A STUDY OF THE EFFECTS OF CLASSICAL CONDITIONING ON THE CORRELATION OF UNIT ACTIVITY AND THE AVERAGED EVOKED POTENTIAL

by

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TO JANET

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INTRODUCTION

Orientation to the problem:

This dissertation is basically concerned with three things: (1) A further examination of classically conditioned unit activity as reported by O'Brien and Fox (1969); (2) The testing of the hypothesis that during the development of a conditioned response (CR) the neurons of the cortical primary projection area of the unconditioned stimulus (US) become more synchronous in their patterns of response to the conditioned stimulus (CS) [a hypothesis suggested by John, 1967 and 1972]; and (3) The elaboration of possible neural models that can be constructed from analyses of the correlation of a unit's post-stimulus histogram (PSH) and an averaged evoked potential (AEP) recorded simultaneously through a single microelectrode.

Nearly a century ago William James characterized neural tissue as being "plastic" since it could exhibit different responses to an unchanging stimulus (Thompson, 1967). Phenomena such as habituation and sensitization have been described as types of plasticity (Groves, DeMarco, and Thompson, 1969). Likewise, conditioning or learning has been considered as a form of plasticity (Thompson, 1967). Durup and Fessard, as early as 1935, discovered that unique patterns of neuroelectrical potentials could be classically conditioned by the temporal pairing of two stimuli. Doty and others (Doty, 1969), have found evidence for conditioning of neuroelectrical activity when the CS and US were direct electrical stimulation of the cerebral cortex.

Plasticity has been demonstrated at virtually every level of neural complexity (Thompson, Patterson, and Teyler, 1972). The present study was not undertaken solely to demonstrate plasticity, but rather to use its effects to help evaluate inferences which have been made by some researchers about the "informational" properties of neuroelectrical field potentials--both averaged evoked potentials (AEP) and electroencephalograms (EEG) (Fox and O'Brien, 1965; Fox and Rudell, 1968; Fox and Rudell, 1970; Rosenfield and Fox, 1972; Rosenfield and Fox, 1971; and John, 1967 and 1972).

Fox and his co-workers have demonstrated that AEPs (Both early and late components of the wave form) may be highly correlated with the probability of cell firing. Based on this evidence Fox and Rudell (1968 and 1970) and Fox and Rosenfield (1971 and 1972) have conducted further studies on the "coding" functions of the brain assuming that when recording from gross electrodes the field potentials accurately represent the response tendencies and firing activity of a majority of neurons in the recording area. Implied by their work is the idea that single cell recording is superfluous since the PSHs of cells only tend to reproduce the various components of the AEP wave form. John (1972) has also attacked the value of single cell data as a measure of information in the brain since; (1) units typically show a wide range of spontaneous rates, (2) they exhibit great variability in response to unchanging stimuli, and (3) many units respond to stimuli of different sensory modalities.

Whereas several researchers have looked for correlation between

unit activity and electrical potentials recorded from macroelectrodes (Creutzfeldt and Watanabe, 1966; Pollen, 1964; Nacimiento, Lux, and Creutzfeldt, 1964; Rall and Sheppard, 1968; Gerstein, 1961; Green, Maxwell, Schindler, and Stumpf, 1960; Verzeano and Negishi, 1960; Verzeano, 1963; and Verzeano et al., 1965), none have really attempted to explore the validity of the assertions made by Fox and John.

In addition, then, to the general concerns listed in the initial paragraph above, this dissertation will attempt to investigate the issue of information processing in the brain and the question of the superiority of AEPs over unit activity as an index of information processing.

A definition and discussion of information:

Information as it will be utilized in the present study incorporates the concept that a stimulus event and a neuroelectrical event may both contain information. A stimulus event, for instance, has characteristic features of intensity, duration, etc. The registration of the presence and characteristics of such an event by neural tissue represents information processing. The transduction of energy and the transmission of events from peripheral sensory mechanisms to more central brain areas constitutes the processing and transmission of information. Thus, a recorded neural event may be viewed as a symbolic representation of the evoking stimulus.

In a recent article, John (1972) has discussed the point that unit activity is an inappropriate measure of information. He reasons; (A) "If nerve cells in the central nervous system fire spontaneously with high incidence" (Burns and Smith, 1962), (B) "if they respond in a variable way to any given stimulus" (Gerstein and Kiang, 1964), and (C) "if they respond to multiple stimuli in various sense modalities" (O'Brien and Fox, 1969; Buser and Imbert, 1958; Amassian and Devito, 1954), then "how is the brain to evaluate the significance of a discharge by a specific cell in a particular pathway?".

Each of the discreditable characteristics John attributes to unit activity is present with apparent equal magnitude in AEPs. The AEP is superimposed upon a baseline of spontaneous activity, its variability to constant input is universally observed and comparable to that of unit activity (John and Morgades, 1969) and AEPs recorded

from a fixed position in the brain may occur as responses to polymodal stimulation (Majowski and Sobieszek, 1971; Albe-Fessard and Fessard, 1963; Buser and Bignall, 1967). _A priori_ then, there seems to be no justification for a bias, based upon these grounds, for either type of data relative to its capacity to reflect information processes in the brain.

The study conducted in this dissertation was designed to determine if (1) unit activity could convey information by exhibiting detectable changes in CS evoked activity attributable to a classical conditioning paradigm of pairing two stimuli, and (2) to assess if such informational representation was reflected in the AEP by correlating conditioned unit activity with the AEP both within and across trials.

Neurons of the pericruciate cortex:

The spontaneous reponse properties of neurons may define the limits within which "symbols" of information can be generated by changes in spike rate. Also, an understanding of afferent and efferent connections provides insight about the possible "sources" and "receivers" of information, if the brain was to be viewed as a communication system (Shannon and Weaver, 1949). Thus, an evaluation of possible information transfer by neurons of the postcruciate cortex must begin with a delineation of the response properties of its member units and their input and output connections.

The response activity of postcruciate neurons reflect a convergence of input. Buser and Imbert (1958), found neurons in this area that would respond to visual, auditory, and somatic stimulation. Patton, Towe, and Kennedy (1962), reported that 70% of the neurons of the postcruciate cortex, that sent fibers into the pyramidal tract, could be driven by somatic stimulation of either side of the body. Some units also responded to auditory and visual stimuli. The central as well as peripheral afferent connections to postcruciate cells have been explored (Patton et al., 1962; Towe, Whitehorn, and Nyquist, 1968; Blum, Halpern, and Ward, 1968; Baker, Tyner, and Towe, 1971; Teyler, Roemer, and Thompson, 1971). A summary of these findings appear in Table 1.

The spontaneous activity of pyramidal cells are different depending on the size and general morphology of the cell (Granit, 1970). The smaller cells which have a relatively lower conduction

Table 1: THE AFFERENT AND EFFERENT PROJECTIONS OF PYRAMIDAL NEURONS. (Composed from results of Patton et al., 1962; Towe et al., 1968; Baker et al., 1961; and Blum et al., 1968).

Layer V pyramidal cells:

Input	Output
*Hair deflection (medium latency)	Pyramidal tract
*Shock & skin tap (medium latency)	
*Visual	
*Auditory	
VL	
CM	
SI	
CM-SI convergence	

Layer III pyramidal cells:

Input	Output
*Hair deflection (latest latency)	Pyramidal tract
*Shock & skin tap (latest latency)	SI
*Visual	Trans collosale
*Auditory	
VL	
CM	
SI	
CM-SI convergence	

Table 1 (continued)

S cells:

Input	Output
*Hair deflection (medium-early latency)	1/6 to pyramidal tract
*Shock & skin tap (earliest latency)	PT III neurons
*Visual	PT V neurons
*Auditory	SI
VL	
CM	
VL-CM convergence	

*These inputs represent only one out of a polymodal array of stimuli to which any given cell may respond.

VL, ventralis lateralis; CM, centre median; SI, somatosensory area 1.

velocity tend to have tonic discharges in the absence of movement. The larger pyramidal neurons, in contrast, tend to have a very low spontaneous activity with phasic bursts of discharges which are associated with limb movement. Tonic pyramidal discharges without movement were observed as long ago as 1940 by Adrian and Moruzzi. Furthermore, Kostiuk and Vasilenko (1968) have confirmed the basic differentiation of pyramidal cells according to their tonic or phasic spontaneous response properties.

In summary, some neurons of the postcruciate cortex are known to receive polysensory input, have projections into the pyramidal tract and thus possible motor influence. They also have spontaneous spike frequencies allowing for both excitatory and inhibitory post-stimulus changes. These characteristics would allow this population of neurons to reflect spike rate dependent transfer of information. Such a population of neurons was needed to test the relative capacities of AEPs and units to reflect information processes in the brain.

"Statistical Configuration Theory" and PSH-AEP correlation:

John (1967, 1972) has formulated a "Statistical Configuration Theory" which states that learning is the consequence of the establishment of "representational systems" composed of a large number of neurons. These systems are presumably established by the spatio-temporal association of stimulus-generated activities in the nervous system. The representational system of neurons is responsible for the development of a "common mode of activity" which is represented by the AEP recorded from a macroelectrode located in the representational system.

John's (1967, 1972) theory makes the assumption that the AEP reflects the summed activity of individual neural units. Basically, the relationship among these phenomena rests on a few fundamental assumptions: (1) It is assumed that a volume of neural tissue contains a number of neural loops or reverberating circuits, whose frequency of cyclic phases of activity are determined by the length of the neuronal loop. (2) The EPSPs (excitatory postsynaptic potentials) resulting from reverberation of action potentials at any given neuron in the circuit will be, in most cases, relatively brief compared to the complete epoch of the loop. (3) Other cells in the system exhibit IPSPs (inhibitory postsynaptic potentials) with durations longer than those of the EPSPs. Thus, an electrode placed to monitor the activity in this neural population would detect the superimposing of these two types of transmembrane potentials which exhibit individually distinct durations but which have a common dependence on the reverberating

frequency of the circuit to which they belong. (4) In addition to IPSPs and EPSPs there would be the transmembrane potential shifts accompanying recovery from action potentials and perhaps similar phenomena with still longer and more varying durations. (5) The frequency correspondence between loop activity and slow wave (EEG and average evoked potentials) would depend upon the time course and shape of the membrane responses. (6) The amplitude of a particular frequency component or component of the average evoked potential would be dependent upon some initiating force bringing neural activity into a coherent or synchronous phase.

Having outlined the above assumptions, John (1967) then proceeds:

> Were the above suggestions correct, how might the activity of a single neuron be related to the shape of the evoked potential? Since the duration of an evoked potential is much longer than a single unit discharge, the discharge (pattern) of those neurons that are not influenced by the stimulus over an extended period (perhaps a half second or longer) cannot be expected to display any correlation with the evoked potential. In order for neurons to become involved in <u>sustained</u> activity as a consequence of the afferent input, they must be members of loops around which the recirculation of activity takes place [p. 240].

John then proposes this example. "Suppose that a given neuron belongs only to one such loop. The activity resulting in that neuron because of events in that loop will occur at some frequency corresponding with the length of the particular loop to which it belongs." In other words, activity by any member neuron will tend to occur at a frequency unique to and corresponding with the length of the particular loop to which it belongs. "The maximum correlation that could be expected between the activity of that neural unit and the macropotential recorded from the neural ensemble would be proportional to

the relative contribution of the frequency component to the wave shape of the evoked potential."

It must be made clear that the frequency component mentioned above is the frequency at which reverberating activity occurs at some point in the hypothetical neural loop. Thus, if the frequency component is a salient factor contributing to both unit and evoked potential activity and if the unit isolated for recording is a member of the representational system of loop then a relatively high correlation should exist between the neural unit and the macropotential. John's theory would predict a progressive shift towards a higher and more positive correlation between unit activity and the AEP during conditioning if the monitored neuron was a member of the loop which was reflected in the "common mode of activity." In regard to the establishment of a "common mode of activity" John writes (1972):

> The critical event in learning is envisaged as the establishment of representational systems of large numbers of neurons in different parts of the brain, whose activity has been affected in a coordinated way by the spacio-temporal characteristics of the stimuli present during a learning experience. The coherent pattern of discharge of neurons in these regions spreads to numberous other regions of the brain. Sustained transactions of activity between participating cells permit rapid stimuli as well as the subsequent spread. This initiates the development of a _common mode of activity_, a temporal pattern which is coherent across those various regions and specific for the stimulus complex. As this common mode of activity is sustained, certain changes are presumed to take place in the participating neuronal populations, which are thereby established as a representational system [pp. 853-854].

Apparently the neuronal loops that John postulates are the same thing as "representational systems" or a "representational system" might be composed of several such loops. He has used the term

"representational system" to refer to both the original population of neurons influenced by the respective stimuli employed in a learning situation, i.e., the CS and US, and to the neural tissue responsible for the "common mode of activity." Presumably the "representational system" which emits the "common mode of activity" can be viewed as the neuroanatomical space within which a conditioned response is present. This assumption is based on the fact that both the CR and the common mode of activity develop "during the learning experience," and are a consequence of the learning situation.

Let's assume the situation of recording from a cell that is a member of a potential representational system for a common mode of activity, but at the commencement of recording the new common mode of activity and consequently its representational system has not yet developed. What effect will the establishment of the common mode of activity have upon this particular cell's correlation with the AEP? Given that the neuron was not a member of the representational system elicited by the CS, one would expect (according to John's theory) the PSH-AEP correlation to increase during the learning procedure. Specifically, in light of results which showed that the positive peak in the AEP usually corresponded with an increase in probability of cell firing (John and Morgade, 1969), one would expect a trend toward a more positive (+) correlation during learning.

The present study was designed to classically conditioned CS evoked unit activity (O'Brien and Fox, 1969) and to assess if such conditioning would be reflected by an increase in PSH-AEP correlation.

Relationship between macropotentials and unit activity:

The source of macropotentials has been an object of considerable research and theorizing (Bremer and Stoupel, 1958, 1959; Eccles, 1951). Excitatory and inhibitory postsynaptic potentials have several characteristics which make them suitable candidates. Firstly, they exist in the absence of action potentials; secondly, they exhibit graded changes of amplitude in contrast to the all-or-none nature of action potentials; thirdly, their duration is variable and often attains values of several hundred milliseconds in the case of IPSPs. Considering these properties and the fact that the population density of neurons in the cortex is in the order of 10,000 to 30,000 per mm. (Sholl, 1956), the postsynaptic potential has been considered a reasonable candidate as a generator of macropotentials.

Experimental evidence supporting these views has been provided by Elul (1968) who recorded transmembrane potentials through microelectrodes resting inside cortical cells. He found that virtually all frequencies comprising EEG were present in the transmembrane potentials. He concluded that the transmembrane potentials, which exhibited amplitudes of 20 mv in some instances, were not a passive reflection of an extracellular source since he found no extracellular potentials of that magnitude or larger. Elul (1968) did not find similar fluctuations of transmembrane potentials in glial cells.

Evoked potentials are usually larger in amplitude than EEG since they represent synchronous events time locked to a stimulus. They also have characteristic wave forms which vary depending on

modality and intensity of the evoking stimulus and recording site. A considerable amount of research has been conducted in an attempt to correlate neuronal postsynaptic potentials with evoked potentials and the data have frequently been contradictory. For example, Creutzfeldt and Watanabe (1966) reported finding EPSPs during surface negative barbiturate spindles, and these results agreed with those of Nacimiento et al. (1964) who reported observing IPSPs associated with surface positive waves. Against these findings are those of Pollen (1964) who reported IPSPs produced surface negative waves.

The relationship of IPSPs and EPSPs to surface voltages is frequently interpreted in terms of the "dipole" concept and data that initially seem contradictory may be found to be congrous when the dipole concept is applied. The concept assumes that a depolarization at a given point on a neuron renders that point negative to regions of the membrane distal to it. Thus, a pyramidal cell whose soma or proximal dendritic process is depolarized will at that instant cause an electrode near the tip of the cells apical dendrite (e.g., resting on the cortical surface) to "see" an initial positive going fluctuation in its voltage. As the depolarization spreads and invades the distal regions of the apical dendritic processes, the electrode will "see" a negative going fluctuation in voltage. It becomes clear, then, that whether a surface negative wave is due to an EPSP or an IPSP depends on the portion of the cell membrane being synaptically effected. The same, of course, is true for surface positive waves.

An accurate interpretation of evoked macropotentials is difficult

unless the anatomy, cytoarchitecture, and synaptic inputs of the recording site are well known. From evoked potentials Rall (1970) and Rall and Sheppard (1968) were able to make predictions of dendrodendritic synapses which were later verified by electron microscopy. Antidromic stimulation was used to minimize synaptic activity in the recording area. The work of Rall and Sheppard (1968) supports the dipole concept and the view that neuronal transmembrane potentials are the generators of both EEG and evoked macropotentials.

Other researchers have looked for a correlation of the all-or-none action potentials of neurons with macropotentials. These experimental approaches were not undertaken to explain, necessarily, the AEPs from unit activity, but merely to describe the relationship between the two. If evoked potentials are the summed activity of membrane depolarization and hyperpolarization, and the initiation of an action potential also depends upon the level of membrane depolarization, one might expect a unit-EP correlation to exist.

Gerstein (1961) obtained poststimulus histograms of unit firing and average response curves of slow potentials from the auditory cortex of the cat and found both to be time locked to the stimulus and a sizeable covariation existed between the two curves. Likewise, Green et al. (1960) were able to show a correlation between hippocampal theta rhythm and the firing patterns of hippocampal neurons.

Other researchers have sampled an appreciable number of units simultaneously using multiple microelectrodes (Verzeano and Negishi, 1960; Verzeano et al., 1965; Verzeano, 1963). Their findings correspond

well with those of Green et al. (1960) in that there is a correlation between the activity of the units and the occurrence of short-duration, high amplitude macropotential waves. Creutzfeldt and Jung (1961), using a longitudinal array of microelectrodes in the thalamus, found a high correspondence of unit activity to the presence of traveling waves through this structure. An increase in the amplitude of the gross waves was accompanied by increased activity of a larger number of neurons involved in the pathway.

Fox and O'Brien (1965) found correlations as high as r = .80 between unit PSHs and AEPs recorded from the same electrode. It was their observation that the PSH, for a number of cells, would duplicate all components, both early and late, of the AEP. John and Morgades (1969) found that the occurrences of action potentials were highly correlated with positive peaks of the AEP. They further reported that during conditioning this correlation increases.

Plasticity of neuro-electrical macropotentials:

It is not understating the facts to say that literally volumes of data have been collected verifying the plastic nature of the brain. A recent review of the subject (Thompson, Patterson, and Teyler, 1972) cited over two hundred forty publications and this involved a "specific focus on electrophysiological studies of learning, particularly those done in the past 5 years." Twenty-two of these references were also reviews.

Morrell and his associates have studied the development of electro-cortical conditioned responses (Morrell and Jasper, 1956; Morrell, Roberts, and Jasper, 1956; Morrell, Naquet, and Gastaut, 1957; Morrell, 1958; Morrell, 1960). When an auditory CS was paired with a flicker light US, the tone began to elicit flicker frequency discharges in the occipital lobes. There were other EP changes in other cortical regions that were characteristically associated with the development of the CR. In early trials (17-60) the tone induced a generalized response which appeared first in all cortical regions, but gave way with further trials to a more discrete response localized at the occipital leads. Morrell (1960) also has reported that the developing CR appeared first in superficial layers of the cortex and then in deeper layers as more conditioning trials were presented.

In 1958 Rusinov and Rabinovich reviewed Russian research on EEG correlates of learned behavioral responses. They reported that Livanov, in a series of articles between 1947 and 1955, described the electrical potentials monitored from various regions of the cortex during acquisition of a "defensive conditioned reflex." The general

experimental procedure in these experiments was a flickering light (3/sec.) CS followed by a US--a peripheral electrical stimulation having a rhythmic pattern the same as the CS. Livanov noted that initially the occipital cortex responded to the CS with evoked potentials having the same frequency as the photic stimulus. As the CR developed these potentials disappeared. In contrast, the motor areas showed no initial response to the flickering light, but such responses became apparent as conditioning progressed. Activity in the parietal cortex was different from both the striate and motor cortices. It did not reflect the CS frequency until a number of conditioning trials had been given. Its response was transitory and disappeared as the motor cortex began to respond to the CS.

Dumenko in 1955, while working in Livanov's laboratory, recorded EEG during the pairing of a complex CS of both sound and light with an electric shock to the skin of a rabbit. She found that initially there was an increase in activity in both the auditory and optic areas with no response occurring in the motor areas. Later on, the increase in activity of the cortical auditory and somatic centers disappeared and by the time the conditioned motor reflex appeared, the cortical reactivity to the CS was limited to the optic and motor areas.

Collaborative evidence for Morrell's (1960) observations of conditioning first in shallow cortical layers followed by CRs in the deeper levels of the cortex was reported by Knipst (Rusinov and Rabinovich, 1958). Rusinov and Rabinovich claim she demonstrated that the rhythm of the CS is first reproduced in the upper layers of

the cortex and then in the lower. By the time the conditioned motor reflex appears, the oscillations of the electrical activity of the upper and deeper levels of the cortex become synchronous.

In man (Wells, 1959) and less frequently in lower animals (Morrell, 1956 and Morrell, Naquet, and Gastaut, 1957), when the procedure is sensory-sensory conditioning in which neither stimulus elicits a behavioral consequence, the evoked potential response to both CS and US may disappear with repeated trials (Morrell, 1961).

Several consistencies emerge from these reports: (a) the establishment of the "conditioned response" follows specific phases of development; (b) the conditioned response is unstable and transitory; (c) experimenters using sensory-sensory conditioning procedures report a gradual localization of the conditioned response at the projection area of the US; (d) the activity of the upper and deeper layers of the cortical US projection area becomes more synchronous; (e) such conditioned responses extinguish more rapidly than behavioral responses; and (f) some habituation to both stimuli frequently occurs during the pairing of two neutral stimuli (Morrell, 1961).

Single cells and conditioning:

Bures and Buresova (1967) paired an acoustical CS with direct microelectrode stimulation of the cell isolated for recording. They found that only about 12% of the cells exhibited response changes to the CS. They observed that 14 of the 17 cells exhibiting response changes were located in the inferior colliculus. These cells were initially more responsive to the CS than units isolated in other areas; thus, the possibility exists that strong responses were required before they could detect conditioned changes (see O'Brien and Fox, 1969). These results have provided the valuable observation that mechanisms capable of mediating plastic changes may be contained within a single neuron.

Jasper, Ricci, and Doane (1958, 1960) made one of the first reports of recording single cell activity during learning. Neurons were sampled from sensory, motor, frontal and parietal cortical areas and their initial response to the CS was recorded. Conditioning was carried out until the subjects were avoiding at 90% accuracy before additional units were monitored. They reported that unit activity changed when EEG wave changes occurred, but no "identifiable sensory message" related to the temporal characteristics of the CS arriving at the sensory-motor area concomitant with a conditioned motor response could be found. They postulated that "important switching mechanisms" necessary for conditioning were probably located in the parietal cortex.

Another early study of this type, by Morrell (1960), reported

differences in neuronal response to the CS relative to a cell's depth in the cortex. During the development of the CR, rhythmic potential changes elicited by the CS appeared first in the superficial layers of the cortex and did not appear in deep cortical layers until the final stages of conditioning. Recordings were taken from areas adjacent to epileptogenic lesions in the visual cortex of the cat. In such subjects, if a tone CS is paired with a flicker light US, the unconditioned epileptic spiking produced by the light will become conditioned to the tone. It was this spiking frequency that appeared first in the more shallow cortical layers and later in deep layers. Morrell (1960) concluded that this phenomena argued for a dendritic locus of closure during conditioning.

In further study, Morrell (1960) sampled neurons in the mesencephalic reticulum, the ventral anterior nucleus of the thalamus and the hippocampus along with the visual cortex. He found that the initial presentation of light US caused increased unit activity in the visual cortex, the mesencephalic reticular formation, and hippocampus. During the first stage of conditioning, the US continued to elicit increased unit activity in these same structures plus the ventral anterior nucleus of the thalamus. By the second stage of conditioning, units were decreasing their response in the ventral anterior nucleus and the mesencephalic reticular formation and were maintaining an increase in the visual cortex and the hippocampus. When conditioning was complete, the ventral anterior cells were again increasing their response to the US as were the cells in the visual cortex. Cells in

the mesencephalic reticulum and hippocampus displayed no noticeable response frequency change.

Unit response to an acoustical CS presentation was slightly different. The mesencephalic reticular formation was the only site of cellular response to the initial CS trials. Stage I of conditioning found all areas except the thalamic nucleus excited by the CS. By stage II of conditioning thalamic cells were responding, and this was also true of the visual cortex. Stage III was characterized by an increase in the activity at the visual cortex and the ventral anterior nucleus of the thalamus.

A more recent study designed to investigate anatomical sites of conditioning has been reported by Disterhoft and Olds (1972). A trial-by-trial analysis revealed that there was a general increase in unit responsiveness to both a CS+ and a CS- in all parts of the brain sampled during early conditioning trials. Indications of "initial learning" appeared first in the posterior dorsomedial and nonspecific thalamic nuclei, and then later at the cortex. In contrast to the "initial learning" measure which was taken from post-CS activity, the intertrial or spontaneous rates for cortical cells showed changes during the early stages of conditioing with similar changes in rate in thalamic cells occurring later. In fact, the change in spontaneous activity of cortical cells preceded the CS evoked learned responses of the thalamic nuclei neurons in the trial sequence.

When the chain of neural events between the CS and US were analyzed (Olds, Disterhoft, Segal, Kornblith, and Hirsh, 1972) the

earliest CR effects were noticed within 20 msec. following CS presentation. The posterior thalamic nucleus exhibited the greatest number of such responses and these responses were larger in this area than at any other. Some early learned responses (< 20 msec.) were also seen at the cortical level, but these responses were generally smaller and more specific; generalized responses to a CS- were absent in the cortex, but present in the posterior thalamic nucleus.

Again using the same conditioning procedures as those producing the results cited above, Segal and Olds (1972) found that during pseudoconditioning most cells in the hippocampus did not respond to the CS. During conditioning, dentate units established a brief accelerated response to the CS during early trials; this response was generalized to a CS-. Units in the CA3 nucleus of the hippocampus exhibited CRs during later trials and these CRs were characterized by an acceleration of discharge rate which lasted throughout the CS-US interval; this response was not generalized to a CS-. Half of the hippocampal CA1 neurons responded like CA3 cells and the other half were like dentate neurons.

The work by Morrell and Olds has reaffirmed that conditioning is reflected in many areas of the brain. The effects of conditioning are as observable using unit data as AEPs. The experiments of Disterhoft and Olds (1972) and Olds et al. (1972) employed operant conditioning procedures which make it difficult to draw parallels between their results and those of Morrell. Apparent in all studies, however, is the trend to see CR changes in thalamic or reticular formation areas before the cortex.

Woody and Engel (1972) have reported that the "significance" of a stimulus can affect the unit activity which it evokes. In their experiment, units of the coronal-pericruciate cortex in the cat were monitored. A hiss and a click stimulus were both utilized. An initial response to these stimuli was determined and then a classical conditioning paradigm was imposed, which consisted of one of these stimuli being the CS with a glabella tap serving as a US. A comparison of conditioned activity to preconditioned responses showed that conditioning resulted in increases in unit responsiveness to the US. Such an increase was seen for both hiss and click stimuli. Also, a preconditioning to conditioning comparison revealed that unit CRs to the different stimuli were more similar in magnitude than were the initial preconditioning responses.

These same researchers (Woody and Engel, 1972) further found that when an electrical stimulus directed to the coronal-pericruciate area served as a CS, that facial movements could be elicited with lower current values following classical conditioning. Woody and Yarowsky (1972) reported similar results when an eye blink response was conditioned by pairing electrical stimulation of the pericruciate area with glabella tap.

The work by O'Brien and Fox (1969), which has served as a prototype for the present experiment, provided convincing evidence that cortical neurons may reflect conditioning. More conditioning units were found to exhibit changes in their response to the CS than did pseudoconditioning cells. Also reported were cells that showed

development of inhibitory responses to the CS during conditioning. Previous studies had emphasized conditioned increases.

Units recorded by O'Brien and Fox (1969) exhibited extinction, savings, and spontaneous recovery--all phenomena common to conditioned behavioral responses. They further reported that in general only cells showing initial responses to the CS conditioned. This observation is reminescent of Bures and Buresova's (1967) report that only cells with large responses to the CS exhibited CRs.

The work by O'Brien and Fox included pseudoconditioning controls which were not present in most of the earlier studies. Their work was chosen as a format for the present study for several reasons:

(1) Their experimental design included appropriate control conditions.

(2) Their paradigm was essentially a sensory-sensory conditioning procedure, i.e., light-weak electric shock. In the present experiment a light-air puff pairing was added to accommodate the possibility that electric shock (even 0.5-2.0 V) could be adversive and thus carry motivational components.

(3) Their recording site, the postcruciate cortex, is the primary projection area for a somatic US and this area is known to also serve a motor function.

(4) Units of the postcruciate cortex exhibit spontaneous rates and polymodal responses which would make them viable candidates as possible transmitters and receivers of information.

(5) The hypothesis of E. Roy John's Statistical Configuration

Theory that during conditioning the PSH-AEP correlation increases was testable with the O'Brien-Fox paradigm.

METHODS

Subjects:

Mature cats weighing between 2.5 and 4.0 kg were used as subjects. Surgical procedures included cannulation of the saphenous vein of the right hindlimb, insertion of an endotracheal tube, and exposing the posterior cruciate area of the cortex for placement of a microelectrode. A total of 83 cats were utilized in the pilot work plus the final experiment reported here. Forty-five subjects contributed to the data reported in this study with the procedures common to these subjects being highly standardized.

Animal preparation:

Thirty of the subjects were ether anesthetized in a wooden box with a transparent glass front which permitted observation of anesthetic level. Depth of anesthesia was judged from respiratory rate, corneal reflex, and motor tone. The larynx and throat were topically anesthetized with Cetacaine spray to prevent reflexive gagging, and an endotracheal tube was inserted with the aid of a laryngoscope. The tracheal tube was secured in position with adhesive tape connected to the lip with Michel clips. The exterior end of the tube was attached to a small bottle containing ether and appropriate intake and exhaust openings to allow for extended anesthesia.

A small incision was made to allow exposure of the saphenous vein of the right hindlimb. The vein was dissected free of adjacent tissues and the distal end was tied off. The vein was then cannulated with 1 mm outside diameter polyethelene tube which was secured to the vein by tying with thread. A gauze pad was saturated with Xylocaine

jelly applied to the incision and bandaged with adhesive tape.

The animal was then mounted in a Kopf model 1204 stereotaxic apparatus and placed in a double electrically shielded sound attenuating room (IAC). A longitudinal incision along the full length of a midline of the skull was made. The exposed muscle tissues adjacent to the incision and all stereotaxic pressure points were infused with 2% or 4% Procain HCl or Xylocaine. The skull was cleared of periostum and tissue with a periosteal elevator, the reflected musculature was covered with gauze pads and the skull was washed with physiological saline and allowed to dry.

The cruciate sulcus of the right cerebral hemisphere and the cortex immediately posterior to it were exposed with the aid of a Foredom electric dental drill and a no. 8 Ransoni and Randolph right angle flat headed burr. The dura matter was punctured and cut free on three sides and layed back to expose the underlying cortical surface (the dura was not reflected when a tungsten microelectrode was used). A second opening was made just to the right of the median sagittal crest about 5 mm anterior from the posterior lip of the parietal eminence to allow implantation of a macroelectrode to stimulate the pyramidal tract. Ether anesthesia was discontinued and the animal was immobilized with injections of gallimine triethiodide through the cannulated saphenous vein.

Fifteen of the forty-five subjects underwent the above preparations with the exception that they were physically restrained during cannulation of the vein. The restraining device was a full body cast made of Orthoplast. Upon being secured in the restrainer the tissue

surrounding the saphenous vein was locally anesthetized with subcutaneous injections of 5% Procaine HCl or Xylocaine. The vein was cannulated as described above and gallimine triethiodide injected. The animal was immediately freed from the restrainer, Cetacain applied to the throat, an endotracheal tube inserted and the subject put on an artificial respirator. Elapsed time from injection of gallimine triethiodide to the commencement of artificial respiration was usually from 30 to 60 seconds. In no case was the interim period beyond 4 minutes.

Local anesthetic agents, Procaine HCl or Xylocaine, were injected into the locations of anticipated stereotaxic pressure points, along the midline of the scalp, and underlying musculature. An interval of from 10-20 min. was allowed for analgesia to occur with the previous vein cannulation operation being used as a good estimate of analgesic latency. The remaining surgical procedures followed those outlined above.

Seven of the fifteen animals subjected to the surgical procedures while under the effects of gallimine triethiodide had been equipped a day or two before with chronic fittings attached to the top of the skull. These fittings consisted of two hard plastic sleeves to which a Kopf chronic headholder device could be attached. The plastic sleeves were fitted under nembutal anesthesia and secured to the skull with the standard screws and cranioplastic cement technique. Animals were allowed several days to recover before being used in the acute procedures. The chronic headholder eliminated all stereotaxic pressure points while maintaining stereotaxic accuracy.

During the experiment gallamine triethiodide was injected hourly (about 1 cc/hr) except during actual conditioning procedures which took 1-1/2 hours to complete. Artificial respiration was maintained with a Harvard pump, the frequency and volume adjusted to maintain 3.5-4.0% tracheal CO_2 level (usually 26 strokes per minute, and a stroke volume of 50-80 cc per stroke). Tracheal CO_2 was monitored on a Godard capnograph. Body temperature was maintained near 37° C with a hot water bottle during recording sessions, and an electric heating pad between recording sessions.

Electrode construction and implantation:

Macroelectrode Construction: The macroelectrodes utilized in this study were of a concentric bipolar type constructed of 22 gauge diameter tubing and a .01 inch diameter stainless steel insulated wire, type 316, purchased from Driver Harris.

The center wire extended beyond the end of the stainless steel tube by 1/10 mm with only the cross section of its cut end being free of insulation. The 22 gauge tube was coated with Insulex such that only the cross sectional end remained exposed.

Microelectrodes: Several types of microelectrodes were used in the course of this research project. Among these were glass or epoxolite coated tungsten wire electrodes. The 125 micron diameter tungsten wire, ordered from Sylvania Electric Chemical and Metal Supply of Tiwanda, Pennsylvania, had been electrolytically etched with potassium nitrate to a 2-5 micron tip, after which it was placed inside of a .016 O.D. 27 gauge stainless steel tube purchased from

Tube Sales of Los Angeles, California. The outer tube was crimped to hold the tungsten wire firmly. Glass tubing was drawn over the electrode with a micropipette puller in such a manner as to coat the tubing and the wire except for the extreme tip of the tungsten wire. Another type of metal electrode was used, made of a 2.5 cm length of .001 in. diameter stainless steel glass coated wire fused to the inside wall of a .016 in. O.D. 27 gauge stainless steel tube. The wire was placed inside of the tubing with 1 cm of the wire extending beyond the end of the tube. A butane torch was used to heat the tubing causing the glass coating on the wire to melt, simultaneously creating a circuit between the tube and the wire. The tube was then coated with epoxolite.

In some instances micropipettes were used which were made of .032 in. O.D. glass tubes with a .006 in. wall drawn on a horizontal puller to a 1 to 2 μ diameter tip and filled with a 3 M NaCl or KCl solution using the standard boiling in alcohol technique.

Macroelectrode Implantation: The macroelectrode was zeroed in the stereotaxic at about a 22° angle sloping downward from posterior to anterior. The electrode was then implanted at coordinates P, 8; V, 0; and L, 1. Exact placement was determined by recording from the macroelectrode while simultaneously stimulating the pericruciate cortex electrically through silver ball bipolar electrodes to activate pyramidal neurons. When evoked responses capable of following high frequencies of electrocortical stimulation were detected having latencies of 1.5-4.0 msec., the electrode was judged to be in the

medullary pyramidal tract. In the experiment, only 5 cells were identified as pyramidal units based on their responses to pyramidal tract stimulation. Pyramidal units were not selected out for special analyses since their number was so small.

Equipment and stimuli:

The recording and data collection equipment is schematically represented in Figure 1. The subject, cathode follower and Tektronix 122 preamplifiers were all located inside a walk-in double walled, electrically shielded sound-proof room. A marble table supported the animal and stereotaxic which was firmly mounted to reduce vibratory effects on recording and electrode stationarity.

Electrocortical potentials passed from the microelectrode to the cathode follower which was single-ended producing in essence a monopolar recording system. The signal was then divided and passed through two parallel 122 preamplifiers with frequency pass settings for EP (0.2-50 cps) and unit action potentials (.8-3.0 k cps). The EP signal was then led to a Tektronic 2A63 amplifier to allow for constant amplitude adjustment and similarly the unit signal passed through a Tektronix 2A60 for the same purpose. Next, both signals were monitored visually on a multichanneled CRO. A PDP 12 was used for A to D conversion, storage in digital form, and data analysis.

The intertrial interval and the occurrence of stimuli were controlled by a tape programmer allowing for closure of a microswitch which initiated a timing cycle on a Devices Digitimer. The start of each cycle was represented by TØ. The intertrial interval was 15 sec.

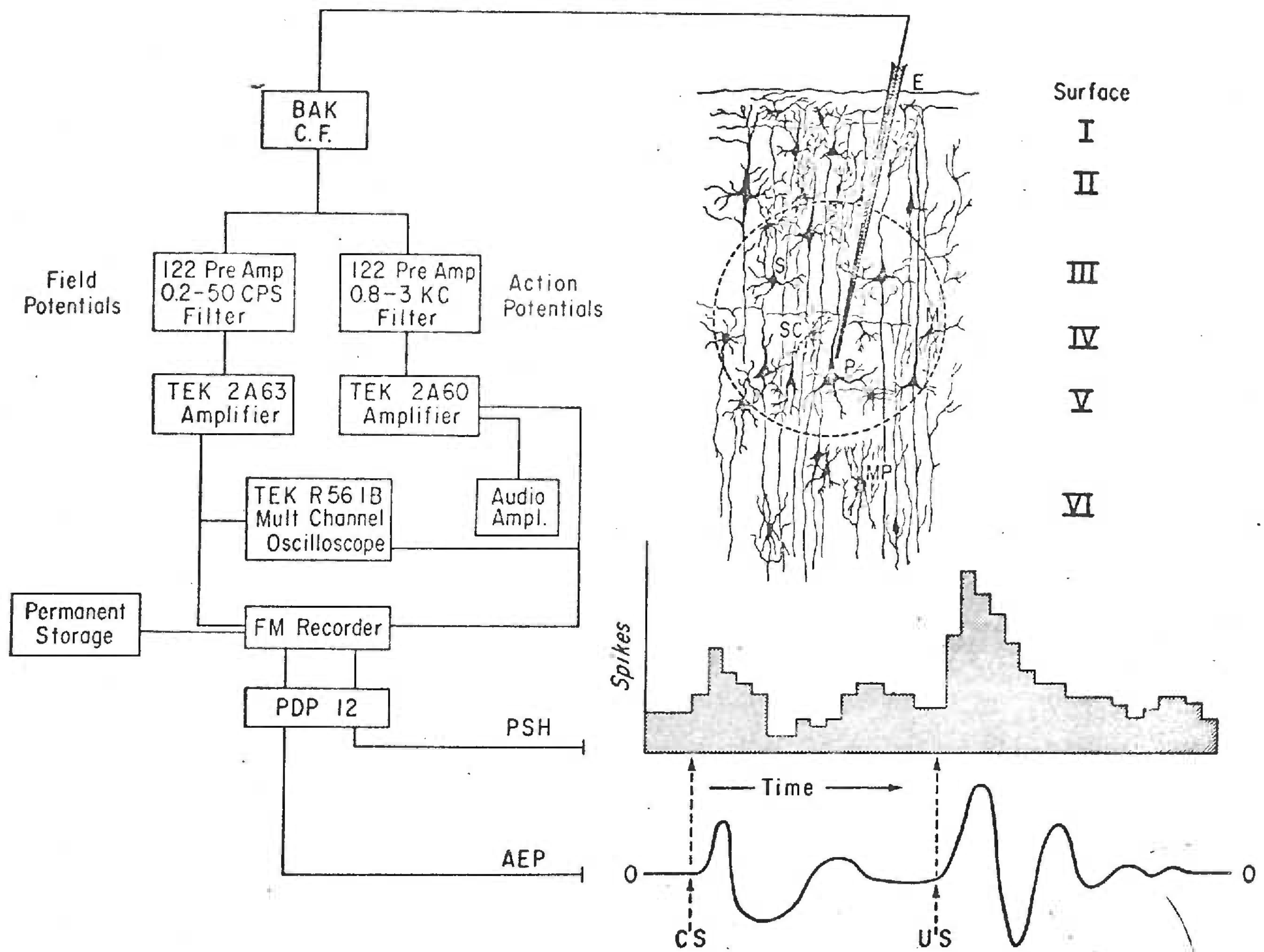


Figure I A drawing to illustrate the various cortical lamina of typical six layered neopallial cortex, and the procedure for recording PSHs and AEPs from a single microelectrode (E) located in the cortex. SC, subject cell, a pyramidal neuron whose action potentials form the PSH; S, stellate cells; M, martinotti cell; MP, modified pyramidal cell. The broken circular line symbolizes an imaginary spherical boundary within which electrical potentials contribute significantly to the AEP. The Roman numerals at the side of the figure indicate cortical layers. Electrical potentials "seen" by the electrode tip are led through a BAC cathode follower and a pair of Tektronix 122 preamplifiers where frequency filters separate unit activity from slower electrocortical potentials.

with a total variance of $\pm$ 6 sec. Thus, a trial could be initiated, at the earliest, 9 sec. following the start of a previous trial; or as late as 21 sec. The actual sequence of varying intertrial intervals was programmed to be randomized around the mean for a series of 25 trials.

The digital cycle duration of the Digitimer was set at a value greater than 2 sec., but less than 9 sec. (usually 4-5 sec.). The Digitimer, operating by counting impulses from a built-in 100 KHz clock generator, provided time delays from TØ accurate to within 0.1 msec. At 1 sec. after TØ, the Digitimer activated an auxilliary pulse generator which in turn delivered a triggering pulse to a Grass PS2 photic stimulator the CS light flash. The CS, held constant through all procedures, was a light flash of 10 μsec. duration with an intensity setting of 8.

A Devices Mark IV stimulator was used to generate the unconditioned shock stimuli which were delivered to the animal's left hindlimb via subcutaneously placed hypodermic needles. The placement of these electrodes was dependent upon eliciting a unit response when a pulse was delivered. In all cases, the needle placements were below the heel in the hindpaw digitigrade. Frequently, a plantar-dorsal arrangement was used, but, in some instances, the best unit responses could be evoked with other placements, e.g., plantar-plantar; dorsal-dorsal, or lateral-medial. No attempt was made to identify specific nerves being effected; however, it is safe to say that the unconditioned stimuli effect was detected by the tibial nerve and its

immediate branches, the medial and lateral plantar nerves; or the superficial and deep peroneal nerves and perhaps, in some instances, the shock exerted some influence on all of them.

Two different shock stimuli were used as unconditioned stimuli. The voltage ranged from 1-10 volts. Both stimuli consisted of 5 pulses at a frequency of 250/sec., with the duration of the individual pulses differentiating the two. The "short" shock US had a pulse duration of 0.1 msec. whereas the "long" shock US had a 1.5 msec. pulse duration.

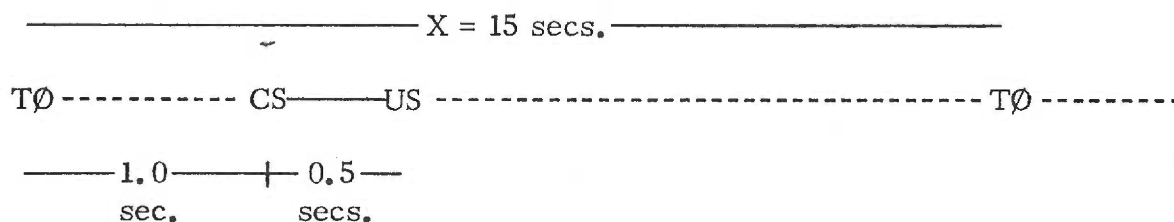
One group of subjects received an air puff delivered to the hind-foot as a US. The air source was a tank of compressed air. A Pan Asco 12 volt D.C. solenoid (cat. no. 8263A2) was placed outside the sound attenuating room between the air source and the subject. The solenoid was activated by a 15 msec. pulse passed from a D.C. source through a Devices relay unit. The latency between solenoid activation and stimulus arrival at the hindfoot was 25 msec. As with the electric shock stimuli, the air puff was directed to the receptive field area of the isolated cortical neuron. The only sound associated with the air stimulus was a "puffing" sound produced by air passing through the nozzle used to direct the air flow onto the receptive field.

Experimental design:

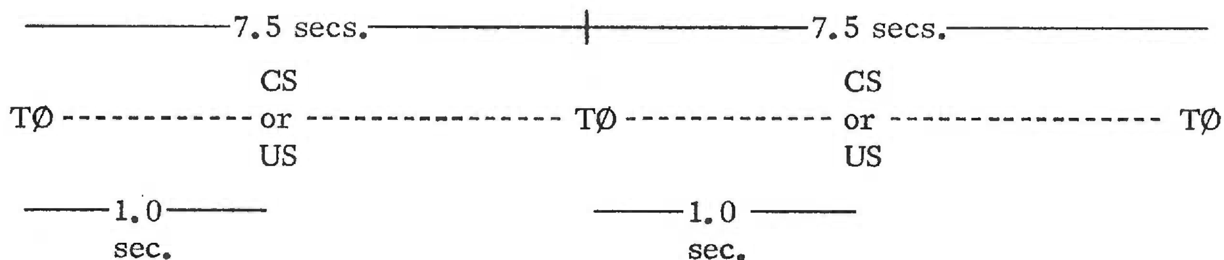
Table 2 outlines the basic experimental design. There were three experimental groups receiving identical habituation, association, and extinction trials with the exception that the US intensity or modality was different. Subjects in these groups received CS-US pairing during association trials. Pairing consisted of the US following the light

Table 2: BASIC EXPERIMENTAL DESIGN

Conditioning association trials:



Pseudoconditioning association trials:



Conditioning:

	Hab	Association	ExT
Group I US = Five 0.5 msec. pulses	75 CSs	225 CS-US	75 CSs
Group II US = Five 1.5 msec. pulses	75 CSs	225 CS-US	75 CSs
Group III US = Air Puff	75 CSs	225 CS-US	75 CSs

Pseudoconditioning:

	Hab	Association	ExT
All Units US = Five 1.5 msec. pulses	75 CSs	225 CSs & USs	75 CSs

flash CS on every trial during the association session. During habituation and extinction procedures the CS was presented alone with the same 15 sec. mean ITI as was used during association.

For pseudoconditioning subjects the association session consisted of the presentation of a US or CS every 7.5 sec. The sequence of stimulus pattern, e.g., CS-CS-US-US-CS-US etc., was determined with a table of random values. These subjects also received habituation and extinction training identical to that of the conditioning groups. Both experimental and control procedures required an hour and a half to complete.

Procedures and data collection:

For subjects receiving a general anesthetic at least an hour was allowed to elapse following removal of either before recording was started. Recording was initiated immediately on those subjects prepared under local anesthesia. The microelectrode was lowered with the aid of a Kopf hydraulic microdrive capable of gauging vertical movement in microns. When a unit was isolated, the left hindfoot was stimulated manually in a punctate manner to discern the receptive field of the isolated cell. The hypodermic needle electrodes were slipped under the skin and test presentations of the US were delivered to determine the exact electrode placement. One to two cc of gallamine triethiodide were injected, the door to the shielded room closed, and the lights turned out. The tape programmer was started and the CS only trials for habituation were started. Following the 75th habituation trial, the US was turned on and the CS-US

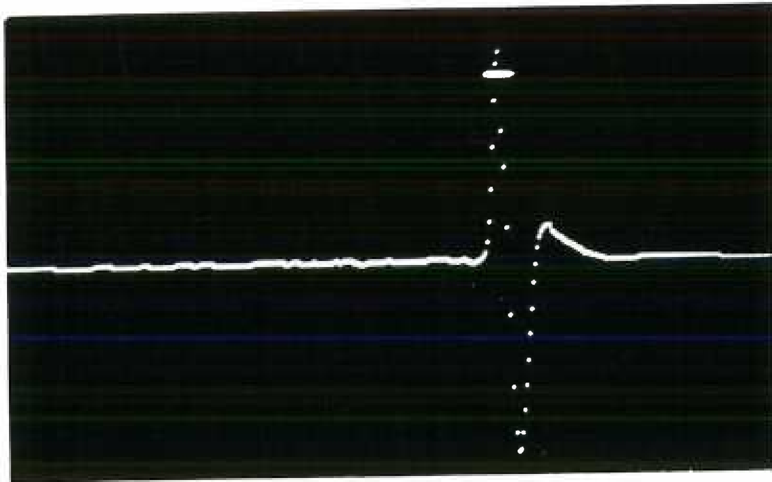
pairings began on the next trial. Thus there was no delay (beyond the regular ITI) between habituation and association sessions. The change from association to extinction was effected in a like manner by simply turning off the US after 225 association trials.

At the end of a recording period, the animal was given an injection of gallimine triethiodide and the temperature was noted. Following the completion of whatever was needed to be done to maintain a viable preparation the microelectrode was further advanced until a second unit was isolated. Cells isolated following an initial experimental run were referred to as "second cells," "third cells," etc. or simply "other cells."

In the event that a recording procedure was started and not completed before loss of the cell, or deterioration of a significant signal to noise ratio, the number of association trials completed was registered in a log book. If the total association trials from uncompleted recording sessions surpassed 150 trials the next cell surviving the entire conditioning procedure was referred to as a "second cell" or "other cell" for that subject. Otherwise, the first completed cell retained its "first cell" status.

Examples of the best and the worst unit signals are shown in Figure 2. The horizontal cursors at the apex of the action potentials indicate that the computer has registered the occurrence of a spike. The entire recording session, including the intertrial interval activity, was recorded by a Sangamo FM magnetic tape recorder. Readout from the recorder was monitored on the CRO to assure accuracy of data collection.

A



B

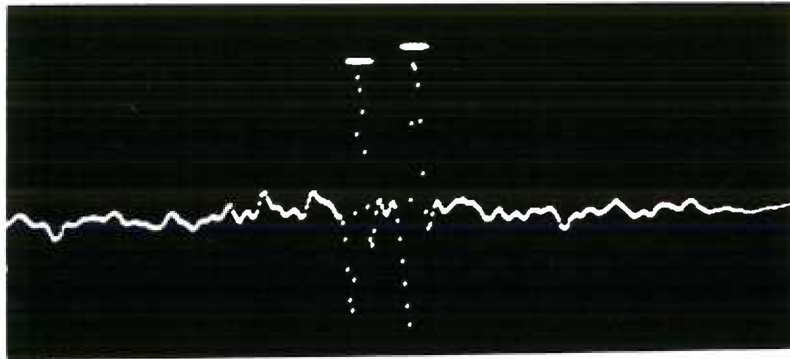


Figure 2 Representative photographs of unit action potentials illustrating signal-to-noise ratios.

A. Cell 123A recorded through a glass-coated tungsten microelectrode. Identified as a pyramidal tract neuron by frequency following characteristics.

B. Cell 91A recorded through a micropipette filled with 3M NaCl. A nonpyramidal cell.

TØ markers were placed on channel 1; unit activity on channel 2; and the EEG on channel 3.

Data processing:

Virtually all cells were recorded "off line" from the PDP-12 computer to allow for a more complete examination of the analogue data before converting it to digital form. This was valuable in that on several occasions, marginal signal to noise ratios could be improved by passing the analogue signal through a Krohn Hite filter with band pass and rejection setting adjusted to reduce the noise amplitude disproportionate with that of the spike amplitude.

When the signal left the FM recorder (or the Krohn Hite filters when adjustment was required), it was led to a Tektronix 2A60 amplifier to produce an adequate signal to be received by the PDP-12. The TØ was also subject to amplitude manipulation.

A program for accepting the analogue data, changing it to digital form and storing it on computer linc tape, was written. The PDP-12 allows for 3 simultaneous inputs (Schmitt Triggers) which can detect voltage amplitude. TØ was led to one of these A to D converters and the unit signal was led on parallel lines to the remaining two. This dual unit input provided for selective recognition of particular spikes based on their amplitude. The occurrence of a TØ initiated sampling of the unit activity being received by one of the Schmitt Triggers. This sampling lasted for 3.5 sec. following TØ resulting in a collection of unit activity commencing at 1 sec. before the onset of the CS and continuing through the 0.5 sec. CS-US interval and for 2 sec.

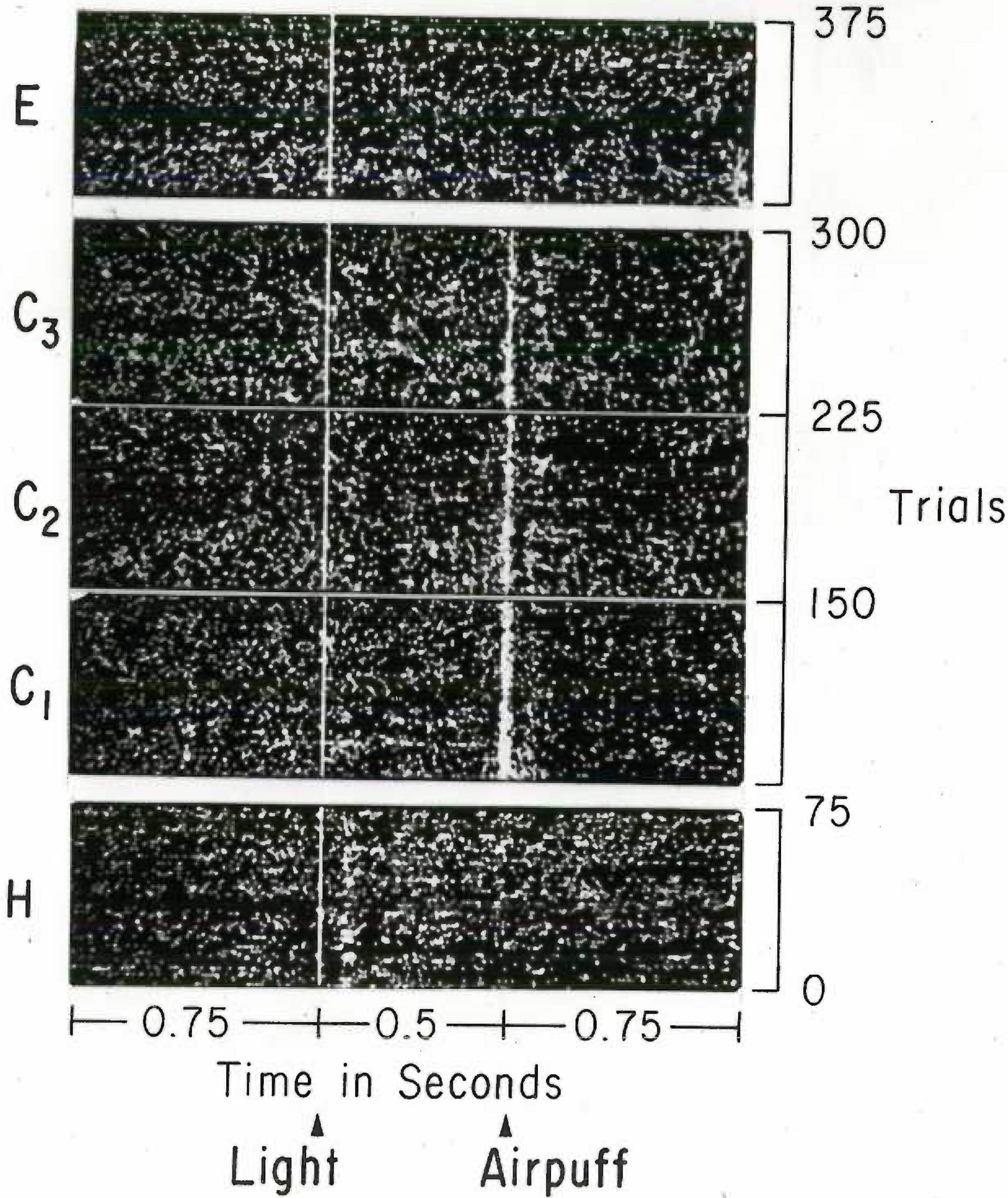
following the US. The location of a spike in time was identified by its latency following TØ. Data was stored on linc tape in a continuous trial series.

The electrocortical potentials were fed directly into the PDP-12 A/D converters with TØ again initiating computer sampling. The amplitude of the EP was sampled every 2 msec. starting 20 msec. before the onset of the CS. The first two hundred fifty-six sampling addresses resulted in a total of 512 msec. of data or in other terms, the CS-US interval was converted to digital form. In like manner the first half-second following the US was sampled, i.e., the voltage was detected by 256 two-msec. samples. In terms of responses then, the first 256 addresses recorded the CR while the second 256 addresses registered the UR.

Twenty-five trials were summed algebraically and the averaged evoked potential (AEP) for the 25 trials was stored on linc tape. After all 375 trials had been converted to digital form, AEPs based on 75 trials were computed from the original 25 trial block data and both the 25 and 75 trial AEPs were recorded on tape. Seventy-five trial PSHs from the trial by trial data previously recorded were also constructed. Thus, the trial by trial unit activity and 75 trial PSHs were recorded on linc tape along with the AEPs for 25 and 75 trial blocks.

Data quantification to response t-scores:

The first step in quantifying a unit's response consisted of visually examining the pattern of occurrence of action potentials for



Cell 99B3
E
C3
C2
C1
H
375
300
225
150
75
0
Trials
0.75
0.5
0.75
Time in Seconds
Light
Airpuff

consecutive trials. Figure 3 shows a "dot" display of such response patterns. Each dot represents the occurrence of a spike. In Figure 3 time runs along the abscissa from left to right and the trials sequence progresses from bottom to top. Each section of "dots" represents 75 trials. From the dot displays portions of the CS-US interval which appeared as areas having high or low concentrations of dots (e.g., the vertical cluster of dots in Figure 3, Habituation block, at about 80-100 msec. post-CS) were identified and noted as a possible response.

With these observations recorded, PSHs for the same unit were constructed and the temporal limits of the response were determined with the aid of the computer. For example, assume that from the dot display and the PSHs a response was detected which had a latency of onset following the CS of 50 msec., and the response features were present for 100 msec. The computer was programmed to calculate the mean spike rate per second for adjustable post-CS periods (in this case 100 msec.) using data from 25 consecutive trials. In this example, the temporal limits of the response, 1050-1150 msec. post-TØ, would be set by the computer operator and the mean spike rate and the across-trials variance for this portion of the CS-US interval would be calculated. In a like manner an equivalent interval (100 msec.) would be chosen from the pre-CS activity and a mean spike rate and an across-trials variance for that interval would be computed. Both of these means, the pre-CS and the post-CS mean rate, would then be compared to the mean spike rate of the remainder of

the 1 sec pre-CS interval (a 900 msec. segment of baseline activity extending from TØ). The method of comparison chosen was a student t-formula. The t-score resulting from this type of comparison is called a response t-score. In effect then a pre-CS t-score and a post-CS response t-score were both computed. The need for the pre-CS t-score will be shown in the Results section.

Conditioning t-score:

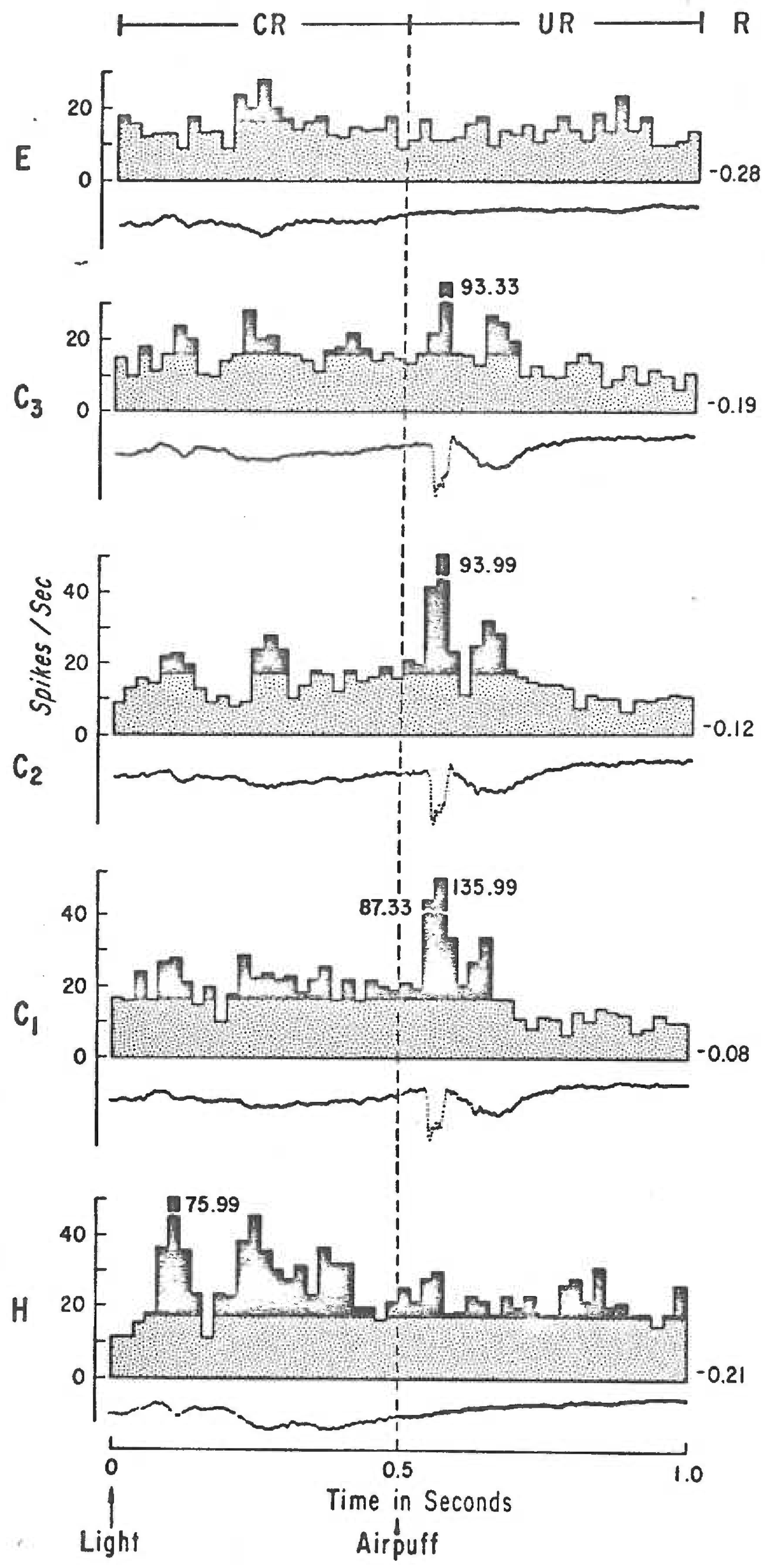
A measure was devised to quantify the amount of change in a unit's response to the CS during the association session as compared with habituation and extinction. Assuming the same hypothetical response described in the response t-score section above, a change in spike rate starting at 50 msec. post-CS and lasting for 100 msec., a conditioning t-score was calculated in the following way: the difference between the spike rate of the response period and the 900 msec. pre-CS baseline period was calculated for every trial. Then a mean difference score was determined for every 25 trial block through habituation, association, and extinction. This resulted in 15 mean difference scores; 3 for habituation, 9 for association, and 3 for extinction. Next the 3 mean difference scores of habituation and those of extinction were pooled to form a distribution of 6 mean difference scores and a grand mean of this distribution was calculated. This grand mean of habituation plus extinction was then compared to the distribution of mean scores, 9 in all, for association. Again a student t-formula was employed to make this comparison and the values resulting from this comparison were called conditioning t-scores. In essence then a conditioning t-score is a quantitative statement of the

amount of change in response during association trials as compared with the mean response activity of habituation and extinction.

PSH-AEP and other correlation values:

As previously described in the Data Processing Section, 75 trial PSHs and AEPs were constructed by the computer. An example of PSH and AEP data is represented in Figure 4. Specifically there is one PSH for habituation (H), 3 for association (C_1, C_2, C_3), and one for extinction. The same number of AEP wave forms were also recorded. Since both the PSHs and the AEP wave form were composed of data sampled every 2 msec., they in essence represented two distributions temporally paralleled, and composed of 256 consecutive points. These two distributions were then compared by means of a Pearson Product Moment Correlation which provided an r value that represented the closeness of fit between the two distributions. This procedure was conducted by the PDP-12 which had further been programmed to allow for time shifts in the two distributions, i.e., the juxtaposition of two points on the two distributions could be altered such that a PSH point could either precede or lag a previously contemporary AEP point. Such time shifts in the distributions were made within limits. It was reasoned that a unit's action potential could be associated with EPSPs of varying slope depending upon the temporally and spacially summed input. For this reason time shifts of up to 20 msec. were allowed. Therefore, the highest correlation r value resulting from the comparison of the PSH and AEP over a $\pm$ 20 msec. time shift became the r value used in data analyses.

Figure 4 Poststimulus histograms of unit activity and the averaged evoked potentials recorded simultaneously through a single micro-electrode. Each PSH and AEP was formed by summing 75 trials. H = habituation trials. C_1, C_2, C_3 = blocks of 75 trials during CS-US pairings. US = airpuff introduced at the beginning of C_1. E = extinction trials. The border between stippled and solid portions of the PSHs defines the mean spontaneous rate of the cell.


Cell 99B3
CR
UR
R
E
20
0
-0.28
93.33
C3
20
0
-0.19
Spikes / Sec
93.99
40
20
0
-0.12
C2
135.99
87.33
40
20
0
-0.08
C1
75.99
40
H
20
0
-0.21
0
0.5
1.0
Time in Seconds
Light
Airpuff

Also possible with the aid of the computer was a PSH-PSH correlation and an AEP-AEP correlation. In the first instance the PSH for H could be correlated for similarity with the PSH for C_1, C_2, C_3, and E. In a similar manner the AEP for H could be correlated with subsequent blocks of trials. When PSH-PSH and AEP-AEP comparisons were run no time shifts between the two distributions were used.

RESULTS

CONDITIONING REFLECTED IN UNIT ACTIVITY

Establishing a criterion response:

The response t-scores for each cell were plotted for blocks of 25 trials across habituation, association, and extinction. An example of such a graph is depicted in Figure 5, part A. The final 25 trial response t-score of habituation of each cell was chosen as indicating its habituated response level and any response t-score of 0.7 or larger which had a sign opposite to that of the habituated response was called a criterion response. In Figure 5 part A, cell 119 exhibits criterion responses for the last 3 blocks of 25 trials during the association session. Graphs were then made of the interpolated number of association trials during which criterion response activity was present for each cell as indicated in Figure 5 part B. Cell 119 is shown at the top of a series of such plots made for first conditioning cells of the Long US group. (Similar plots were made for Short US, Air US, and pseudoconditioning cells.) When the criterion response trials for a group of units were accumulated in a vertical manner a histogram similar to the one in the lower part of part B of Figure 8 was formed. The number of trials containing criterion activity, indicated by the height of the histogram bars, was then converted to a percentage value by dividing the total number of trials of criterion activity in each histogram bar by 200 (25 trial blocks x 8 cells = 200) and multiplying the dividend by 100 ($\frac{X}{200} \times 100$ = percent criterion response trials where X = number of trials containing criterion activity.)

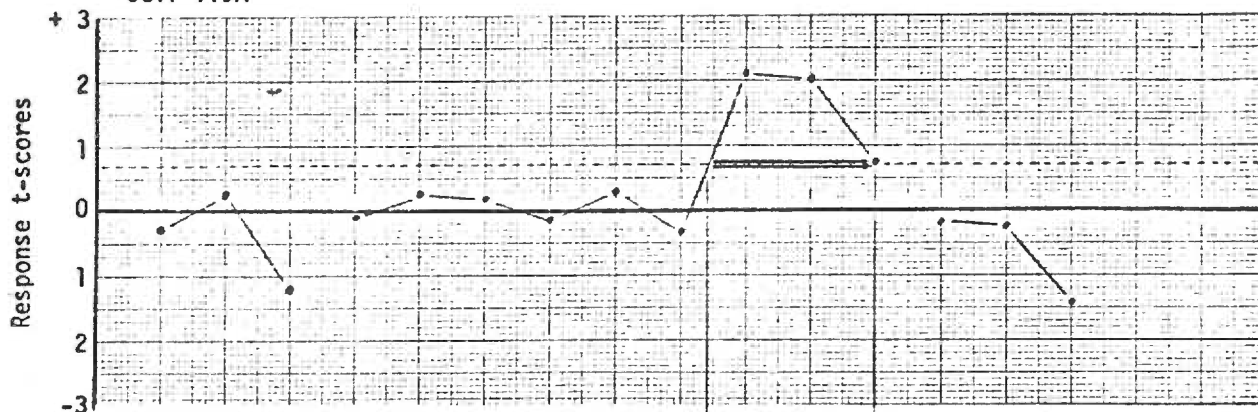
Figure 5 Determination of percent criterion response curves. In Part A, the response t-score for each block of 25 trials is shown for cell 119A. This same type of graph was made for all cells reported in this study. The first 3 points represent habituation trials with the third point being accepted as the "habituated state" of the cell's response. The tenth, eleventh, and twelfth points are the last three 25 trial blocks of paired CS-US trials and qualify as criterion responses since their response t-scores are beyond 0.7 and are opposite to the sign of the habituated response (point 3 in the graph). The number of trials during each 25 trial block on which criterion responses may have occurred was interpolated by assuming that each small square on the graph paper represented 2.5 trials. The number of squares falling under an 0.7 response t-score was thus multiplied by 2.5 to determine the number of criterion response trials. This value is represented on a horizontal scale in the upper part of Part B. The criterion response trials for the 8 first conditioning cells of the Long US group are also shown here.

The criterion responses were summed across cells for each 25 trial block and represented in histogram form (Part B, lower portion). Criterion response trials were converted to a percent value as follows:

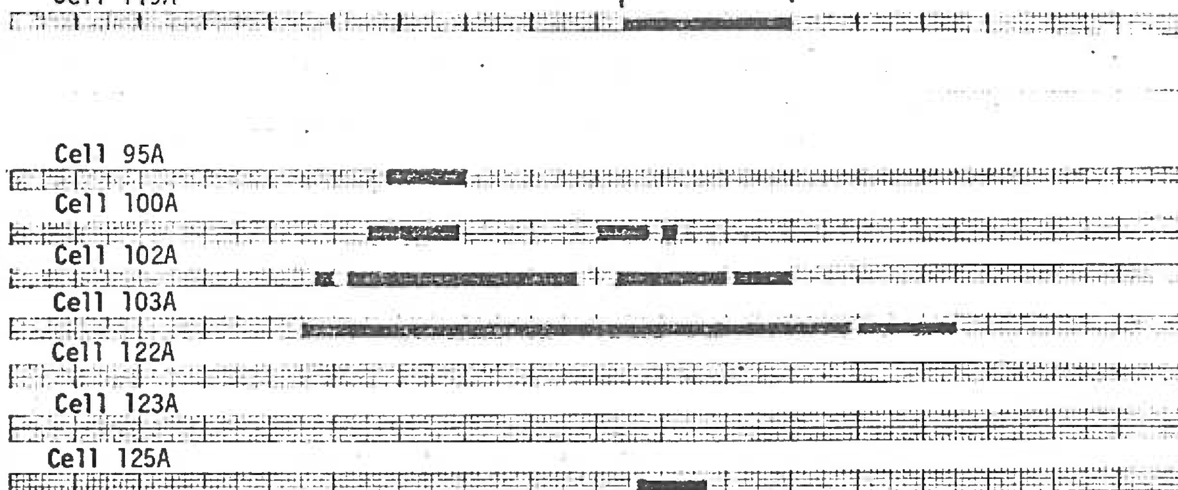
$$100 \left(\frac{X}{200}\right) = \text{percent criterion response trials.}$$

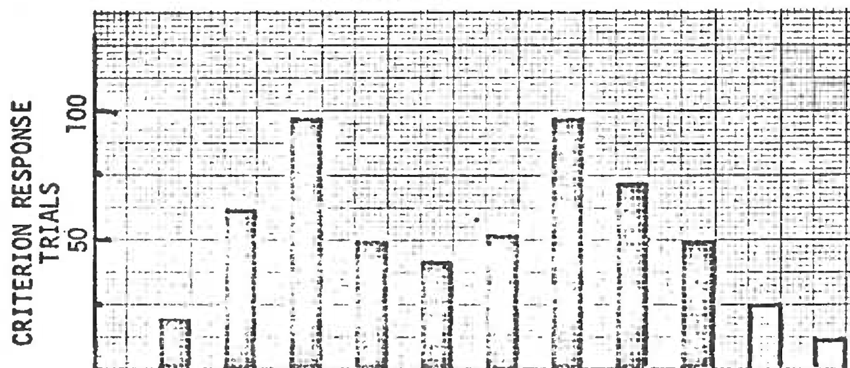
where X = the sum of criterion responses for a particular 25 trial block, and 200 = 8 cells x 25 trials to give the total number of trials given.

PART A



PART B





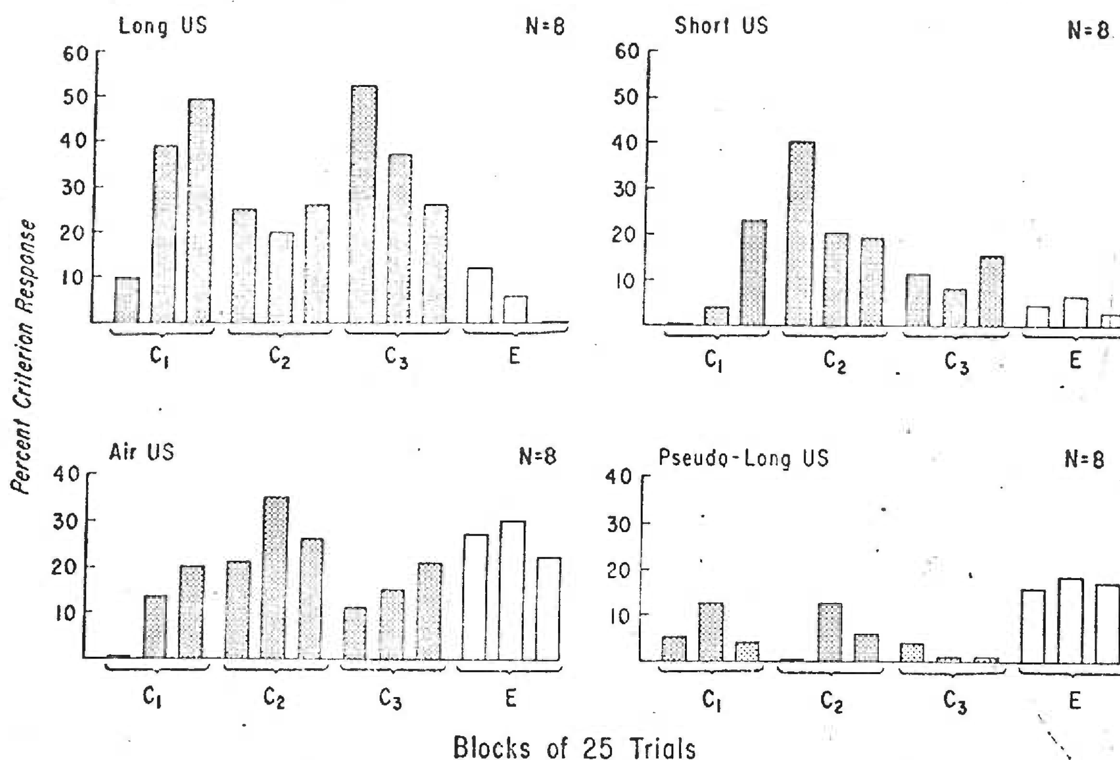


Figure 6 Percent criterion response activity of experimental and pseudoconditioning units. The interpolated number of trials per 25 trial blocks, exhibiting criterion activity (see procedural outline for this interpolation in Figure 5) was divided by 25 and multiplied by 100 to arrive at a percent value. Thus, the percent of trials on which criterion activity was present was determined for each block of 25 trials for each cell. Cells were grouped according to US modality and the percent criterion activity was summed across units for each block of 25 trials. For example, the 10 percent criterion response value shown by the first bar in the Long US histogram may be interpreted as indicating that of the 200 trials associated with the first 25 association trials for the 8 units (N=8), 20 trials exhibited response t-scores of 0.7 or greater. Units receiving long shock USs show a developmental increase in trials of criterion activity to an initial maximum level within 75 trials; short shock cells required 100 trials, and airpuff units 125 trials to develop their initial maximum peaks of criterion activity.

that, whereas a very weak US, such as air puff, is sufficient to produce conditioning, the developmental time course of the CR is longer.

An additional control used to demonstrate conditioning was the establishment of a pre-CS t-score between two segments of the pre-CS interval which was then compared to the post-CS response t-score for the same 25 trial block. The control procedure here assumed that if the CS evoked a change in baseline activity, then to demonstrate conditioning, the response t-scores across trials should be independent from the baseline change reflected in the t-score generated by the two time segments selected from the pre-CS interval. In Figure 7, the percent of trials on which activity (t-score of $> \pm 0.7$) occurred for both the pre- and post-CS activity is shown for the three experimental groups. The pre-CS criterion response activity, which had a t-score sign opposite to that of the post CS t-score, is shown projecting downward from the abscissa and represents a baseline trend which was reversed by the introduction of the CS. The graphs reflect the statistical results which showed the post-CS response t-score for all three groups to be independent of changes in the intertrial interval activity (Long US, $t = 5.36$, $df = 10$, $p < .05$; Short US, $t = 1.92$, $df = 10$, $p < .05$; Air US, $t = 6.01$, $df = 10$, $p < .05$).

In summary, then, all three conditioning procedures produced conditioning changes in unit responses to the CS. The conditioned changes were found to be unique from both baseline, intertrial interval, changes and from CS evoked responses during a psueudo-conditioning procedure. In the case of the Air US group, these

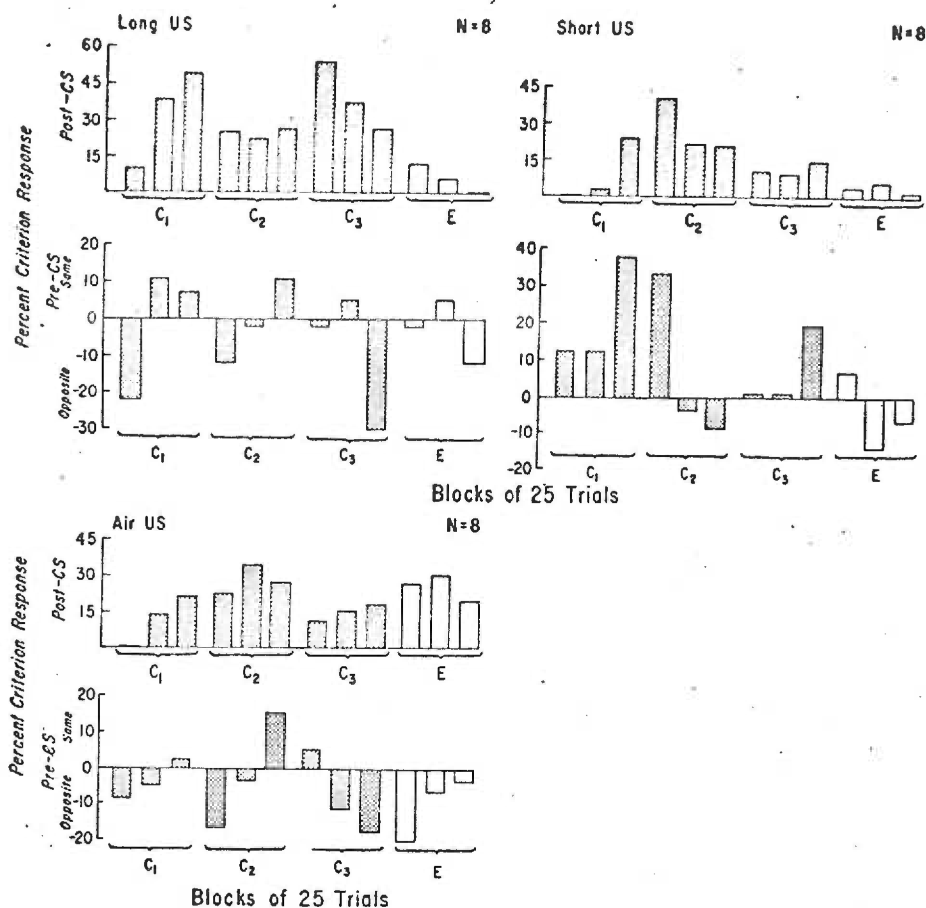


Figure 7 Criterion response activity evoked by the CS compared to baseline change. Data from eight first cells (N=8) in each of the US conditions were used in the construction of this figure. Post-CS criterion activity (percent of trials having response t-scores of ± 0.7 or greater) for the three experimental groups is represented in the top of each pair of histograms. The lower histogram in each pair represents pre-CS criterion activity. Pre-CS criterion activity occurring in the same direction, i.e., having a t-score with the same sign as the post-CS t-score, is shown by the histogram bars pointing upward. Histogram bars pointing downward indicate baseline activity in the opposite direction to that of post-CS activity.

results demonstrate that conditioning can be detected at the unit level when two very weak and non-noxious stimuli are paired. Thus, these observations support the view that contiguous pairing of sensory input is a sufficient condition to produce associative bonds. However, as the intensity, and perhaps the noxiousness of the US is increased, the number of trials required to establish an initial maximum level of CR activity is reduced. This point will be developed further in the discussion.

RESPONSE COMPONENTS

An examination of unit discharge following the light flash CS made clear the fact that in most cases there was recurrent fluctuation from excitation to inhibition within the CS-US interval. This oscillation in poststimulus activity presented a dilemma. Should the entire CS-US interval serve as the time interval from which a "response" mean rate and t-score should be calculated or could some fractional portion of the interval more accurately represent the presence of stimulus evoked changes?

A mean firing rate based on the total CS-US interval was often found to be misleading. Very dynamic alterations could be observed in some poststimulus histograms, but when these fluctuations were averaged, their mean did not differ substantially from the mean spontaneous rate. This fact, plus reports of single units exhibiting multicomponent responses to single stimulus events (Towe, Patton, and Kennedy, 1963), seemed to justify a component analyses of the CS-US interval activity.

After examination of the poststimulus histograms and the dot displays of many of the units, each cell was found to have two and sometimes three response components. The earliest component usually had a post-CS latency of 15-20 msec. and a duration of 50-100 msec. The earliest response components from all cells were placed on top of each other on a post-CS time scale (Figure 8, top left hand histogram) to form a histogram representation of the location of these components in the CS-US interval. Specifically, the CS-US

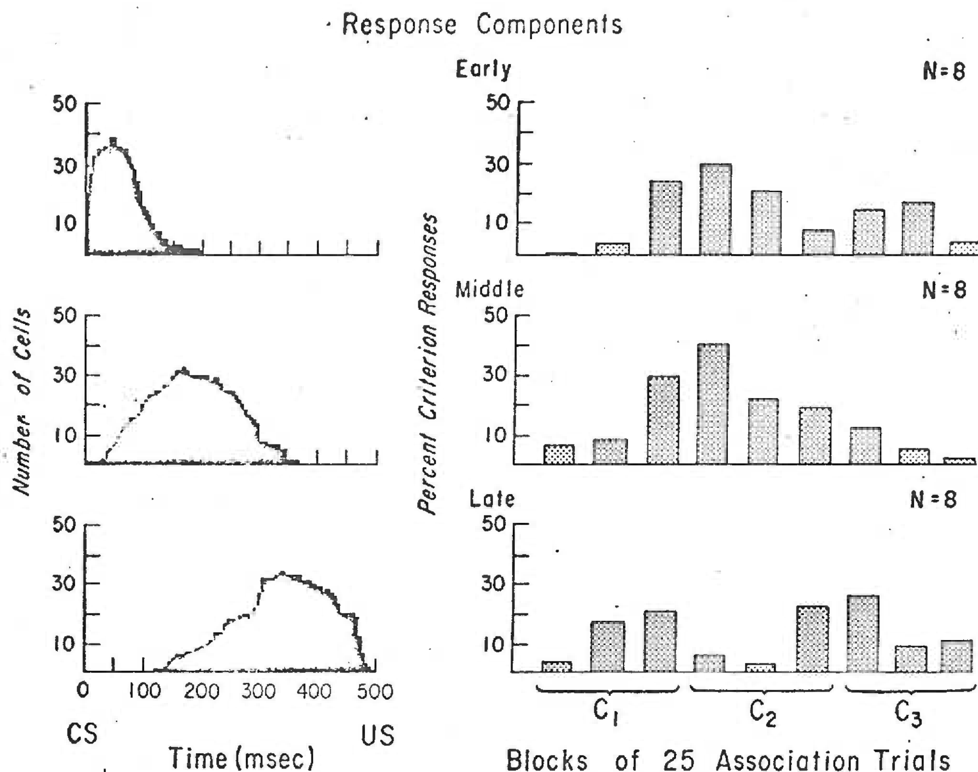


Figure 8 Response components: Their location in the CS-US interval and their respective learning curves. The frequency distributions on the left hand side of the figure depict the location of the early, middle, and late response components in the CS-US interval. The distributions were generated by registering the duration of the respective components for each cell, therefore, the ordinate is number of cells. The absissa is the CS-US interval or 500 msec. post-CS time.

The percent criterion activity exhibited by the respective components of the Short US group (N = 8 cells in this group) is represented in the histograms on the right side of the figure, and representative of the learning curves of the respective components.

interval was divided into 10 msec. lines. The temporal limits of each cell's early response component was determined from the dot display and PSHs. Each 10 msec. line in which the response was present received a vertical increment on the "cell" scale of the ordinate. This was done for each response component for every cell recorded during conditioning (Figure 8, left-hand histograms).
A second or middle response component usually followed in close succession to the earliest one (Figure 8, center left-hand histogram). The range of latencies for the onset of this second components was wider than for the earlier response. Nonetheless, its mean latency was around 100 msec. following the CS and the duration of this middle response component was typically around 200 msec. A third and final component identified in a majority of cells extended from the termination of the middle component to within 25 msec. of the US (Figure 8, bottom left-hand histogram).

Response and conditioning t-values were calculated for all three response components for each of the fifty-one cells recorded during CS-US pairing procedures. Fifteen units showed their highest conditioning t-score in their earliest response component. Eighteen cells exhibited their highest conditioning t-score during the middle response component and an identical number of units showed best conditioning during the third response component.

With respect to the 24 cells recorded during initial conditioning procedures, the highest conditioning t-values were distributed as follows: Early component = 7; middle component = 7; late component =

10. Twenty-seven units were recorded after at least one conditioning sequence had been completed, i.e., these units represented a repeated measure. The number of these cells showing their highest conditioning t during the respective component intervals were: early component = 8; middle component = 11; late component = 8.

When the percent criterion response measure was plotted across trials, the respective response components exhibited marked differences in the trial-to-trial development of conditioned changes (Figure 8, right-hand column). Early and middle components showed their maximum percent criterion response (PCR) level between 75 and 100 conditioning trials whereas the third component showed a large PCR within 50 conditioning trials. The absolute level of the PCRs were quite different also with the middle component peaking at 41% and the third component reaching only 26% at its highest point. Therefore, despite the near equal distribution of highest conditioning t-scores between response components, differences exist in the time course of the development of conditioned changes in the respective components.

REPLICATION OF O'BRIEN AND FOX

Conditioning of unit activity:

The present experiment employed conditioning procedures and stimulus parameters that were used in an earlier study of unit conditioning (O'Brien and Fox, 1969). In an attempt to assess the replicability of this previous experiment the data collected in the present study were submitted to analyses according to the methods of O'Brien and Fox (1969).

To measure unit conditioning, the former authors computed a conditioning t-score based on the difference between the grand mean spike rate during association trials and the mean rate of unit discharge during habituation plus extinction. Thus, for 97 cells, conditioning t-scores reflected the quantity and the direction of change in the mean rate of firing during association trials as compared with the combined habituation-extinction mean rate.

Their data were grouped into 15 trial blocks resulting in a total of 15 such blocks used in computing the conditioning t-score. For twenty degrees of freedom a t value of $\pm$ 2.09 represents a .05 confidence level. This t value, $\pm$ 2.09, was arbitrarily selected as a cutoff level and the number of cells whose conditioning t-scores equalled or surpassed it were noted for the conditioning and pseudoconditioning groups. From a total of 17 pseudoconditioning cells, only 2 exhibited conditioning t scores beyond $\pm$ 2.09. In comparison, the 0.5 sec. CS-US interval conditioning group, N = 53, produced 10 cells exceeding the cutoff level. The probabilities by the binomial

expansion that these numbers of high t-scores could have arisen by chance are: (1) pseudoconditioning, 2/17, $p < 0.2$; conditioning, 10/53, $p < 0.0003$.

In the current study a total of 50 conditioning cells were recorded and conditioning t-scores were computed for each response component in each of the 50 cells using methods similar to those of O'Brien and Fox. The major difference was that in the current analyses the spike rate for the grand means was based on blocks of 25 trials rather than 15 trials and all trials were utilized in the present analyses. In the earlier study the first 15 trials were utilized in the present analyses. In the earlier study the first 15 trials of habituation, conditioning, and extinction were deleted before further analysis was undertaken. Using blocks of 25 trials, the conditioning t-score in the present study was based on a distribution of means with 14 degrees of freedom as compared to 20 degrees of freedom in the O'Brien and Fox experiment. The cutoff t for a .05 confidence level with 14 degrees of freedom is $\pm$ 2.14, and this value was, therefore, chosen as the cutoff level in this study. Further, if any response component of a given cell exhibited a conditioning t-score beyond the 2.14 level, the cell was scored as exceeding the criterion level.

Of the 50 conditioning cells in the present study, 10 were found to have conditioning t-scores higher than the cutoff level. From a total of 16 pseudoconditioning units only 2 produced t-scores surpassing the assigned cutoff level. Thus, the ratios of high conditioning t-scores to total number of recorded cells in this study, 10/50 and 2/16 for conditioning and pseudoconditioning, respectively, are

impressively similar to 10/53 and 2/17 reported for these same procedures by O'Brien and Fox (1969).

O'Brien and Fox reported that the direction of conditioning change was inversely related to the sign of the original response to the CS. Specifically, an increased firing rate to the CS during conditioning tended to occur in cells which initially exhibited inhibitory responses to the CS and vise versa. In 79% of the cells they studied the modification during conditioning was actually a reversal of the sign of the original CS response.

In the present study, the direction of the response to the CS during habituation was determined for each response component. From 50 cells, 141 response components were identified. Of this total, 104 response components exhibited conditioning t-scores opposite in sign to that of the response t which had been based on the final 50 trials of habituation. When only response components with conditioning t-scores exceeding $\pm$ 1.20 (N = 45) were used, 89% of them exhibited the reversal phenomenon.

Therefore, in respect to both the quantity and the direction of conditioned changes in unit activity, the results of the present study are similar to those reported by O'Brien and Fox (1969).

CROSS CORRELATION OF PSHs AND AEPs

The criterion response (a response t-score of >0.7 during conditioning which had a sign opposite to the response t-score of habituation) was established to provide a means of selecting units which showed a relatively large change in their CS evoked activity during conditioning. Similar response requirements have been used by other researchers (Disterhoft and Olds, 1972). As indicated in Figure 5 the interpolated number of trials having criterion activity was determined for each cell and these values were summed to produce a group criterion response curve (Figure 5, bottom). This was done for each of the US conditions and for pseudoconditioning. Referring to Figure 5, it may be noted that cells 95A, 100A, 102A and 103A seems to contribute the most to the group criterion response curve. These units were selected as displaying the "best" plastic changes since it was their activity which contributed most to the group criterion response curve. These "good" conditioning units were chosen for the PSH-AEP correlation analyses since they demonstrated the "best" plasticity or good conditioning when the conditioned response (the criterion response) was a reversal of response polarity with the response t-score being >0.7. In a similar fashion the four best conditioning units from each of the other US conditions or groups were chosen and these 12 units became the groups of cells used in the PSH-AEP correlation analyses.

Pearson product moment correlation coefficients were computed based on 256 points from the two distributions created by the PSH and

AEP. In general, the r-values were low, ranging from .03 to .47 (see Table 1 of the Appendix). The actual magnitude of the r-values is less critical to the hypotheses to be tested and conclusions sought by this study then is the changing of the r-values during trial sequences.

This can be explained best when the material illustrated in Figure 1 is considered. The PSH and AEP are both sampled simultaneously through a single microelectrode. The PSH represents the probability of a unit spike occurring at any given point following the stimulus event. The AEP represents the activity (possibly the IPSPs and EPSPs) of all neural elements surrounding the subject cell with the degree of contribution to the AEP by a unit being a function of its proximity and solid angle relative to the electrode tip. The level of synchrony or congruence existing between the subject cell's probability of firing and the average probability of adjacent cells to fire will presumably be reflected in the PSH-AEP r-value. A high r-value would indicate a corresponding high degree of congruence with smaller r-values indicating less congruence. An increase in PSH-AEP correlation could occur following a starting habituation correlation of $\pm$ .75 or $\pm$ .05. The magnitude of the initial r-value would not put restrictions on this basic assumption: A trend toward a more homogeneous response by the neuron population will be reflected by an increase in the PSH-AEP cross correlation value.

The twelve cells selected for analyses in this section were chosen because they demonstrated dynamic changes in their response to

the CS during association trials. These changes in unit response consisted of (1) a reversal in sign of the response t-score, and (2) the criterion response was required to exceed a $\pm$ 0.7 response t value. It was reasoned that if the PSH-AEP correlation was sensitive to changes in unit activity then the PSH-AEP r-values for these cells should change across association trials. An initial expectation was that the average amount of r-value change would be proportionate to changes in the average amount of criterion response activity exhibited by these neurons. The pattern of r-value change across trials would, therefore, parallel the pattern of criterion response activity across trials.

In Figure 9 the average change (absolute difference between H and C_1, H and C_2, etc.) in PSH-AEP r-value and the criterion response activity is represented. The criterion response activity increases from H to C_1 and from C_1 to C_2 but then declines in magnitude from C_2 to C_3 and is reduced even more during E. Similar to this unit activity pattern is the change in PSH-AEP correlation from H to C_1, and an even greater change from the original habituation r-value during C_2. In C_3, the PSH-AEP r value is more similar to H than it was in C_2; this is also the case during E. Thus, absolute shifts in PSH-AEP correlation tend to parallel the pattern of criterion response development and extinction. These changes in PSH-AEP correlations are unique to conditioning as indicated by the results of pseudoconditioning cells also shown in Figure 9.

With these results having supported the initial hypothesis that PSH-AEP correlation is sensitive to known unit response changes, the

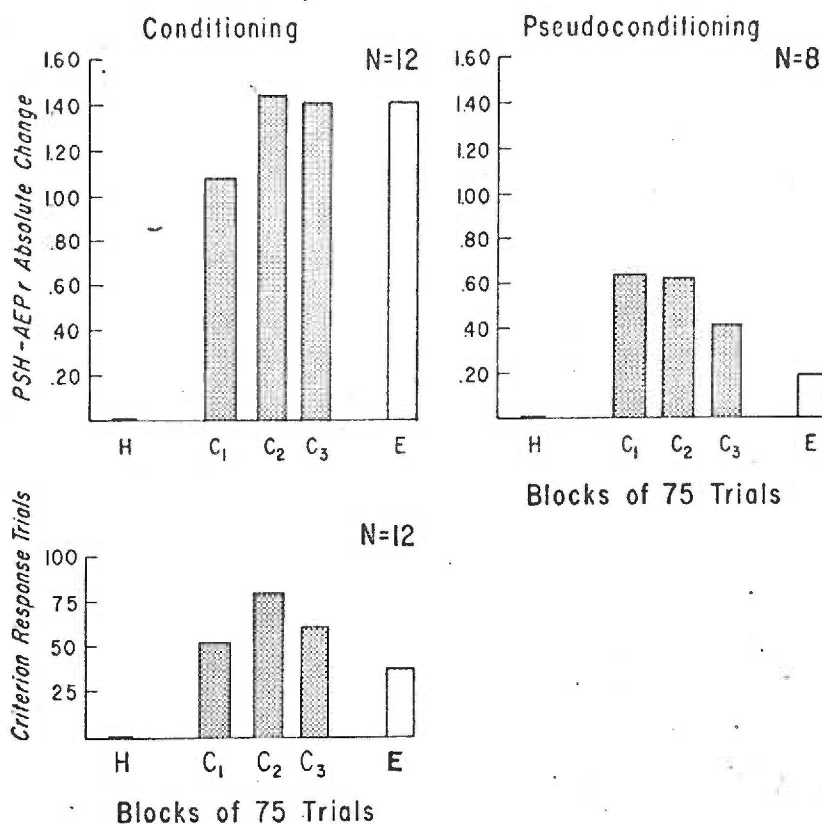


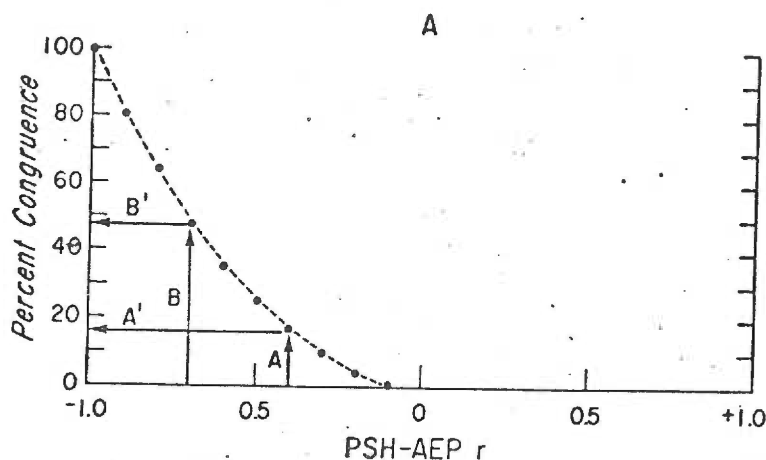
Figure 9 The absolute shift in PSH-AEP r-value during conditioning. The ordinate scales for the top two histograms represent the summed differences in PSH-AEP correlation for twelve units (N = 12) recorded during initial conditioning procedures. For each of the 12 (N = 12) units the PSH-AEP correlation for the 75 habituation (H) trials was determined. Likewise, PSH-AEP r-values were found for the 3, 75 trial blocks of the association (CS paired with US) session (C , C , C represented by stippled bars). Extinction (E) trials (CS alone) are represented by a clear bar. Each unit's r-values of C_1, C_2, C_3, and E were subtracted from it's H r- value. These difference scores, H-C_1, H-C_2, etc., were summed across units to produce the vertical extensions of the histogram bars of the top two histograms. The lower right histogram is the percent criterion response activity during conditioning for these same cells.

next hypothesis of interest was: The PSH-AEP reflects the degree of congruence of synchrony of probability of subject cell firing and the sources of the AEP.

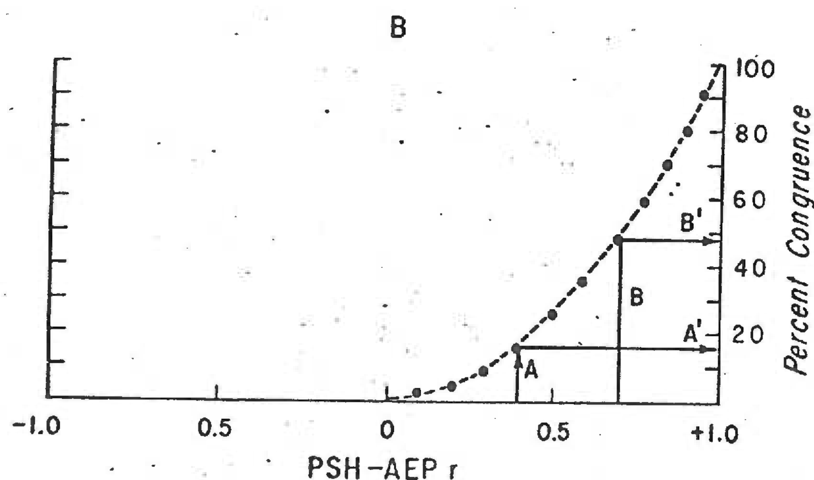
Inferences drawn from PSH-AEP correlations about the effect of conditioning upon the congruence of subject cell activity and the activity of neighboring neurons are totally dependent upon the assumptions one holds about how congruence would effect the PSH-AEP correlation. The assumption which produced results most similar to a traditional conditioning curve contained the following reasoning: Given a particular neuronal population, and an unchanging repeated stimulus such as a CS, the response activity of any given neuron in that population would have some preponderance for either excitation or inhibition. If this tendency were similar to the majority of other cells in the population, then a positive r-value would be observed. If the subject cell was linked in parallel with a majority of the cells contributing to the AEP, but was inhibited by the stimulus while the remaining units were excited, a negative correlation would result.

Schematic representations of these two types of hypothetical units and the expected relationship between their PSH-AEP correlations and congruence are shown in Schematics A and B.

In albebraic terms, the assumptions can be represented by: For A, $-(C_1\text{-}H)$, $-(C_2\text{-}HO)$, $-(C_3\text{-}H)$, and $-(E\text{-}H)$; for B, $C_1\text{-}H$, $C_2\text{-}H$, $C_3\text{-}H$, and $E\text{-}H$.



A. This instance would apply when the PSH-AEP correlation during H was negative. The cell would be judged to be predominately opposite in its response tendencies from the adjacent neuron population, e.g., inhibited by the CS while the majority of neighboring units were excited. Thus, an increase in congruence, a shift from A' to B' would be indicated by an observed shift in PSH-AEP r from the origin of arrow A to the origin of arrow B on the correlation scale.



B. The type of cell hypothesized in this schematic is one where an increase in a (+) r would reflect an increase in congruence consisting of both subject cell and AEP being effected in the same way by the stimulus.

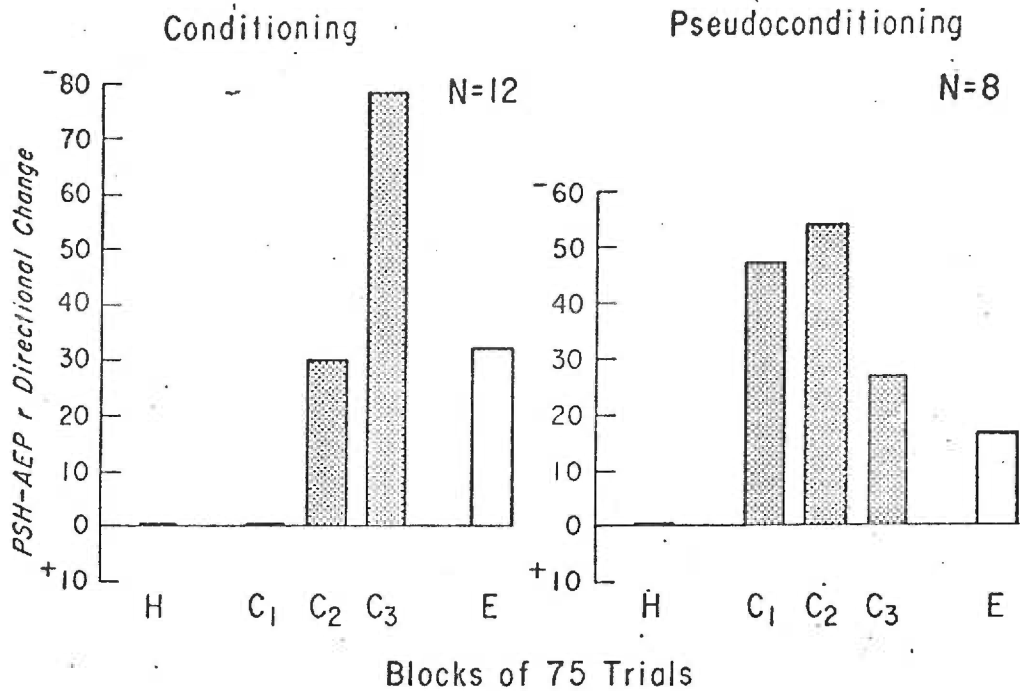
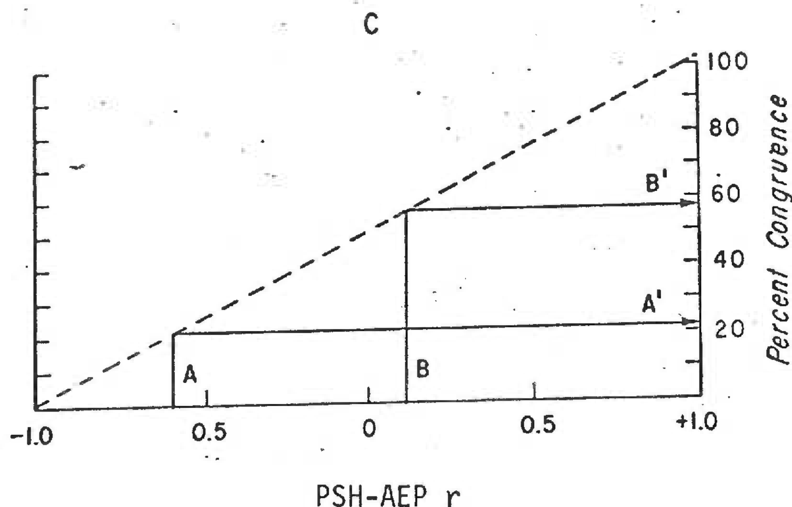


Figure 10 Directional shifts in PSH-AEP r-value during conditioning. Using habituation as a reference, the PSH-AEP values of C_1, C_2, C_3, and E were compared. If the r-value increased in size and maintained the same sign as the initial H correlation, the amount of change was given a plus polarity. If the r decreased or changed sign, the difference score was given a minus polarity. The ordinates in this figure represent the sums of scores calculated in this way with decreases in PSH-AEP correlations plotted upwards on the ordinate. Thus, the negative values of this figure indicate that the majority of r-values of habituation either decreased during conditioning or changed sign or both.

When the r-values of Table 3 were submitted to the operations dictated by the above assumptions, the values in Table 5 were generated (see Appendix). A minus value in the latter table indicates a loss of congruence if assumptions A and B were to hold true in nature. The results are given in the histogram in Figure 10. It can be seen that there is a gradual decrease in congruence over conditioning trials as indicated by the negative values. In other words, the average tendency was to either reduce the PSH-AEP r-value during conditioning or the r-value actually changed sign. The pattern of decrease in these difference scores is unique to conditioning. This is borne out by the results of the pseudoconditioning cells (Figure 10) which exhibited an immediate shift in r-value at the commencement of conditioning and sustained a comparable level in C_3 and E. This appears to be a sensitization effect.

Employing the assumptions outlined above, one must conclude from these data that conditioning actually produced a decrease in congruence of neural responding. This is the reverse of what would be predicted by John's theory (1967 and 1972).

A second assumption that could be imposed to evaluate the meaning of PSH-AEP changes has been suggested by John and Morgade (1969) who reported that during conditioning the unit-EP correlation always shifted to a more positive r-value. The difference between this assumption and the previous one may best be illustrated by the following schematic:



PSH-AEP r

From the schematic it can be seen that any correlation value to the right of an initial r-value, e.g., a shift from A to B, would indicate an increase in congruence, from A' to B'. Thus, a trend toward greater congruence would be signalled by a PSH-AEP correlation shift to a more positive value.

The imposing of this assumption upon the data of Table 3 again produced results which were very similar to traditional conditioning effects with the added feature that the pattern of development of this measure parallels exactly the pattern of criterion response development (see Tables 6 and 7 and Figure 11). There is an increase in the average amount of shift toward a more positive r-value from H to C_1 and from C_1 to C_2, but from C_2 to C_3 this trend attenuates and is reduced even further during E.

These results, therefore, are in harmony with the previous observations of John and Morgade (1969) and parallel the pattern of development of conditioned criterion responses. During pseudoconditioning,

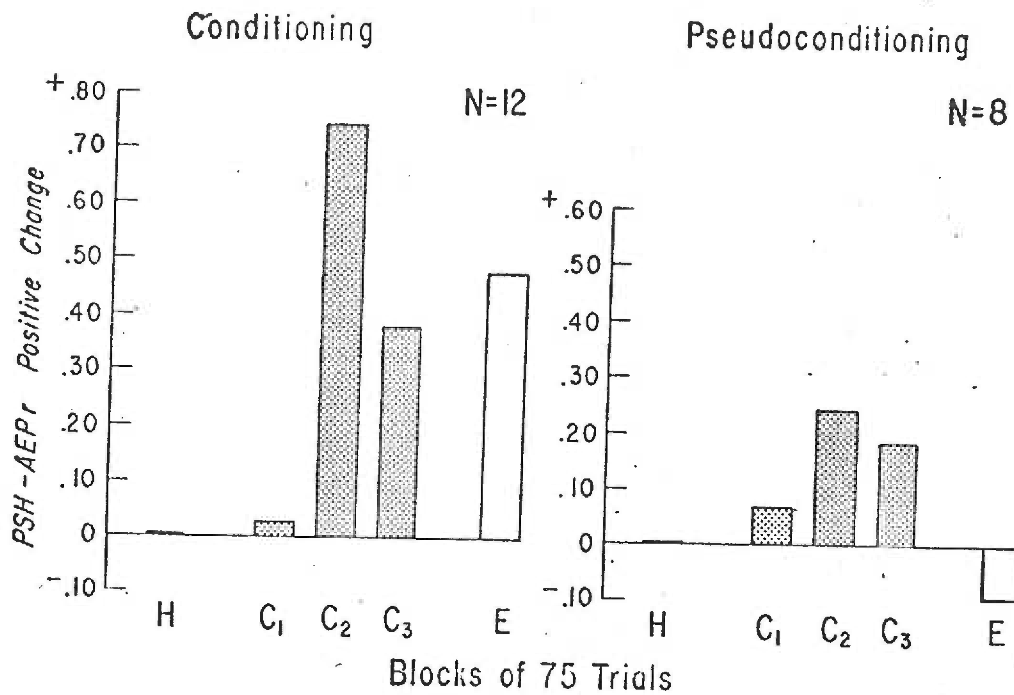


Figure 11 Positive shifts in PSH-AEP r-value during conditioning. A difference score between H and C_1, C_2, C_3, or E was given a + value if the shift in r was to a less negative or more positive value. A negative difference score indicated the reverse of this kind of change. The (+) and (-) difference scores of twelve conditioning and eight pseudoconditioning cells were summed to indicate the "net shift in r to a more positive level" marked on the ordinate. The negative net score during E of pseudoconditioning indicates that during this trial block cells had a net shift in r toward a negative value.

the pattern of positive shifts is identical to that of conditioning. The magnitude of these shifts is not as great, but the similarity of pattern between conditioning and pseudoconditioning introduces some doubt as to its dependence upon the contingent pairing of stimuli.

Cells were then segregated according to their criterion response sign. Specifically, six units were observed to exhibit positive response t-scores during criterion response periods and six exhibited negative response t-scores during intervals of criterion responding. It will be recalled that a positive response t-score indicates an excitatory response to the stimulus, and a negative response t-score an inhibitory response.

A comparison of these two groups of cells is shown in Figure 12. The data for positive criterion response units are in the left hand column while data for negative criteria response units are in the right hand column. In section A of the figure the absolute change in PSH-AEP correlation for the two groups is shown. It will be noticed that the positive response units produce a pattern of PSH-AEP change across trials which parallels the criterion response changes (Figure 9, part B). In contrast, the negative response units mirror the criterion response pattern and the PSH-AEP correlations of the positive response units.

Parts B and C of Figure 12 show the results for these two groups of cells when their respective PSH-AEP r-values are analyzed utilizing the two assumptions outlined above concerning the possible relationship of r-value change and response congruence. Part B of Figure 12

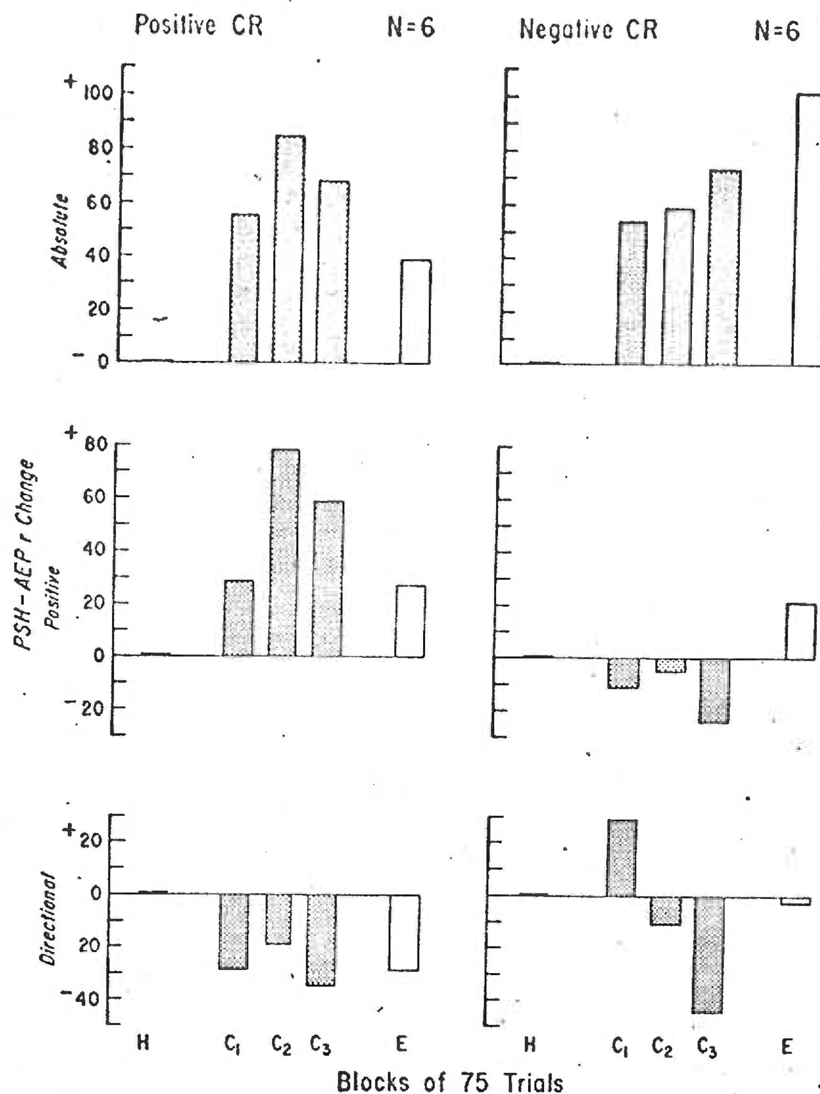


Figure 12 The PSH-AEP r-value changes for cells developing positive or negative CRs. The left-hand column represents data from cells that developed excitatory responses to the CS during conditioning. The right-hand column represents identical PSH-AEP correlation measures, but for cells that developed inhibitory responses to the CS. A, absolute change in r-values; B, shifts toward more positive r-values; C, amount of r increase when increase is defined as a shift to a larger r having the same sign as the r-value of habituation. (A = top; B = middle; C = bottom)

illustrates the trend towards more positive r-values for the two groups. The positive response cells comply with the observations of John and Morgade (1969) and parallel criterion response patterns. The negative response group on the other hand demonstrates an average trend toward more negative r-values with this trend decreasing from C_1 to C_2 but then increasing during C_3 and E. Apparently, it was the influence of the positive criterion response units which determined the paralleling features between PSH-AEP r-value shifts toward more positive score and conditioned criterion response activity shown in Figure 4.

In part C of Figure 12, positive criterion response units and negative criterion response units were analyzed assuming that the PSH-AEP could only reflect increased response congruence by shifting to an r-value of higher magnitude while maintaining the sign of the r-value of habituation. The negative values in the histograms of part C indicate that neither group of cells increased its response congruence as a consequence of conditioning. Also, it makes clear the significant contribution of the negative criterion response group to the "conditioning effect" described in Figure 10. This is shown in the progressive trend toward negative scores from C_1 to C_2 and then to C_3 (see Figure 11, part C, right-hand histogram).

To this point, the data indicate that when a unit's response to the CS becomes more excited, i.e., when the mean spike rate increases during conditioning, the correlation of that response's PSH to the AEP tends to increase. The PSH-AEP correlation for units exhibiting an inhibition of activity to the CS usually decreases during association trials.

THE INTERRELATIONSHIP OF PSH-AEP CORRELATION,

AEP-AEP CORRELATION AND UNIT CONDITIONING

PSH-AEP Correlation - Two Groups of Cells:

In the previous section, data of units judged to exhibit strong conditioned responses were analyzed (N = 12). This limited analysis was conducted to test the relationship between the AEP and the activity of cells which exhibited prominent changes in response. In this section, results will be presented for a total of 46 cells studied with conditioning procedures. Specifically, the analyses in this section will examine the differences between cells that show increases and decreases in their PSH-AEP correlations.

Cells were divided into two groups depending upon whether their PSH-AEP correlation coefficient increased or decreased during conditioning. These groups and their respective r-values are shown in Tables 15 and 16 in the Appendix. Twenty-seven units exhibited decreases in their PSH-AEP correlation values from habituation to C_3 of conditioning (D cells) whereas nineteen units showed increases (I cells). Figure 13 shows the changes in the mean of the absolute r-values for both types of cells. The average r-value during habituation for these two groups is significantly different at the .05 level ($t = 4.52$, $df = 44$, $p < .05$). The progressive changes in these two groups of cells nearly mirror each other with the mean r-values of the I group during C_2 and C_3 being larger than the analogous mean r-values of the D group. Thus, these reciprocal changes do not represent a passive convergence toward a common point of correlation level. The

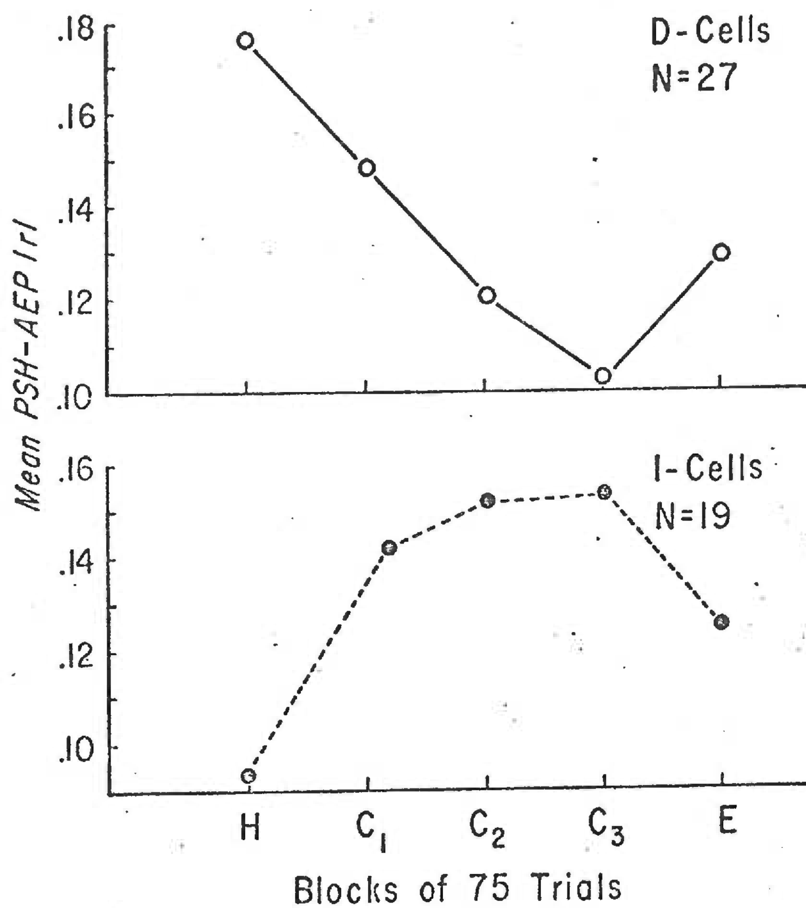


Figure 13 Mean PSH-AEP correlations for D-cells and I-cells. Units which exhibited a decrease in absolute PSH-AEP r-value during conditioning were called D cells. Similarly, units exhibiting increases in r-value were classified as I cells. The mean r-values for both groups are shown in blocks of 75 trials.

alterations in PSH-AEP r-values for both groups develop in a progressive way across conditioning trials and then partially return to their basic habituated levels during extinction.

AEP-AEP Correlation:

The data presented in this section are the cross correlation coefficients from comparing the AEP wave forms of habituation to subsequent AEP wave forms averaged during C_1, C_2, etc., for the same cell. I cells and D cells constituted the groups used for comparison of this AEP-AEP correlation conditioning effect. Figure 14 shows the mean AEP-AEP correlation values for both groups of cells. Tables 17 and 18 contain the correlation values for the individual units. It will be noted that the correlation of the habituation AEP to the C_1 wave form is larger than it is with C_2. In the case of the D group, the AEP-AEP correlation drops to its lowest level during C_3 and then increases some during extinction. A reduction in closeness of fit means that the AEP wave form is altered in C_1 and C_2 with the alterations of C_2 being more drastic than those in C_1. In a similar way, the wave form of C_3 in the D group is less like H than is the AEP of C_2. The increase in AEP-AEP correlation during extinction for this group indicates that during CS only trials the evoked response to the CS becomes more similar to its original form which existed during habituation.

Figure 14 further indicates that the changes in AEP-AEP correlations are different from the I and D groups. The D group exhibits AEP-AEP correlations which reflect progressive change during conditioning trials and then a partial return to a pre-conditioning habituated state during

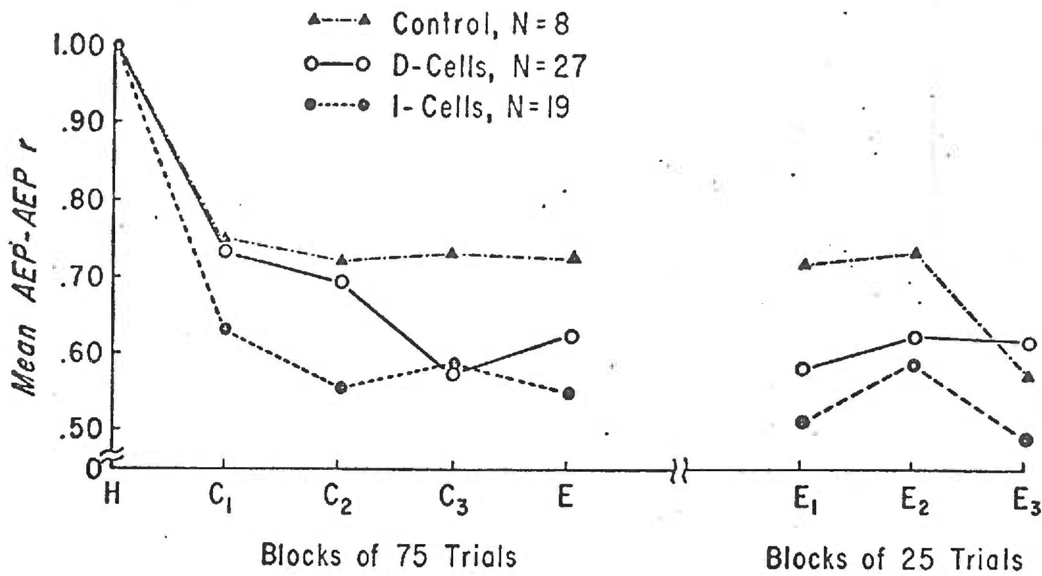


Figure 14 Mean AEP-AEP correlations for D cells and I cells. The AEP waveform for (H) was correlated with that of C_1, C_2, etc. As the AEP waveform during conditioning becomes more dissimilar from the original AEP evoked by the CS during habituation, the AEP-AEP r-value becomes smaller. The right side of the figure illustrates mean r-values for extinction based on blocks of 25 trials. All groups of cells show an initial drop in r-value during C_1. Both the I cells and pseudoconditioning units tend to continue at the new level of correlation through the remainder of the conditioning and extinction trials. The D cells, on the other hand, exhibit a progressive decrease in r-value across C_2 and C_3. During extinction trials the r-value for D cells increases slightly.

extinction. In contrast, the group of I cells produce AEP-AEP correlation means which decrease during early conditioning trials and then remain at a reduced level throughout the remainder of association trials. During extinction, the correlation value does not indicate a return to the habituation wave form since the AEP-AEP correlation drops in magnitude from C_3 to E.

Unit Responses of I and D Cells:

A comparison of conditioning t-scores for both groups of cells showed that D cells exhibited the greater change in unit activity during conditioning (mean conditioing t-scores; D cells = -.75; I cells = -.49). These results were substantiated by response t-score data (D cells: H = +.75, C_3 = +.36; I cells: H = -.08, C_3 = -.12). The +.75 response t-score during habituation for the D cells represents an appreciable average response. In comparison, the -.08 response t-score for I cells is very small. By C_3, the average response t-score for I cells is virtually unchanged (t = -.12), while a +.36 for D cells represents a sizeable drop in t-score magnitude.

The Relationship Between CR and UR PSH-AEP Correlations and the Tendency for a Unit to Develop a Conditioned Response:

In Table 11, all first session conditioning cells are rank ordered according to the magnitude of their respective PSH-AEP correlation values for activity evoked by the US. The mean for this distribution is $\overline{r}$ = .37. Asterisks identify those neurons whose percent criterion response curves most represented conditioning. The majority of these conditioning cells had a PSH-AEP correlation for the US that was below

Table 11: RANK ORDER OF PSH-AEP CORRELATIONS FOR THE UR BASED ON 225 TRIALS FOR FIRST CONDITIONING CELLS

Unit	UR_{225}
123A	-.74
*100A	-.61
91A	-.53
130A	+.52
82A	-.50
86A	-.50
133A	-.47
*92A	+.44
98A	-.43
122A	+.39
*76A	+.36
*95A	+.38
132A	+.35
*80A	-.32
*97A	+.32
*127A	-.27
119A	-.25
*126A	+.25
83B	+.23
*99A	-.23
125A	-.22
*103A	+.18
*74A	+.17
*102A	-.17

*Good conditioning neurons

$\overline{X}$* versus $\overline{X}$: $t = 2.08$, $df = 22$, $p < .05$

Table 12: PSH-AEP CORRELATIONS FOR THE CR AND UR FOR FIRST CONDITIONING CELLS. CELLS ARE RANK ORDER ACCORDING TO THE MAGNITUDE OF THE SUM OF THE CR AND UR VALUES.

Unit	CS-US Hab	UR	CR + UR
123A	+.16	-.74	.90
86A	-.30	-.50	.80
91A	+.25	-.53	.78
*100A	+.08	-.61	.69
82A	-.17	-.50	.67
122A	+.27	+.39	.66
*95A	-.27	+.38	.65
98A	+.20	-.43	.63
130A	-.07	+.52	.59
*92A	-.15	+.44	.51
133A	-.03	-.47	.50
119A	+.24	-.25	.49
*76A	+.11	+.36	.47
*103A	-.20	+.18	.38
*80A	+.06	-.32	.38
*127A	-.10	-.27	.37
*126A	-.11	+.25	.36
*97A	+.04	+.32	.36
*99A	+.12	-.23	.35
83B	+.11	+.23	.34
125A	+.10	-.22	.32
+102A	-.13	-.17	.30
*74A	+.09	+.17	.26
132A	+.11	——	.11

*Good conditioning neurons

$\overline{X}^*$ versus $\overline{X}$: $t = 1.267$, $df = 22$, $p < .05$

the mean value for the distribution, and the difference between the mean correlation value for the US for the best vs. poorer conditioning cells was significant at the .05 level ($t = 2.08$, $df = 22$). There is also a significant difference between good and poor conditioning cells when the correlation values for both the CR and UR are summed ($t = 2.76$, $df = 22$, $p < .05$) [Table 5]. This CR and UR analysis was prompted by the observation that in most instances when relatively high r-values existed for the CR (in good conditioning cells), they were matched with a relatively low UR r-value. Also, high UR r-values were usually found with relatively low CR r-values in good conditioning cells.

The high correlations (e.g., $r = .60$) between PSH shapes and AEP wave forms reported by Fox and O'Brien (1965) were computed from, in some cases, thousands of stimulus presentations, and was from data taken in the visual and visual association areas. Few cells analyzed in the present study reached correlations as high as those reported by Fox and O'Brien. In agreement with their findings, the correlation values in this study were influenced by the number of trials summed to generate the AEPs and unit PSHs. The AEP-unit correlations for 75 trials was compared to correlations computed on 225 trials for the US. The r-values for the 225 summed trials were significantly higher than those for 75 trials ($t = 2.965$, $df = 43$, $p < .05$). Since the correlation value has been shown to be influenced by the number of stimulus presentations, it is impossible to determine whether the lower correlations in this study are due to trials or to the anatomical difference between postcruciate and visual areas.

Another result which substantiates the uniqueness of the decrease in PSH-AEP correlation during conditioning, for units shown in Tables 3, 5, and 7, is that the mean correlation for the UR increases from earlier to later conditioning trials (Tables 13 and 14) for these same neurons. Thus, the PSH and AEP generated from the CS is independent of intertrial interval changes as shown above in the criterion response data, and furthermore, their correlation values change in a direction opposite to those for the US. It can be concluded that (1) the phenomenon of conditioning reflected in these data is not a "generalized" phenomenon effecting all responses identically, and (2) spontaneous, post-CS, and post-US activities all change but they do so independently.

Summary of Results

Units:

(1) Compared to pseudoconditioning changes, all three US modalities effected significant conditioning.

(2) Early conditioning trials (first 75-125 trials) showed different CR development by units receiving the three different US conditions.

(3) All three experimental groups, Long US, Short US, and Air US, exhibited CR changes independent of intertrial baseline activity.

Response Components:

(4) The components having the highest conditioning t-score were nearly equally distributed between early, middle, and late segments of the CS-US interval.

(5) The trial-by-trial development of conditioned criterion responses were unique for each of the response components. The earliest component showed no conditioning in the first 25 trials. The latest component exhibited a major CR within the first 75 trials, and the middle component reached the highest percent criterion response levels of all components.

(6) Approximately the same proportion of sampled units showed conditioning in the present study as were reported by O'Brien and Fox (1969).

(7) Eighty-nine percent of the first conditioning cells showed a reversal of polarity of response t-score from habituation to association trials.

PSH-AEP Correlation:

(8) The PSH-AEP correlation is sensitive to conditioned changes in unit activity.

(9) When the PSH-AEP correlation sign for habituation was assumed as a referent, the r-value changes during conditioning implied a decrease in unit-evoked potential congruence. However, when conditioned shifts in r-value toward a less negative or more positive correlation value were considered, the trial-by-trial changes paralleled those of unit CR development.

(10) Cells that exhibited conditioned increases in CR spike rate likewise showed an increase in PSH-AEP correlation. In contrast, units which developed decreases in CR spike rate tended to exhibit a decrease in correlation with the AEP.

(11) When cells were divided into two groups, those that decreased (D cells) and those that increased (I cells) their PSH-AEP correlation during conditioning, the D cells were observed to have a larger mean conditioning t-score than did I cells. I cells exhibited virtually no mean response during habituation and this state remained unchanged during conditioning.

(12) Cells exhibiting the best conditioning were observed to have lower PSH-AEP r-values for the US evoked response than poorer conditioning cells. Also, when a unit's PSH-AEP r-values for both the CR and UR were considered, those cells observed to have the best conditioning had the lower PSH-AEP correlations.

(13) The number of trials summed to create the PSH and AEP distributions effects the magnitude of correlation between them.

(14) The PSH-AEP correlations for the US were higher than for the CS. These data indicate that given an equal number of trials, the PSH-AEP correlation from the primary projection area for the evoking stimulus will be higher than for activity recorded from nonprimary areas.

(15) The PSH-AEP correlation for the UR increased during association trials such that the PSH-AEP r-value for C_1 was lower than for C_3.

AEP-AEP Correlation:

(16) The AEP-AEP correlation for D cells followed traditional conditioning changes during association trials and exhibited a trend toward extinction. I cells did not show such developmental changes across trials.

DISCUSSION

CONDITIONED UNIT ACTIVITY

Conditionability of cortical neurons:

That cortical neuron activity reflects conditioning has been reaffirmed by the results of this experiment. The response of cells to the CS were found to change significantly during association trials of conditioning in a manner different from changes occurring during pseudoconditioning. The results reported by O'Brien and Fox (1969) were replicated nearly exactly by the present study, and a similar learning curve for conditioned leg movements has been reported when these same conditioning paradigm and stimulus parameters were used (O'Brien and Packham, 1973).

Projection pathways implied by response components:

The establishment of criterion response activity provided a means of detecting the relative amount of conditioning each cell exhibited. It also allowed measurement of conditioning reflected by CS evoked response components. The earliest response segment following the CS is actually the last component to show conditioning. Conditioning was not observed during the first 25 trials and only slight changes in activity occurred from 25-50 trials for this component. In contrast, the second and third components showed conditioning in the first block of 25 trials. The latest response component in the CS-US interval, actually exhibits one of its largest response changes during the first 75 trials.

These data, on the trial-by-trial development of a CR by components of the CS elicited response, may be interpreted as supporting the projection view of EP components. The traditional projection view assumes

that early components of the EP represent input from the most direct primary afferent connections while later components are believed to be routed through the reticular formation (RF) and other nonspecific nuclei. Early and late orthodromic responses which utilize different pathways have been well documented for neurons of the sensorimotor cortex (Towe, Patton, and Kennedy, 1963; Amassian, 1954). In research presently underway utilizing reversible lesion techniques, early response components from somatic stimulation (with latencies of 10-15 msec and response durations of 20-30 msec) remain unaffected by cooling of the CM-PF non-specific thalamic area while later response components are reduced considerably (Rosenblum and O'Brien, 1973). It will be recalled that the work by Yoshii and Ogura (1960) and Kamikawa et al. (1968) indicated that conditioned unit changes occurred in the RF within the first 25 trials and changes in the thalamus followed at 25 to 50 trials. Conditioned cortical unit activity required from 75-150 trials in most cells (O'Brien and Fox, 1969). Thus, the active topographical sites of conditioned change progresses from RF to thalamus to cortex, and this shifting of activity can be correlated with the progressive development of conditioned changes in sequential components of the response following the CS. Specifically, the third or latest component, which presumably represents input from the RF shows conditioned criterion responding within the first 25 conditioning trials with the following 50 trials exhibiting a major conditioning effect. In contrast, the earliest response component shows no conditioning in the initial 25 trials of association. The 25-50 trial block contains some conditioned activity and a maximal level is not attained until 100 trials into conditioning.

In support of the projection theory, there is evidence that there are several pathways by which visual input reaches the sensorimotor cortex (Buser, Kitsikis, and Wiesendanger, 1968; Dubrovsky and Garcia-Rill, 1971; and Garcia-Rill and Dubrovsky, 1971). Buser et al. (1968), using cooling and KCl reversible lesion methods in combination with subcortical incisions, concluded that activity from the visual cortex reaches the sensorimotor cortex by subcortical pathways. Dubrovsky and Garcia-Rill (1971) studied the response characteristic of neurons in the pericruciate cortex to stimulation of the visual cortex and the superior colliculus. Excitatory responses elicited from stimulation of the visual cortex had a latency of 16 $\pm$ 3 msecs whereas those elicited from the superior colliculus had a latency of 9 $\pm$ 2 msec. Inhibitory responses (found in 55% of the cells) had latencies of 35 $\pm$ 5 and 27 $\pm$ 4 for the respective stimulation sites. The authors concluded that these data argued for different pathways for inhibitory and excitatory input to pericruciate neurons.

The likelihood of there being two separate pathways for inhibitory and excitatory projections from the visual system to the sensorimotor area is further supported by differences found in the conditioning and extinction response characteristics of CS inhibited and CS excited neurons (O'Brien and Fox, 1969). Cells that have an original excitatory response to a light flash CS and then develop an inhibitory response to this stimulus during conditioning also show an almost immediate extinction of that CR. In contrast, units having an initial inhibitory response to a light flash which are then conditioned to an excitatory

response, show a gradual extinction trend requiring at least 15 trials. These workers also found that conditioned spike rate increases were usually time locked to the CS while decreases were associated more with the US. The fact that response components within the CS-US interval, as shown in the present study, can exhibit different learning curves is in harmony with all of the preceding evidence arguing for multiple projection pathways to neurons of the postcruciate cortex.

Disterhoft and Olds (1972) observed unit CRs developing in the thalamic nuclei with 30-40 conditioning trials. Cortical units didn't show similar changes until about 60-70 conditioning trials. The question arises, if the thalamic activity seen at 30-40 trials is projected upon the cortex (such a projection is implied by the present experiment), why weren't those changes seen by Disterhoft and Olds until 30 trials later? This apparent inconsistency may be a function of methodology. Disterhoft and Olds (1972) "decided to choose the main component period during the CS-US interval individually for each unit" in order to maximize the probability of seeing conditioned changes. In comparison, several components from each unit were analyzed in the present study, and the percent criterion activity was summed across cells for each component. Therefore, since Disterhoft and Olds chose only one response component, it is possible that cortical units activity in remaining portions of the CS-US interval might have reflected thalamic conditioning.

The mean number of trials required for cortical unit conditioning was 68.7 as reported by Disterhoft and Olds, but the standard deviation for that distribution was 31.4 trials; therefore, some of the cortical

response components observed may have been analogous to the second response component of the present study. The second component has been associated by implication with nonspecific thalamic input.

Effects of US modality and intensity on conditioned unit activity:

Long shock, short shock, and air puff stimuli all produced a CR to a light flash CS, but the development of the CR followed different time courses for the respective conditions. Long US units exhibited an initial peak of criterion activity between 50 and 75 trials. The Short US group required about 100 trials to reach its maximum level and the Air US cells took 125 trials to achieve their maximum levels of CR activity. Conditioned response activity during trials following its original development was also different depending on the US intensity and modality. The fact that there was conditioning in all experimental groups supports the position that convergence is a sufficient condition for conditioning given appropriate CS-US intervals. However, the present study was selective to neurons with moderate to high spontaneous rates of activity. In comparison, Vassilevsky and Trubatchev (1959) found that units with slower spontaneous rates did not show conditioning.

PSH-AEP CORRELATION

The number of trials summed when making the PSH effect the PSH-AEP r-value. This has been found both in the present study and the original report by Fox and O'Brien (1965). Given an equal number of trials the correlation of the PSH-AEPs is higher when recording from the primary projection areas of the evoking stimulus. Thus, in the present study the PSH-AEP r-values were higher for shock and hair deflection than for light flash.

This fact seems to demonstrate that whereas the AEP might reflect the activity of a majority of neurons in some areas of the brain it may do so with less reliability in others. Specifically, the weaker the effect of a stimulus on a particular neural volume the lower the PSH-AEP correlation will be. "Weaker effect" as used here only refers to the relative number of units in an area effected in a synchronous manner by the stimulus. To the extent that individual cells within a neural volume have specific nonsynchronous responses which carry information, the AEP will not reflect information processing. The AEP will only reflect information processing when that information constitutes synchronous activity in a majority of cells in a particular volume. For this reason the AEP may better serve as a representation of information in the primary projection area of a stimulus than in nonspecific nuclei or nonprimary cortical areas.

Deficiencies of the statistical configuration theory:

John's (1969, 1972) theory, which postulates reverberating neural loops that generate the AEP and PSH components, cannot account for the differential development of conditioned criterion responses by the three response components analyzed in the present study. The theory does not provide for independent changes in reverberating activity occurring with different latencies to the CS.

The statistical configuration theory has drawn heavily on data taken from the lateral and medial geniculate nuclei and other portions of the visual and auditory systems--the primary projection systems for the CSs most frequently employed. The large disparity between the magnitude of

PSH-AEP r-values for the CR and UR in the present study points out clearly that the degree to which the AEP may reflect the processes of sampled neural populations depends on whether the recording is taken from a specific or nonspecific area relative to the evoking stimulus. Therefore, the assumptions which John makes about AEP and information carried by neurons contributing to the AEP may only be applicable to AEPs taken from primary projection areas.

The data of the present experiment tend to confirm John's findings, when cells show a positive (excitatory) CR, a shift toward a more positive r-value occurs during association trials for these cells. The PSH-AEP correlation data further indicate that for a majority of the cells showing a decrease in the PSH-AEP correlation, the conditioned unit activity is inhibitory; the average response t-score drops from habituation to C_3 of association trials. This fits well with the observation made on the six best conditioning cells which developed inhibitory criterion responses during association trials--the PSH-AEP r-values dropped during conditioning for these units. These results point out another weakness in the assumption that AEPs must represent information processed by the monitored neural population. The weakness is that the magnitude of the AEP-PSH correlation for a given cell may well depend upon whether the unit's activity rate is increased or decreased during the supposed presence or transfer of information. Information could be transferred through a particular neural volume by a discrete decrease in the activity of a majority of the member neurons. During such an interval, the quiescent neurons would be contributing a relatively small amount to the

AEP. Thus, by recording only the AEP in such a case, one could conceivably misinterpret random or unrelated neuron activity for information or perhaps conclude that no information was passed when in fact there had been.

The PSH-AEP correlation for the UR, recorded from the primary projection area of the US, increases during conditioning. This was demonstrated by the higher PSH-AEP r-value of the UR for C_3 as compared to C_1. It should be pointed out that virtually all unit URs had a major excitatory component. The fact that the C_3 r-values were higher than the C_1 correlations might indicate that there is a process producing more synchronous activity in the primary projection areas of a stimulus as sequential trials are presented.

SUMMARY AND CONCLUSIONS

Averaged evoked potentials and unit activity in the postcruciate cortex was recorded simultaneously through a single microelectrode during a classical conditioning procedure given to 45 awake cats immobilized with Flaxedil. Twenty-four units were isolated during initial conditioning sessions and 22 were recorded during repeated conditioning sessions. Both unit and averaged potentials were also recorded during a pseudoconditioning procedure for 8 additional cells as a control.

Conditioning consisted of 75 trials of CS (light flash) alone followed by 225 trials of CS-US pairing and then 75 CS only extinction trials. Pseudoconditioning was identical except for the 225 presentations of light and US were unpaired. There were three experimental groups which were distinguished by three different USs; a long shock, a short shock, and an air puff.

Unit responses were quantified by comparing pre to post-CS spike rate with a student t formula--means and variances were determined from blocks of 25 and 75 trials. Post-CS activity was segregated into response components with each neuron exhibiting 2 or 3 such components in the CS-US interval.

Results of unit activity confirmed earlier reports (O'Brien and Fox, 1969) of conditioned unit activity in the postcruciate cortex. The percent of units exhibiting CRs, the number of trials to maximum CR level, and the tendency for a unit to reverse its response polarity from its habituated state during conditioning seen in the present study were convincingly similar to the earlier report.

The number of trials required to develop a maximum percent criterion level during conditioning was different for the three experimental groups. Thus, US modality effects the time course of CR development, but the sensory-sensory paradigm did produce conditioning even in the case of an air puff US.

A major finding of this study was the existence of response components which exhibited different plastic characteristics within individual units. Typically, the component falling at the end of the CS-US interval exhibited changes very early in conditioning. Next, the middle component developed criterion activity and the component with the shortest latency to the CS was the last component to begin to condition. These findings support (A) the projection hypotheses of AEP components, and (B) earlier observations that units in RF and thalamus exhibit CR changes previous to cortex. The hypothetical "neural loops" postulated by John (1969, 1972) seem to be inadequate to account for the response component observations.

The correlation of unit activity with AEP was found to change during conditioning. Predictions of an increase in PSH-AEP correlation during conditioning deduced from John's statistical configuration theory were observed to hold with some qualifications: (A) Increases only occurred when the unit PSH was generated by a cell that developed an excitatory response to the CS during conditioning. (B) The PSH-AEP correlation for pseudoconditioning cells also increased thus introducing some question about the phenomenon's dependence upon contingent pairing of the CS and US.

Changes in PSH-AEP correlations unique to the experimental groups were observed when a directional assumption was made about the relationship between r-values and congruence of response patterns of units comprising the sampled population. Adopting these assumptions produced results which could be interpreted as indicating a decrease in PSH-AEP correlation during conditioning.

Magnitude of PSH-AEP correlation is sensitive to the number of trials summed when making the PSH and AEP. Also, higher correlations were observed to the US than to light flash implying that the unit-AEP correlation will be higher when recording from the primary system of the evoking stimulus.

It was concluded that unit, as well as AEP, can reflect conditioning and, thus, may represent information processing in the brain. It was further concluded that since the AEP may only reflect a majority of unit response probabilities in the primary projection pathways and areas, one should not rely upon the AEP as a representation of information processing occurring at the unit level.

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APPENDIX

Table 3: PSH-AEP CORRELATIONS FOR CONDITIONING

	Correlation values				
Unit	H	C	C	C	E
74A	+.09	+.22	+.42	+.26	+.12
76A	+.11	+.11	+.08	+.08	+.07
80A	+.06	+.06	-.08	-.13	+.05
92A	-.15	-.18	-.12	-.12	+.18
95A	+.08	+.04	+.11	+.05	+.23
100A	+.08	+.21	+.11	-.04	+.03
102A	-.13	-.38	-.31	-.27	-.47
103A	-.20	-.09	-.09	-.07	-.08
97A	+.04	-.09	+.04	+.04	+.04
99A	-.12	-.12	+.08	+.05	+.06
126A	-.11	+.07	+.07	+.07	-.13
127A	-.10	-.02	+.08	+.11	+.03
Sum (absolute)	1.37	1.59	1.59	1.39	1.49
Mean	.114	.132	.132	.107	.124

Table 4: CHANGE IN PSH-AEP CORRELATION FOR CONDITIONING NEURONS

Unit	Absolute difference in correlation values			
	$1C_1$-H1	$1C_2$-H1	$1C_3$-H1	1E-H1
74A	.13	.33	.17	.03
76A	———	.03	.03	.04
80A	———	.14	.19	.01
92A	.03	.03	.03	.33
95A	.04	.03	.03	.15
100A	.13	.03	.12	.05
102A	.25	.18	.14	.34
103A	.11	.11	.13	.12
97A	.13	———	———	———
99A	———	.20	.17	.18
126A	.18	.18	.18	.02
127A	.08	.18	.21	.13
Sum	1.08	1.44	1.40	1.40
Mean	.091	.120	.117	.117

Table 5: CHANGE IN PSH-AEP CORRELATION FOR PSEUDOCONDITIONING NEURONS

Unit	Absolute difference in correlation values			
	$1C_1$-H1	$1C_2$-H1	$1C_3$-H1	1E-H1
106A	.07	.28	.23	———
107B	.28	.01	.01	———
111A	.03	———	.03	.03
112A	.05	.06	.01	.05
113A	.17	.05	.05	———
116A	.06	.19	.05	———
118A	.01	.04	.02	.01
121A	———	.01	.01	.10
Sum	.67	.64	.41	.19
Mean	.08	.08	.05	.02

Table 6: DIRECTIONAL PSH-AEP CORRELATION CHANGE WITH REFERENCE TO r VALUES OF HABITUATION FOR CONDITIONING NEURONS.

Unit	C_1	C_2	C_3	E
74A	+.13	+.33	+.17	+.03
76A	——	-.03	-.03	-.04
80A	——	-.14	-.19	-.01
92A	+.03	-.03	-.03	-.33
95A	-.04	+.03	-.03	+.15
100A	+.13	+.03	-.12	-.05
102A	+.23	+.18	+.14	+.34
103A	-.11	-.11	-.13	-.12
97A	-.13	——	——	——
99A	——	-.20	-.17	-.18
126A	-.18	-.18	-.18	+.02
127A	-.08	-.18	-.21	-.13
Sum	——	-.30	-.78	-.32

Assuming that the sign of the r value during habituation represents a habituated state, an increase signified by a (+) sign indicates change toward a larger r value of the same sign as the habituated r value. A (-) sign refers to any drop in r value or change in r value during C_1, C_2, etc., resulting in a polarity opposite to that of habituation.

Table 7: DIRECTIONAL PSH-AEP CORRELATION CHANGE WITH REFERENCE TO r VALUES OF HABITUATION FOR PSEUDOCONDITIONING NEURONS.

Unit	C_1	C_2	C_3	E
106A	+.07	-.28	-.23	——
107A	-.28	-.01	-.01	——
111A	+.03	——	-.03	-.03
112A	-.05	-.06	-.01	-.05
113A	-.17	+.05	+.05	——
116A	-.06	-.19	-.05	——
118A	-.01	-.04	+.02	+.01
121A	——	-.01	-.01	-.10
Sum	-.47	-.54	-.27	-.17

Assuming that the sign of the r value during habituation represents a habituated state, an increase signified by a (+) sign indicates change toward a larger r value of the same sign as the habituated r value. A (-) sign refers to any drop in r value or change in r value during C_1, C_2, etc., resulting in a polarity opposite to that of habituation.

Table 8: POSITIVE SHIFTS IN PSH-AEP CORRELATIONS FOR CONDITIONING NEURONS

Unit	C_1	C_2	C_3	E
74A	+.13	+.33	+.17	+.03
76A	——	-.07	-.03	-.04
80A	——	-.14	-.19	-.01
92A	-.18	+.03	+.03	+.33
95A	-.04	+.03	-.03	+.15
100A	+.13	+.03	-.12	-.05
102A	-.25	-.18	-.14	-.34
103A	+.11	+.11	+.13	+.12
97A	-.13	——	——	——
99A	——	+.20	+.17	+.18
126A	+.18	+.18	+.18	-.02
127A	+.08	+.18	+.21	+.13
Sum	+.03	+.74	+.38	+.48

Any decrease in negative r value or increase in positive r value from habituation to C_1, C_2, etc., is represented by a (+) sign in the table. Negative (-) signs in the table represent the opposite changes.

Table 9: TREND TOWARDS POSITIVITY, PSH-AEP r VALUES - PSEUDOCONDITIONING NEURONS

Unit	C_1	C_2	C_3	E
106A	-.07	+.28	+.23	—
107B	+.28	+.01	+.01	—
111A	+.03	—	-.03	-.03
112A	+.05	+.06	+.01	+.05
113A	-.17	+.05	+.05	—
116A	-.06	-.19	-.05	—
118A	+.01	+.04	-.02	-.01
121A	—	-.01	-.01	-.10
Sum	+.07	+.24	+.19	-.09

10: PSH-AEP CORRELATIONS FOR UNITS HAVING POSITIVE OR NEGATIVE CONDITIONED CRITERION RESPONSES.

Part A

	H	C_1	C_2	C_3	E
	(+).09	(+).22	(+).42	(+).26	(+).12
	(+).11	(+).11	(+).08	(+).08	(+).07
	(+).04	(-).09	(+).04	(+).04	(+).04
1	(-).12	(-).12	(+).08	(+).05	(+).06
1(	(-).11	(+).07	(+).07	(+).07	(-).13
	(-).20	(-).09	(-).09	(-).07	(-).08
Su bsolute s	.67	.70	.78	.57	.50

Th AEP crosscorrelation coefficients for the best conditioning cells which had a po +) criterion response during conditioning.

Table 10 (continued)

Part B

Unit	H	C_1	C_2	C_3	E
80A	(+).06	(+).06	(-).08	(-).13	(+).05
92A	(-).15	(-).18	(-).12	(-).12	(+).18
127A	(-).10	(-).02	(+).08	(+).11	(+).03
95A	(+).08	(+).04	(+).11	(+).05	(+).23
100A	(+).08	(+).21	(+).11	(-).04	(+).03
102A	(-).13	(-).38	(-).31	(-).27	(-).47
Sum of Absolute Values	.60	.89	.81	.72	.99

The PSH-AEP crosscorrelation coefficients for the best conditioning cells which had a negative (-) criterion response during conditioning.

Table 13: PSH-AEP CORRELATIONS FOR THE UR BASED ON 75 TRIALS FOR THE 12 BEST FIRST CONDITIONING CELLS.

Unit	C_1	C_2	C_3
74 A	+.29	+.30	+.28
76A	+.32	+.37	+.30
80A	-.09	-.07	-.28
92A	+.31	+.38	+.45
95A	+.06	-.07	-.20
97A	-.35	-.42	-.30
99A	-.07	-.17	-.30
100A	-.60	-.58	-.56
102A	-.16	-.17	-.15
103A	+.15	+.17	+.13
126A	+.18	+.11	+.11
127A	-.11	-.20	-.10
Sum	2.69	3.01	3.16
Mean	.224	.251	.263

Table 14: PSH-AEP CORRELATIONS FOR THE UR BASED ON 75 TRIALS FOR ALL FIRST CONDITIONING CELLS.

Unit	C_1	C_2	C_3
74A	+.29	+.30	-.28
76A	+.32	+.37	-.30
80A	-.09	-.07	-.28
82A	-.52	-.52	-.42
83B	+.23	+.23	+.25
86A	——	——	——
91A	-.57	-.54	-.48
92A	+.31	+.38	+.45
95A	+.06	-.07	-.20
97A	-.35	-.42	-.30
98A	-.42	-.41	-.48
99A	-.07	-.17	-.30
100A	-.60	-.58	-.56

Table 14 (continued)

102A	-.16	-.17	-.15
103A	+.15	+.17	+.13
119A	-.17	-.24	-.24
122A	+.36	+.37	+.43
123A	-.53	-.53	-.57
125A	-.16	-.27	-.22
126A	+.18	+.11	+.11
127A	-.11	-.20	-.10
130A	+.48	+.52	+.50
132A	+.02	——	-.05
133A	-.38	-.42	-.40
Sum (absolute)	6.53	6.96	7.20
Mean	.284	.316	.313

Table 15: PSH-AEP CORRELATIONS FOR CELLS SHOWING A DECREASE IN CORRELATION WITH THE AEP DURING CONDITIONING

Unit	H	C_1	C_2	C_3	E
76A	+.11	+.11	+.08	+.08	+.07
81D	+.15	+.13	+.22	+.11	+.18
82A	-.17	-.09	-.04	+.03	+.13
83C	-.28	-.20	-.18	-.12	-.03
84B	-.25	-.26	-.31	-.18	-.22
84E	+.18	+.18	+.08	+.16	+.07
86A	-.30	-.21	-.23	-.13	-.16
86B	+.14	+.18	+.15	+.08	+.09
90B	+.21	+.22	+.08	+.04	+.06
91A	+.25	+.18	-.13	-.14	+.22
91B	+.17	+.18	+.11	+.12	-.09
92A	-.15	-.18	-.12	-.12	+.18
92B	-.09	-.20	+.02	-.07	-.21

Table 15 (continued)

92C	-.26	+.16	+.07	+.07	-.09
94E	+.09	+.15	+.14	+.05	——
97B	+.15	+.09	+.08	-.11	+.15
98A	+.20	+.18	——	+.18	+.16
98B	+.12	-.12	-.12	-.08	-.07
99C	-.10	-.10	-.11	-.07	-.12
100A	+.08	+.21	+.11	-.04	+.03
99B	-.21	-.08	-.12	-.19	-.28
103A	-.20	-.09	-.09	-.07	-.08
119A	+.24	+.16	+.22	+.08	+.22
122A	+.27	+.18	+.09	+.20	+.22
123A	+.16	-.08	-.07	-.13	-.05

Table 15 (continued)

126A	-.11	+.07	+.07	+.07	-.13
132A	+.11	+.24	+.07	+.03	+.05
Sum	4.75	4.28	3.17	2.75	3.36
Mean	.176	.159	.120	.102	.129

Table 16: PSH-AEP CORRELATIONS FOR CELLS SHOWING AN INCREASE IN CORRELATION WITH THE AEP DURING CONDITIONING

Unit	H	C_1	C_2	C_3	E
74A	+.09	+.22	+.42	+.26	+.12
74B	+.05	+.24	-.10	-.14	+.05
80A	+.06	+.06	-.08	-.13	+.05
81C	+.06	+.09	+.17	+.15	+.09
90C	-.06	+.22	-.13	+.08	—
94F	+.16	+.33	+.37	+.26	—
95A	-.27	-.07	+.11	+.27	+.23
96E	+.08	+.08	—	+.14	+.05
96F	-.08	-.08	-.15	+.18	+.07
96H	-.12	+.08	+.10	-.15	+.08
98C	+.08	+.09	-.08	-.10	-.13
97A	+.04	-.09	+.04	+.04	+.04

Table 16 (continued)

102A	-.13	-.38	-.31	-.27	-.47
102C	+.12	+.10	+.19	+.30	+.34
125A	+.10	+.20	+.15	+.12	+.10
127A	-.10	-.02	+.08	+.11	+.03
130A	-.07	-.07	-.03	-.07	-.07
133A	-.03	-.17	-.07	-.05	—
Sum	1.78	2.69	2.71	2.92	2.00
Mean	.094	.142	.151	.153	.125

Table 17: AEP-AEP CORRELATIONS FOR CELLS SHOWING A DECREASE IN CORRELATION OF PSHS AND AEPS DURING CONDITIONING.

Unit	H to C_1	H to C_2	H to C_3	H to E
76A				
81D	+.32	+.02	-.11	-.24
82A	+.95	+.63	+.72	+.91
83C	+.98	+.95	+.92	+.94
84B	+.88	+.87	+.65	+.76
84E	—	—	—	—
86A	+.93	+.84	+.78	+.92
86B	+.71	+.65	+.62	+.62
90B	+.50	+.53	+.32	+.40
91A	+.78	+.77	+.32	+.55
91B	+.85	+.83	+.82	+.82
92A	+.74	+.71	+.34	+.39
92B	+.68	+.22	-.10	+.32
92C	+.81	+.93	+.85	+.85

Table 17 (continued)

94E	+.23	+.25	+.47	+.42
97B	+.46	+.69	-.12	+.28
98A	+.93	+.92	+.85	+.92
98B	+.74	+.81	+.76	+.78
99C	+.45	+.67	+.19	-.10
100A	+.52	+.51	+.45	+.28
99B	+.79	+.76	+.69	+.53
1003A	+.72	+.69	+.71	+.70
119A	+.88	+.79	+.69	+.82
122A	+.88	+.86	+.80	+.87
123A	+.96	+.95	+.92	+.89
126A	+.73	+.72	+.68	+.65
132A	+.89	+.90	+.87	+.89
Sum	18.31	17.47	14.31	15.65
Mean	.732	.699	.572	.626

Table 18: AEP-AEP CORRELATIONS FOR CELLS SHOWING AN INCREASE IN CORRELATION OF PSHS AND AEPS DURING CONDITIONING

Unit	C_1	C_2	C_3	E
74A				
74B	+.65	+.82	+.24	+.28
80A	+.58	+.28	+.14	+.44
81C	+.58	+.36	-.64	+.75
90C	+.52	+.58	+.37	+.47
94F	+.22	+.33	+.54	+.38
95A	-.07	—	+.17	-.08
95B	+.17	-.07	+.11	+.08
96E	+.70	+.62	+.70	+.73
96F	+.64	+.55	+.65	+.56
96H	+.69	+.08	+.60	+.27
98C	+.74	+.72	+.67	+.70
97A	+.74	+.76	+.72	+.46

Table 18 (continued)

102A	+.92	+.90	+.89	+.90
102C	+.82	+.85	+.83	+.83
125A	+.82	+.79	+.74	+.83
127A	+.92	+.89	+.86	+.81
130A	+.87	+.75	+.87	+.87
133A	+.78	+.78	+.63	+.55
Sum	11.29	9.99	10.37	.983
Mean	.627	.555	.576	.546

Table 19: CONDITIONING t-SCORES FOR D AND I CELLS

D Cells		I Cells	
Unit	Cond-t	Unit	Cond-t
76A	+0.78	74A	+1.33
81D	-1.14	74B	+1.20
82A	-0.78	80A	-1.71
83C	-1.13	81C	+2.02
84B	+0.69	90C	-2.21
84E	-1.50	94F	-1.44
86A	-1.01	95A	-1.22
86B	+0.61	95B	-1.66
90B	+1.22	96E	+0.63
91A	-3.54	96F	-1.45
91B	-2.97	96H	-1.82
92A	-2.01	98C	+2.02
92B	+1.08	97A	+1.12

Table 19 (continued)

92C	-1.60
94E	-1.75
97B	-3.50
98A	-1.44
98B	-2.49
99C	-0.53
100A	+1.07
99B	-3.64
103A	+2.96
119A	+2.45
122A	-0.66
123A	-1.15
126A	+1.549
132A	-1.71
Sum	-20.14
Mean	-0.75

102A	-1.31
102C	-3.06
125A	-1.56
127A	+0.39
130A	+0.36
133A	-0.86
Sum	-9.29
Mean	-0.49

Table 20: HABITUATION AND C_3 RESPONSE t-SCORES FOR D CELLS

Unit	H resp. t	C_3 resp. t
76A	+1.17	-0.29
81D	-1.79	+0.48
82A	+0.56	+0.52
83C	+1.26	+0.01
84B	+2.75	+2.70
84E	-0.38	-0.97
86A	+6.53	+3.58
86B	+0.47	+0.82
90B	-0.35	+1.18
91A	+1.45	-0.34
91B	+1.45	-0.43
92A	+1.22	+0.20
92B	-1.21	-0.21

Table 20 (continued)

92C	+0.78	-0.05
94E	+0.57	+0.04
97B	+1.89	-0.09
98A	-1.51	-2.49
98B	+0.22	-1.09
99C	+1.69	-0.35
100A	-0.90	+0.47
99B	+3.39	+0.74
103A	-0.75	+1.41
119A	-0.52	+1.63
122A	+0.50	+1.77
123A	+1.08	+0.60
126A	-0.78	-0.38
132A	+0.66	+0.29
Sum	+19.45	+9.75
Mean	+0.75	+0.36

Table 21: HABITUATION AND C_3 RESPONSE t-SCORES FOR I CELLS

Unit	H	C_3
74A	-1.89	-.081
74B	-1.93	+0.37
80A	+0.33	-0.24
81C	-0.93	+0.55
90C	+0.70	-0.21
94F	+0.43	-0.83
95A	+1.30	+0.73
95B	-0.06	-0.37
96E	+0.15	+0.48
96F	+0.01	+0.04
96H	+0.06	-1.64
98C	-2.42	-0.72
97A	+0.49	+0.38

Table 21 (continued)

102A	+1.34	-0.77
102C	+1.75	-0.12
125A	+0.75	+1.02
127A	+0.31	-0.08
130A	-1.90	-0.47
133A	-0.16	+0.24
Sum	-1.67	-2.45
Mean	-0.088	-0.129

Table 22: SUMMARY TABLES FOR ANALYSIS OF VARIANCE BETWEEN PERCENT CRITERION RESPONSE TRIALS OF LONG US, SHORT US, AIR US AND PSEUDOCONDITIONING GROUPS.

Summary table:

Source	SS	df	MS	F	P
Treatment	3,271.52	3	1,090.51	9.832	<.001
Error	3,549.09	32	110.91		
Total	6,820.62	35			

Duncan multiple range test:

	Long US	Short US	Air US
Short US	13.50*		
Air US	16.00**	2.50	
Pseudo	26.78**	13.28*	10.78*

$$\sigma_{\bar{x}} = \frac{110.91}{9.0} = 3.5105$$

* P = <.01
** P = <.05