the stimulus features that were most closely associated with procurement of food. Similarly, owl monkeys trained to detect an increase in the envelope frequency of a sinusoidally-modulated 1 kHz tone developed increased sensitivity to small changes in envelope frequency. Even the processing of sound intensity (level) is specifically

shifted by associative processes. Rats were trained in a sound maze to move to a place in a small arena guided only by changes in the changing loudness of ongoing sound bursts. A1 responses became selective to relevant sound levels. Moreover, attentional demands can switch plasticity between stimulus parameters, such as frequency and intensity.

These findings are illustrative and we can expect further demonstrations that sensory processing in A1 is shaped by learning. It is likely that most, if not all, acoustic parameters are subject to specific associative plasticity. Moreover, other sensory systems are undoubtedly operating on the same principle: “Behaviorally relevant stimuli receive preferential processing and gain both processing capacity via tuning shifts and representational area, within primary sensory cortices.”

Additional Cognitive-Based Plasticity

The A1 is involved in many other cognitive processes. Space limitations permit only a listing. They include specific neurophysiological correlates of working memory, reference memory, attention, concept formation, and expectancy.

Moreover, cross-modality interactions are prevalent in A1. For example, in monkeys trained in a complex auditory discrimination task, the cue light that signaled trial availability developed the ability to elicit responses in A1. In humans, the sight of speech without sound elicits neural activity in A1. A recent anatomical study in the gerbil may provide an anatomical basis for some cross-modality effects. The authors found a surprisingly large number of inputs to A1 from nonauditory regions of both the cortex and the thalamus.

Perhaps one of the most surprising findings is that learning strategy, rather than the type or amount of learning determines auditory cortical plasticity. Thus, different groups of rats learned to bar press for water reward

contingent on the presence of a tone. Although both groups achieved high levels of correct performance, specific plasticity in A1 (CS-specific decrease in threshold and bandwidth) developed only for subjects that used a strategy based on attention to tone onset rather than tone duration.

Does the Auditory Cortex Form and Hold Specific Long-Term Memory Traces?

A specific long-term memory trace (SMT) is an enduring neural record of a particular aspect of experience. How might one determine if specific RF plasticity does index actual long-term memory traces? One might expect that destruction of A1 should remove its long-term memory traces, which would in turn be revealed by behavioral tests showing a specific loss of auditory memories. This apparently simple and decisive test proves to be neither because A1 is both sensory and mnemonic. Lesions will therefore interfere with both processes, so that any deficits cannot be attributed to either.

If not lesions, then what might be done? One approach is to attempt to defeat the proposal that long-term memory traces form in A1. As A1 does form associative plasticity (above), what line of attack might be taken? It could be argued that in addition to such plasticity, SMTs should possess the major characteristics of behavioral associative memory itself. This would impose a second level of criteria that have not previously been demanded of any neurophysiological studies of learning and memory. Nonetheless, this is not an unreasonable demand.

What are these characteristics? In addition to being associative, SMTs should also exhibit specificity, fairly rapid formation, long-term retention, and even consolidation, that is, continued strengthening over time after training in the absence of additional reinforcement. Another feature of memory is that it can be formed in a wide variety of learning tasks, rather than being confined to, for example, classical conditioning. A further key feature of memory is that it transcends a particular type of motivation, but develops in both appetitive and aversive situations. Additionally, one would expect SMTs to be manifest for whatever the type of CS or signal stimuli used in training, as is the case for genuine associative memory. That is, SMTs should not be limited to plasticity of frequency representation but should develop for any acoustic parameter that can serve as a signal for reward or punishment. Finally, as in the case of memory, SMTs should be biologically conserved, that is, develop across diverse taxa.

Convergent findings reviewed above show that specific plasticity in A1 meets all of these criteria. Moreover, as this is an active area of inquiry, new acoustic parameters are continually being studied. Although this article can

never be up-to-date, at least one prediction can be made: If an acoustic parameter can serve as a signal or gain behavioral relevance through learning, then its processing in A1 will develop specific representational plasticity.

Conclusions

A1 can no longer be considered to function merely as an acoustic analyzer. Nor is it likely that either the primary visual or primary somatosensory cortices differ fundamentally from A1. The auditory cortex is simply that sensory structure which has been most extensively investigated in learning and memory. In fact, both primary visual and somatosensory fields do exhibit some specific learning-based associative plasticity.

The findings reviewed above should be understood to transcend most approaches to neurophysiological correlates of learning and memory. Of course, demonstrations of such correlates are a necessary starting point but it is not in, and of, itself an ending point. In the absence of another level of inquiry, which seeks to understand the functional significance of learning-related plasticity, we are left largely with a list of plastic places and justified, but not fully satisfying conclusions, that these regions are involved in learning and memory. The evidence to date strongly suggests that at least one of the functions of specific associative tuning shifts and related plasticity in A1 is to store information, that is, serve as locus of specific long-term memory traces. To be sure, most memory substrates probably involve widespread networks of neurons. However, that in no way lessens the need to identify a component of such a network. By both determining the degree of specificity of A1 plasticity and delineating its attributes and characteristics in detail, it is possible to meet the criteria for identifying specific long-term memory traces.

The larger-scale implication of a modern concept of A1 is that the S–A–R model is no longer tenable. Despite understandable attempts to separate the analysis of stimuli from the comprehension and assignment of behavioral importance to stimuli at the level of the cerebral cortex, this approach simply cannot account for the data. It is time to seek a new brain–behavior organizational principle.

See also: Active Avoidance and Escape Learning; Animal Models of Learning and Memory; Cholinergic Systems in Aging and Alzheimer's Disease; Neurotrophic Molecular Analysis; Drug Cues: Significance of Conditioning Factors in Drug Abuse and Addiction; Fear Conditioning; Fear, Anxiety, and Defensive Behaviors in Animals; Memory Consolidation; Neural Basis of Classical Conditioning; Neural Basis of Working Memory; Neural Substrates of Conditioned Fear and Anxiety.

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