CORTICAL AND SUB-CORTICAL AVERAGE AUDITORY EVOKED POTENTIALS ELICITED BY A CONDITIONED STIMULUS DURING WAKEFULNESS AND NATURAL SLEEP

bу

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ABSTRACT

The purpose of the study was to monitor the brain's responsiveness to significant stimuli during wakefulness and natural sleep.

Tones whose significance had been established by Classical or Operant conditioning procedures were used as the stimuli. Averaged auditory evoked potentials (AEPs) were recorded from both cortical and reticular areas in the brain of squirrel monkeys.

Analysis of the AEP waveform was undertaken with a multivariate procedure.

Changes in the overall form of the AEPs were evident after the training procedures, and there were indications that the brain, particularly in the reticular area was selectively responsive to the CS during natural sleep.

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I. INTRODUCTION

A. Selective sensitivity during sleep

For Pavlov, "the fundamental and most general function of the hemispheres is that of reacting to signals presented by innumerable stimuli of interchangeable significance". (Pavlov, 1929).

What are the mechanisms that enable an organism to respond selectively to different stimuli? What nervous structures are involved in the discrimination of these innumerable stimuli? How does it recognize the significant from the non-informative?

Such questions, raised long before Pavlov, are still encouraging much research into the relationships between brain and function behaviour. Somehow the nervous system encodes the information it receives, checks it against a store of previous data, and responds in an appropriate fashion.

It is a common-place observation that we can block out input from certain sources and attend to only a significant or important message. The mother, we are told, will waken readily to the small sound of her baby crying, but will sleep through the sound of jet planes that habitually fly over her house. She would appear, in other words, to be selectively responsive to important sounds even while asleep.

How the brain performs such selection and what it does with the rejected input is still largely a mystery, but it seems clear that, in spite of Pavlov, the cortex is not all important in the analysis of incoming stimuli— conditioned or unconditioned. For instance, since the classical description of the reticular activating system (Moruzzi and Magoun, 1949), much attention has been paid to the role that the mid-brain reticular system plays in the recognition and elaboration of incoming signals. This lower brain area that receives input from all the afferant pathways could provide the anatomical possibility for much modification of stimulus input outside the cortex. Various studies have shown that the development and maintenance of a stimulus "signalling capacity" involves such corticosubcortical relations. (Anokhon, 1961; Galambos, 1961; Magoun, 1961; Morrell, 1961; Adey, 1962; Hernandez-Peon, 1966; John, 1967.).

More will be said later concerning the role of the reticular system, but first, evidence relating to the abilities of the "sensitive mother" previously mentioned will be considered. Is there, in fact, any evidence, outside of anecdote and folklore that would lead us to believe that the brain is selectively sensitive during natural sleep?

Clearly, to be certain that the selective sensitivity is to the meaning of the stimulus we must control for both stimulus intensity and stimulus novelty. The mother may be responding to the child's cry not because it is of particular significance to her but because, within the context of the ordinary background stimuli that are present during sleep, it is a novel event. Again, a person may respond to his own name and not others only because it was spoken more loudly. Such confounding influences are, however, relatively easy to control.

In a series of studies, Oswald (1960; 1966) demonstrated rather simply that people are selectively responsive to names of particular significance to them. Volunteer subjects slept in the laboratory where their scalp EEG was continuously recorded. A list of

about 50 tape recorded names of the same physical intensity was played to the subjects while they slept. Previous instructions required the subject to clench his fist whenever he heard his own name. Although spontaneous arousals during sleep (defined by slow waves in the EEG) were rare, fist clenching and cortical arousal (elicitation of the K complex) contingent on presentation of the subject's own name, occurred frequently. Even more interestingly, the cortical arousal response was evident even though the fist clenching response sometimes failed to occur. The brain was responsive even though the called-for behavioural response was apparently not made.

In a similar vein, Wilson and Zung (1966) have also demonstrated selective sensitivity during sleep. In this study, a response was defined as any change in the EEG to a lighter stage of sleep from the on-going level. "Motivating" sounds, i.e.; those previously specified as target signals, produced more responses than "neutral" sounds, such as gongs and animal noises. Incidentally, Wilson and Zung report that females in their study were more responsive to the neutral sounds than males. There was, however, no difference between men and women in their responsiveness to the motivating stimuli.

Four different sleep stages were distinguished according to the system proposed by Davis (Davis, et. al.; 1937), and the subject's responsiveness during different sleep levels was analysed separately. Although responsiveness to the "motivating" sounds was uniformly high during all sleep stages, responsiveness to the neutral sounds diminished linearly as the subjects moved deeper into sleep. Thus,

for the subjects as a whole, 90% of the "motivating" stimuli produced a response even during the deepest stage of sleep, but only 25% of the neutral sounds were effective in producing a change in the EEG from level 4 to a lighter stage of sleep.

In Oswald's previously mentioned study, the subjects were shown to be selectively responsive to their own names, whereas Wilson and Zung's subjects were differentially responsive to "target" sounds, i.e. - they were told that they would be rewarded if they awakened when a particular sound occurred, e.g.; a telephone ringing. The "motivating" nature of these sounds was, therefore, artificially created. We might assume that the sound of one's own name would be more naturally motivating, however, it should be noted that Oswald's subjects were instructed to respond to their own name. He did not show that subjects were selectively responsive without prior instructions. Nevertheless, both studies would seem to demonstrate that the brain, as evidenced by changes in the cortical EEG, is selectively responsive to certain "crucial" sounds during natural (i.e.; non drug-induced) sleep.

B. Learning During Sleep.

(i) Complex Verbal Material.

of relevance to the question of responsiveness during sleep are studies concerned with the reported phenomena of learning during sleep. Such studies, particularly those that attempt to establish a discriminatory response, are germane in that the brain must be selectively responsive if a conditioned response is to be elaborated during sleep. Some years ago, Emmons and Simon reviewed the existing work that purported to show that learning could take place during sleep (Emmons and Simon, 1955). All of the studies that claimed positive results were considered inconclusive because of methodological inadequacies. A particular criticism concerned

the lack of proper criteria to determine whether the subjects were, in fact, asleep while the stimulus material was being presented.

Subsequent, well controlled studies by Emmons and Simon (Simon and Emmons, 1956; Emmons and Simon, 1956), supported their belief that learning could not occur while subjects were asleep.

In the first study, subjects were presented with tape recorded questions and answers, e.g.; "Where did General Grant work before the Civil War?" Answer: "In a hardware store". Subjects were required to report immediately if they heard any of the answers. The next day, they were tested for retention of the material in a multiple choice test.

The occipital EEG was continuously monitored, but the stimulus material was presented, regardless of the stage of sleep that was evident. The sleep stages were defined in terms of how much Alpha activity was present. Results indicated that both the number of items answered correctly and the number of immediate reports of having heard the answer during the previous night were directly related to the amount of Alpha present in the EEG when the stimulus material was presented. When Alpha activity was completely absent, virtually no items were recalled, and there were no immediate responses. In other words, when the subject was clearly deeply asleep, no learning occurred.

The second study (Emmons and Simon, 1956), was performed to test the effect of repetitive stimulation. A list of 10 one-syllable nouns was presented repeatedly, but only when the EEG showed an absence of Alpha activity. There was no evidence in a recall test that the subjects had learned the nouns during sleep.

(ii) Conditioned responses.

More recently. Beh and Barratt (1965) reported a series of experiments indicating that a classically conditioned discrimination, elaborated during wakefulness, is retained during medium level (Stage C) sleep. They also report that they were able to establish the discrimination during stage C sleep. In the first experiment. random presentations of both a 500 and a 300 cps. tone were made until they no longer produced blocking of the on-going Alpha activity. After this habituation session, the experimental group received presentations of the 500 cps. tone paired with painful shock to the finger. Presentations of the 300 cps. tone were also made, but were never paired with shock. The control group simply received presentations of both tones without any shocks. Analysis of the data revealed that the experimental subjects showed significantly more conditioned Alpha blocking to the 500 cps. tone than the control group. In subsequent tests during sleep the criterion for a conditioned response was a cortical arousal response (K-complex). During stage C sleep, the experimental group again showed more conditioned discriminative responses than the control group. Beh and Barrett concluded from this that the subjects were differentially responsive during sleep to a stimulus whose significance had been "built in" by the conditioning procedure.

The next experiment by Beh and Barratt demonstrated that it was possible to establish a conditioned cortical arousal response during sleep. This time the 300 cps. tone was paired during sleep with the shock (the US for the elicitation of the A-complex) for the experimental subjects, while the control group again received both

tones unpaired with shock. Once again, the experimental group showed more conditioned responses than the control group. It should be noted that in the latter experiment the subjects were administered a dose of Chloral Hydrate (0.6 gm.) to help induce sleep.

From Beh and Barratt's data, then, it would seem that a classically conditioned discriminatory response can be retained and established at least during medium levels of sleep. However, as the authors point out, we cannot conclude from this data that similar results would be found if the stimuli were more complex, e.g.; verbal instructions.

Granda and Hammack (1961), in an experiment employing operant conditioning techniques, also report positive results with regard to conditioning during sleep. Five subjects were required to learn 2 switch closing responses. A Sidman avoidance schedule was set up under control of the left hand. The shock-shock interval was 3 secs: thus, a subject could avoid all shocks, which were delivered to the right leg, by responding at a rate higher than one response every 3 seconds. A fixed ratio schedule of "time-out" periods was programmed on the right-hand switch; that is, the subjects could get time out from the Sidman schedule by making a fixed number of right-hand responses. Ten seconds before the end of these "time-out" periods, a loud buzzer was sounded next to the subject's ear. A signal light mounted in front of the subject's head was turned on after ten seconds of the buzzer - this light signalled the beginning of the next Sidman avoidance session. Grands and Hammack's treatment of the results is very superficial. They claim, however, that the subjects learned to respond appropriately on both the Sidman schedule and the "time-out"

schedule "without returning to the electroencephalographically defined "waking state". The implication is that the subjects neither heard the "loud buzzer" nor saw the signal light, but, as the authors point out, the bulk of their positive data came from "light" sleep stages. It seems quite possible, then, that Granda and Hammack's subjects were more awake than asleep.

An experiment in which care was taken to see that the subjects were not awake during the conditioning procedure was performed by Weinberg (Weinberg, 1966). Subjects received 25¢ if they were able to close a manually operated switch within 15 seconds of the onset of the "positive" tone. If they failed to respond correctly within the 15 second limit they were "punished" by being awakened by a loud bell. They also received the 25¢ reward if they did not close the switch when the "negative" tone was presented.

The EEG was sampled aperiodically throughout the night, and if the subject showed stage C, D, or E activity (medium through deep sleep) he was tested for responsiveness by being presented with five 100 volt, condenser discharged shocks. These shocks had been previously tested while the subjects were awake, and they were found to be sufficiently intense to elicit peripheral vasoconstriction and to be described as painful. The conditioning procedure was begun only if there was no vasomotor response and no behavioural or EEG arousal. With this cautious procedure, the subjects received on the average, one tone (either positive or negative) an hour throughout the night. To complete the experiment, subjects returned to the laboratory 2 to 4 times a week for up 7:3 months.

Three out of five of the subjects gave clear indication of a gradual acquisition of a discriminatory response to the 2 tones. The remaining 2 subjects seemed to make the discrimination from the beginning of the experiment. It seems, then, that Weinberg, admittedly with a limited number of subjects, has demonstrated the possibility of establishing a conditioned discrimination during relatively deep sleep.

We can add at this point that studies using animal subjects confirm that discriminations learned in the waking state are still evident in terms of selective EEG desynchronization responses during sleep. But even here, as of course in the case of the human studies, direct readings from the reticular area have not been made. Also, results have been presented in terms of EEG de-synchronization or the elicitation of the K-complex. Reticular recordings would be particularly important in this regard since it is now known that the K-complex is elicited in the cortex via the reticular system "rather than via the direct specific afferent pathways, as previously thought (Brazier, 1968).

To summarize briefly; it would seem that although there is no evidence to support the notion that complex psychological material can be learned during sleep, there is some evidence that subjects are responsive to certain "crucial" or significant sounds. The significance of the sound may be relatively "natural", such as the subject's own name, or it might be built in by means of a Classical or Operant conditioning procedure. Conditioned discriminations elaborated during wakefulness are retained during sleep.

Deep sleep and wakefulness may be viewed as widely separated states so far as the organism's responsiveness is concerned. Whether a stimulus will be responded to will depend on both the subject's level of arousal and the importance of the stimulus. In deep sleep, a state of relatively complete inattention, the brain might respond (even though an overt, motor response is absent) only to stimuli of "crucial" importance. In order to monitor the responsiveness of various cortical and sub-cortical brain areas to these stimuli, some stable and qualifiable index is needed. The following section presents some of the research that has employed the Average Evoked Potential (AEP) as such an index.

- C. The Average Evoked Potential as an Index of Cortical and Sub-Cortical Responsiveness to Significant Stimuli During Different States of Attention.
 - (i) General Arousal.

Deep sleep has been referred to earlier as a state of relatively complete inattention. The organism's behavioural responsiveness to external stimuli in general is greatly diminished. It is to be expected also that the brain's responsiveness, directly measured, will be affected by the sleep state. Studies of the effects of successively deeper stages of slow wave sleep on the brain's responsiveness, as measured by the AEP, have been studied under such headings as, for example, "the effects of general arousal". It might be noted here that some confusion might arise as to the meaning of "arousal". In the literature the term sometimes is applied to arousal in a behavioural sense and at other times it clearly refers to a neural arousal response as measured by changes in the EEG (eg., in the

Oswald studies previously mentioned). Particular difficulties arise, for instance, with regard to so-called paradoxical sleep, which is characterized by an EEG pattern more similar to low amplitude, high frequency aroused state than to the high amplitude, low frequency EEG pattern that is recorded during deep sleep. During paradoxical sleep, the brain appears aroused, but other indices, eg., lack of responsiveness to external stimuli and the presence of muscle atonia, indicate that the organism is deeply asleep. In the studies reported below, eg., Huttenlocher, 1960; Winter, 1964; and Shagass and Trusty, 1966, the authors talk of the effect of a decline in general arousal. The level of arousal here is defined by changes in the EEG from "fast" activity to low frequency, high voltage, "slow wave" sleep. Responsiveness during paradoxical sleep in these studies is treated as a separate phenomena.

The effect of a decline in general "arousal" on the AEP has, then, attracted a certain amount of attention. (Allison et al., 1966; Shagass and Trusty, 1966). For instance, Shagass and Trusty (1966) report results concerning visual and somatosensory cerebral evoked potentials in humans. Briefly, they find changes that include a systematic lengthening of latencies as sleep progresses to deeper levels. So far as the amplitude of the AEP is concerned they report that the initial components are enhanced while later components are decreased. In a similar vein, Herz (1965), recording cortically and subcortically in cats, reports an increased amplitude of cortical AEP to auditory stimuli except during stages of paradoxical sleep.

Again, using cats, Hattenlocher (1960) has demonstrated a

diminution in the amplitude of click elicited AEPS, in the mesencephalic reticular formation during naturally occurring slow-wave sleep. Although during the waking state the click responses remained undiminished for hundreds of presentations, the reticular response during slow-wave sleep habituated to about 50% of it's waking state level. However, if a period of silence intervened between series of 5 to 10 clicks, large reticular responses were again elicited. The habituation, then, was somewhat reversible, but occurred quite rapidly, i.e.; within 5 to 10 presentations of the clicks. It should be noted, however, that the habituation was never complete even after hundreds of click presentations.

Cortical responses to the clicks in the same animals were clearly present during slow-wave sleep, although there was a decrease in the late, (later than 50 ms. after stimulus onset) slow-wave, components of the AEP waveform. This diminution, also reported by Shagass et al. (1966), was not evident until after several hundred click presentations.

When recordings were made during so-called paradoxical sleep stages, there was almost complete suppression of the reticular response. Similarly, there was an absence of the slow-wave component in the cortical response, although the short latency responses were maintained essentially the same as in the awake state.

Huttenlocher's report suggests that there is a <u>decreased</u> responsiveness of the reticular system during slow-wave sleep, but suppression of response is never complete except during paradoxical sleep. Responsiveness in the cortex remains essentially the same,

except for the marked diminution of later, slow-wave components of the AEP. As Huttenlocher points out, these late components probably reflect a spread of activity to secondary areas, and therefore, it appears that during sleep this secondary activation is diminished.

In a similar study, Winter (1964), results indicate that the AEP to click stimuli does not decrease at all in amplitude during sleep. If anything, his data appears to show a slight increase in amplitude compared to that found during the waking state. One possible reason for this contradiction of Huttenlocher's results is that Winter used a variable interstimulus interval specifically to decrease the possibility of habituation. In Winter's study, the inter-click interval varied between 0.5 and 6.0 seconds, whereas in the Huttenlocher study, it was maintained constant at 3.2 secs.

The stimuli used in the previously mentioned studies were of no particular significance to the subjects, ie; they were neutral clicks. Although there is conflicting evidence concerning the habituation of the reticular response during sleep, it is clear that habituation is nowhere near complete, even after hundreds of presentations. It can be noted also that analysis of the changes in the waveform of the AEP were confined mostly to the observations of changes in amplitude alone. Attempts were not made to deal with the configuration of the waveform as a whole.

(ii). Selective Responsiveness.

As we noted earlier, subjects are sometimes responsive only to stimuli of particular significance. Although they may be quite awake in general, it is as though they were asleep so far as certain, usually habituated or non-important, stimuli are concerned.

Much recent research investigating AEPs during these states of what might be termed, "selective responsiveness", has been done under the heading of shifts in attention. The later findings tend to support Hernandez-Peon's early paper concerning the effects of visual distraction on the amplitude of auditory evoked potentials in the cochlear nucleus of the cat. (Hernandez-Peon et. al., 1956). In general, it seems that AEPs are greatest to stimuli that are of most significance to the organism. (Haider, et. al., 1964; Garcia-Austt. et. al., 1964; Guerro-Figueroa and Heath, 1964; Satterfield, 1965; Spong, et. al., 1965). The Haider et. al. paper deserves some special attention in that they recorded AEPs to both significant and nonsignificant stimuli during different phases of a signal detection experiment. They used a vigilance situation in which the subjects. (humans), were required to detect a particular visual stimulus in a series of other non-significant flashes. Over the course of the experimental session, as general vigilance declined, the amplitude of the AEPs decreased. However, they note in particular that the evoked potentials to signals that a subject failed to detect were reduced in amplitude in comparison with the AEP to the same stimulus when it was detected. The differences in the AEPs to detected versus missed signals were equally evident both early and late in the vigilance session, thus indicating that the differences were not due to a general decline in vigilance.

(iii) The AEP and Conditioned Stimuli.

So far, mention has been made of the effects of arousal and attention on AEPs elicited by neutral and important stimuli. The "importance" of the stimulus was typically established by instructions or, as in the case of Hernandez-Peon's cats, a basically neutral

stimulus was made even less important by introducing an 'innately' distracting stimulus." Another way, however, to make a stimulus important, as was pointed out above, is to use it as a conditioned or discriminative stimulus for some response.

Typical findings report that a stimulus which no longer elicits a high amplitude AEP due to habituation, will do so again if it is made significant by pairing the stimulus with positive or negative reinforcement. (Galambos, 1961; John and Killam, 1961; Gasanov, 1966; Pribram, et. al., 1967; Mark & Hall, 1967; Hall & Mark, 1967).

A typical example, Hall and Mark (1967), reports amplitude changes in click evoked AEPs recorded both cortically and in the reticular area of rats. Trains of the click stimuli were used as a CS in a fear conditioning (Conditional Emotional Response) situation. The amplitudes of late components of the AEPs recorded from auditory cortex, medial geniculate body and reticular formation increased during conditioning, fell back to preconditioning levels during extinction, and increased again with further conditioning sessions.

We might note here, as Galambos points out, that the particular training method affects the changes that occur in the AEP over the course of training. For instance, if, instead of simply pairing the stimulus with some form of reinforcement, it is used as a signal for an operant response, the AEP to the CS is often found to decrease during acquisition. We might further note once again that, in these studies, the analysis of the AEP was concerned with changes in the amplitude of the response. The amplitude of the AE' is, of course, only one of a number of parameters that could be examined.

Some studies that attempt to deal with some more complex aspects of the AEP waveform will be mentioned below.

D. The AEP: Index or Code?

In dealing with the AEP as a measure of brain activity, we must distinguish, as Uttal (1965; 1967) points out, between signs and codes. Does the waveform of the AEP in some way accurately reflect the physiological code for the elicitation of some specific behavioural response? Can it be shown that the differences in AEPs elicited by "meaningful" as opposed to "non-meaningful" stimuli do, in fact, constitute the informational value of the stimulus rather than merely reflecting a general change in the cortical activity of the subjects? Are the changes in the AEP that are contingent on changes in the independent variables merely "signs" that the brain is in a different state or do they accurately indicate the particular way that information has been encoded and stored?

In the animal studies mentioned above (Huttenlocher, 1960; Winter, 1964) the authors are clearly using the changes in the AEP to reflect general changes in the brain's responsiveness. The AEP is used as an index, or tracer device, to indicate what areas of the brain are more or less responsive during different states of arousal.

Hall and Mark (1967), in the previously mentioned paper and a subsequent study (Mark and Hall, 1967), specifically argue that the changes in the AEP during conditioning result from a general change in the state of the animals rather than being due to associative factors. They demonstrate that the same amplitude changes in the click-evoked responses are evident when the animals have been fear-

conditioned, using a visual CS. They argue, then, that the observed changes occur because the animal is fearful, rather than as a result of the conditioning procedure per se. The AEP amplitude changes index the state of conditioned fear, rather than indexing changes in the way the CS is encoded as it becomes associated with the UCS. some other recent conditioning studies (Pribram et al., 1967; Ruchin and John, 1966; John, 1967; John, et al., 1969), and in the human studies that seek to establish physiological correlates of specific behaviours (Donchin et al., 1963; Davis, 1964; Shipley et al., 1965; Donchin, 1966; Donchin and Lindsley, 1966; Lifshitz, 1966; Sutton et al., 1967), the authors are more concerned with the AEP as, in Uttal's terms. a code. Pribram (1967), for instance, using monkeys, reports that he can detect a differential "intention" response in flash evoked AEPs that are recorded prior to a right or left panel push. John (1967; 1969), argues even more strongly that the AEP specifically relates to endogenous brain processes. That is, the waveform of the AEP specifically indicates stored information. The AEP is, like the printout of a computor, the "readout" of stored information. For example, in his latest report, John et al. (1969), trained cats to make differential responses to flickering lights of different frequencies. After extensive training, reliably different AEPs were recorded prior to the performance of each response. If a third stimulus, intermediate in frequency between the two training stimuli, was then presented, the "confused" cats would sometimes perform the response appropriate to training stimulus A, and sometimes that appropriate to stimulus B. The AEP to the new stimulus, when it elicited response A, was similar

to the waveform of the AEP elicited by training stimulus A. Similarly, when the response appropriate to stimulus B was elicited, the AEP, to the new stimulus, was like that originally elicited by stimulus B. Such data do, in fact, seem to indicate that the stimuli were triggering differential neural codes.

Similar results have also been reported in human studies where it has been found that an "evoked" response to an expected, but deleted, stimulus is similar to that elicited by the stimulus itself, (Lindsley, 1969; Weinberg, 1969; Sutton et al., 1967). In such studies, it is as though the response was "emitted" rather than "externally evoked".

For example, in the Sutton et al. study, 1967, subjects were uncertain as to whether an initial click would be followed by a second click which occurred 180 or 580 msec. later. The AEP waveforms elicited by the initial click showed a large positive deflection at the point in time where a second stimulus could have occurred but did not. It is the absence of the second click, or the passage of a certain amount of time, i.e., 180 or 580 msec., that resolves the uncertainty of the situation. That is, after the time in which a second stimulus might occur has elapsed, the subject knows for certain that it will not be forthcoming. Sutton et al., argue that the large positive deflection reflects the resolution of uncertainty. In that it is not "evoked" by a stimulus they argue that the deflection reflects an endogenous brain process, that is related to the subject's reaction or attitude towards the stimulus rather than to the physical characteristics of the situation itself. Sutton's and John's findings, then, constitute evidence suggesting that a

stimulus-specific pattern of neural activity is laid down in the nervous system during the conditioning process.

It is important to note that, although John talks of "neural readout" of stored material, the actual mechanism of information storage, e.g., in electrical or bio-chemical terms, is left open. If we can use the computer analogy again, the printed output may result from information stored in a variety of ways.

E. Factor Analysis as a Method for Evaluating Changes in AEP Waveforms.

Part of the usefulness of John's work derives from his use of more objective, correlational, techniques to measure waveform similarity. The correlational measures, such as those reported by John et. al (1969), have been extended via the application of Principal Component Factor Analytic techniques. Donchin (1966), for instance, used a Principal Component technique to analyse AEPs from human psycho-physical experiments. And similar techniques were employed in some of John's earlier conditioning studies (John, et. al., 1964).

In addition to providing an objective index of waveform similarity, the Factor Analytic technique allows for an analysis of the AEP into separate time related components, each of which contributes a certain percentage of the variance in the total AEP.

The AEP can be broken down into the independent components that make up the original waveform by plotting "factor scores" for each of the factors that accounts for variance in the AEP.

Essentially, the digitized AEP is treated as a variable. Each of the digitized time points or addresses of the AEP is treated as a

"person" in a factor analytic study. AEPs collected under different conditions, e.g.; during successive conditioning days are intercorrelated as the first step in the generation of a matrix of factor loadings. The similarity of AEP waveforms is reflected in the extent to which they load on the same factors. Condensation of the original data matrix occurs to the extent that a small number of factors are found to account for most of the variance in the original AEPs. Each time point ("person") of the AEP has a score on each of the extracted factors. If as many factors as variables were extracted, the exact shape of the AEP could be reconstructed by re-combining the factor scores of all the factors. The usefulness of the technique, however. lies in it's condensing power, in that the shape of the AEPs can be reconstructed from the scores of a small number of factors. For instance. in the data to be reported later, it will be seen that about 80% of the variance in 30 or 40 AEP waveforms can be accounted for by as few as 3 factors. Of course, as noted above, the idea is not so much to reconstruct the AEP waveform from the factor scores, but to analyse it into a small number of components that account for most of it's variance.

There are, however, limitations in the method; such limitations show up most obviously when we are dealing with a small number of variables, or when it is necessary to deal with the configuration of a single, isolated waveform that was gathered under conditions that occur only once in the experiment..

With few variables, a clear factor structure may not emerge.

In the case of the single waveforms previously mentioned, the problem is that there are no other waveforms collected under the same

experimental conditions, to correlate with it. It will tend, therefore, to appear as a specific factor; i.e., it will be the only variable with a high loading on a particular factor, or it will have low loadings on a number of factors. In the latter case, significant features of the waveform might be overlooked if we do not revert to visual inspection of the AEP. The particular power of the method, once again, exists in its ability to differentiate between large numbers of visually highly similar waveforms.

The procedure as it applies to the present research will become clearer when the specific results are presented.

In the research to be reported, evidence will be presented which suggests (1) that specific components of the AEP are identifiable after a stimulus has been made significant via a conditioning procedure, and (2) that the stored information can be "readout" while the animal is asleep.

II. PROCEDURE

A. Subjects and Apparatus.

Subjects were six, male, squirrel monkeys (Saimiri sciureus) whose weight at the beginning of training was between 600-900 grams. They were housed in a large colony cage and were maintained on a diet of Purina Monkey Chow, supplemented by fresh fruit. Drinking water was freely available, but feeding occurred only once a day after the training session.

All training and recording took place in a Lehigh Valley monkey chair, which was housed in an electrically shielded, sound attenuating chamber. Amplification was performed by Grass model, 7P5A wide bank AC EEG amplifiers, and the evoked potentials were averaged on the model 1052 LS, 1024 address, FabriTek signal averager. The AEP waveforms were displayed on an oscilliscope, photographed, and digitized on a Tally paper tape punch machine.

Evoked potentials were elicited by a brief (approximately 0.10 sec.), 90 db., tone. Frequency settings of the tone generator were either 500 or 1000 cps. All AEPs consisted of the average of 64 stimulus presentations. Stimuli were programmed on standard tape timers.

B. Electrode Placement.

Electrodes were implanted during Nembutal anaesthesia.

Bipolar electrodes were placed in both the left and right mesencephalic reticular areas. The electrodes were made from insulated Nichrome wire. Separation of the electrode tips was 1.5 mm. The zero reference for the anterior-posterior coordinates was a line

through the animal's external auditory canal. Zero for the vertical coordinates was a line 1 cm. dorsal to the line through the auditory canal. The midline zero reference was the saggital skull suture. (Emmers and Akert, 1963). With these references, the reticular bipolar electrodes were placed 4.0 mm. anterior, 1.5 mm. lateral (left and right), and were lowered to a depth of 1 mm. dorsal to the vertical zero. Electrodes were arranged in a 7 pin Amphenol connector, which was anchored to the skull with jewellers screws and dental cement.

Evoked potentials were also recorded from the surface of both temporal and occipital cortex. Cortical electrode 1 was placed approximately 20 mm. posterior, and 5 mm. lateral. Cortical electrode 2 was placed 5 mm. more lateral than 1. Lateral placements were to the left, thus electrodes 1 and 2 were placed over the left occipital cortex in the visual association area. The temporal electrode was placed 13 mm. left lateral, and 2 mm. anterior. This electrode was thus placed towards the posterior portion of the mid-temporal gyrus.

Auditory evoked potentials were recorded between electrodes 2 and 3. Evoked activity from the visual area was recorded between electrodes 1 and 2.

C. Conditioning Procedure.

(i) Classical Conditioning.

Monkeys B-1, B-2, B-3 and C-1 were trained, using a Classical discriminative procedure. After the monkeys had learned to scoop up the reinforcement pellets, training proceeded in 3 phases.

In phase I, the monkey was presented with both the 500 and 1000 cps. tones randomly intermixed with .045 gram Noyes sucrose pellets which were delivered to a food cup directly in front of him. Phase I thus constituted a "pseudo-conditioning" control session, in which reinforcement was never reliably contingent (or non-contingent) on either tone, (cf. Rescorla, 1967). Stimuli were presented aperiodically on separate 25 second VI schedules. Each training day the monkey received 64 presentations of each tone plus about 128 pellets.

The signal averager could be programmed to record potential changes evoked by either stimulus. AEPs were recorded from both stimuli on every training day. Since recordings were being made from four different areas simultaneously, there were 256 averager addresses available for each recording channel. Voltages were sampled every 2 msec. after stimulus onset. The total duration of the AEP, therefore, was 512 msecs. Each address was digitized so that every waveform was described by 256 data points.

The number of phase I training days varied from 3 to 7 for different monkeys.

Phase II of training was the conditioning phase in which the sucrose pellet was always delivered 0.5 sec. after one of the tones. Presentations of the other, negative, tone were still independently programmed along with positive tone presentations. For monkeys B-1 and B-3 the 500 cps. tone was positive, whereas for B-2 and C-1 the 1000 cps. tone always signalled the arrival of a pellet.

AEPs were collected in exactly the same way as in phase I, and the number of phase II days varied somewhat from monkey to monkey.

Phase III consisted of a repetition of from 5 to 7 days of Phase I training. These final sessions could be thought of as constituting an extinction session.

In all phases of training AEPs to the 500 and 1000 cps. tone were collected first on alternate days.

It might be noted that for the monkeys trained with the classical procedure no overt behavioural response is recorded. Evidence concerning the establishment of conditioning consists solely of changes in the waveform of the AEP. The "conditioned response". then, is purely a brain response. This brain response is treated conceptually as though it were the "conditioned response" in a traditional classical conditioning situation. For example, instead of looking for changes in rate of salivation or amplitude of GSR, we are directly monitoring cortical and subcortical changes in the brain responsiveness over the course of training. Such a procedure, is, indeed, extremely useful, particularly in cases where, although there is reason to believe that the animal has developed a CS-UCS association, overt behavioural evidence is precluded; for instance, as when the animal is deeply asleep. Direct monitoring of the brain's response to the CS can be used to show evidence of conditioning when an overt response is, for some reason, precluded.

We might note also that the particular classical conditioning design used here incorporates good controls for such artifacts as pseudo-conditioning, sensitization, and habituation. Indeed, few studies employing the AEP as an index of conditioning have included preconditioning ("random") sessions, discriminative conditioning

sessions, and extinction sessions in a within animal study.

(ii) Operant Conditioning.

For two monkeys, M-8 and M-9, an operant rather than a Classical conditioning procedure was used. The discriminative stimulus was a 1000 cps., 90 db. tone. Over the course of 4 to 5 weeks of daily sessions, the monkey learned to press a lever for a sucrose pellet only during tone presentations. Duration of the tone, (S^d), was gradually decreased until finally the monkey had to press within 1.5 seconds of the occurrence of a 0.10 sec. tone "blip". The extent to which he had learned the discrimination was expressed in terms of the ratio of reinforced presses to total presses. Since the AEP was based on the average of 64 stimulus presentations, the monkey could earn a maximum of 64 reinforcements each session. Both monkeys learned the "go, no-go" discrimination almost perfectly in that they obtained all of the possible pellets while making very few extra presses. The stimulus was presented on a 30 second VI schedule.

AEPs were taken during each session once the monkey had begun to respond to the shortest tone duration. Tests during natural sleep were made after the discrimination was completely established, and again after it had been extinguished.

D. Recording of the AEPs during natural sleep.

Evoked responses to both stimuli were recorded during a sleep session after each phase of the training. Prior to the sleep test, animals were kept awake for either 1 or 2 nights by being slowly rotated in a cage. Whetherthe monkey was deprived of 1 or 2 nights sleep depended on how readily he fell asleep on the night set for the

first sleep test. If he fell asleep readily (within 0.5 to 1.0 hours) after only 1 night's deprivation, all subsequent sleep tests were made after 1 night's deprivation. If he did not fall asleep readily, he was kept awake a further night and henceforth sleep tests were made after 2 night's deprivation.

The EEG was monitored throughout the test session and stimuli were presented only when the record indicated slow-wave sleep.

Frequent behavioural observations were also made — without disturbing the monkey. Because of the infrequency of arousals, the stimuli could be presented on almost the same schedule as during phase II training.

None of the monkeys were agitated by the sleep deprivation procedure, primarily because of the slow rate of rotation and the fact that they could see out of the cage and cling to it easily.

Earlier sleep deprivation procedures using a round, opaque drum to rotate the monkey had been found to cause them considerable distress.

All monkeys fell asleep readily after 1 or 2 night's deprivation.

E. Summary of Training Procedure.

A summary of the testing procedure is presented in table 1.

s	Phase I Random	Phase II Conditioning	Phase III Extinction	Sleep Deprivation
B-1	3	8	5	2
B-2	3	10	7	2
B - 3	3	10	5	1
C-1	5	18	10	1

Table 1. Showing the number of days spent in each phase of training for each of the Classically trained monkeys.

III. RESULTS

A. Introduction and Summary of Histology

Results are presented primarily in terms of factor loadings and plots of the factor scores. Representative AEP waveforms are also presented for comparison with the factor score plots. Data are presented separately for each of the 6 monkeys.

A summary of the histological verification of the electrode placement is presented in figure 1. As can be seen, the right reticular electrode was grossly misplaced, due to electrode bending in monkeys M-8 and B-2. For the sake of consistency and economy of data presentation only the results from the left reticular site are presented.

B. Stimulus Contingent Cortical Arousal

Table 2 shows, for each monkey, the number of stimulus contingent arousals that occurred during each sleep test. We might have expected that more EEC defined arousals would have been elicited by the positive tone after it had been made significant by the conditioning procedure, however; only in the case of B-3 is there any indication of this effect. For this one monkey there were 28 arousals in the sleep test after conditioning as compared to only 4 in the test prior to the training sessions. There is no tendency for more frequent arousal after training in any of the other monkeys.

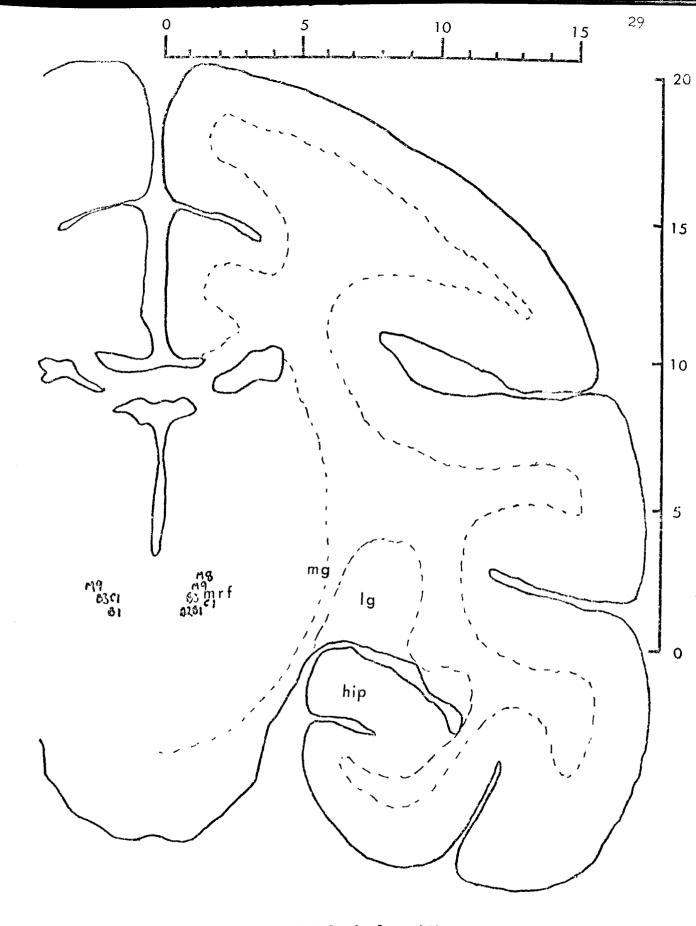


Figure 1. Summary of the histological verification of electrode placement. Section was cut at 4.0 mm anterior. Electrode tips aimed at the reticular area are identified with each monkey's number; e.g., B-1, B-2, etc. Structures identified are: mg - medial geniculate; lg - lateral geniculate; hip - hippocampus; mrf - mesencephalic reticular formation.

		efore tioning		After Conditioning		After Extinction	
	+	-	+	-	+	-	
B-1	5	4	4	2	3	5	
B-2	11	10	6	8	16	7	
B - 3	4	12	28	12	16	10	
C-1	10	10	13	14	8	6	
M-8			3		16		
M-9			11		17		

Table 2. Showing the number of stimulus contingent EEG arousals to the positive and negative tones during sleep tests.

In the factor analytic results to be reported, the AEP waveform is treated as a variable. The 256 digitized time points of the AEP are analogous to "people" in a typical factor analysis.

AEPs for both the positive and negative stimuli were collected each day throughout the 3 phases of training. There is, therefore, one variable (AEP) for each day, for each stimulus.

If we think of each day of training as a "test", then each of the 256 "people" has a score on that test. These scores are intercorrelated as the first step in the extraction of Principal Component factors. The Principal Component factor loading are then rotated by the Varimax procedure. The Varimax method of rotation, while maintaining the orthogonality of the factors, rotates the loadings so as to produce some high, and some near zero loadings for each factor. By such a procedure, which essentially attempts to get rid of medium factor loadings, a more unambiguous and hence more interpretable factor structure is created. Successive rotations of

from 2 through 9 of the Principal Component factors were made to find a set of factors that could most meaningfully be related to the AEPs (variables). The actual factor loadings from the selected rotation appear as appendix II, but day by day changes in the loadings on selected factors are presented graphically. The loadings for sleep-test days are dealt with separately. By thus plotting the factor loadings it is possible to see how, as training proceeds, a different factor begins to account for successively more or less variance in the variables. Plots of the factor scores reproduce the "shape" of each factor. These plots are then directly compared to the actual AEP waveform.

Occasionally the AEP record appears "up-side-down". This is because the baseline setting of the signal averager was occasionally, inadvertently, set incorrectly, with the result that positive/negative deflections are reversed. On such occasions, for the sake of consistency of visual presentation, the AEP record was traced "up-side-down". However, the digitized version of the AEP could not be reversed with the result that such AEPs will enter into negative correlations, and will show negative loadings on the underlying factor.

C. Detailed Results.

(i) B-1

Figures 2 and 3 show samples of the EEG in the awake and asleep animal, respectively.

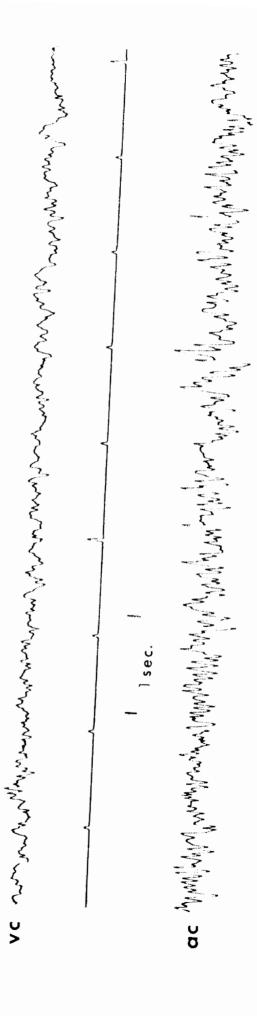
Figure 4 shows the factor loadings derived from a rotation of 3 of the principal component factors. The variables are the AEPs elicited by the positive and negative stimuli in the <u>reticular</u> area. Together, the 3 factors account for 80% of the total variance. Included in the graph are loadings for days 1 through 3 of phase I of training (random presentations of both stimuli and einforcements); days 2, 3, 4, 6, 7 and 8 of phase II (conditioning), and days 1, 3, and 5 of phase III (extinction).

The left side of the graph shows how, over the course of training, the AEPs (variables) load progressively higher and higher on factor 1. The curves for the positive and negative stimuli do not separate, and loadings for the extinction days are still high on factor 1. Psychologically, this implies that over the course of the conditioning days the monkey has not discriminated, at least at the reticular level, between the two stimuli. AEPs for both positive and negative tones load on the same factor. However, if we think of factor 1 as a "conditioning" factor, the successively higher loadings indicate that some non-discriminative conditioning might have taken place.

The conditioning is referred to as <u>non-discriminative</u> in that there is evidence that the monkey had learned a tone-food association, but did not show that he had discriminated between the two tone stimuli.

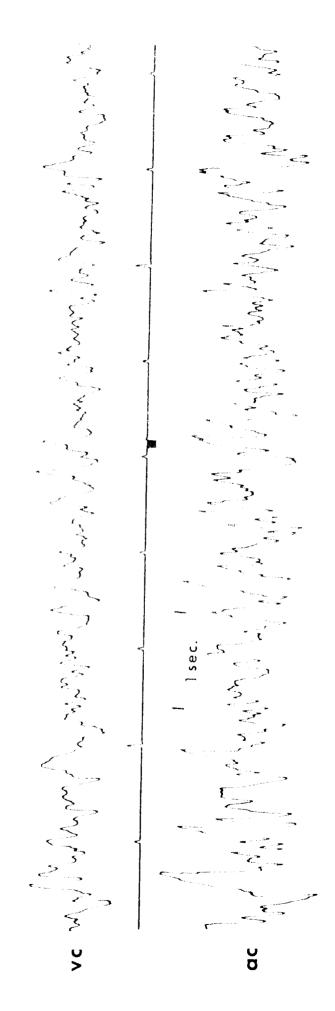




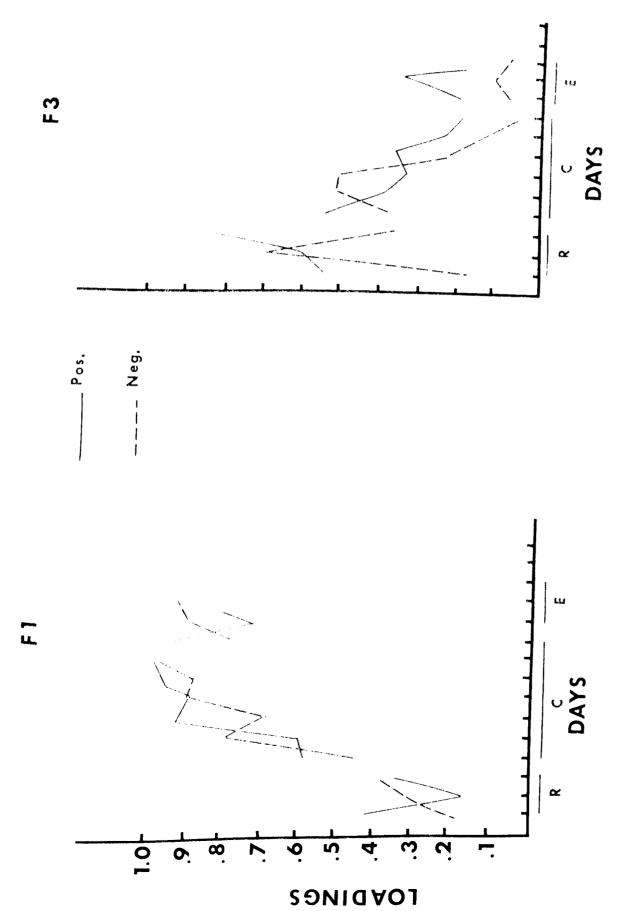


Awake EEG for monkey 8-1; mrf - mesencephalic reticular formation; vc - visual Figure 2.





Asleep EEG for monkey 8-1; mrf - mesencephalic reticular formation; vc - visual cortex; ac - auditory cortex. Figure 3.



R - Random days; 8 - Conditioning days; Factor leadings for reticular AEPs, 5-1. Extinction days. Figure 4.

The interpretation of factor 1 as a conditioning factor is complicated by the fact that extinction day AEPs continue to load highly on it. It could be that the monkey had not extinguished within the 5 days, or it could be that factor 1 is not related to the conditioning process. The decision as to whether we should label factor 1 a "conditioning" factor in this instance is aided by a comparison with the data from C-1. The results for C-1 will be presented in detail later, but we can note here that a similar factor was obtained, and C-1's data clearly indicate that even discriminative conditioning had taken place.

It can be seen from figure 5 that factor 1 is related to the slow negative deflection that occurs in the second half of the AEP. The factor scores plotted in figure 5 should be compared with the representative AEP waveforms in figure 6. It can also be seen that factor 3 (loadings are graphed in the right panel of figure 4) is related to the early portion of the AEP and consists essentially of 2 relatively high amplitude negative peaks that are probably representative of stimulus registration.

It should be noted that the plots of the factor scores are stretched out in time in comparison with the AEP waveforms. Also, they are somewhat smoothed in that only every fifth out of the total 256 points was plotted.

The slow, late appearing, negative deflection in the reticular AEPs, then, is tentatively considered to be related to the acquisition of conditioned acticipation of the delivery of a reminforcement.

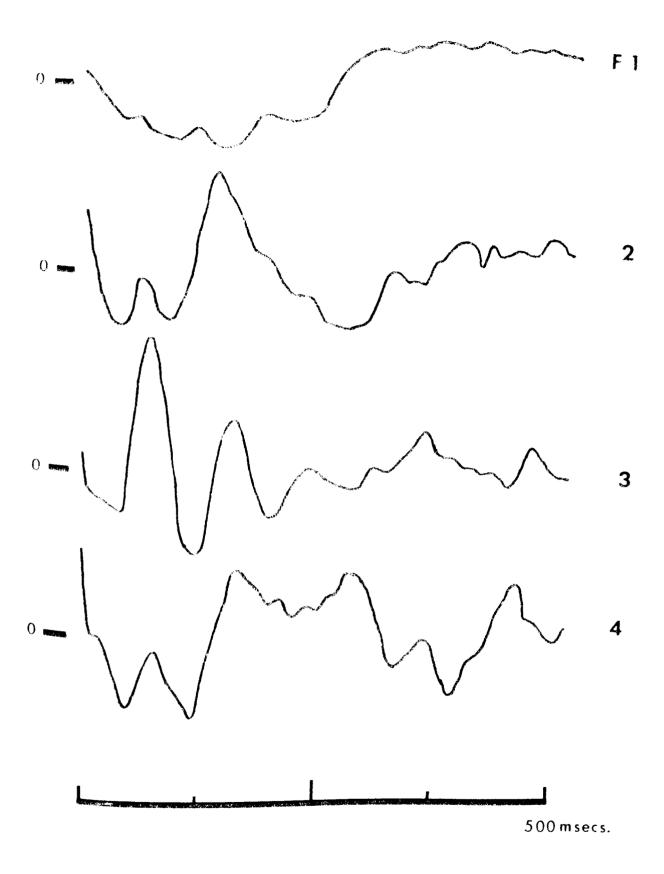
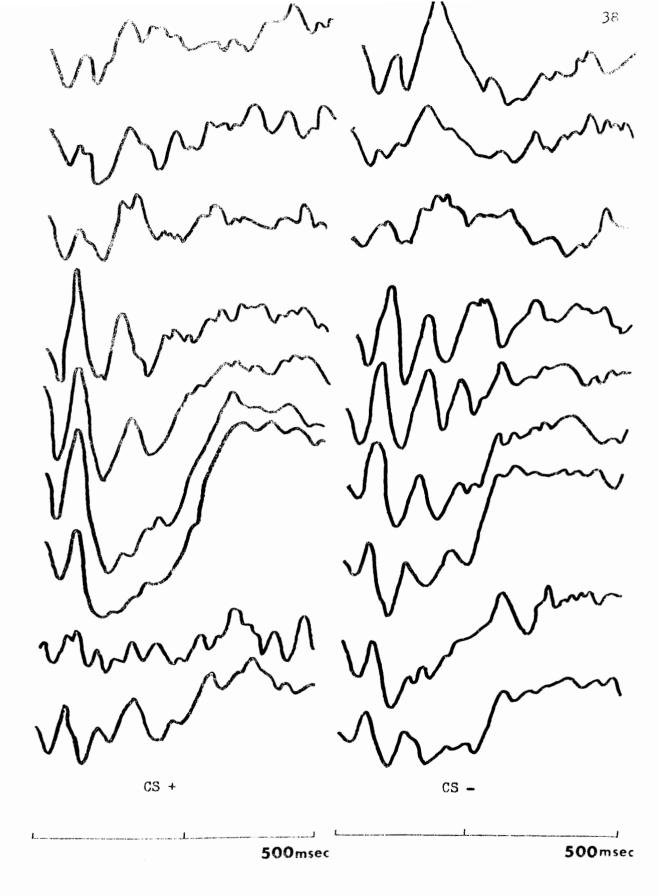


Figure 5. Plots of factor scores for reticular AEPs, B-1.



Sleep Before Cond.

Sleep After Cond.

Sleep After Ext.

R 3

C 3

C 6

g o

E 3

E 5

Figure 6. Sample reticular AEPs, B-1. R - Random days; C - Conditioning days; E - Extinction days.

Data from the sleep tests will now be examined to see if there is any evidence that the stimuli elicit AEPs with characteristics like those elicited in the awake animal. Table 3 presents factor loadings for each of the AEPs elicited by the positive and negative tones during sleep.

		Factor		
		1 2 3 4 5		
	Before cond.	.33 .6404 .4537		
Positive tone	After cond.	.81 .27 .23 .24 .03		
	After ext.	37 .47 .15 <u>.63</u> .22		
Negative tone	Before cond.	13 <u>.96</u> .03 .00 .03		
	After cond.	.10 .9013 .11 .07		
	After ext.	30 .20 .03 <u>.83</u> 22		

Table 3. Factor loadings of the AEPs elicited during the sleep test. Loadings above .50 are underlined.

As can be seen from table 3, three of the sleep AEPs load most highly on factor 2, and 2 of them load on factor 4. The remaining sleep AEP, that elicited by the positive tone after conditioning, loads highly on factor 1.

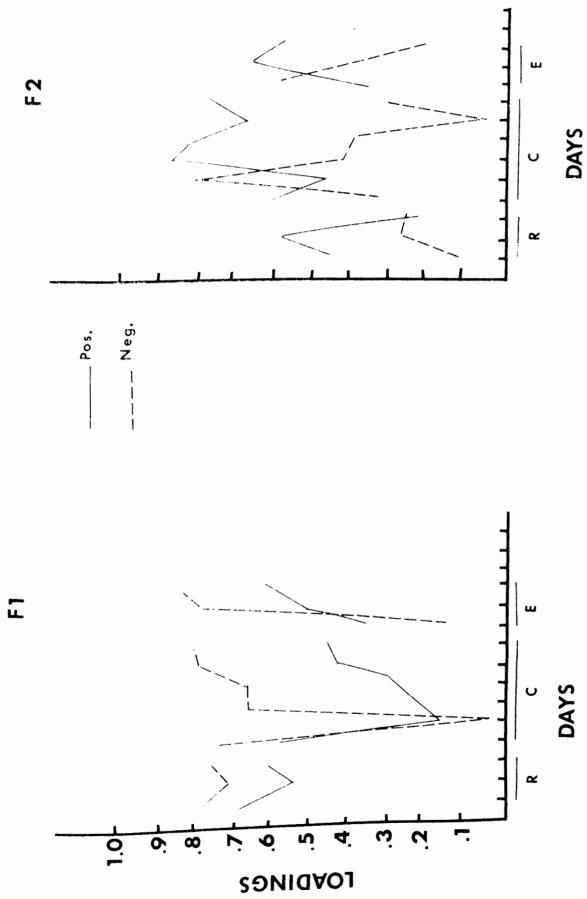
The shift from a high loading on factor 2 to a high loading on factor 1, outlined in the table, is unique to the sleep-test after conditioning for the positive stimulus. It has been argued previously that there is no evidence of discrimination between the 2 tones, at least on the basis of the reticular recordings, but here we find the post-conditioning sleep AEP to load highly on the "conditioning" factor 1. It is as though there was a discrimination

which is only evident during sleep. Such a surprising conclusion may not be so far-fetched, for, as we shall see, there is evidence for a discrimination at the cortical level.

Figure 7 shows the AEP loadings from a 3 factor rotation day, that were recorded from the auditory cortex. It is clear that as training proceeds, factor 2 begins to account for more of the variance. It is clear, also, that the positive and negative curves are separated. Referring to figure 8, it can be seen that factor 2 is characterized by the presence of a slow, negative wave "hump" in the middle of the waveform. Comparing the factor score plots with representative AEP waveforms in figure 9, it is noted that the previously mentioned "hump" is not clearly evident in the waveform of any single AEP. It does, however, appear clearly as a factor.

It is also evident, from the right panel of figure 7, that positive-tone AEP loadings fall off F2 during extinction to a level similar to the loadings of the "random" day AEPs.

Table 4 presents the factor loadings for sleep test AEPs. The cortical AEPs elicited during sleep after conditioning, from both the positive and negative stimuli, load most highly on the same factor, namely factor 1. However, these loadings of about .70 in each case indicate that about 50% of the variance in each of these AEPs is accounted for by other factors. If it could be shown that this residual variance is accounted for by different factors for the positive and negative tones, we would have some evidence that a discrimination during sleep after conditioning is evident, ortically, also. It could, then, admittedly tenuously, be argued that the



R - Random days; C - Conditioning days; Figure 7. Factor loadings for cortical AEPs, B-1. E - Extinction days.

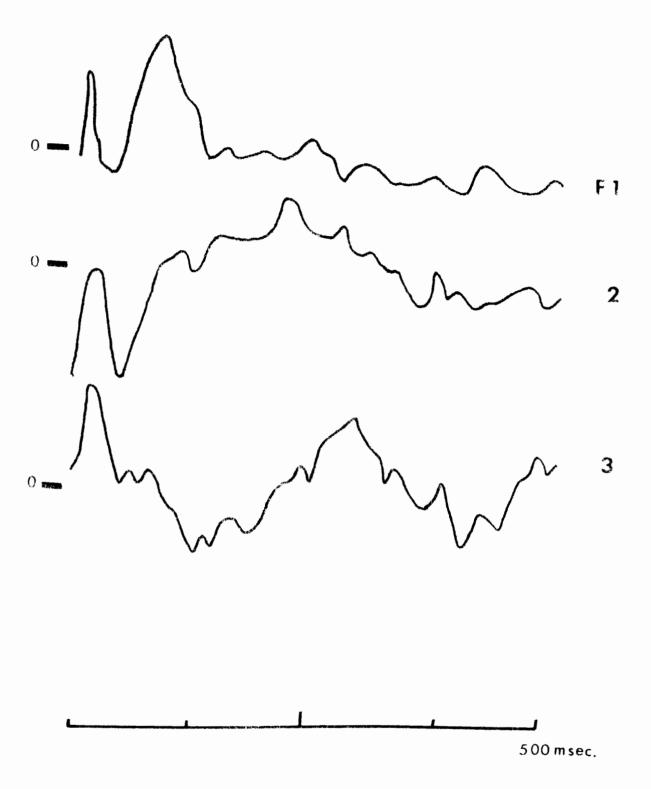


Figure 8. Plots of factor scores for auditory cortex AEPs, B-1.

apparent reticular discrimination during sleep was produced by a cortico-reticular interaction. In fact, if we look at the results from the rotation of 7 factors (which does not appreciably change the factor loadings on conditioning days) there is evidence that the AEPs from the positive and negative stimuli during sleep after conditioning are composed of different factors. Factor loadings from the 7 factor rotation solution show that the negative tone AEP increases it's loading on factor 1 slightly to .74 while the positive loading drops to .54 with the residual variance being accounted for primarily by the second and fourth factors.

Inspection of the AEPs in figure 9 also shows that the waveforms of the AEPs elicited during sleep after conditioning, for both the positive and negative tones, are different from those elicited before conditioning. In particular, there is an accentuation of the second, positive/negative deflection that peaks positively at about 80 msecs.

Although the point cannot be pressed strongly, if at all, there is, then, some evidence that the positive stimulus is being registered during sleep, both cortically and sub-cortically, as being different from the negative stimulus.

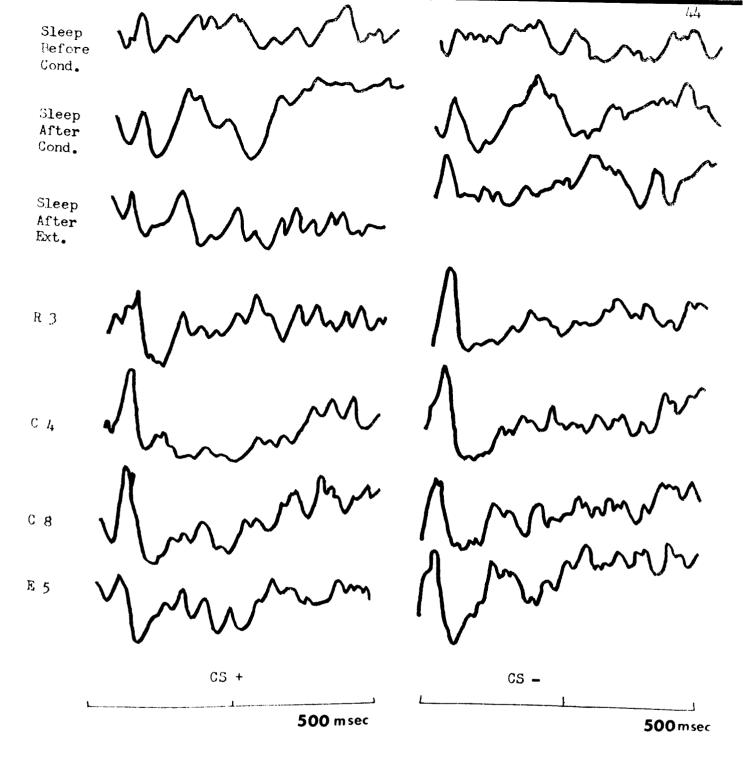


Figure 9. Sample auditory cortex AEPs, B-1. R - Random days; C - Conditioning days; E - Extinction days.

		Factor		
		1	2	3
	Before cond.	<u>.62</u>	05	<u>.52</u>
Positive tone	After cond.	<u>•70</u>	.28	.25
	After ext.	.12	.42	.12
	Before cond.	09	.09	<u>. 69</u>
Negative tone	After cond.	<u>•72</u>	03	•46
	After ext.	23	.12	•75

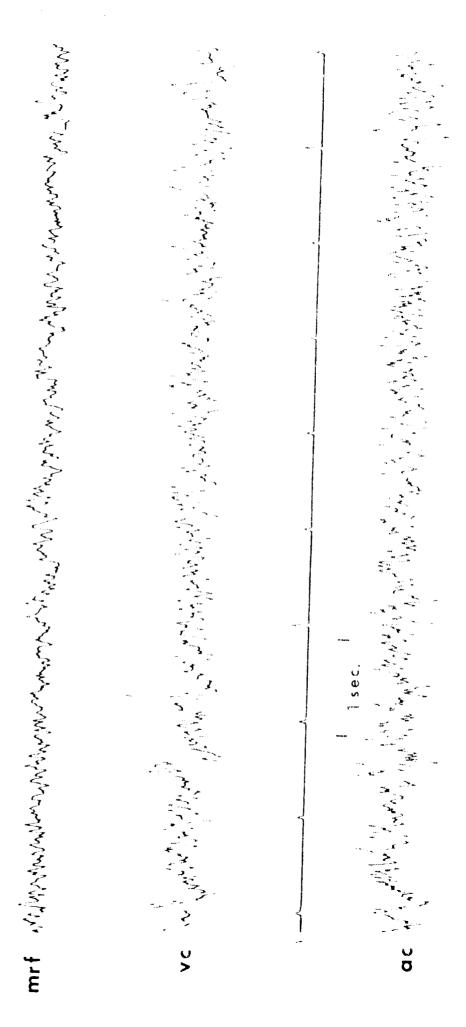
Table 4. Factor Loadings for Cortical AEPs Elicited During the Sleep Tests.(B-1).

Although recordings were also made in the occipital cortex, there was no evidence of a clear stimulus locked evoked activity, except in the case of M-9. The occipital cortex data is, therefore, not included in the analysis.

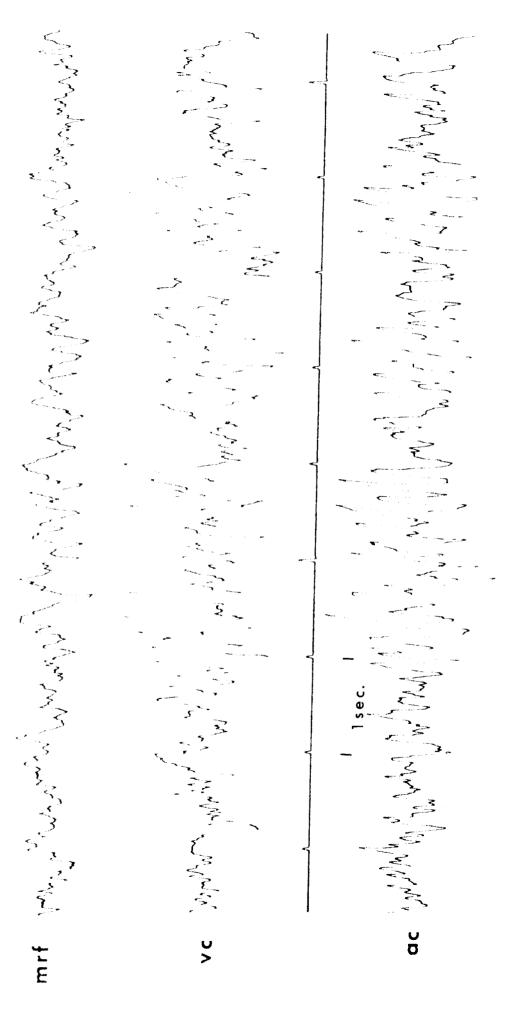
(ii) B-2

Examples of the EEG record for the awake and sleep states are shown in figures 10 and 11 respectively. Figures 12 and 13 show factor loadings from the unrotated Principal Component solution (PC) and for the 7 factor rotation derived from the reticular AEPs.

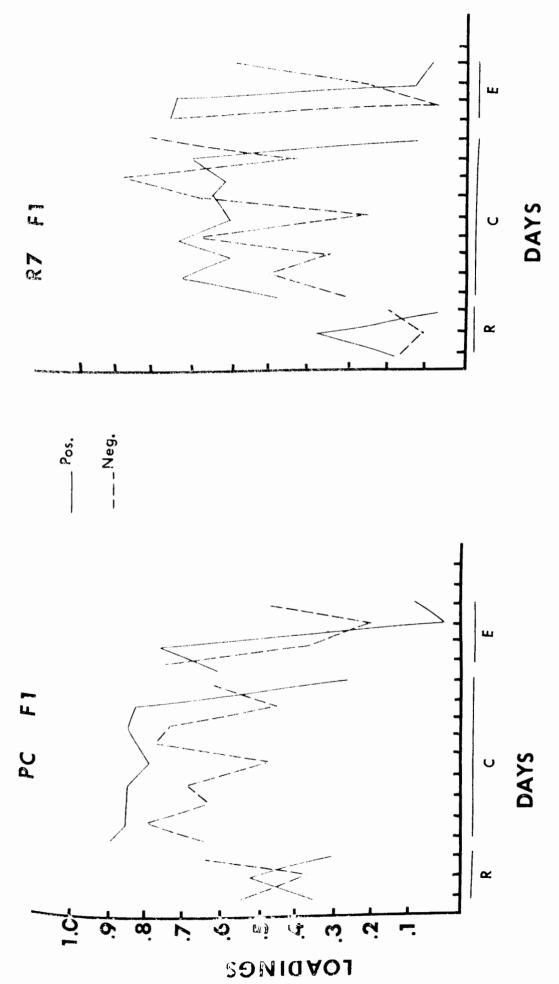
None of the rotations provided a more easily interpretable structure than the PC solution. Approximately 90% of the variance was accounted for by the 7 factors. "Random" days 1-3; conditioning days 1-10 (excluding day 3), and extinction days 1, 2, 6 and 7 are represented in the grapus. Further discussion (1) the factor loadings will use the "



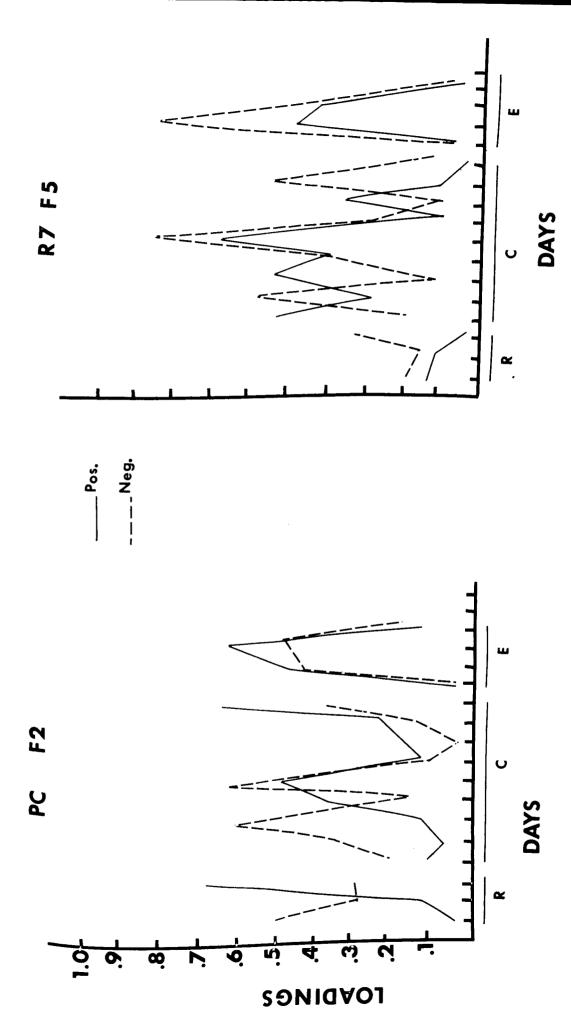
Awake EBG for monkey B-2; mrf - mesencephalic reticular formation; vc - visual cortex; Figure 10.



Asleep EEG for monkey B-2; mrf - mesencephalic reticular formation; vc - visual cortex; ac - auditory cortex. Figure 11.



PC - Principal Components; R7 - Rotation Loadings for reticular AFPs on Factor 1, B-2. of 7 factors. Figure 12.



PC - Principal Components; Loadings for reticular AEPs on Factor 2 and 5, B-2. R7 - Rotation of 7 factors. Figure 13.

factor rotation solution, although essentially the same conclusions could be drawn from the PC solution. The majority of the AEPs load most highly on factor 1 or 5, and, as can be seen, there is little evidence of a consistent tendency for the loadings to move from one factor to another over the course of training. There is some indication that factor l is a conditioning factor, in that the "random" days have no appreciable loading on it. The loadings. are, however, quite variable and the positive and negative curves are not clearly separated, particularly on later conditioning days. The 2 curves do seem more clearly separated in the PC solution, but this is not substantiated by the rotational solutions. that can conservatively be claimed, then, is that there is some evidence that non-discriminative conditioning is represented in the reticular data. Factor scores for the first 5 factors are shown in figure 14. As can be seen by comparing these shapes with those of the sample AEP waveforms in figure 15, the double humped F1 and F5 shapes are characteristic of the majority of the conditioning day The difference between the 2 factors lies in the latency of AEPs. the 2 negative going humps; both are slightly earlier in F5. As is evident from the factor loadings, there is no clear indication that one or other of the waveforms is more characteristic of the positive stimulus. We might note, however, that the late, slow, negativegoing deflection is reminiscent of that seen in data from the previous monkey, although it falls off about 125 msecs. earlier.

Table 5 shows the loadings for the reticular AEPs collected during the sleep tests. There does not seem to be any interpretable

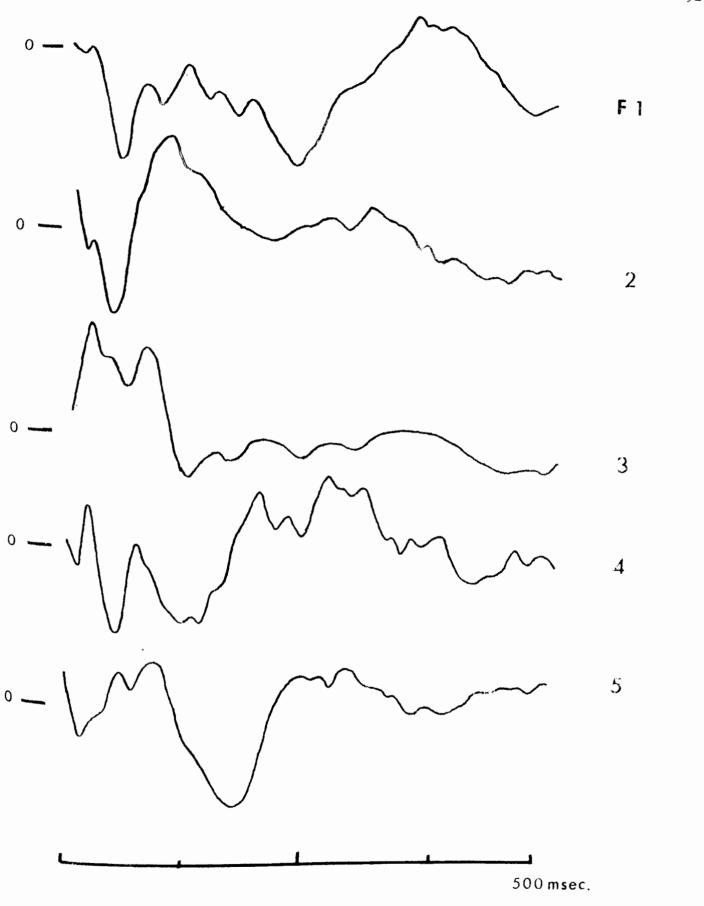


Figure 14. Plots of factor scores for reticular AEPs, B-1.

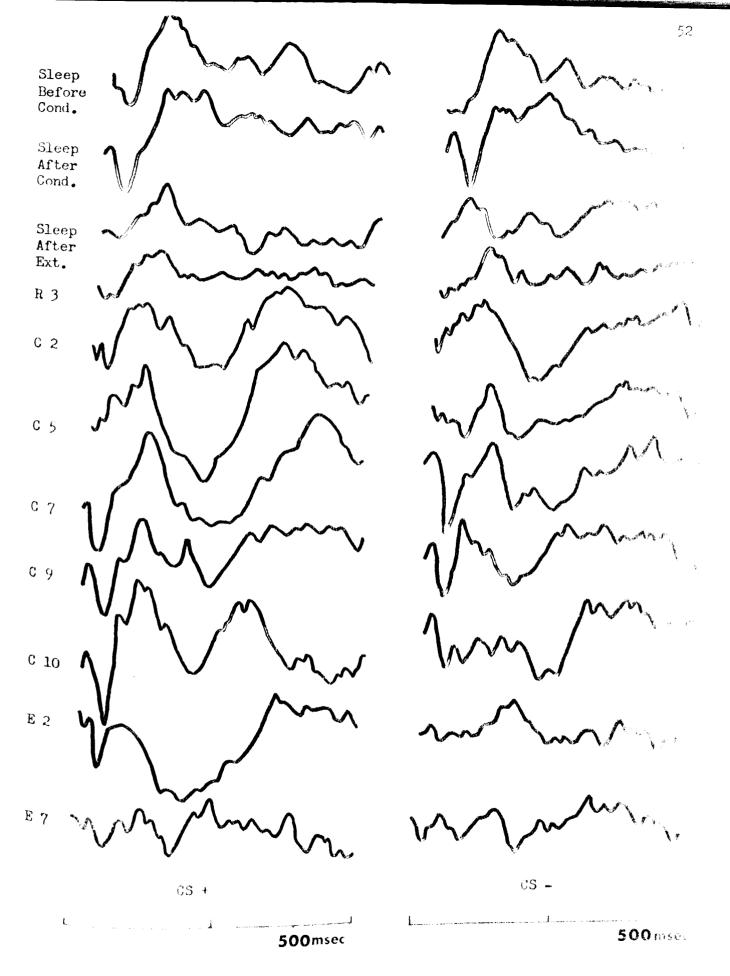


Figure 15. Sample reticular AEPs, B-2. R - Random days; C - Conditioning days; E - Extinction days.

pattern to the loadings. None of the sleep AEPs has appreciable loadings on either Fl or F5 factors.

						Fact	or	
			1	2	3	4	5	6
		Before cond.	•00	- <u>.84</u>	.37	.08	.00	.07
Positive	Positive tone	After cond.	.04	<u>.51</u>	- <u>.61</u>	.16	44	.22
		After ext.	13	.68	.07	40	40	.17
		Before cond.	.04	- <u>.57</u>	<u>.69</u>	.28	.11	11
Negative	Negative tone	After cond.	10	<u>.56</u>	29	.24	<u>54</u>	.35
		After ext.	.22	02	.20	.21	.2 3	8 2

Table 5. Factor Loadings for Reticular AEPs Elicited During the Sleep Tests (B-2).

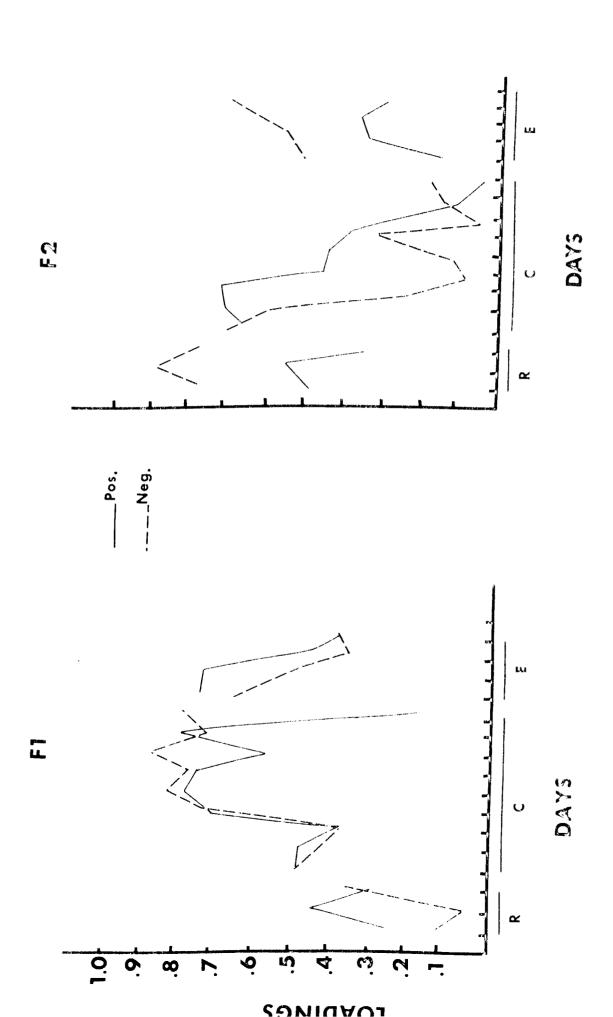
moment and examine the actual AEP waveforms that are shown in figure 15, it does look as though the AEPs elicited during sleep after conditioning are highly similar, and different in form from those elicited during the other sleep tests. After conditioning, the AEPs have a more pronounced initial negative deflection, and the subsequent positive deflection is flatter and of longer duration. This description is supported by the actual correlations amongst the 6 AEPs which are shown in table 6. The highest correlation, .79, is between the 2 after-conditioning waveforms. Other correlations involving these AEPs are low or negative. There is, then, some evidence from the reticular data that the stimuli are analysed differently after conditioning.

		Negative Tone		
	(1)	(2)	(3)	
Before cond. (1)	•75	54	.07	
Positive tone After cond. (2)	 72	<u>•79</u>	38	
After ext. (3)	47	<u>.53</u>	38	

Table 6. Showing the Correlations Between the Sleep Test Reticular AEPs Elicited by the Positive and Negative Tones (B-2).

Figure 16 shows the factor loadings from a 7 factor rotation for the cortical recordings. As can be seen, the AEPs load progressively higher on Fl as they fall off F2. The AEP elicited by the positive stimulus on conditioning day 10 is an unexplained exception. The high loadings on Fl fall off systematically over the course of extinction days, and the "random" day loadings are negligible. There is good evidence, then, (with the exception of the abberant day 10 loading) that Fl is a "conditioning" factor. In that the curves for both stimuli follow the same trend there is no evidence that a discrimination had taken place.

From the plots of the factor scores in figure 17, it is clear that factor 1 has a second, sharply defined, negative deflection that is not present in F2. Comparison of these plots with the representative AEP waveforms in figure 18, show that factor 1 characterizes the late conditioning AEPs, whereas factor 2 is characteristic of "random" and early conditioning AEPs.



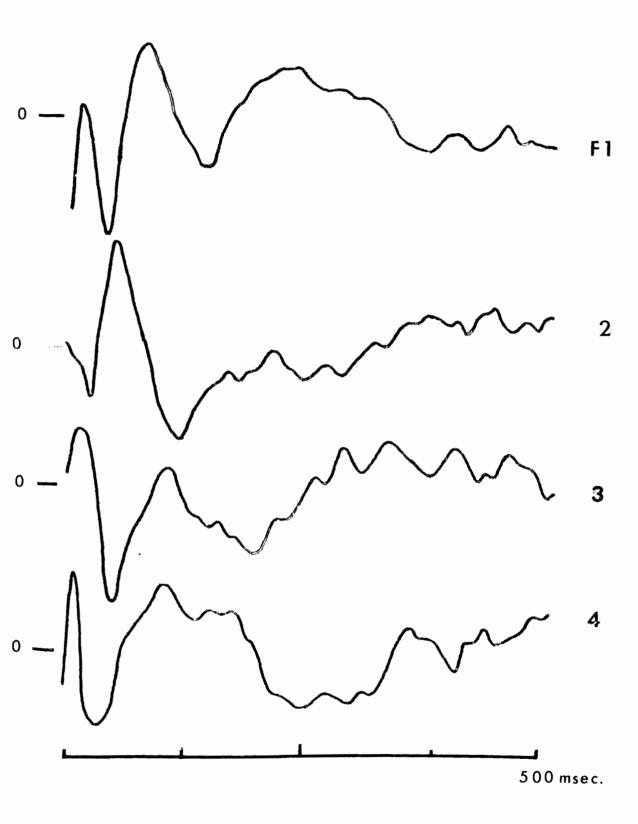


Figure 17. Plots of factor scores for auditory cortex AEPs, B-2.

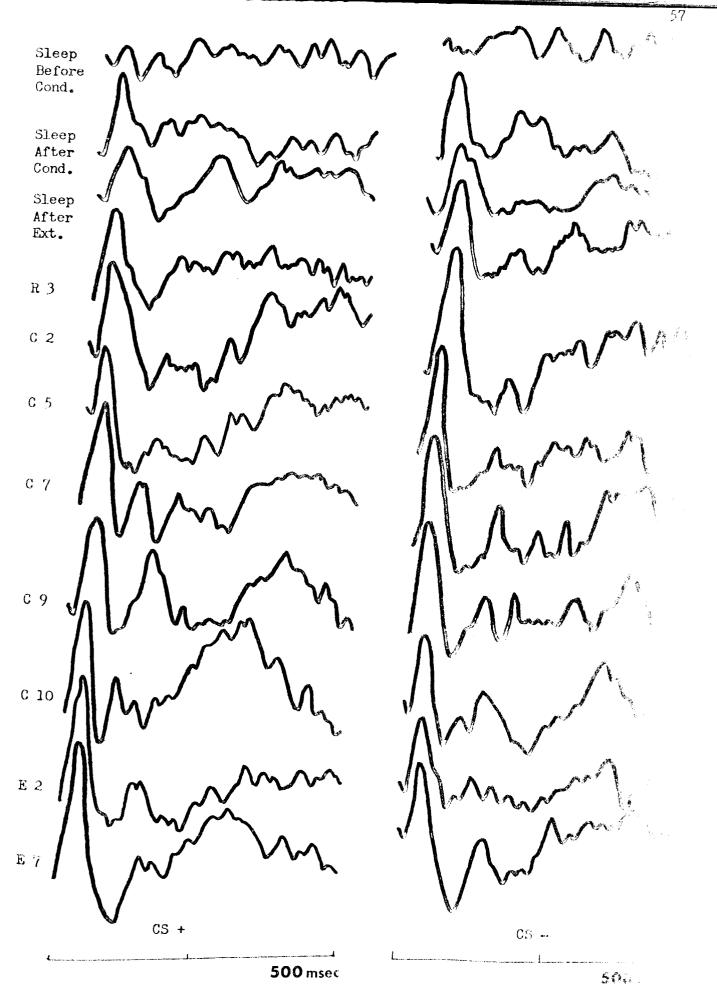


Figure 18. Sample auditory cortex AEPs, B-2. R - Random days; C - Conditional days; E - Extinction days.

So far as the sleep test data are concerned, both the positive and negative tone AEPs for the sleep test after conditioning load highly, .89 and .84, on factor 3. No other AEPs have even moderate loadings on this factor. The configuration of F3 is somewhat similar to that of F1, but the second, negative deflection is of longer duration and the waveform does not end with a long, low amplitude, negative swing as does F1. In that neither the reticular data nor the cortical data give evidence that this monkey had made a clear discrimination between the tones, it would seem reasonable to expect that these sleep AEPs should load on the same factor. That the AEPs from the other sleep tests do not load on the same factor, (F3), is also consistent with the evidence that at least some non-discriminative conditioning had taken place. Although the sleep-after-conditioning AEPs do not load on the "conditioning" factor, they are treated exactly alike in terms of their loadings.

Although, as it was pointed out above, the factor loadings of the reticular sleep-test data were difficult to interpret, visual inspection, and correlational data suggested that the AEPs for the after-conditioning, sleep test data were different from the other sleep-test data. The cortical sleep-test data directly support the notion that the stimuli are being analysed differently after conditioning. Both the reticular and the cortical data seem to show that, even during sleep, conditioned stimuli, as compared to neutral stimuli, are analysed or encoded differently. The two stimuli are, however, not treated differentially.

(iii) B-3.

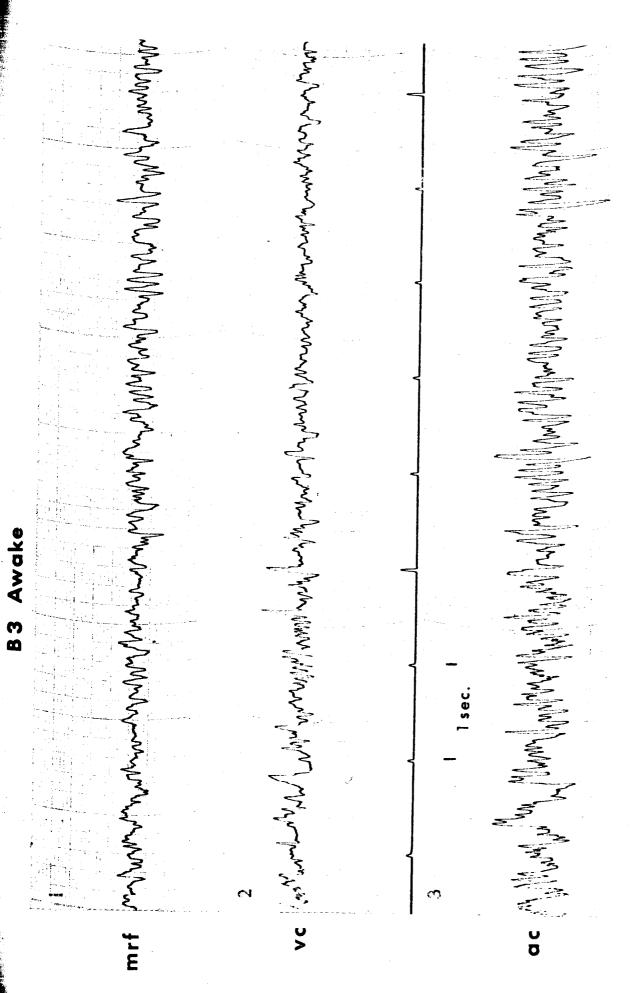
Samples of the EEG from the awake and asleep states are shown in figures 19 and 20.

So far as evidence for conditioning goes, the results from B-3 are disappointing. Referring first to the AEPs collected from the auditory cortex, samples of which appear in figure 21, it seems that there is little evidence of any systematic, stimulus-locked activity. The AEP waveforms do not have clearly identifiable peaks. Factor analysis of the data did not produce an interpretable factor structure in that the AEPs did not load un-ambiguously on any factors. The reason for the lack of any clearly evoked activity is not immediately apparent. The auditory electrode was not misplaced, and the on-going EEG records show that apparently normal activity was being picked up. It is clear, however, that we cannot make use of the cortical data.

as can be seen in the sample records in figure 22. Figure 23 shows the AEP loadings on the first 2 factors from a 7 factor rotation.

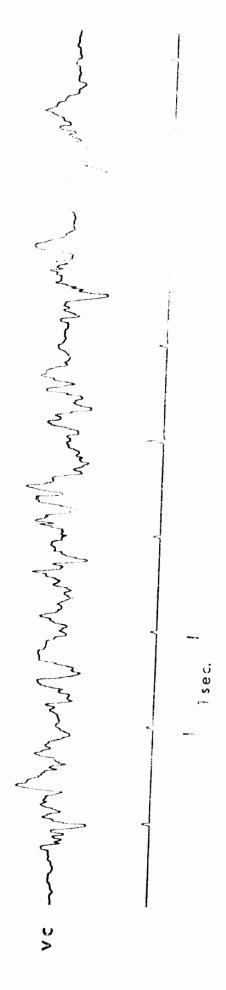
"Random" days 1 to 3, conditioning days 1 through 10, and extinction days 1 through 5 are included. Only an occasional AEP, from the "random" and extinction day records, had appreciable (>.70)

loadings in factors other than F1 or F2. It is apparent also that loadings in general tend to be split between the two factors. Most of the conditioning day AEPs for both positive and negative stimul. have a moderate loading on both factors. There is, however, a



Awake EEG for monkey B-3; mrf - mesencephalic reticular formation; vc - visual cortex; - auditory cortex, Figure 19.







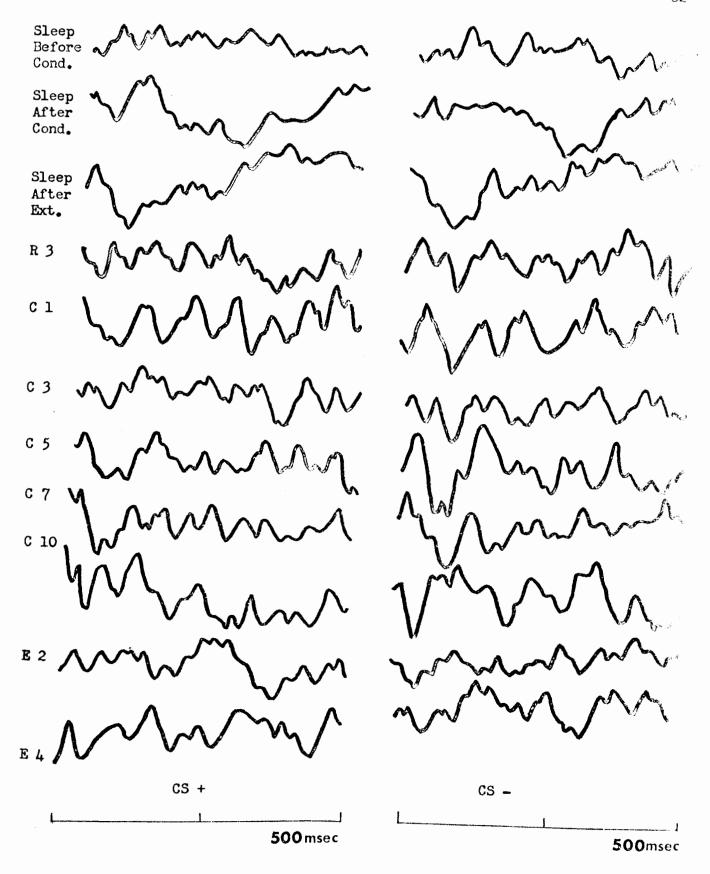


Figure 21. Sample auditory cortex AEPs, B-3; R - Random days; C - Conditioning days; E - Extinction days.

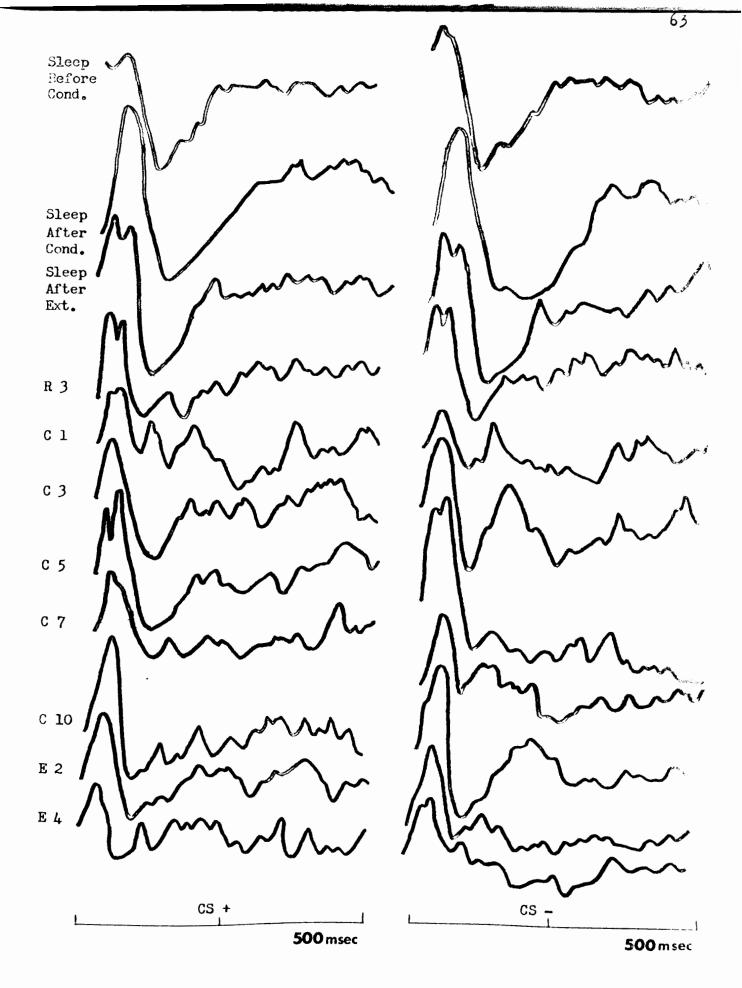
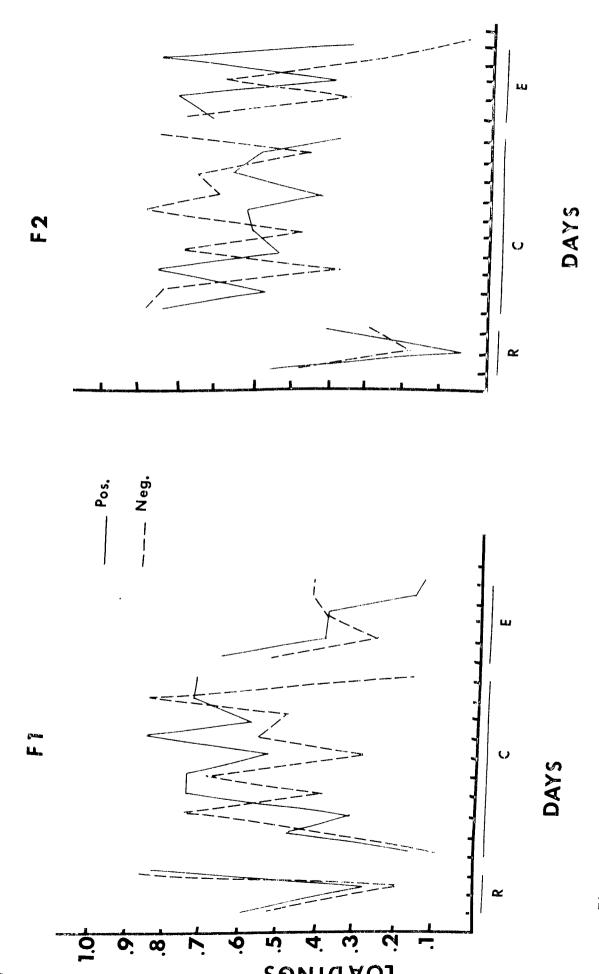


Figure 22. Sample reticular AEPs, B-3. R - Random days; C - Conditioning days; E - Extinction days.

tendency for the AEPs to load progressively more highly on Fl over the course of conditioning days. Interpretation of Fl as even a nondiscriminative factor is, however, complicated by the fact that the AEP for "random" day 3, for both positive and negative stimuli are highly loaded on F1 (>.82 and .86). Loadings on F1 during extinction days do, however, gradually fall off, particularly for positive-tone AEPs. The right panel of figure 23 shows the loadings on factor 2. Here, the separation of "random" from conditioning days is more clear, but the shift to F2 is not acquired gradually over days. Comparison of the sample AEP waveforms in figure 22, with the plots of factor scores in figure 24, shows that both Fl and F2 shapes are represented in the positive and negative tone records. The prime difference between the two shapes appears to be the direction of the late, slow wave deflection that begins 130 msec. after the stimulus. For factor 1, this deflection is negative, but positive for F2. might recall that for B-1, the factor defined as a conditioning factor, also possessed such a slow, negative deflection. It may be. then, that Fl is to some extent a conditioning factor, and perhaps with more conditioning days for B-3, it would have appeared clearly as The conclusion from the data is, however, that there is no substantial evidence that conditioning, as reflected in the AEPs, had occurred in B-3. We should expect, then, that the AEPs collected during sleep should all load highly on the same factors. do is clear from table 7, which shows the loadings on the first 2 factors.



R - Random days; 3 - Senditioning days; Factor loadings for reticular AEPs, B-3. E - Extinction days. Figure 23.

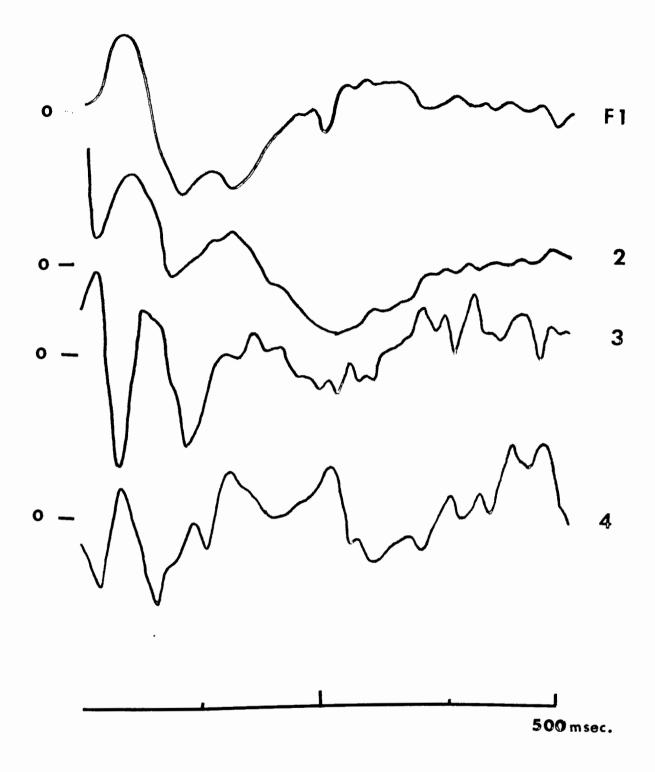
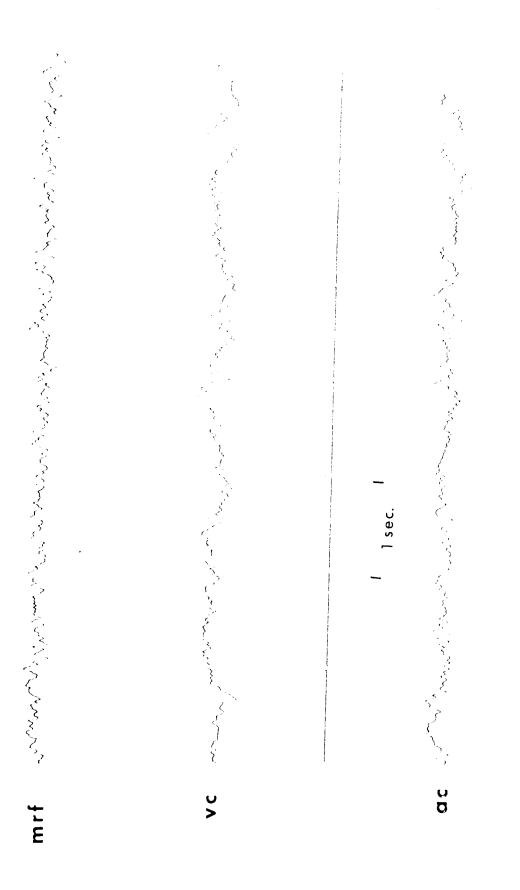


Figure 24. Plots of factor scores for reticular AEPs, B-3.

				F	actor
				1	2
]	Before	cond.	- <u>.91</u> *	09
Positive	tone	After	cond.	<u>.73</u>	.32
		After	ext.	.81	.32
		Before	cond.	- <u>.88</u> *	.02
Negative	tone	After	cond.	<u>.92</u>	.18
		After	ext.	.90	-17

(iv) C-1.

Samples from the awake and asleep EEG records are shown in figures 25 and 26. The loadings of the reticular AEPs on the first 2 factors from a 7 factor rotation are shown in figure 27. Shown in the figure are "random" days 1,2,3,5, and 6; conditioning days 3 through 18, and extinction days 1 through 6, and day 10. The positive and negative stimulus AEPs load moderately on Fl during "random" days, but throughout the conditioning days the positive tone AEPs load very highly on Fl, while the negative tone loadings drop off and begin to load on F2 after conditioning day 6. It can be noted also that on extinction days 3 and 5, the positive tone AEPs again load very highly on Fl; this might be a result of "spontaneous-recovery" of the conditioning effect.



Awake EEG for monkey C-1; mrf - mesencephalic reticular formation; vc - visual cortex; ac - auditory cortex. Figure 25.

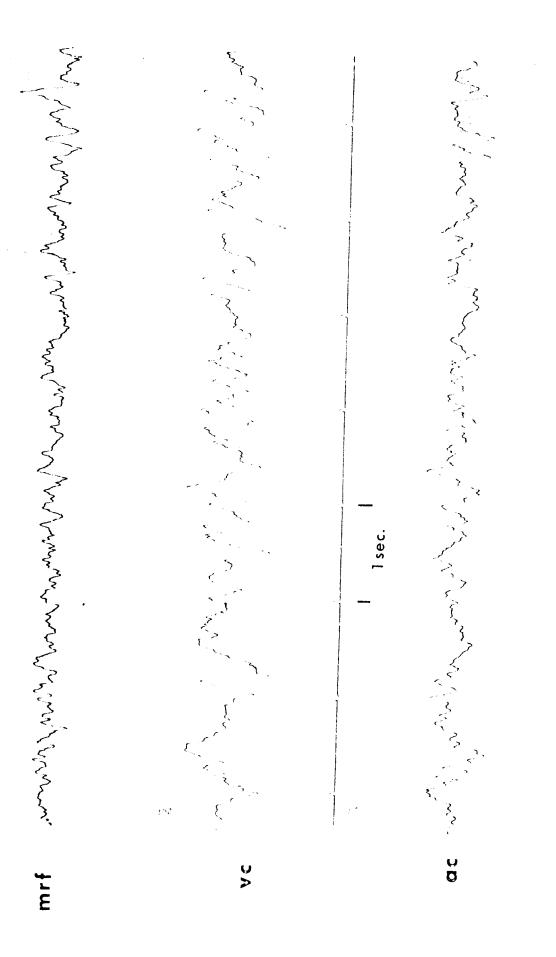


Figure 26. Asleep EEG for monkey C-1; mrf - mesencephalic reticular formation; vc - visual cortex; ac - auditory cortex.

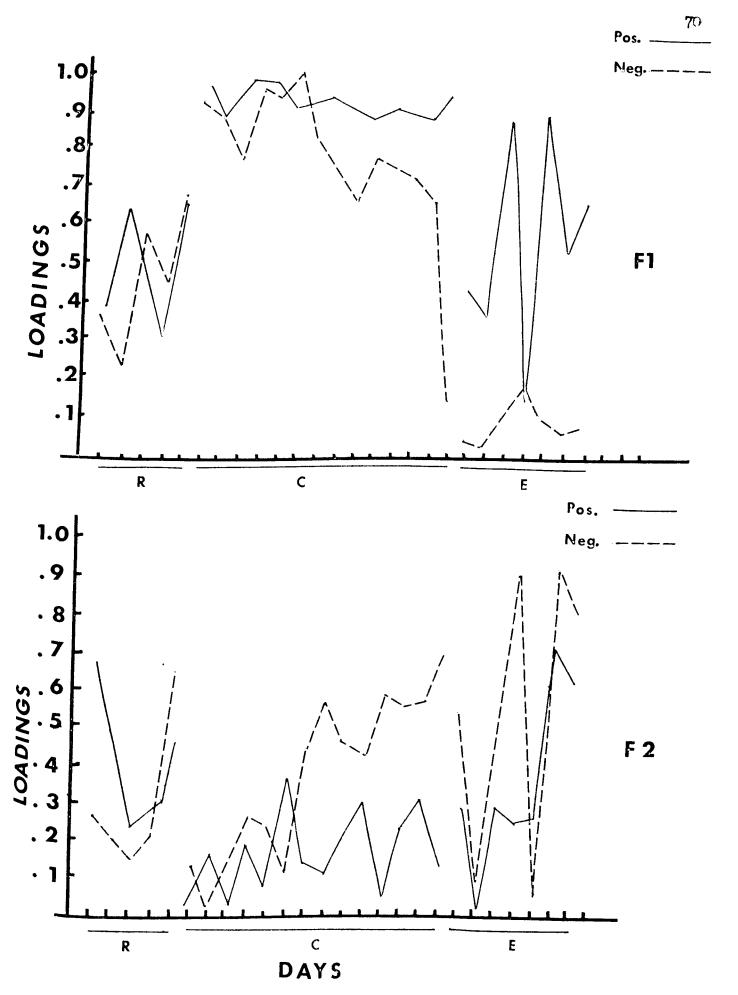


Figure 27. Factor loadings for reticular AEPs, C-1. R-Randon days; C - Conditioning days; E - Extinction days.

The shape of these factors can be seen in the plots presented in figure 28. Fl, the conditioning factor, is characterized by an initial positive deflection followed by a relatively low amplitude, negative/positive, hump which is followed by a long, slow, relatively high amplitude negative deflection. As can be seen from a comparison with the sample AEPs in figure 29 (complete day by day tracings of the AEPs appear in Appendix I), this factor characterizes the conditioning AEPs, particularly from the positive tone. AEPs elicited by both the positive and negative tones during conditioning are visually quite similar, but the first negative/positive "hump", and the slow negative deflection are more pronounced, late in conditioning, in the records of the positive AEPs. Factor 2 seems most characteristic of negative tone AEPs elicited during the extinction days. We shall see also that the records elicited during sleep also load highly on factor 2.

On the basis of the systematic shifts in the loadings on the factors that underlie the AEPs, C-l evidently has discriminated between the two stimuli.

Factor loadings for the reticular AEPs elicited during the sleep tests are presented in table 8. As is evident from the table, the sleep AEPs load most highly on factor 2. Such a pattern of loadings would indicate that the AEPs to the stimuli during sleep after conditioning are similar, and not different from those elicited during the other sleep tests. Characteristic of the sleep waveforms is the absence of the early negative/positive "hump" that appears in the conditioning records. Considering once again a visual analysis of the AEP waveforms shown in figure 29, it appears



Figure 28. Plots of factor scores for reticular AEPs, C-1.

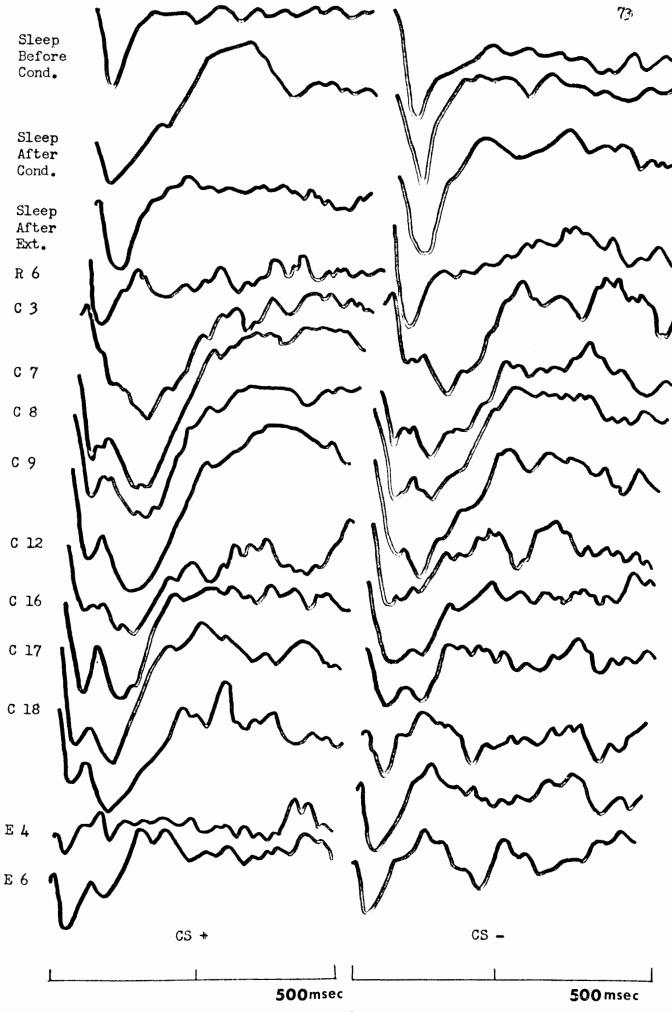


Figure 29. Sample reticular AEPs, C-1. R - Random days; C - Conditioning

that the positive AEP elicited in sleep after conditioning is somewhat different from the others. Only in this one record is there a small peak which appears about 125 msec. after stimulus onset superimposed on the ascending portion of the slow, negative deflection. The peak of this slow deflection is later and greater

		Fa	ctor
		1	2
	Before cond.	.24	.80
Positive tone	After cond.	.23	<u>•91</u>
	After ext.	<u>.66</u>	<u>.61</u>
	Before cond.	•33	<u>•77</u>
Negative tone	After cond.	.27	<u>•92</u>
	After ext.	.40	.86

Table 8. Factor Loadings of Reticular AEPs, Elicited During the Sleep Tests (C-1).

in amplitude than in all the other sleep records. Examination of the matrix of inter-correlations of the AEPs showed that this record is highly correlated with the positive tone records elicited during the other sleep tests - this does indicate overall similarity of the waveforms. The problem with the analysis of this particular AEP points out one of the drawbacks of the factor analysis technique. Here we are concerned with one isolated variable which in gross respects is similar to many other variables. It is highly correlated with other variables, and, accordingly, it loads on the same factor. However, were there more variables that it was even more highly correlated with, another factor could be extracted. On the other hand, we have seen

already, in the conditioning, data, that the factoring technique has high discriminating power in that it enabled the separation of a set of highly similar AEPs into separate factors. In this case, there were enough records to allow the production of the two different factors.

Tentatively, then, it is argued that the reticular AEP elicited by the positive tone during sleep after conditioning, is sufficiently different from other sleep records to allow us to conclude that the reticular area is "recognizing" the positive stimulus as being different from the negative.

The loadings of the cortical AEPs on the first 2 factors of a 7 factor rotation are presented in figure 30. Although the loadings across training days are more variable than for the reticular data, Fl does seem to emerge as a "conditioning" factor. Extinction day loadings remain high in Fl, but falls off precipitously on the final session. The shape of the factors is shown in figure 31 and may be compared with the sample AEP waveforms in figure 32. The major feature of Fl is a high amplitude positive/negative deflection that returns to a little above baseline at approximately 140 msecs. The remainder of the waveform consists of a very shallow, slow, positive/negative deflection. The configuration of F2 is basically similar, but the major positive/negative peak is less pronounced. The ascending, negative deflection reaches its peak earlier, at 125 msecs. The following, slow positive deflection is steeper and more pronounced than in factor 1. Factor 1 character-

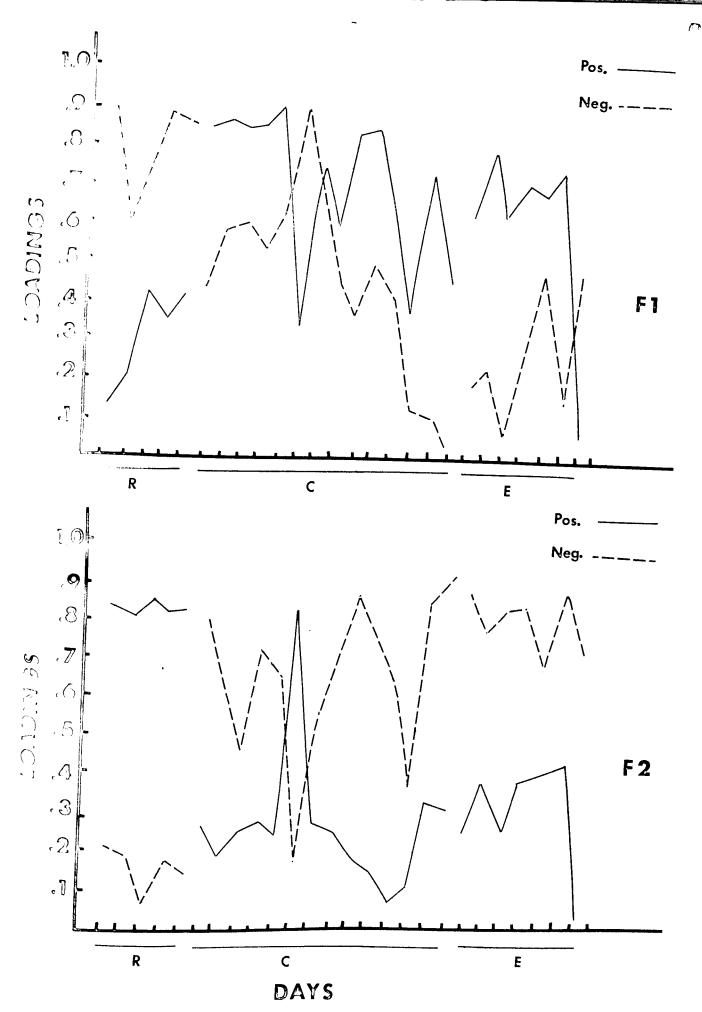


Figure 30. Factor loadings for auditory cortex AEPs, C-l. R - Random days; C - Conditioning days; E - Extinction days.

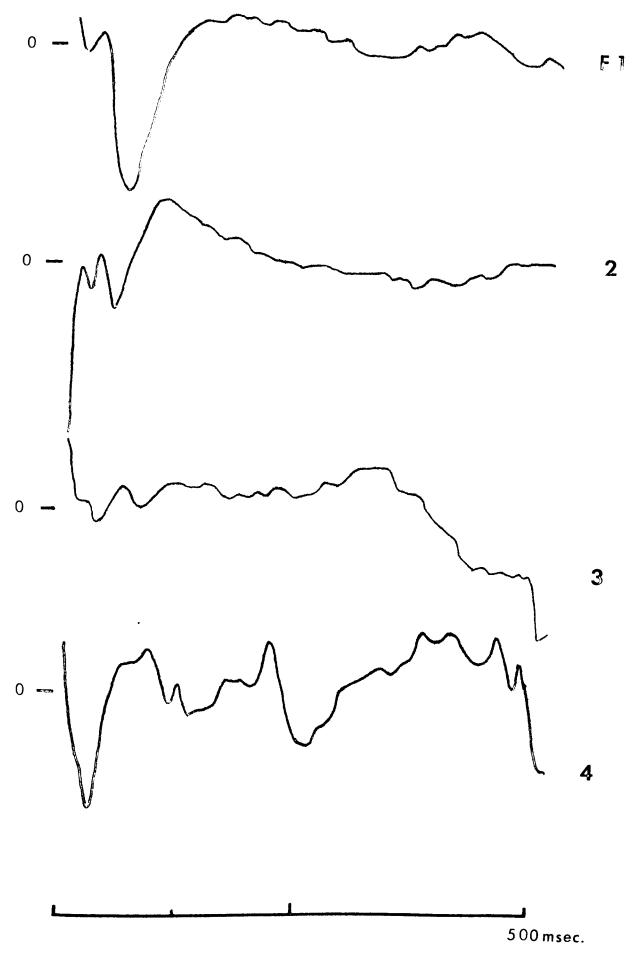


Figure 31. Plots of factor scores for cortical AEPs, C-1.

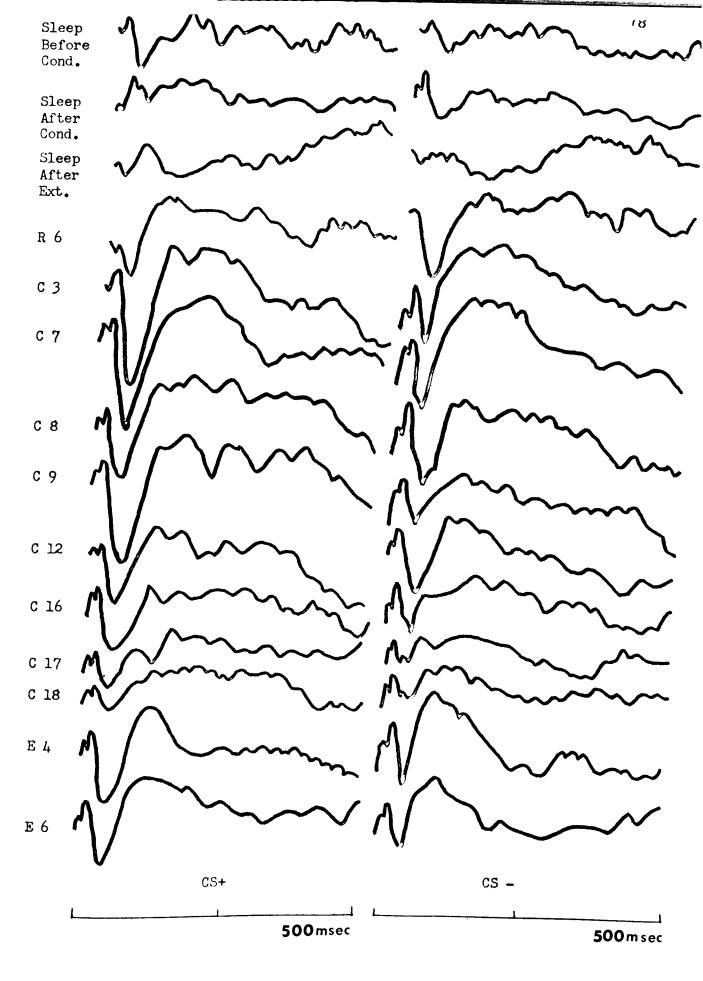


Figure 32. Sample auditory cortex AEPs, C-1. R - Random days; C - Conditioning days; E - Extinction days.

izes the late conditioning AEPs for the positive tone, while F2 characterizes the early positive AEPs and the later negative AEPs. Once again, as for the reticular data, the factoring technique has discriminated the slight differences underlying visually similar AEP waveforms.

Reference to the sample AEPs in figure 32 shows that the amplitude of the AEPs was much diminished during all of the sleep records. Table 9 (see under table 8), shows the unsystematic, and relatively ambiguous nature of the factor loadings for the cortical AEPs elicited during the sleep tests. The state of the data here does not seem to allow even speculative interpretation concerning how the cortex is responding to the 2 stimuli during sleep.

					racto	r		
		1	2	3	4	5	6	7
	Before cond.	- <u>.74</u>	24	.04	03	13	14	.3:
Positive tone	After cond.	03	<u>.50</u>	.09	17	.68	.05	.20
	After ext.	09	18	<u>-77</u>	•44	34	04	13
Negative tone	Before cond.	44	22	04	<u>.72</u>	05	18	26
	After cond.	•47	.26	.26	- <u>.71</u>	.04	.06	06
	After ext.	19	48	¬1 2	•30	28	13	- <u>.66</u>

Table 9. Factor Loadings for Cortical AEPs Elicited During the Sleep Tests. (C-1).

Attention may be drawn to the extreme diminution in the amplitude of the cortical AEPs to both took during the final 3 conditationing days. Although relative amplitudes of the various deflections were maintained, the overall amplitude declined considerably, but

recovered on subsequent days. Such a decrease in amplitude was not observed in the other monkeys, nor was it evident in the reticular recordings. The decrease is thought to be related to the fact that C-1 developed an infection that produced suppuration around the electrode cap at precisely this stage of training. Administration of antibiotics cleared up the suppuration almost immediately. If the suppuration had seeped under the skull around the electrode site, the increased resistance could have accounted for the temporary decrease in AEP amplitude.

(v) M-8.

We turn now to the data from the operantly trained animals, M-8 and M-9.

As described in the procedure section, these monkeys were trained to make a lever press within 1.5 seconds of the tone signal. They could obtain a maximum of 64 reinforcements if they pressed within the time limit. They both learned this go, no-go response almost perfectly, without making more than a few extra responses.

The AEPs from various training and extinction days, and for the sleep tests after training and after extinction are shown in figures 33A and 33B. (Examples of the awake and asleep EEG are presented in figures 34 and 35.

As the monkey learns to perform the task without extra presses, the reticular AEP develops 2 high amplitude negative/positive peaks, each of which has a small positive/negative "jog" superimposed at the top. The second major peak seems to be slightly lower in amplitude.

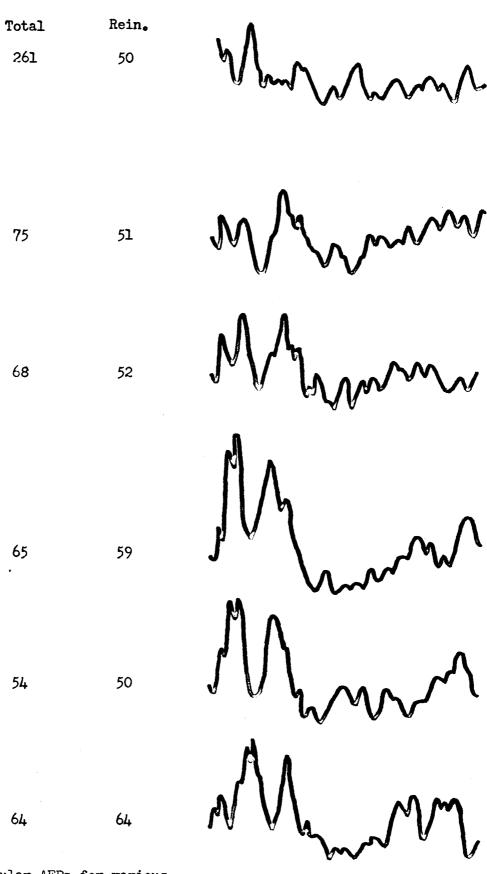
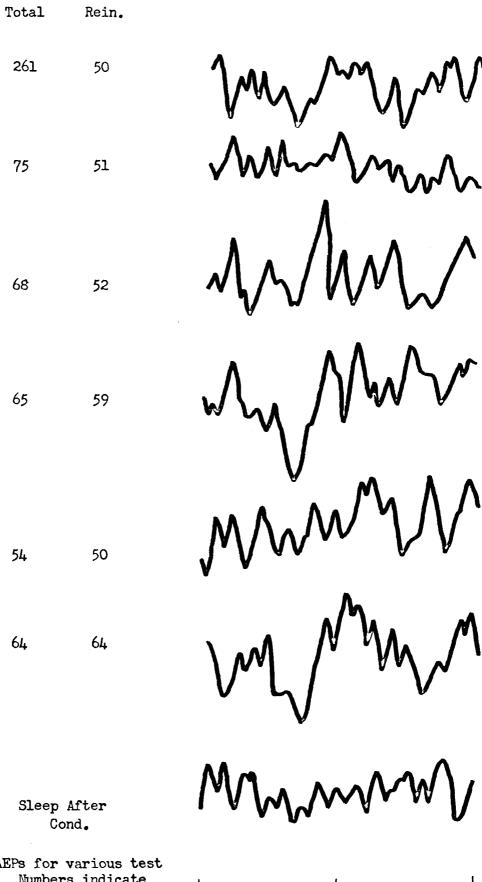


Figure 33A. Reticular AEPs for various test days, M-8. Numbers indicate total bar presses and total reinforcement for

Total Rein. Sleep After Cond. Sleep After Ext.

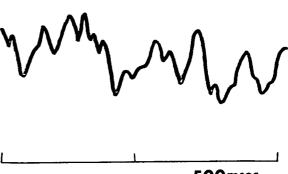
Figure 33A Con'd



gure 33B. Cortical AEPs for various test days, M-8. Numbers indicate total bar presses and total reinforcement for each day.

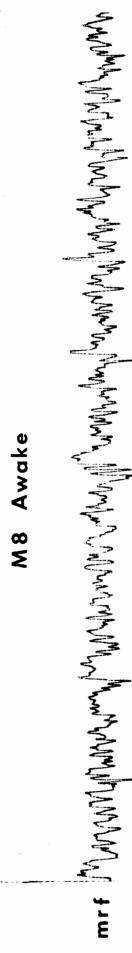
Total	Rein.	1 2 M 20 2 A2 A2
150	0	
35 7	37	Www.W
7	4	
0	0	

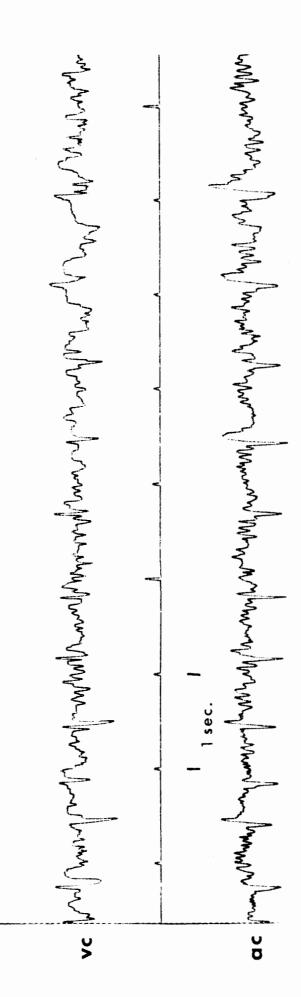
Sleep After Ext.



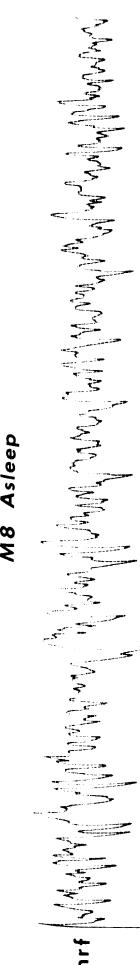
500msec

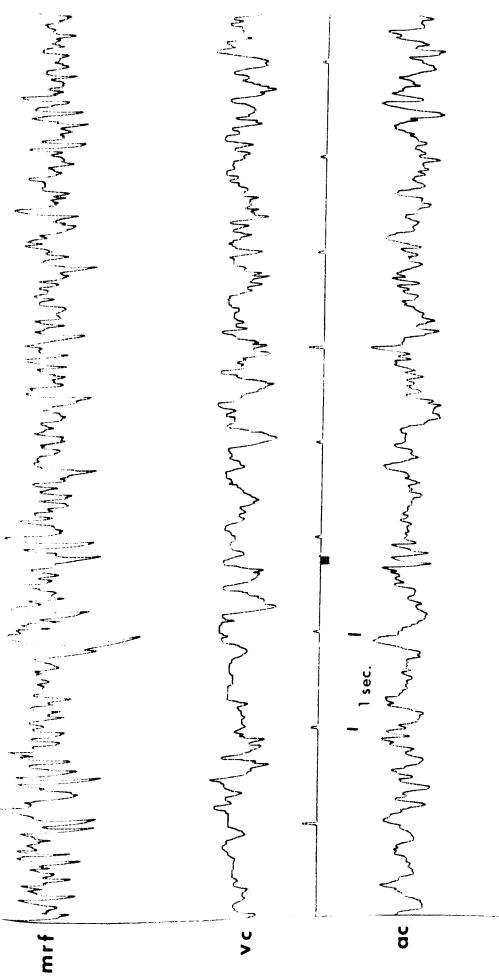
igure 33B Con'd





Awake EEG for monkey M-8; mrf - mesencephalic reticular formation; vc - visual cortex; ac - auditory cortex, Figure 34.





Asleep EBG for monkey M-8; mrf - mesencephalic reticular formation; vc - visual cortex;

Factor loadings from a 5 factor rotation are shown in table 10. Days 3 through 6 load highly on factor 1, the shape of which is shown in figure 36. (In comparing the factor shapes with the AEP waveforms, it should be noted that the factors are stretched out in time, relative to the AEPs). The day 6 waveform, which seems to have the major peaks displaced a few msecs. to the right, was recorded after the monkey had been re-trained after some extinction The similarity of this AEP to the other "trained" AEPs attests to the reliability of the records. Also evident in the "trained" AEP waveform is a slow, shallow negative deflection. Two separate extinction factors appear in the data. Extinction days 3 and 4 load highly on factor 2. It will be noted that extinction on these days was almost complete; in fact, no responses at all were made on day 4. During the first 2 extinction days the monkey pressed the lever indiscriminately. This generally agitated state produced much "noise" in the AEP records. This noise is reflected in factor 4, on which extinction day 2 is highly loaded.

	Factor						
	1	2	3	4	5		
Training day l	<u>•59</u>	.12	11	•33	41		
2	.12	.10	.03	.17	.88		
3	<u>.82</u>	.11	.13	.29	05		
4	<u>.89</u>	.05	.26	04	•03		
5	.84	26	.11	.13	.20		
6	.82	.04	20	05	12		
7	<u>.72</u>	.3 9	08	05	.12		
1	<u>.58</u>	.18	37	.04	49		
2	.09	10	.02	<u>•91</u>	.14		
3	.36	<u>.82</u>	09	19	05		
4	13	<u>.91</u>	02	•04	.08		
Sleep after training	.56	31	- <u>.51</u>	13	33		
" " extinction				.00	03		

Table 10. Factor Loadings for Reticular AEPs (M-8) (See table 11 for bar Press Data).

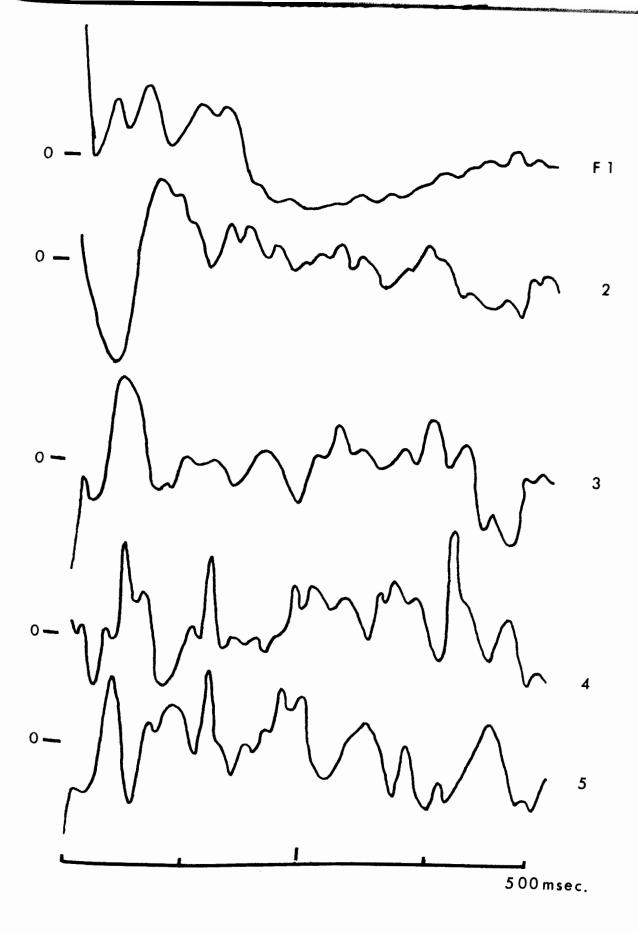


Figure 36. Plots of factor scores for reticular AEPs, M-8.

The AEP from the sleep test after conditioning has moderate and low loadings on factors 1, 2, 3, and 5. The AEP, although difficult to classify, does seem to have a slow, negative deflection towards the end, which might account for its moderate loading on Fl. However, training day 1, in which the monkey made many extra responses also has a moderate loading on Fl.

The AEP recorded during sleep after complete extinction, is the only variable with a high loading on factor 3. (In comparing the AEP with the factor shape in this case, the factor should be "reflected", i.e., turned up-side down.) That the 2 sleep AEPs are uncorrelated, and hence, of course, load on different factors is, again, some evidence that the reticular area is responding to the signal differently during sleep after conditioning, compared to after, extinction.

Cortical recordings from M-8 are quite disappointing (most likely because the temporal electrode was placed too far posteriorly). The AEPs are shown in figure 33B. In general, they can best be described as "noisy", with little evidence of any clearly stimulus—locked evoked deflections. The factor loadings from a 7 factor rotation are shown in table 11. No discernible factor structure is evident. Visual inspection of the AEPs, presented in figures 33B

does not reveal any systematic changes, either.

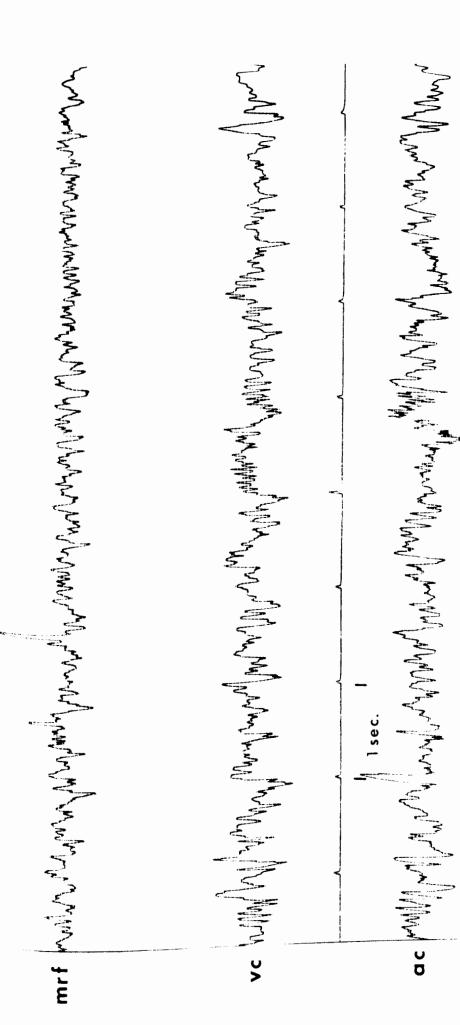
The data from M-8, then, are primarily interesting in that they show clear changes in the reticular AEP waveforms, contingent on changes in level of training.

		Facto	Total Resp.	Reinforced Resp.			
	1 2	3 4	5	6	7		
Training day 1	0210	11 <u>.85</u>	02	•03	05	261	50
2	2002	.0401	03	•09	<u>•96</u>	75	51
3	.31 .03	<u>.69</u> .16	24	28	.04	68	52
4	.44 .02	.1218	.36	- <u>.67</u>	.14	65	59
5	.22 .07	<u>.61</u> 45	.03	29	16	54	50
6	•35 - <u>•63</u>	06 .04	.08	48	05	73	60
7	<u>.73</u> 20	.3009	03	23	23	64	64
Extinction day 1	.08 .86	1101	01	18	04	150	10
2	.1733	35 - <u>.60</u>	.00	29	15	357	37
3	.31 .28	- <u>.71</u> .05	04	29	15	7	4
4	<u>.90</u> .07	0807	.01	.02	11	0	O
Sleep after cond.	0104	0901	<u>•97</u>	04	03		
Sleep after ext.	.0407	06 .12	.06	.88	.16		

Table 11. Factor Loadings for Cortical AEPs (M-8). Total Responses and Number of Reinforcements Gained are Also Shown.

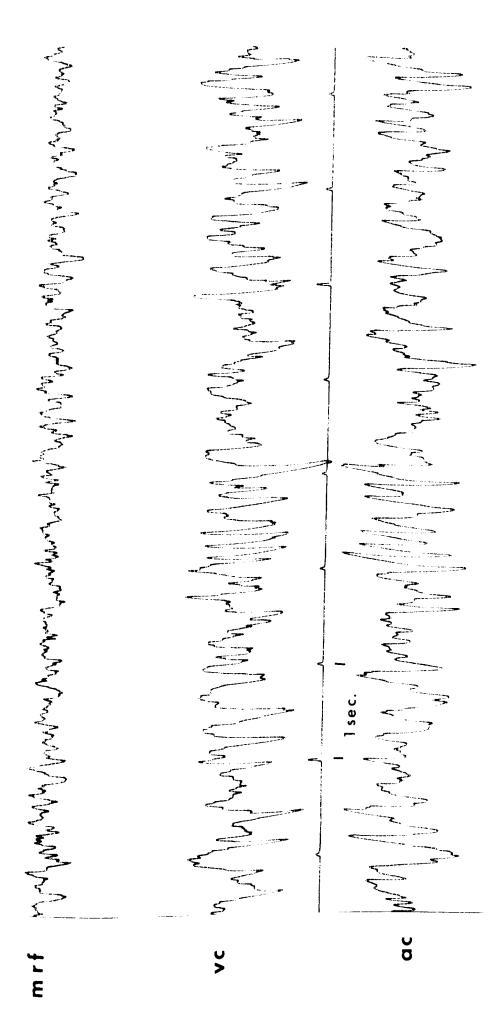
(vi) M-9.

Awake and asleep EEG records are shown in figures 37 and 38. The reticular AEPs from various training days are presented in figure 39. The AEPs from the pre-trained and extinction records are characterized by a short latency, high amplitude, positive/negative deflection. As the monkey learns the task, the initial peak diminishes in amplitude and a later, at about 130 msecs., high amplitude, negative/positive peak becomes predominant. Another, late, negative peak is evident on training days 3, 6, and 7. Factor loadings for the reticular AEPs are shown in table 12. The fact is scores as a presented in figure 40, (which should be compared with figure 39). Factor 1, which seems best described as a "non-trained" factor, clearly shows a shape



M9 Awake

Awake EEG for monkey M-9; mrf - mesencephalic reticular formation; vc - visual cortex; ac - auditory cortex.



Asleep EEG for monkey M-9; mrf - mesencephalic reticular formation; vc - visual cortex; Figure 38.

Total Rein.

No training

39 16

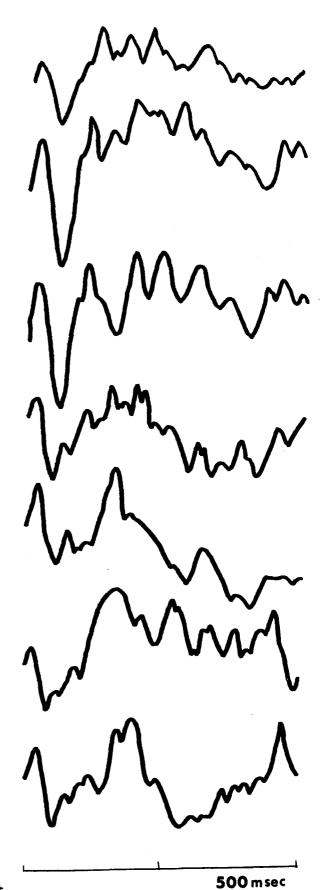
49 17

115 59

114 50

87 58

70 58



igure 39. Reticular AEPs for various test days, M-9. Numbers indicate total bar presses and total reinforcement for each day.

Total Rein.

Sleep After Training

69 63

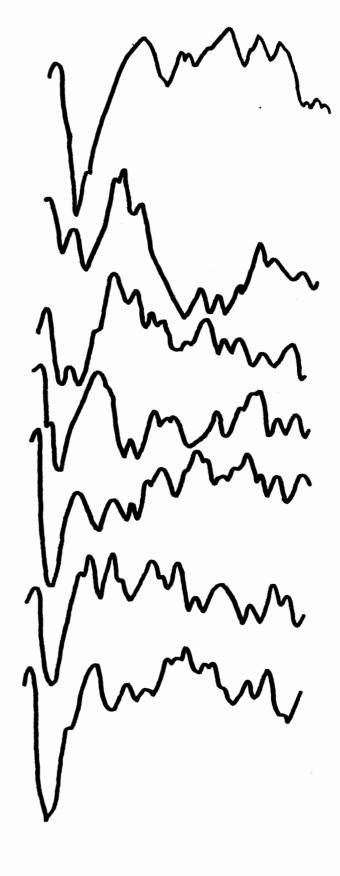
72 63

49 46

38 33

0 0

Sleep After Ext.



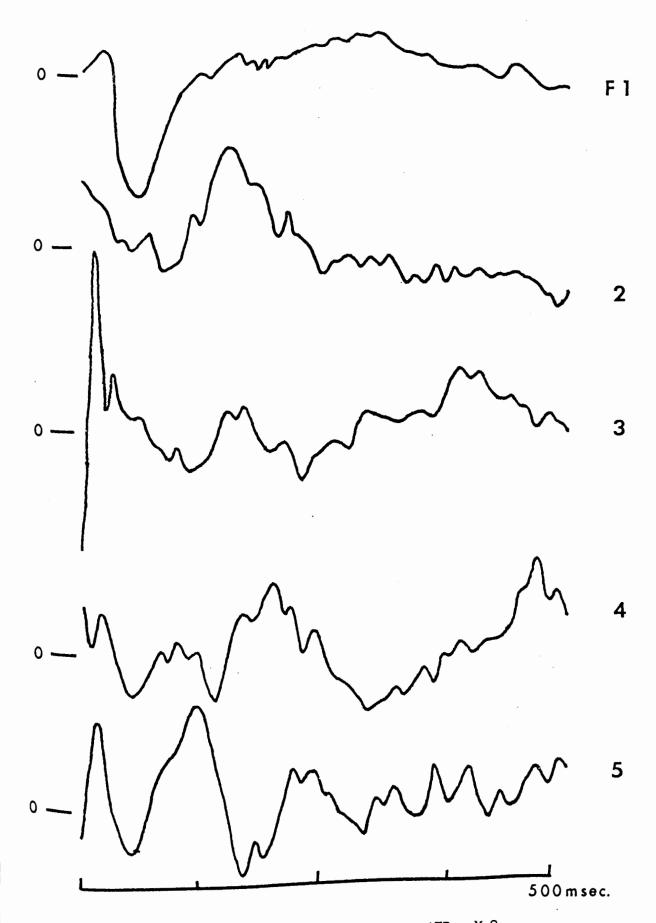


Figure 40. Plots of factor scores for reticular AEPs, M-9.

characteristic of the early training days, the last 2 extinction days, and both the sleep test days. The training days 7 and 8, where discrimination is at its best, load most highly on factor 2, which most clearly shows the large, negative/positive peak. Training day 4, where there are still many extra responses, also loads highly on the same factor. Other discrepancies in the loadings of the training day AEPs are also clearly evident. For instance, day 5 reverts to a moderately high loading on Fl, while day 6 loads very highly, and almost uniquely, on F4. Although a basic waveform pattern for the training days is evident, it seems that slight changes in the latency of the major negative/positive deflection at around 130 msecs. are destroying any neat factor structure. Contributing to the instability of the factor loadings also is the presence or absence of the late negative deflection that can be seen in the records of days 3, 6, and 7. It is as though the late training day AEP waveform, though clearly different from the extinction and early training day patterns, had not completely stabilized. Had there been more training day AEPs to enter into the analysis, a more stable factor structure should have emerged.

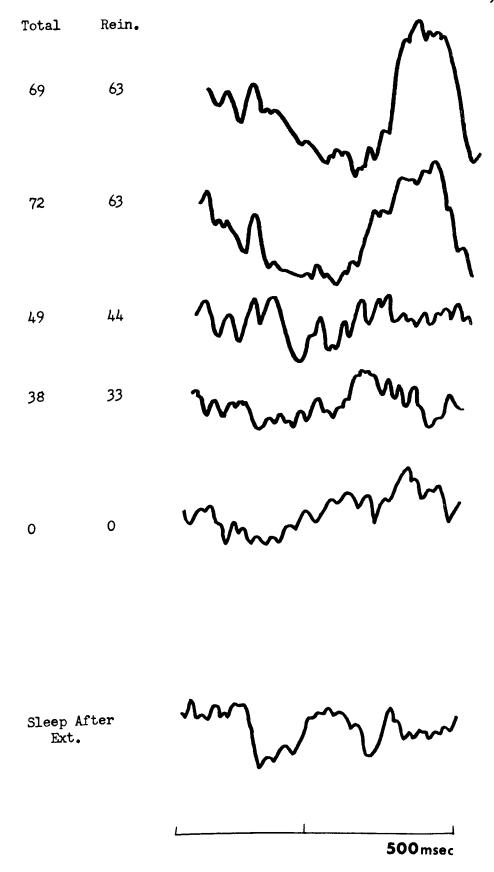
	1	2	3	4	5	Total Resp.	Reinforced Resp.
Prior to any training	.14	01	79	01	25		
Training day l	<u>.86</u>	.08	31	. 22	•06	39	16
2	<u>•77</u>	16	 36	.18	.24	99	17
3	•33	<u>.56</u>	25	<u>.60</u>	•07	115	59
4	04	<u>.87</u>	12	.21	.03	114	50
5	<u>.71</u>	.27	07	.14	53	87	58
6	.13	.20	.07	<u>•93</u>	05	7 0	58
Sleep before cond.	- <u>•94</u>	05	02	12	•06		
Training day 7	24	.80	.32	.25	.02	69	63
8	<u>.60</u>	<u>.72</u>	05	09	12	7 2	63
Extinction day 1	.24	.27	.25	•00	.85	49	46
2	<u>.73</u> -	36	.32	.07	.16	38	33
3	<u>.77</u>	.27	 30	.16	.18	0	0
Sleep after extinction	<u>.94</u> -	.04	.01	09	•09		

Table 12. Factor Loadings for Reticular AEPs (M-9). Total Responses and Reinforcements are also Shown.

As noted above, the 2 sleep test AEPs load squarely on Fl. They are clearly quite similar to each other and different from the "trained" AEPs. If neural encoding of the signal has taken place, it is clearly not being read out in the reticular area during sleep.

Cortical AEPs are presented in figure 41. The dominant feature is the late, high amplitude, negative deflection that drops off just before the end of the waveform, that is present after the animal has learned the task. It is also present in reduced form in the early

Figure 41. Auditory cortex AEPs for various days, M-9. Numbers indicate total bar presses and reinforcement for each day.



training days 3 and 4, where the animal is still making many extra responses, but earning most of the possible reinforcements. factor loadings, from a 5 factor rotation shown in table 13, present a perplexing picture. The AEPs from training days 4, 5, and 6 do load highly on Fl, whose shape is shown in figure 42, but days 3, 7, and 8, which also show the late, high amplitude, negative peak do not load at all on this factor. Other rotations do not provide a more satisfactory picture. The A possible reason for the lack of a satisfactory factor solution might lie in the fact that much high frequency activity is superimposed on the basic waveform. This "error" variance would substantially lower the correlations between the waveforms. Also, as was pointed out in the discussion of the reticular data, minor discrepancies in the latencies of the major peaks would also tend to attenuate the correlations between AEPs with a generally similar waveform. Perhaps even more important is the fact that for M-8 and M-9, we are dealing with a limited number of variables from which to construct a factor structure.

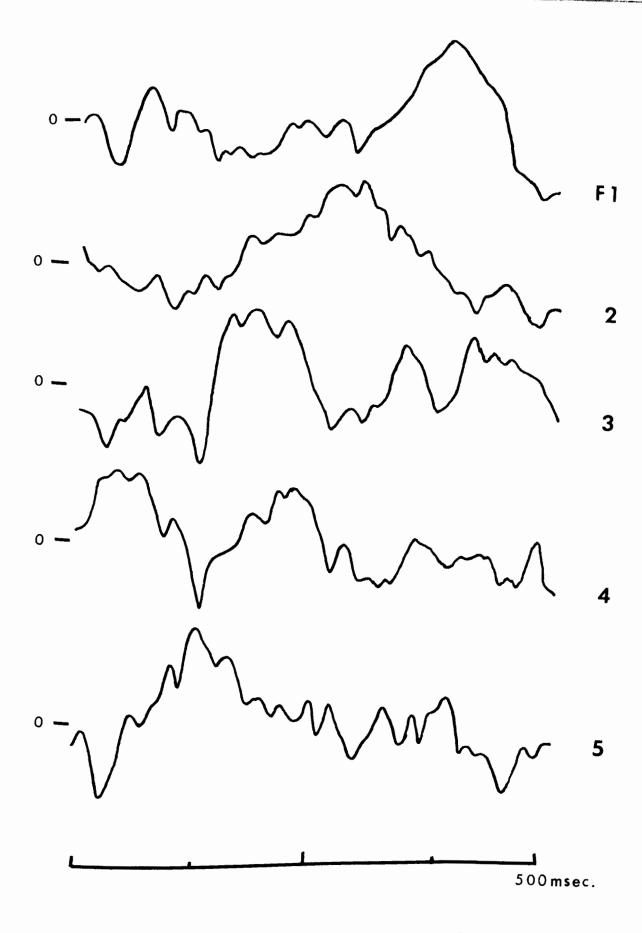


Figure 42. Plots of factor scores for auditory cortex AEPs, M-9.

			Facto	r	
	1	2	3	4	5
Prior to any training	.38	.01	35	25	- <u>.65</u>
Training day 1	.03	- <u>•59</u>	.05	22	- <u>.67</u>
2	.08	- <u>.81</u>	•07	23	.03
3	.19	- <u>.87</u>	•04	12	21
4	<u>.78</u>	32	14	33	23
5	<u>•95</u>	05	01	02	13
6	<u>•74</u>	33	11	19	45
Sleep after training	.19	07	.03	- <u>.91</u>	19
Training day 7	18	<u>.87</u>	•33	03	•20
8	.10	- <u>.59</u>	.10	- <u>.73</u>	20
Extinction day 1	30	•47	.25	02	<u>•75</u>
2 ·	19	.64	•45	.04	.40
3	.41	06	04	42	- <u>.72</u>
Sleep after Extinction	•06	05	- <u>•95</u>	.07	13
		al AFDa	(M 0)		

Table 13. Factor Loadings for Cortical AEPs (M-9).

The AEPs elicited during the sleep tests do not possess any of the major characteristics of the training day AEPs, and they appear to resemble extinction and "pre-trained" waveforms more than anything else. There is no visual evidence to lead to the conclusion that the stimulus is being treated by the cortex more as a discriminative than a neutral stimulus, and we shall conclude, as we did for the reticular data, that the stimulus is not being recognized as significant during sleep.

It will be recalled that the monkey had a 1.5 second interval within which to press the lever for a reinforcement. Although response latencies were not formally recorded, observation of the monkey after he had been trained indicated that the response occurred well beyond the .5 sec. duration of the AEP. It is possible then that the late, negative/positive component of the AEP is related to the monkeys' intention to respond. It is interesting to note that the components of the reticular AEP that were condidered to be related to the discriminative nature of the AEP occurred much earlier than the late cortical response. This was true in both M-8 and M-9, although in the case of M-8, no consistent cortical evoked activity was recorded. It would seem, then, that there is evidence that the reticular area analyses the significance of the stimulus before the cortex.

The data from M-9 are also interesting in that it was the only animal that showed evoked activity in the visual area. On training days 3 through 8, a high amplitude negative/positive peak occurs about 50 msecs. before the high negative peak at the end of the auditory cortex response. This peak may be due to an orienting response to the stimulus after it has become significant. The records from the visual cortex for M-9 appear in figure 43.



msec

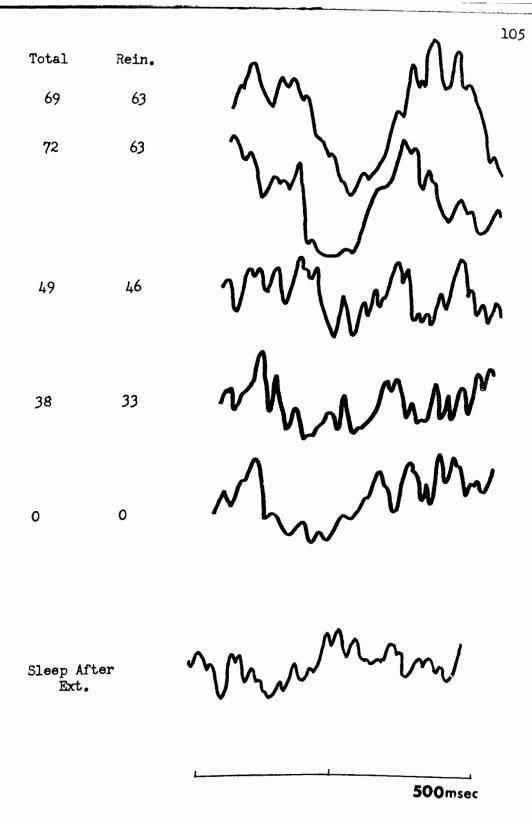


Figure 43 Con'd

CONCLUSIONS AND DISCUSSION.

A conditioning factor was tentatively identified for monkeys B-1, B2, and C-1. The shapes of these factors may be compared in figures 44 and 45. The shape was not identical, but for the reticular data, a late, negative deflection was identified in each. It is assumed that this late component is indicative of the monkeys conditioned anticipation of reinforcement. The three factors identified as conditioning factors from the cortical data are shown in figure 45. Again, the shapes are not identical; however, in B-1 and B-2 there is a slow, negative deflection in the middle portion of the waveform. For C-1, it was noted that the difference between the conditioning factor (F1) and the unconditioned factor (F2) was that the late component of F2 fell off in a slow, shallow, positive deflection. This did not appear in Fl. There is some evidence, then, that the conditioning factors are characterized by a relatively late, negative deflection, both cortically and reticularly. It is not claimed that these deflections constitute the neural code for the conditioned stimuli, but only that they are at least indicative of the monkeys' anticipation of forthcoming reinforcement.

From figure 27, it can be seen that for C-1, where there was evidence that discriminative conditioning had occurred, the reticular conditioning factor appears to separate out on conditioning day 9. Cortically, the separation appears throughout conditioning. It is noted, also, that in B-2, no evidence for discrimination was found in the reticular data, but there was evidence of the development of a discrimination, cortically. Also, the negative deflection previously referred to, occurs temporally prior in the cortical AEPs. There is,

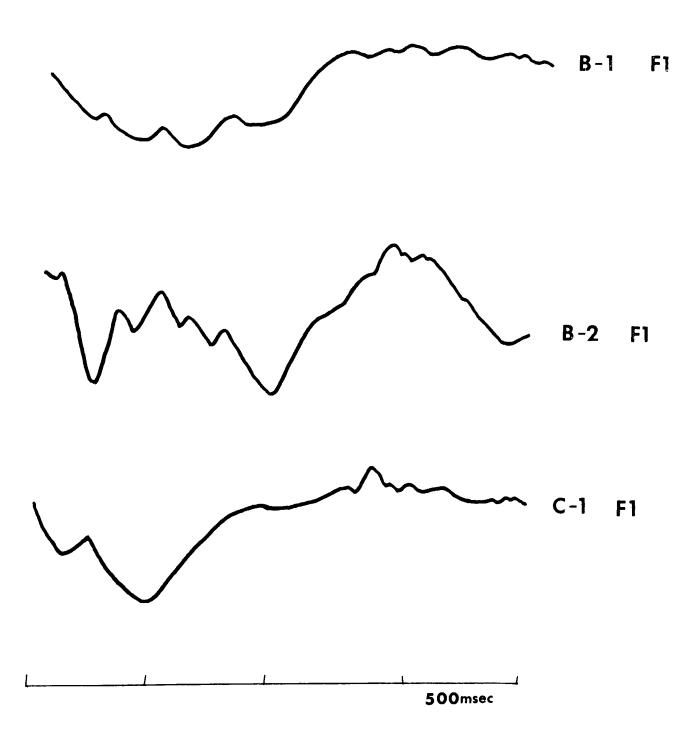


Figure 44. Plots of factor scores for reticular "conditioning" factors.

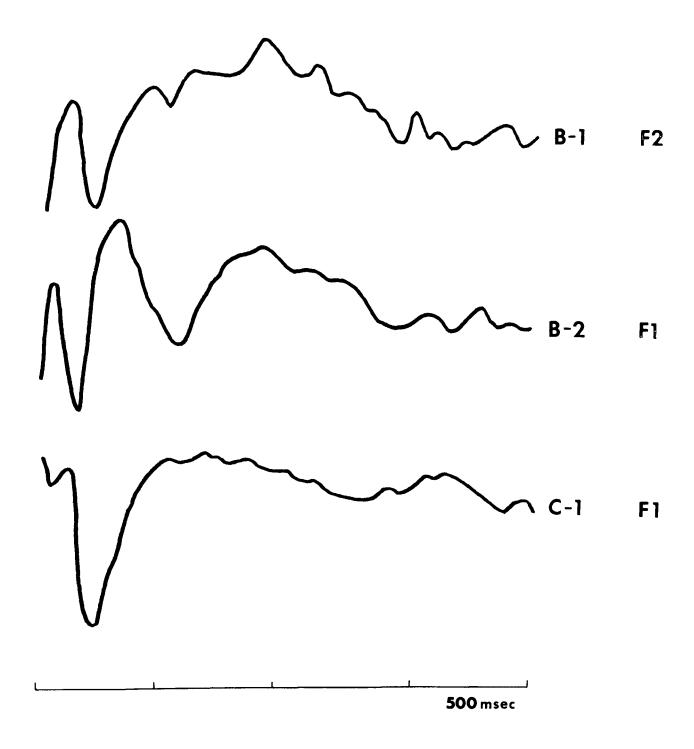


Figure 45. Plots of factor scores for cortical "conditioning" factors.

then, some indication that the discrimination occurs first at the cortex, but is later apparent in the reticular area, also.

Originally, it was thought that it might be possible to show that underlying the AEPs elicited during sleep after conditioning, there was a factor that could be identified with the "awake" conditioning factor. Such was not the case, except for B-1. However, it has been argued that, particularly in the reticular area, the AEPs during sleep after conditioning were sufficiently different from those elicited in the other sleep tests to warrant the conclusion that the brain is recognizing the stimuli as being different from neutral, or unconditioned stimuli. There is no evidence that a permanently established neural code is being "readout" during sleep. As noted above, it is claimed only that the changes in the AEPs are indicative of the changes in brain state that are contingent on the conditioning procedure.

In the operantly conditioned monkeys, changes in the earlier components of the reticular AEPs were clearly evident after they had learned the task. In the case of M-9, a clearly identifiable, negative/positive peak was also evident in the cortical AEPs. It might be noted here that the changes in the AEP that are considered indicative of conditioning appear temporally prior in the <u>reticular</u> records. John, (1967), has also reported that components of the AEP related to conditioning (operant) seem to appear earlier in the reticular, compared to the cortical records.

There was no evidence from M-8 or M-9 that the significance of the stimulus was being recognized either cortically or in the reticular area during sleep.

It is interesting to note that there is evidence that the brain is responding, during sleep, to the significance of a classically conditioned CS, but not to the significance of the operant CS. To speculate briefly concerning the implication of this difference, it might be noted that the operantly trained monkeys' task is, in a sense, two-fold. He learns that a particular CS is a reliable indicator that food is available, but only if he makes a behavioural response; i.e., presses a lever. On receipt of the stimulus, then, the brain must assess it for it's significance — is it the discriminative stimulus? An overt behavioural response, then, must then be emitted if reinforcement is to be obtained; i.e., a particular behavioural response is "attached" to a particular stimulus. The changes in the AEP waveforms that occur as the monkey learns the go, no-go discrimination while he is awake are assumed to reflect the entire process of (1) recognizing the stimulus, and (2) preparation for the emission of the correct response.

The form of the AEP, recorded during sleep after training was complete, was virtually identical to those recorded during the awake states before training and after extinction. During sleep, the brain apparently was not responsive enough to process the information conveyed by the stimulus and emit the appropriate behavioural response. The task of integrating the stimulus information with the appropriate response mechanism is, perhaps, too difficult for the sleeping brain.

In the case of the classically conditioned monkeys, no specific behavioural response has to be attached to the stimulus. Changes in the AEP waveforms overthe course of classical conditioning days are thought to reflect the animals' anticipation of forthcoming re-

inforcement. The reinforcement here is not contingent on his attaching an instrumental response to the stimulus. It might be claimed that, in this case, the brain has a simpler task to perform; the stimulus information does not have to be integrated with a particular motor response. The finding that the AEPs recorded during sleep after conditioning are different from those recorded prior to conditioning indicates that the brain, during sleep, is still responding appropriately enough to recognize the significance of a CS so long as that CS does not carry information that requires the further task of producing a specific behavioural response.

A section of the Introduction referred to the controversy concerning the nature of the AEP. Specifically, does the AEP reflect psychological codes, or is it more accurately described as an index of more general changes that occur in the brain contingent on changes in the independent variables? Put another way, do the differences in AEPs elicited by a "meaningful" as opposed to a "non-meaningful" stimulus constitute the informational value of the stimulus, rather than merely reflecting a general change in the subject's brain activity?

The most impressive evidence that the waveform of the AEP accurately reflects the way the information value of a stimulus is stored comes from the previously mentioned work of John, et. al. (1969), and Sutton et. al. (1967). In the former study, it was demonstrated that an AEP elicited by a new, generalized stimulus was highly similar to that elicited by the original training stimulus only when it also led to the behavioural response appropriate to the original training stimulus. The same physical stimulus could elicit different AEPs,

depending on which behavioural response it produced. If it produced the behaviour appropriate to stimulus A, the AEP was the same as that elicited by stimulus A, but if it led to the behaviour appropriate to stimulus B, the AEP was the same as that elicited by stimulus B. In that the same physical stimulus can elicit different AEPs, John concludes that it is triggering a neural process that accurately reflects the way in which stimulus information is stored. Stimulus A, the signal for response A, is encoded in a particular manner that is reflected in the particular form of the AEP that it elicits. When the animal interprets a generalized stimulus as an "A" stimulus; i.e., when it performs response A, the AEP appropriate to stimulus A is "readout" of storage. Put another way, it is because the generalized stimulus triggers the stored neural code for stimulus A that response A occurs. If it triggers the pattern of neural activity that is specific to stimulus B, response B will occur.

Such findings, then, constitute evidence suggesting that a retrievable, stimulus-specific, pattern of neural activity is laid down in the brain during the conditioning process.

Other researchers; e.g., Hall and Mark (1967), argue that the changes in the AEPs during conditioning reflect a general change in the nervous system that is not reflective of the associative aspect of conditioning per se. For instance, they conclude that the changes visible in the AEP during the acquisition of a conditioned emotional response reflect the animals' state of fear, rather than the establishment of the CS-US connection.

It should be pointed out that it is not necessary to conclude that the AEP reflects a psychological code, or merely indeces general changes, in an either/or fashion. It is quite possible that in some experimental situations the AEP does reflect a stimulus-specific code, while in others it monitors more general changes in the state of the organism. John's study was specifically designed to see if the AEP can be considered as reflective of neural codes, and indeed, his data support the notion.

The Factor Analytic technique employed here did elucidate changes in the AEP that were contingent on the conditioning procedure. The research was not, however, specifically designed to throw light on the status of the AEP as an indicator of neural codes. For the purposes of this work it was sufficient to view the AEP as an index of brain responsiveness that is sensitive to various experimental manipulations.

We might add, as a final note, that so far as the method of analysis is concerned, both strengths and weaknesses were noted. The discriminative power of the factor analytic technique was pointed out in it's ability to reveal underlying differences in visually highly similar waveforms. Short-comings of the procedure were particularly evident when there were few variables to work with, as in the case of M-8 and M-9, and when the concern was with the analysis of the characteristics of the waveform of a single, isolated AEP. In general, however, it does seem that multivariate analytic techniques, such as the Principal Component analysis employed here, can be usefully applied to psycho-physiological data.

V. SUMMARY

For animals trained with the discriminative classical conditioning technique, the CS+ and CS- were tone bursts of 500 and 1000 cps. There were three phases of training. During phase I both stimuli were presented on independent VI 20" schedules. Reinforcement pellets (.045 gm. Noyes sucrose) were also independently programmed. Phase I, which consisted of 3-5 daily sessions, thus constituted a "random" control procedure. Phase II was the conditioning phase in which one of the stimuli (CS+) always occured .5 scecs. before the delivery of a reinforcement. CS- was still presented on an independent schedule. The conditioning phase consisted of from 8-18 daily sessions. Phase III, the extinction sessions, consisted of a return to the "random" procedure of phase I.

An average evoked potential (AEP) based on 64 presentations of each of the tone bursts was collected during each daily session. The data consisted, therefore, of an AEP elicited by the CS+ and the CS- for each training day.

AEPs were collected during natural sleep after each phase of training. Animals were deprived of sleep for 24 or 48 hours before each sleep test. The EEG was monitored throughout the sleep test, and the stimuli were presented only during slow-wave sleep.

Results consisted of descriptions of changes in the waveforms of AEPs recorded from the surface of the temporal cortex and from the left mesencephalic reticular areas of four monkeys.

The AEPs were automatically digitized and a version of the Principal Component factor analytic technique was used to detect aspects of the AEP that were characteristic of the various stages of training.

A "Conditioning Factor" was tentatively identified for monkeys B-1, B-2, and C-1. The conditioning factors, for both the reticular and cortical data, seemed to be characterized by a relatively late, negative deflection. It was suggested that this deflection was indicative of the monkey's anticipation of forthcoming reinforcement. It was also argued that, particularly in the reticular area, the AEPs recorded during sleep after conditioning were sufficiently different from those elicited in the other sleep tests to warrant the conclusion that the brain was recognizing the stimuli as being different from neutral, or unconditioned stimuli even during natural sleep.

Two animals were trained in a "go, no-go" discrimination situation. They were gradually taught to press a lever within 1.5 seconds of a tone burst to get a reinforcement. Dramatic changes in the form of the AEP emerged as the animal became proficient at the task. However, in disagreement with the results derived from the classically trained animals, there was no evidence that the brain was responsive to the "significance" of the stimulus during sleep.

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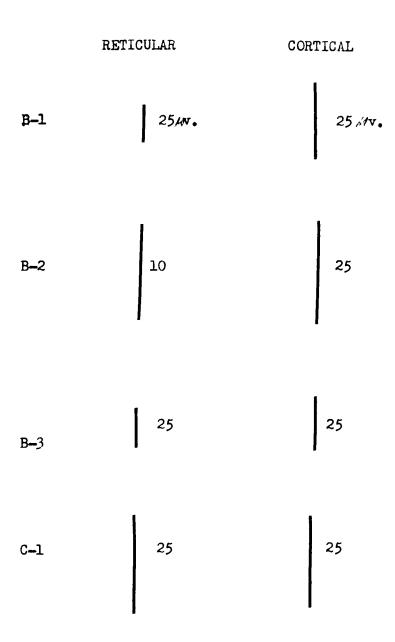
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APPENDIX

A note on calibration

The analysis of the AEPs was not concerned with amplitude changes, however, estimated wv. equivalences for reticular and temporal cortex AEPs are shown below for monkeys B-1, B-2, B-3, and C-1.



The following tables (A - G) show the loadings of the AEPs on the Varimaxed Principal Components.

LOADINGS ON VARIMAXED PRINCIPAL COMPONENTS

			2	03	-43 -51 -75	424648	9 79
	AEPs		7	848	898	389298	19 20 -19
<u>ر</u>	E TONE	FACTOR	m	848	37	6 PK B B B B B B B B B B B B B B B B B B	813
	NEGATIVE TONE AEPS	124	8	888	81 02 17	8 ବିଷ୍ଟ ଓ ବିଷ	24 16 16
ral CC	Z		ч	5100	388	388888	28%
RINCI							
LOADINGS ON VARIMAKED FRINCIFAL COMPONENTS			2	23	10 75	25 116 110 100 100	বৃষ্ঠন্
N VARLE	AEPs		7	5 4 5	5 % G	<u> </u>	876
ח מסאודי		FACTOR	Μ	15	56 61 85	34 34 36 19 19	77,
TKOT	POSITIVE TONE	4	R	64 27 47	462	285825 285825	8948
	ሺ		Н	383	15 34 34	232826	828
				Sleep Test Before Conditioning # After " After Extintion	Random Days	Conditioning Days	Extinction Days

Loadings of Positive and Negative AEPs on Varimaxed Principal Components. B-1, Reticular Recordings. Table A.

LOADINGS ON VARIMAXED PRINCIPAL COMPONENTS

	POSIT	IVE TO	POSITIVE TONE AEPS	NEGAT	IVE	NEGATIVE TONE AEPS	AEPB
		FACTOR	æ		FACTOR	eg Eg	
	Н	~	8	ч	7	Μ	
Sleep Test Before Conditioning " " After " After Extinction	62 12 12	583	25.52 12	222	1493	69 46 75	
Random Days	-68 -52 -61	54.78	-13 -29 28	77- 17- 27-	784	888	
Conditioning Days	\$5,000 \$5	348845	8657932	545558 845558	384848	228322	
Extinction Days	ቋ ፈ		-15 -24 63	12 78 84	58 40 19	6449	

Loadings of Positive and Negative AEPs on Varimaxed Principal Components. B-1, Auditory Cortex Recordings. Table B.

LOADINGS ON VARIMAXED PRINCIPAL COMPONENTS

	7	948	444	ន្ត	11- 10- 38
AEPs	9	<u> ಶಿ</u> ವಜ್ಞ	12.83	557 58 58 57 58 58 57 58 58 58 58 58 58 58 58 58 58 58 58 58	4884
TONE	.jog. 5	3758	148	18 33 33 17 17 18 17 18 17 18 17 18 18 18 18 18 18 18 18 18 18 18 18 18	04 04 04
NEGATIVE	FACTOR	777	88 42 72	123 123 00 128 123 123 123 123 123 123 123 123 123 123	4310
DEN	8	-79 -79	\$ 60	44446466	6999
	N	なれる	-57 -58 -02	4444444	52 5 %
	ч	8 3 4	04 10 22	######################################	2623
	~	7 7 7 7 7 7 8 8 8 8 8 8 8 8 8 8 8 8 8 8	8 <u>4</u> 8	12 99 99 99 97 12 12 12 12 12 12 12 12 12 12 12 12 12	8648
AEPs	9	10 48 05	92	\$4984898	\$448
TONE A	3R 5	ងងខ	849	862121232	8233
POSITIVE '	FACTOR	823	8977	48648434	द्भव्य
POS	9	878	37 61 07	55 15 15 15 15 15 15 15 15 15 15 15 15 1	19 19 19 19
	۵	8609	\$ 42	2889119248	12 77 71
	٦	19 -39 07	9451	22 \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$	2246
		Random Days	Sleep Test Before Conditioning " After After Extinction	Conditioning Days	Extinction Days

Loadings of Positive and Negative AEPs on Varimaxed Principal Components. B-2 Reticular Recordings. Table C.

LOADINGS ON VARIMAXED PRINCIPAL COMPONENTS

	-24x	525	46644694	-18 -10 -27
	855%	04 p	422989894	-26 -15
E AEPs	118 103 103	88 K	ಭಾಕಾಭಿಕತ್ಕ್ಲ ಭಾಕಾಭಿಕಿತಕ್ಕ	-05 30 45
TIVE TONE FACTOR	4825	3 [‡] 5	8273873873873	8 13
NEGATIVE FACT	\$ 5 7 7 7	17 88 72	82252525	3%£
Z	25.82	-25 -02 -57	28 6 5 7 5 6 6 7 6 6 7 6 6 7 6 7 6 7 6 7 6 7	-51 -55 -50
	-25 -36 -36	152	878283878	67 56 37
	19 124 18	-07 08 28	\$554\$\$\$\$\$\$\$	8 8 8 6 8 8
		क्ष्यर्	984982488	119
3 AEPs	26 -17	6969	283612828	822
POSITIVE TONE PACTOR	-122 -123 -125 -126 -126 -126 -126 -126 -126 -126 -126	-26 -05 35	31388118	35 52
POSITIN	15 P P P P P P P P P P P P P P P P P P P	07 27	F8333453	17 75
H	155 155 155 155 155		466242694	
	-2 ⁴ 2 ⁴ 2 ⁷ 30	-07 119 -15	\$24.50 \$2.20 \$20 \$20 \$20 \$20 \$20 \$20 \$20 \$20 \$20 \$	77 78 79
	Rando m D ays	Sleep Test Before Conditioning " After Extinction	Conditioning Days	Extinction Days

Loadings of Positive and Negative AEPs on Varimaxed Principal Components. B-2, Cortical Recordings. Table D.

LOADINGS ON VARIMAXED PRINCIPAL COMPONENTS

POSITIVE TONE AEPs

	FACTOR						
	1	2	3	4	5	6	7
Random Days	58 27 82	54 04 40	19 82 10	-23 00 07	27 18 06	-18 07 17	-01 02 01
Conditioning Days	15 58 30 74 74 53 85 57 72 72	83 56 84 52 60 61 41 66 60 36	13 15 -02 -11 04 -22 01 09 -19 -03	07 02 11 13 -07 -12 00 28 12 23	18 -03 -09 -06 -01 -15 09 17 -02 -34	09 29 25 11 -15 18 12 -01 07 36	05 -29 -07 -06 13 -36 00 -07 -02 -04
Extinction Days	66 38 38 14 -12	70 81 38 86 31	06 -20 02 -13 09	-02 -22 00 -17 -84	03 -10 07 -11 11	03 -04 18 -16 -06	12 01 64 23 -01
Sleep Test Before Conditioning " " After " " After Extinction	-91 73 81	-09 32 32	-16 22 21	09 - 25 03	25 - 09 - 32	07 -46 -02	-08 12 02

Table E(i). Loadings of Positive Tone AEPs on Varimaxed Principal Components. B -3, Reticular Recordings.

LOADINGS ON VARIMAXED PRINCIPAL COMPONENTS

NEGATIVE TONE AEPS

				FAC'	ror		
	1	2	3	4	5	6	7
Random Days	52 18 86	50 -18 30	31 81 03	13 -11 -08	35 -06 15	-36 -24 09	01 01 08
Conditioning Days	07 32 74 36 71 27 55 49 84	86 83 36 78 48 98 70 75 44 85	-01 06 12 17 12 04 -10 07 -19 -36	-19 01 16 04 18 04 -17 -18 -03 -17	-09 01 05 11 -08 -06 -17 05 -03 10	14 27 33 -04 16 10 08 05 15	24 -09 06 33 -01 -06 -05 01 05
Extinction Days	52 72 24 39 -42	78 34 68 31 01	07 -06 -23 -19 10	-10 01 -29 05 -15	06 01 -43 05 78	-08 45 13 74 08	13 14 07 13 08
Sleep Test Before Conditioning " " After " " After "	-88 92 90	02 18 17	-29 16 25	- 05 - 02 05	29 -17 -11	-03 -15 20	- 05 12 05

Table E(ii).Loadings of Negative Tone AEPs on Varimaxed Principal Components. B-3, Reticular Recordings.

LOADINGS ON VARIMAXED PRINCIPAL COMPONENTS

		7	12862	488	846448644848
		9	-142 -130 -142 -130	-29 09 18	\$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$
AEPs		۲۰	82828	10 0 7 04	13738887557 13738887557
E TONE	FACTOR	4	05 05 05 05	1767	255550000000000000000000000000000000000
NEGATIVE	FA	Μ	77 77 77 77 77 77 77 77 77 77 77 77 77	077	34462448
Z		N	822428	77 92 86	8822244445688
		ч	%# 26 7 9 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8	33 27 40	627275388825756
		7	8 448 8	889	446646464686
χp		9	497	-19 17 02	· • • • • • • • • • • • • • • • • • • •
TONE AEPB	~•	٧.	75 75 75 75 75	82	4138498986848
VE TO	PACTOR	4	78688	-35 F	1,59
POSIT.	_	σ	५ ८%%५	‡8‡	08624961486
		8	51 53 53 74 76	88 449	44628421884883
		ת	37 63 49 29 69	Before Conditioning 24 After " 23 After Extinction 66	95 93 94 95 95 95 95 95 95 95 95 95 95 95 95 95
			Random Days	Sleep Test Before " " After " " After	Conditioning Days

Continued on next page

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16 22 16 16 18
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£2387325

Extinction Days

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Table F. Loadings of Positive and Negative AEPs on Varimaxed Principal Components. C-1, Reticular Recordings.

COMPONENTS	
PRINCIPAL (
ON VARIMAXED	
LOADINGS ON	

		7	29 119 65	887	8 488869849
		9	92862	1385	7877888648888888888888
AEPs		2	ខ្ពុខខ្ព	05	4244488989448
E TONE	FACTOR	4	89759	24- 30-	ង្ឋ នៃង្គ នេង នេង នេង នេង នេង នេង នេះ
NEGATIVE	FA	٣	ឯសន្នឧដ	12 % t-	64 115 115 115 115 115 115 115 115 115 11
Z		8	-12 -13 -14	7287	2835738852428383634836363836363636363636363636363636
		т	844.4648	44 47 -19	38849843863218
		7	15 19 19 19 19	585	225222222222222222222222222222222222222
		9	142868	न् ४ ०	4864949649
AEPs		₩.	101- 01- 01- 09-	-13 68 -34	648886666666666666666666666666666666666
E TONE	FACTOR	-4	101 28	17	997577778877575 997777777887757777777777
SITIVE	FA(σ	45,555	-77	382488885444488
8		~	क्षे यं श्रुष्ठे क्षे	-24 50 -18	33 22 23 88 13 25 38 15 32 25 38 15 32 25 35 35 35 35 35 35 35 35 35 35 35 35 35
		г	11-20-1	Before Conditioning -74 After " -03 After Extinction -09	5388877788888 47388888877888888
			Random Days	Sleep Test Before " After " After	Conditioning Days

19	∄	-26	8	-22	q	-17
7	-16	ڳ	-17	7	ö	8
헏	- 05	58	58	27	34	-30
-19	-19	8	-05	77-	9	ដ
ম	7.7	ଷ	18	21	덕	ප
83	22	ಹಿ	ਲੋਂ	69	88	22
					15	
27	78	ઝ	-19	16	8	8
-34	-	-26	-16	-18	8	43
05	õ	ප	33	7	র	7 0-
-24	15	80	6	6	- 12	05
31	ခု	3	39	45	20	7
					43	
63	돲	62	2	69	92	90

Extinction Days

Table G. Loadings of Positive and Negative AEPs on Varimaxed Principal Components. C-1, Cortical Recordings.