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"ADAPTIVE INFORMATION PROCESSING IN AUDITORY CORTEX"

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INTRODUCTION

Central to biological intelligence are the cerebral neocortex and learning. The pronounced expansion of the neocortex relative to other brain structures is a dominant feature of vertebrate evolution including man. Learning involves the incorporation of experience into brain function and so provides the major process by which adaptive behavior is achieved.

In recent years, two basic strategies for understanding brain function and learning have emerged: (1) stimulus-response circuit tracing and (2) information-processing. The first attempts to delineate the complete circuitry involved in the development and performance of a specific behavioral conditioned response (CR), e.g., eyelid CR. It emphasizes learning as the acquisition of specific muscle actions during presentation of a particular stimulus.

The second approach attempts to understand how information is acquired and stored in the brain by determining the transformations in sensory system encoding of information during learning. It emphasizes the multi-potentiality of acquired information, i.e., acquired information can be used as the basis for virtually any adaptive behavioral acts; further, it is available for combination with other information, as required for higher processes (e.g., thought, abstractions, etc.). For this approach, learned (e.g., conditioned) responses serve as indices of information acquisition rather than as ends in themselves (Weinberger et al, 1984a).

Both approaches are complementary but they may lead to very different findings and conceptualizations. For example, the circuit-tracing strategy has resulted in delineation of neuronal constituents within the hindbrain and the cerebellum which are necessary and sufficient for production of slowly-acquired conditioned eyeblink responses in trained animals. In this case, cerebral cortex appears to be unimportant.

In contrast, the information processing approach has continuously implicated the cerebral cortex in physiological and anatomical plasticity during the acquisition and storage of information. Further, such plasticity develops extremely rapidly, well in advance of the emergence of a specific conditioned response (e.g. eyelid, limb flexion) but simultaneously with non-specific autonomic conditioned responses (e.g., bradycardia, pupillary dilation) which index the learning of an association (e.g., tone-shock) (Weinberger, 1982a).

Although the two approaches provide somewhat different answers to issues in the neurobiology of learning, the differences may simply reflect emphasis upon what is generally thought to be two different forms of memory, procedural and declarative memory. Thus, slowly-acquired eyelid CRs appear to be representative of motor skills, i.e., learning how to make a particular response under particular circumstances. In contrast, rapidly-developing plasticity in sensory cortex may represent the acquisition of factual information, i.e., the relationship between environmental events such as, but not restricted to, conditioned and unconditioned stimuli in classical conditioning. The current research program emphasizes the information processing approach (Weinberger & Diamond, 1987).

BACKGROUND

Previously, we have found that learning involves differential plasticity at the thalamic level of the auditory system. The lemniscal ventral-medial geniculate nucleus (MGv) is not plastic. In contrast, discharge plasticity develops rapidly in the magnocellular medial geniculate (MGm) (Ryugo & Weinberger, 1978; Weinberger, 1982a). In brief, the MGv provides the cortex with precise information about the physical parameters of sound, and this information is not subject to modification. On the other hand, the MGm provides the auditory cortex with precise information about the importance of sound, e.g., the extent to which it signals an aversive stimulus. This information is modified to track stimulus significance, e.g., "tone signals aversive reinforcement". The site of convergence of information from the auditory and somatosensory-nociceptive system is in the MGm, the synapses of which can undergo long-term potentiation (Gerren & Weinberger, 1983; Weinberger, 1982b).

At the level of auditory cortex, learning induces a rapidly-developing discharge plasticity which is best revealed in the discharges of single neurons, rather than "clusters" or "multiple-unit" recordings. Associatively-induced plasticity in both the MGm and the auditory cortex develops during discrimination learning and exhibits retention for at least one week post training (Oleson et al, 1975; Weinberger et al 1984; Diamond & Weinberger, 1984b).

The sites of information transformation during learning in the auditory system seem to be confined to the MGm-cortex sub-system. Supportive evidence is that the lemniscal input to the cortex is not plastic. Also, as might be expected, the receptor potential (cochlear microphonic) is not plastic (Ashe et al, 1976). Thus, neither peripheral gating nor putative changes in the lower auditory system can account for associatively-induced plasticity. Finally, direct measures of arousal level (tonic and phasic pupillary size) indicate that the physiological plasticity in auditory thalamo-cortex is associative rather than due to state of arousal (Weinberger and Diamond, 1987; Diamond and Weinberger, in press).

These findings, by themselves, do not directly resolve critical issues involved in the processing of acquired information. Thus, learning-induced sensory cortical plasticity could reflect either (1) a general change in cortical responsivity or (2) a specific change in the way that information is processed by sensory cortex. Direct tests of these alternatives have been attempted, and it has been claimed that the results support the "general change" hypothesis. Detailed critiques of these claims have been presented elsewhere (Weinberger and Diamond, in press). For present purposes, it is sufficient to note that those findings are inconclusive due, in part, to the absence of adequate controls for non-associative factors.

In order to resolve this issue, it is insufficient to test learning effects on neuronal responses to a single stimulus, as done in previous studies. Rather, it is necessary to determine the effects of learning on the processing of a stimulus dimension. Under a prior contract, we have combined sensory physiology and learning paradigms within the same experiment.

Tuning curves were obtained from single neurons before and after each stage of classical conditioning (sensitization, pairing, extinction, retention). It was revealed that physiological plasticity in the secondary (AII) and ventral ectosylvian (VE) auditory fields actually reflects a highly specific change in the frequency receptive fields of single neurons -- the greatest effect is at the frequency of the conditioned stimulus. The receptive fields are stable in the absence of conditioning, and the changes in receptive fields are maintained unless the behavioral learning is altered by extinction, in which case they revert to pre-conditioning status. These effects were found for both narrowly and broadly-tuned cells (Diamond and Weinberger, 1986; Weinberger and Diamond 1988, in press).

These results indicate that the "processing specificity" theory is correct. In other words, the encoding of stimuli whose significance is acquired by experience is accomplished by retuning the receptive fields of single neurons.

From a formal standpoint, the tuning curves of neurons have much in common with the filtering properties of information processing networks. An analysis of cortical tuning curves revealed that tuning curves behave as adaptive filters when learning occurs. However, the processes of induction and expression of physiological plasticity are separable by determining tuning under different contexts (Diamond and Weinberger, in press). Such contextual sensitivity is clearly highly adaptive. Furthermore, it seems unlikely that fixed changes in specific circuits could track context as well as stimulus significance. Rather, each neuron may better be considered as a member of a Functional Mosaic (see Diamond and Weinberger, in press for details). Accordingly, attaining an understanding of adaptive information processing (AIP) as evolved in mammalian sensory neocortex demands a broader conceptual framework than does "skill" or "procedural" conditioning. It also entails more exhaustive experimental designs.

GOALS OF THIS PROJECT

The fact that learning induces frequency-specific modification of receptive fields in auditory cortex implies that the functional organization of auditory (and perhaps other sensory) cortex comprises an adaptively-constituted information base. This project initiates the first systematic investigation of adaptive information processing in cerebral cortex. A major goal is to determine the circumstances under which adaptive information processing is induced by experience. ~~Additionally,~~ this project also addresses central hypotheses about rules that govern adaptive information processing, at three levels of spatial scale: (a) parallel processing in different auditory fields; (b) modular processing in different cortical lamina within fields; (c) local processing in different neurons within the same locus within lamina.

PROGRESS DURING THE FIRST YEAR

Auditory Cortical Fields of Guinea Pig (Cavia Porcellus)

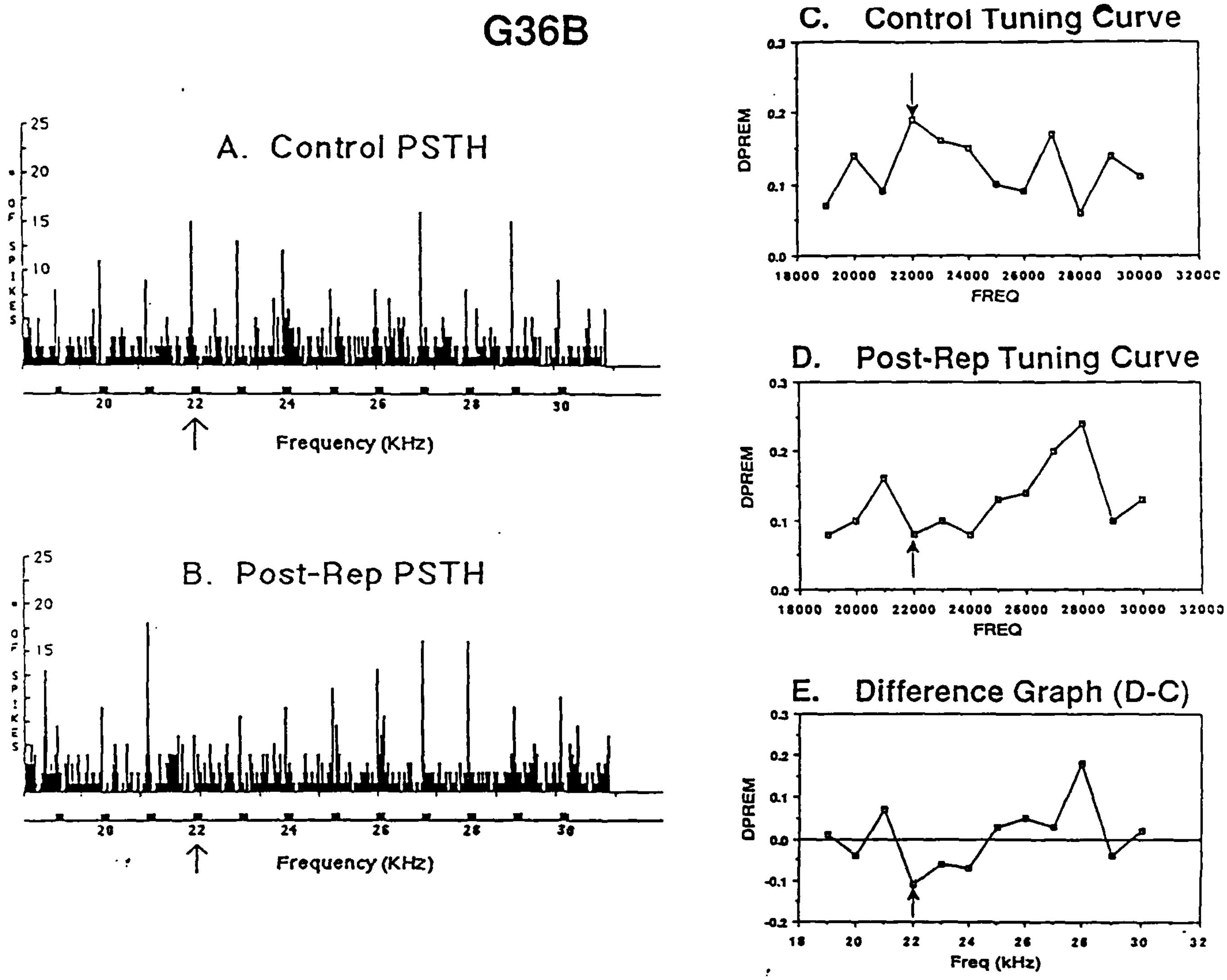
Studies were extended to a rodent, the guinea pig, in order to determine the generality of AIP across families of mammals, bring findings into closer relation with the main corpus of data in brain and learning, i.e., the rodent, and to enable cost-effective experimentation. Regarding the last point, costs for cats including completely sterile surgical procedures, have risen greatly and are presently about 15 times the cost per animal of guinea pigs.

Previous studies have indicated that the guinea pig has two primary-like auditory fields. These are each organized tontopically, on a rostral to caudal axis, but they are mirror images. The anterior field has low frequencies anterior, high frequencies posterior; the adjacent posterior field has the reverse frequency arrangement.

We have undertake systematic mapping of the guinea pig cortical auditory fields using quantative analysis of neuronal responses in the anesthetized (sodium pentobarbital and innovar) guinea pig. A major goal is to determine if there are systematic differences in parameters of frequency organization, e.g., threshold, bandwidth, etc. Work in progress has emphasized the anterior field. A tonotopic organization was validated for this field, by multiple penetrations with low frequencies anterior and high frequencies, posterior. Complete response areas (frequency vs intensity) were obtained for each site, and are undergoing analysis. Efforts during the second year will concentrate on the posterior field. The data are basic for investigating parallel AIP in two cortical fields.

Frequency Specific Plasticity During Habituation in the Guinea Pig

The extent to which different types of learning invoke adaptive information processing is of major interest. In this study, we explored the extent to which AIP is in evidence in a simple form of non-associative learning, habituation. The subjects were guinea pigs bearing chronically-implanted microelectrodes in primary (tonotopically-organized) auditory cortex. The animals were adapted to a hammock and head restraint in an acoustic chamber to provide for constancy of acoustic stimuli at the tympanic membrane. Following determination of tuning curves, a single tone frequency was repeated several hundred times. Response decrements in both clusters of neurons and single cells extracted from clusters were obtained. Post habituation tuning curves showed that a frequency specific decrement centered on the frequency of the repeated stimulus (Figs. 1-2). Adaptation, refractoriness, fatigue, and other non-learning factors were controlled. Therefore habituation produces a frequency-specific change in tuning rather than a general alteration of neuronal excitability. Experience-dependent retuning of frequency receptive fields is not limited to classical conditioning or to the cat auditory cortex.



<u>Figure 1. An example of frequency-specific decrement in tuning in auditory cortex due to habituation.</u> A,B: poststimulus histograms (PSTH) of showing frequency response before and after repeated presentation (not shown) of 22.0 kHz (arrow). C,D:tuning curves before and after habituation, corresponding to PSTH A,B, respectively. E., effect of habituation shown as post minus pre tuning curves. Note that the maximal decrease is at the habituated frequency (22.0 kHz).

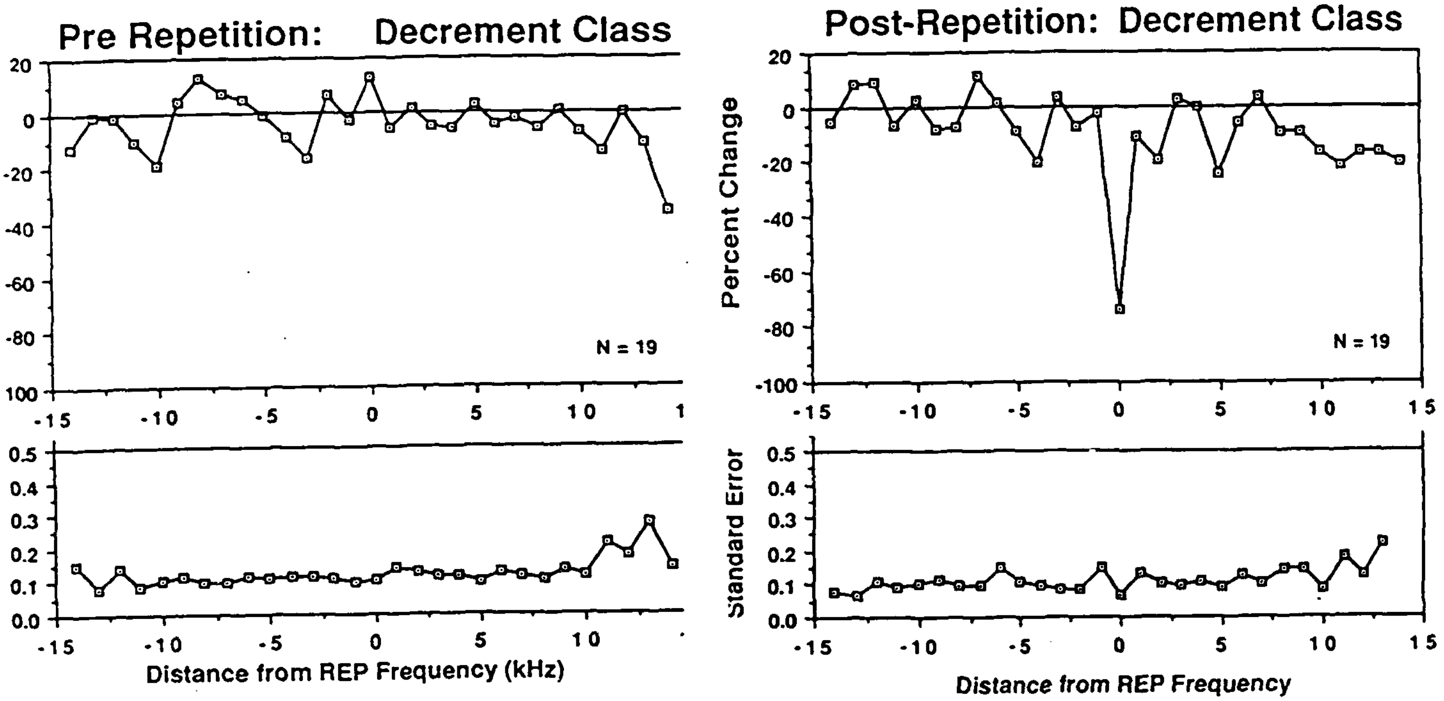


Figure 2. Summary of percent change from control (and S.E.) as a function of distance (kHz) from repeated ("REP") frequency. Left: differences in frequency tuning before repetition of a single selected frequency; tuning curves were obtained twice before repetition to determine the effect of the passage of time. Note the absence of significant change before tone repetition. Right: differences in tuning following repetition. Note in contrast to the preceding data that there is a large decrement in response at the repeated frequency. Further, note the absence of other large changes in tuning.

The Expression of Frequency-Specific Plasticity Under Anesthesia

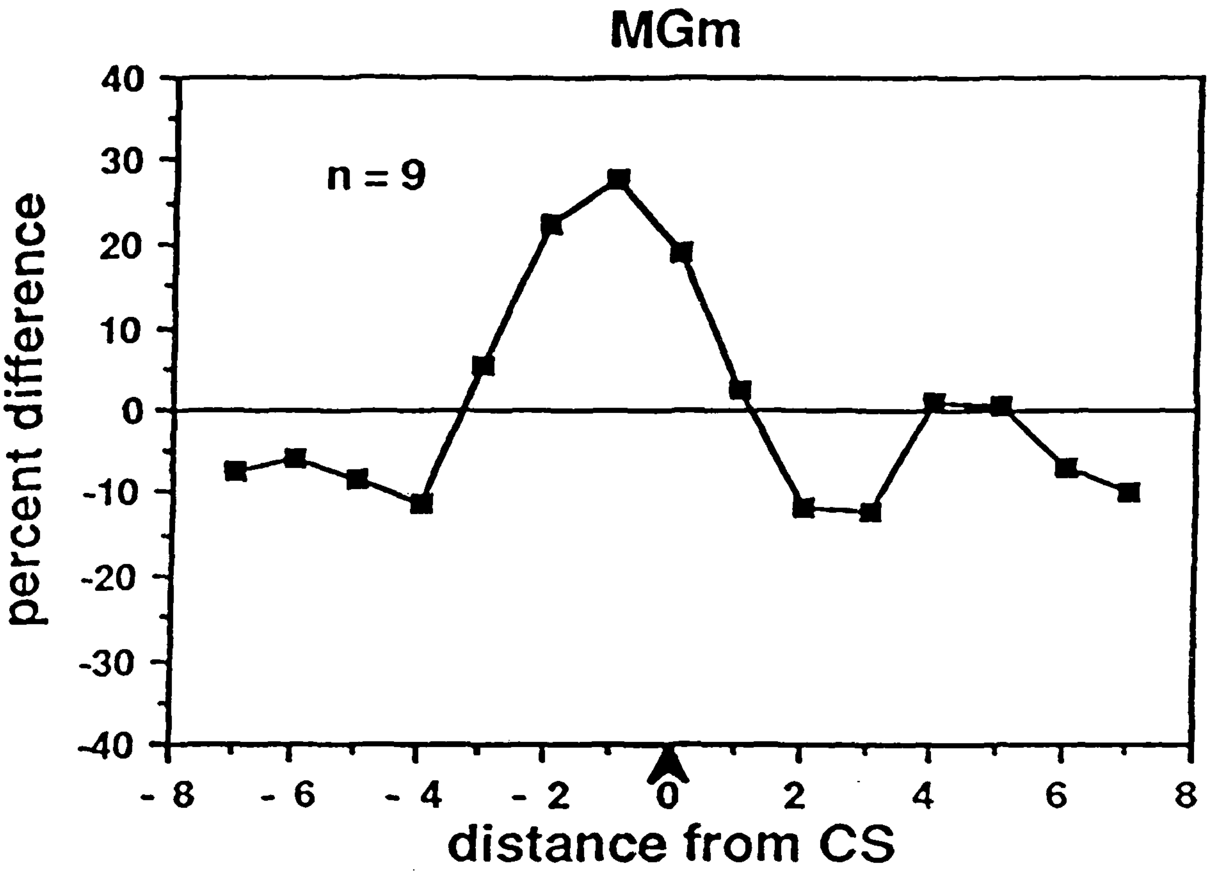
One method of delineating AIP is to seek neurophysiological representations of memories at a time when no new learning is possible. Accordingly, waking guinea pigs underwent classical aversive conditioning (tone-shock). Frequency receptive fields were determined in the magnocellular medial geniculate nucleus before and following fear conditioning, while the subjects were under deep general anesthesia (sodium pentobarbital). Learning produced frequency-specific changes in tuning. The major change was at the frequency of the conditioned stimulus (Fig. 3). These findings provides the first evidence that learning produces sufficiently robust physiological plasticity that it can be "read out" under subsequent anesthesia. It also indicates that learning-induced re-tuning of frequency receptive fields can develop in the magnocellular medial geniculate.

Adaptive Information Processing in Auditory Cortex during Classical Conditioning

In order to determine the effects of associative learning in the primary, tonotopic, auditory cortex, guinea pigs bearing chronically-implanted microelectrodes underwent classical conditioning. Following determination of frequency RF in an acoustic chamber, a frequency within the RF was selected as a CS. Comparison of receptive fields before and after conditioning revealed that classical conditioning induced frequency-specific plasticity in auditory cortex. Interestingly, when the frequency used as the CS was not the best frequency, then it <u>became the best frequency</u> as a result of conditioning. This was accomplished by a coordinated <u>increase in response to the CS frequency</u> and a <u>decrease in response to the previous best frequency</u> (Fig. 4). Therefore, learning can produce <u>shifts</u> in tuning so that re-tuning is centered on the important frequency. In short, neurons exhibit particularly important features of adaptive filters as a result of learning.

Facilitated Discriminative Avoidance Behavior

In order to explore the domain of tuning curve changes, we have trained guinea pigs in an instrumental avoidance situation to complement work in classical conditioning. Guinea pigs were trained in a Brogden wheel using two tones and CS durations of 10 sec. We were able to facilitate two-tone discrimination by reducing responding to the CS- using a response-contingent paradigm. Responses during the CS+ produced termination of the stimulus and avoidance of shock. Responses to the CS- produced <u>another CS</u> (10 sec.) until animals no longer responded during this stimulus. In contrast to a control group (non-contingent), the experimental group exhibited superior discriminative performance (Fig. 5).



<u>Figure 3. Effects of conditioning in the waking state upon tuning curves obtained under general anesthesia from neurons in the magnocellular medial geniculate nucleus (MGm).</u> Tuning curves were obtained from animals under anesthesia 24 hours preceding conditioning and 1 hour following classical conditioning. Data are expressed as percent change of post-conditioning tuning from pre-conditioning tuning, shown as a function of distance (kHz) from the CS frequency employed, for a group of 9 animals. Note the frequency-specific effects of conditioning; the maximum effect is an increase in response 1 kHz below the CS frequency with substantial increase from -2 kHz to the frequency of the CS. Note also the suppression of response at lower and higher frequencies.

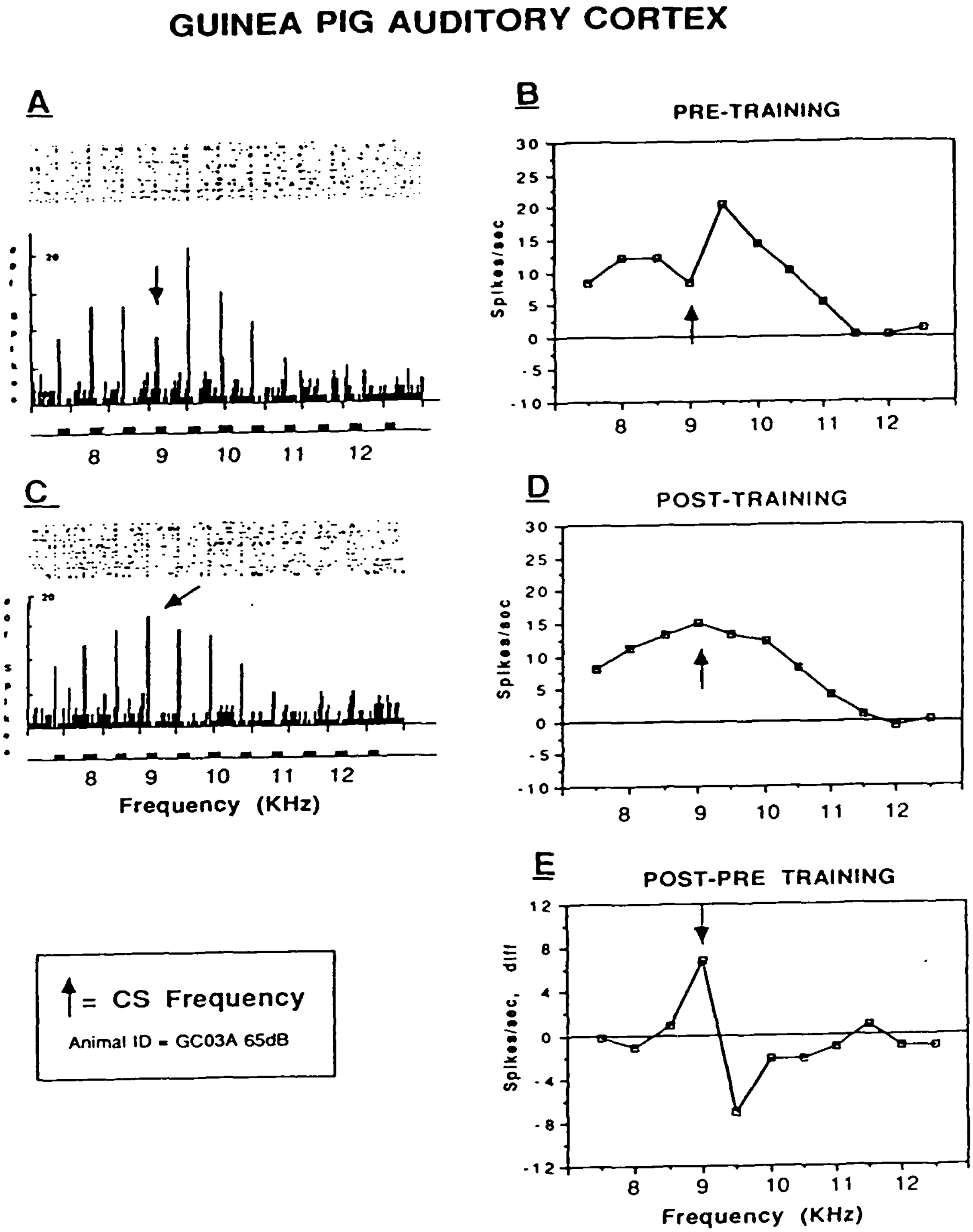
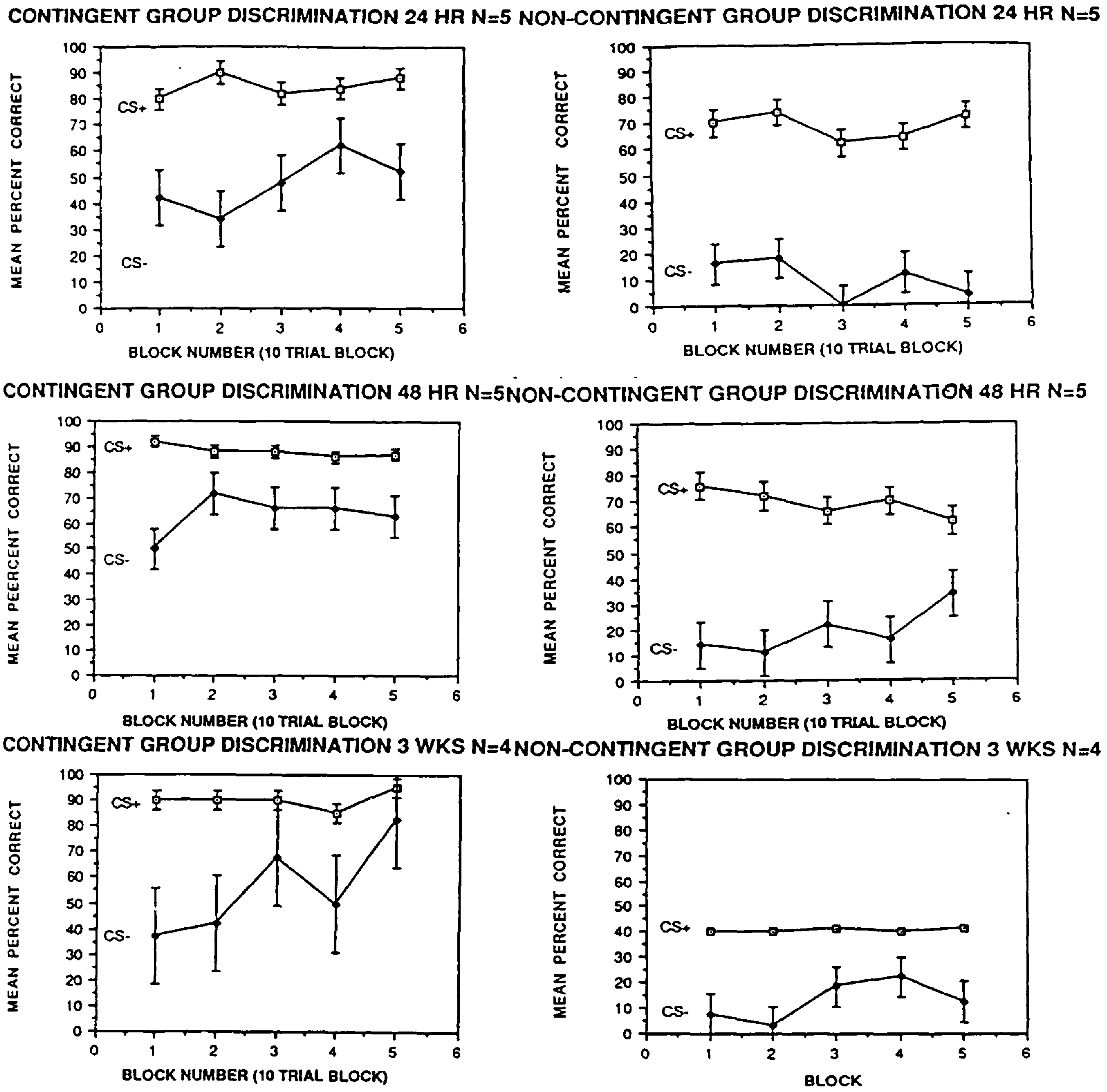


Figure 4. Frequency-specific effect of classical conditioning on receptive fields in auditory cortex of a guinea pig. A,B and C,D, respectively: PSTH and tuning curves for before and after classical conditioning (tone-shock) in which the CS was 9.0 kHz. 65 db (arrows). E: the effects of conditioning presented as difference between pre and post tuning curves. Note that conditioning produced an increase in response to the CS frequency and a suppression of response to the original best frequency (9.5 kHz); the result was a shift in tuning so that the CS feqwuency became the new best frequency; tuning bandwidth was also increased in this case.



CONTINGENT GROUP DISCRIMINATION 24 HR N=5

NON-CONTINGENT GROUP DISCRIMINATION 24 HR N=5

CONTINGENT GROUP DISCRIMINATION 48 HR N=5

NON-CONTINGENT GROUP DISCRIMINATION 48 HR N=5

CONTINGENT GROUP DISCRIMINATION 3 WKS N=4

NON-CONTINGENT GROUP DISCRIMINATION 3 WKS N=4

Figure 5. Facilitation of discriminative avoidance conditioning. The contingent-group received another 10 sec. CS- tone if wheel running occurred during CS- presentation; the non-contingent group received standard training. The contingent group exhibits superior performance at 24 hours, 48 hours, and 3 weeks post-training.

Adaptive Information Processing in Auditory Cortex During Instrumental Conditioning

We used the facilitated avoidance paradigm described above to determine whether AIP in auditory cortex develops for instrumental conditioning as well as habituation and classical conditioning. Frequency receptive fields were obtained before and after successful avoidance training. The CS+ was selected as a frequency, often the best frequency, within the response area of the neuron. The CS- was selected in this initial study as a frequency to which neurons were minimally responsive. Avoidance conditioning resulted in frequency-specific modification of tuning curves. In particular, if the CS+ was also the best frequency, then the major effect was a facilitation of response to the CS frequency (Fig. 6).

GUINEA PIG AUDITORY CORTEX AVOIDANCE CONDITIONING

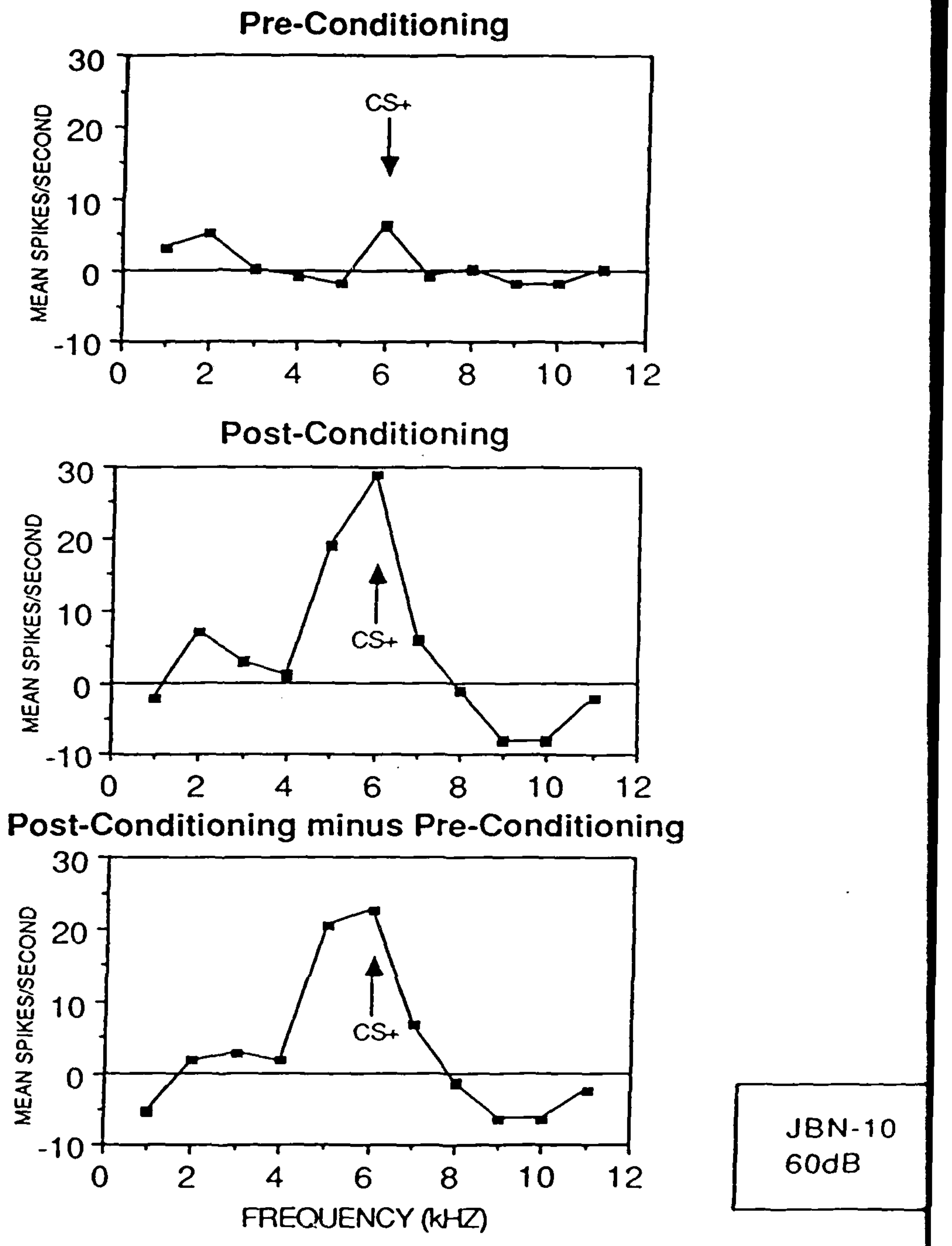


Figure 6. Frequency-specific modification of receptive fields by avoidance conditioning. This subject was trained at the best frequency (6.0 kHz, 60 db), denoted by arrows. Avoidance conditioning resulted in a very large facilitation of response which was maximal at the frequency of the CS; less facilitation was observed within 1 kHz of the CS frequency. Note the suppression of responses at distant frequencies.

CONCLUSIONS

Adaptive information processing has evolved such that sensory system processing is continually modified and updated as it "filters" environmental stimuli. This is best exemplified in observations of the higher auditory system during learning. Auditory neocortex and its related thalamic gateway, the medial geniculate nucleus, synthesize information about the physical parameters of stimuli with information about stimulus meaning, significance and signal value. During the first year of this contract, we have emphasized determining the learning circumstances under which adaptive information processing is invoked by the brain. Current studies reveal that the frequency receptive fields of neurons in the auditory cortex, and the physiologically-plastic magnocellular medial geniculate nucleus, develop frequency-specific modification such that maximal shifts in tuning are at or adjacent to the "signal" frequency. Further, this adaptive re-tuning of neurons develops rapidly during habituation, classical conditioning, and instrumental avoidance conditioning. The generality of re-tuning has established that AIP during learning represents a general brain strategy for the acquisition and subsequent processing of information.

During the second year, additional behavioral learning situations will be studied including retention intervals, extinction, and contextual effects. This will provide the type of neuro-behavioral comprehensive characterization of AIP that is needed for the understanding of mechanism. We will also initiate experiments on the neural bases of AIP within the scope of this contract. This will include obtaining data necessary for analysis of neural mechanisms at three levels of network organization -- cortical fields, cortical lamina within fields, and neuronal local networks within lamina. These data should provide a firm basis for delineation of the neural algorithms and implementations of adaptive information processing that characterize biological intelligence. Emulation of the evolved neuronal solutions to adaptive information processing may then be achievable.

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SUPPORTED BY THIS CONTRACT

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