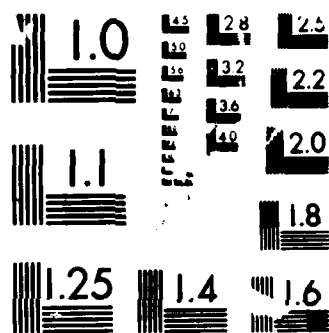


AD-A187 759 MODULATION OF THALAMIC SOMATOSENSORY NEURONS BY AROUSAL 1/1
AND ATTENTION(U) MICHIGAN UNIV ANN ARBOR DEPT OF
PHYSIOLOGY T J MORROW 18 AUG 87 AFOSR-TR-87-1413
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MICROCOPY RESOLUTION TEST CHART

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19. ABSTRACT (Continue on reverse if necessary and identify by block number) Several directions have been followed toward the attainment of our research goals. We have continued recording in the untrained monkey, looking at arousal related changes in spontaneous and evoked thalamic activity, as well as, the effects of various drugs on these responses. We are now recording the responses of thalamic somatosensory neurons in behaviorally trained animals, looking at response modulation during two attentional paradigms, including shifts in arousal. Preliminary experiments have been conducted to develop methods for examining the underlying mechanisms of thalamic modulation. We are continuing to update and validate our computerized stereotaxic atlas of the green monkey brain. We have also developed a unique computer program for the acquisition (PETH) and statistical analysis (HISTSAT) of perievent time histograms. Some of the results in this report have been or will be communicated at scientific meetings, published or are in press.					
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1. Scientific Goals

The primary goals of this study is to identify at the cellular level, those mechanisms involved in the modulation of thalamic somatosensory responses by arousal and attention. To this end the specific objectives are as follows:

- to record from neurons in the ventral posterior lateral thalamus of the awake, behaving monkey that respond to somatosensory stimuli applied to the body surface .
- to detect and quantify any changes in the sensory responsiveness of the above population of thalamic neurons during changes in the level of arousal or attention.
- to determine for units showing attention related changes in activity, whether these changes are 1) non-specific only related to generalized changes in attentional state or 2) are more closely correlated with specific somatosensory attention.
- to physiologically identify (when possible) whether these somatic VP neurons are cortical projection neurons using standard antidromic activation techniques.
- to compare physiological characteristics and anatomical location of the above neurons with those of other somatosensory units showing no behavioral state relationships.
- to determine to what extent the thalamic reticular nucleus may participate in the the behavioral state modulation of somatosensory responses in the ventral posterior thalamus.
- to identify possible cortical mechanisms involved in arousal or attention related somatosensory modulation in the VP thalamus.

The scientific goals of this study are essentially unchanged from those described in the original proposal. Some new techniques for the identification of mechanisms have been tested in pilot experiments to determine their feasibility for use in the awake monkey. These are discussed under the appropriate sections below.

Distribution/

Availability Codes

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2. Status of the Research

This report covers the course our research has followed and accomplishments made toward the successful completion of our project since August 1, 1986.

Stereotaxic Atlas Preparation

Two additional monkey brains were histologically prepared and sectioned and used to update our current atlas database. The anatomical reconstructions from these animals have been used to update our computerized atlas of the Green monkey, confirming and further validating our previous work in this area. This additional data also supplements our estimations of anatomical variation in both the size and location of CNS structures in this species. We have chosen to continue updating our atlas anatomical materials with the idea in mind that this might lead to a future publication of an atlas of the Green monkey thalamus and brainstem.

To date we have concluded that the African green monkey appears to be an excellent choice for primate stereotaxic procedures. Actual, histologically confirmed coordinates from recording experiments have shown only slight variation from animal to animal, and from computed atlas coordinates. Four sample plates from this computerized atlas are shown in figure 1.

Focal Cortical Suppression - Primate Model

A primate model has now been included in our efforts to develop a means of assessing cortical controls on thalamic somatosensory responsiveness. As in our previous experiments in the rat, we found that $MgSO_4$ applied to the surface of the dura above S1 cortex suppresses the spontaneous as well as the activity evoked in cortex, restricted to the area of application of the compound. Concurrent with this reduction in cortical activity, we found that the responsiveness of thalamocortical projection neurons to also exhibit a reduced responsiveness to somatic stimuli. This data, then validates the use of such a technique in the monkey, as a tool to study the behavioral state related modulation of the VP thalamus. We are currently working to adapt this method for use in the awake monkey. It is yet unclear, however, whether the technical problem of applying $MgSO_4$ immediately above and around the area of electrode penetration in a chronic preparation is feasible. We must be sure that none of the $MgSO_4$ diffuses down the electrode track and thereby acts directly on the thalamic recording site. This was not a problem in our previous pilot studies in rat, but differences in the gross anatomy in the monkey make this situation unavoidable. We are currently preparing to conduct a radioactive tracer study to answer this diffusion question.

Development and Implementation of PETH and HISTAT

PETH is the unique program which collects and stores data on the time of each neural discharge, somatic or central stimulus, bar bull or release, signal light onset/offset, EEG synchronization, movement sensor, and other behavioral indicators. Peri-Event Time Histograms of almost any bin width and duration can then be computed off-line around any event and during any specified behavioral state. This analysis is shown schematically in figure 2. Because this program is now well tested and proven effective, a technical paper on this data acquisition approach is planned.

In conjunction with PETH, we have recently completed development of a method and computer program (HISTAT) for the statistical analysis and comparison of differences within and between peri-stimulus time histograms. Because it is essential in our studies to make reliable and accurate statements regarding the presence or absence of significant changes in neuronal responsiveness, we developed the program HISTAT. To our knowledge, no other neurophysiology laboratory systematically compares PET histograms for statistically significant changes as has been recommended in the statistical literature. Using the histogram data from PETH above, this program produces new histograms with superimposed bin by bin 95% confidence limits (based on binomial analysis), an error probability histogram, and the values of statistically relevant variables (for example, firing rate) including the t-statistic with associated levels of significance. When final testing is completed, this should lead to an additional technical publication.

Unit Recording in the Awake, Behaving Monkey

A total of 4 animals have been chronically implanted since the previous yearly report, 2 untrained, naive animals and two behaviorally trained monkeys. Unit responses recorded in the untrained animals have been studied for changes related to the state of arousal. During the early part of this past year we encountered some problem with obtaining good single unit records in the awake monkey preparation. The cause of this situation was fairly quickly identified as a bad supply of electrode insulating material. After replacing the suspect lacquer, good recordings were again obtained. As with our previous work in the squirrel monkey, we find that many of the somatically responsive neurons in VPL show some form of modulation correlated with the behavioral state of the animal.

Unit recording is currently in progress in the latter trained subjects. In these animals as well as in the naive animals, some units have been studied for changes in discharge after the administration of several drugs (namely, morphine, naloxone and halothane). These drugs have been shown to affect

the behavioral state of the animal, and we have looked for possible corresponding changes in thalamic responsiveness. The use of such drugs may prove to be a valuable tool for looking at possible mechanisms in thalamic somatosensory modulation.

An example of the responses of one VPL unit to a light tactile stimulus is shown in the two histograms of figure 3. This unit showed an enhanced responsiveness during the slightly drowsy state as compared to the quiet waking state. We are finding that as with our earlier squirrel monkey recordings, that unit responsiveness is profoundly affected by the behavioral state of the animal.

Technical and Methodological Developments

Additional refinements have been made to the chronic recording system which have led to better, more stable recordings. As we continue to use this method we have found it necessary to further modify the system to increase its utility and ease of use. This will be a continual ongoing evolution.

The development of a computerized data base for the descriptive information as to unit response properties is still in evolution. A version is currently on-line, however, this is still being modified as we learn more about the response properties of the cells from which we are recording.

In my previous Research Progress and Forecast Report, I mentioned that we were pursuing the development of a fine wire electrode array for stimulation in the midbrain spinal lemniscus. This has been abandoned in favor of the more traditional and reliable twisted pair electrodes that we have used in past experiments. Also, we are continuing our investigation into the use of chronic microinjection of glutamate into the Thalamic reticular nucleus. This would provide a more "physiological" means of activating TRN than electrical stimulation of this structure, however, technically this approach may not be feasible. Because of the location and size of all other necessary parts of the chronic implant, there is little or no room for the placement of the catheter, without interfering with the operation of some other part of the system. We have not, however, given up on the possibility of applying this technique in the future.

3. Publications

Journal Articles

Yuan, B., Morrow, T.J. and Casey, K.L.: (1986) Corticofugal influences of S1 cortex on ventrobasal thalamic neurons in the awake rat. J. Neuroscience 6(12): 3611-3617.

Casey, K.L., Morrow, T.J. Terry, L.C. and Craig, R.: Differential effects of partial myelotomies on monoamine levels in cat spinal cord. Brain Res. 408: 377-380.

Casey, K.L. and Morrow, T.J.: Supraspinal nocifensive responses of cats: spinal cord pathways, monoamines and modulation. J. Comp. Neurol. (in press).

Chapters in Books

Casey, K.L. and Morrow, T.J.: (1987) Nociceptive neurons in the ventral posterior thalamus of the awake monkey: Observations on identification, modulation and drug effects. Proceedings of the conference on Thalamic Mechanisms of Pain, LaRocheville, France. (in press).

Abstracts

Morrow, T.J. and Casey, K.L.: (1987) Effect of medial medullary lesions on the excitability and modulation of supraspinal nocifensive responses of cats to thermal pulses. Meeting on Descending Brainstem Controls, Beaune, France.

Morrow, T.J. and Casey, K.L.: (1987) Drug induced changes in ventrobasal thalamic neuronal responses in awake monkey. Vth World Congress on Pain, Hamburg, FRG. Pain (Supp.4), S264.

Yu, L., Morrow, T.J. and Casey, K.L.: (1987) Cocaine: Evidence for CNS analgesic action., Vth World Congress on Pain, Hamburg, FRG. Pain (Supp.4), S48.

Yokota, T., Morrow, T.J., Kniffki, K. and Dostrovsky, J.O.: (1987) Thalamocortical mechanisms of Pain., Vth World Congress on Pain, Hamburg, FRG. Pain (Supp. 4), S105.

Vierck, C., Morrow, T.J. and Maixner, W.: (1987) Animal Models of Pain., Vth World Congress on Pain, Hamburg, FRG. Pain (Supp. 4), S222.

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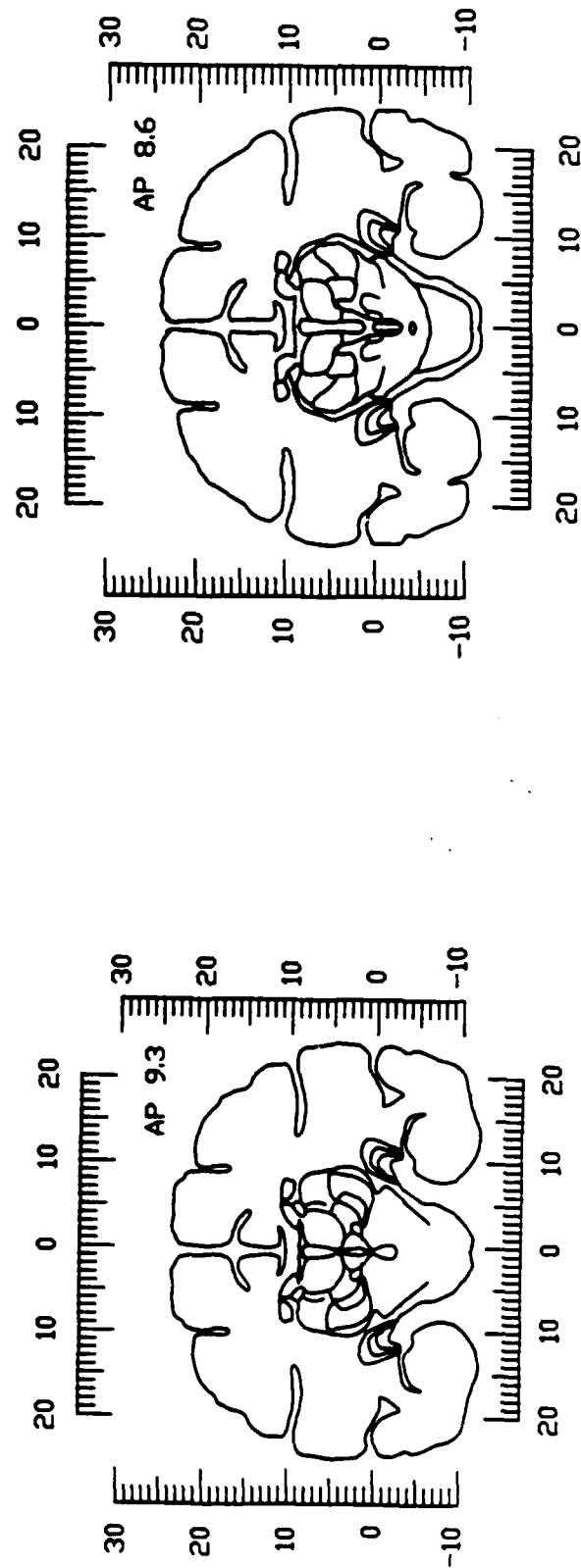
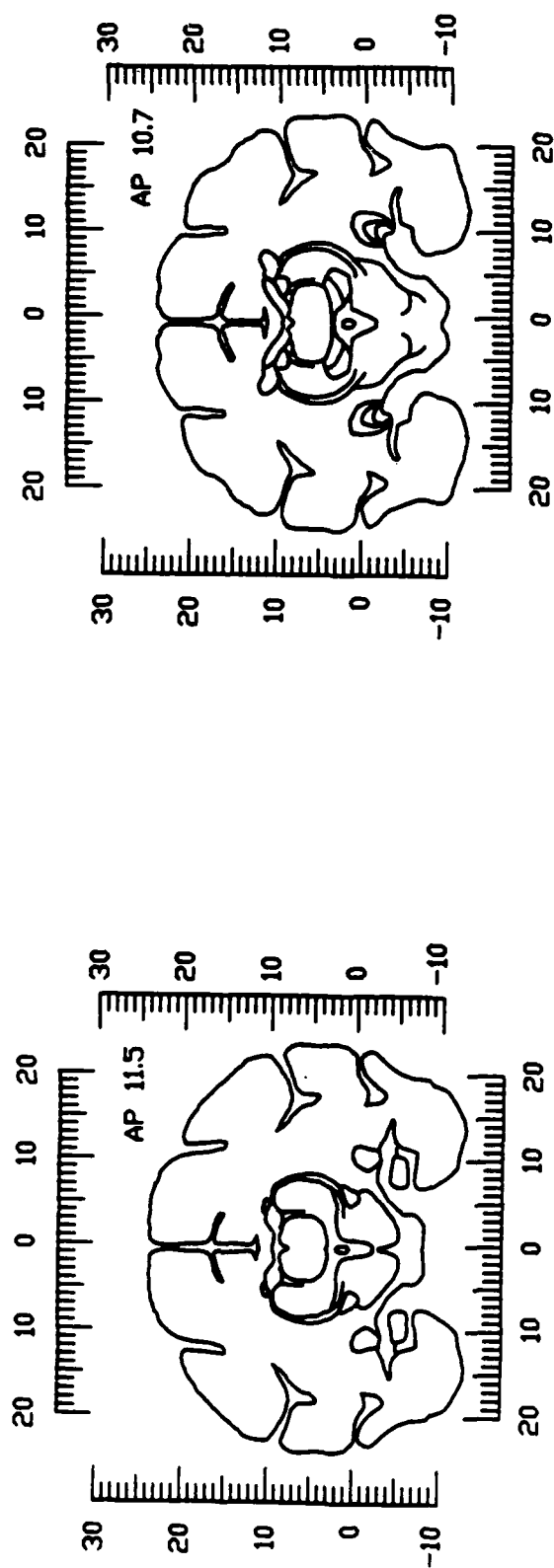
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FIGURE 1



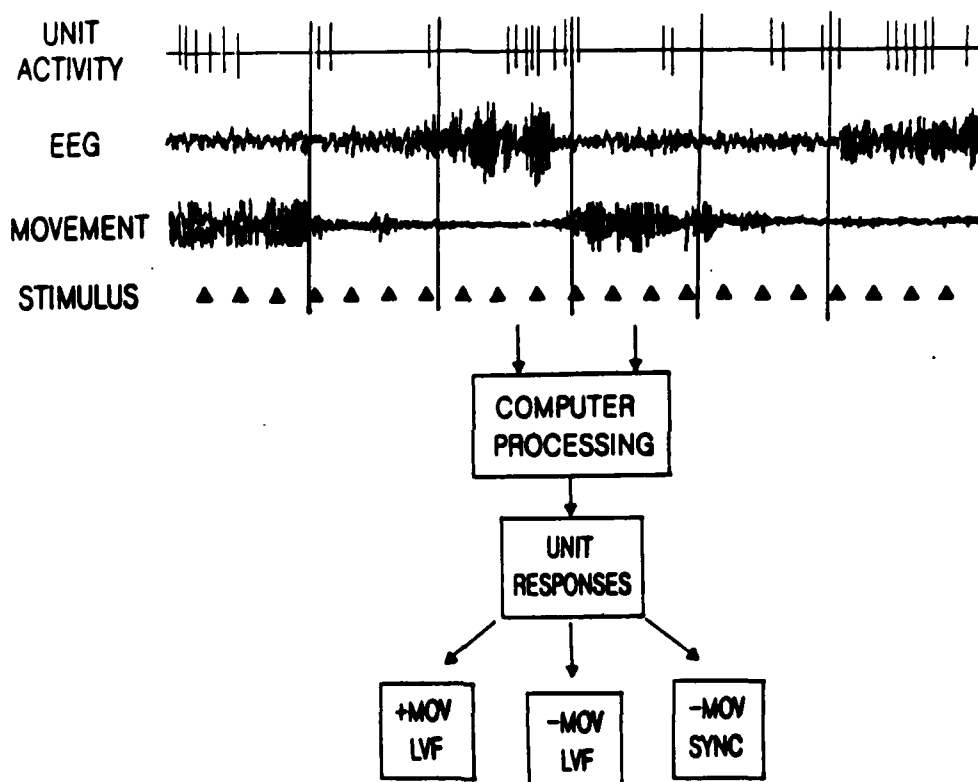
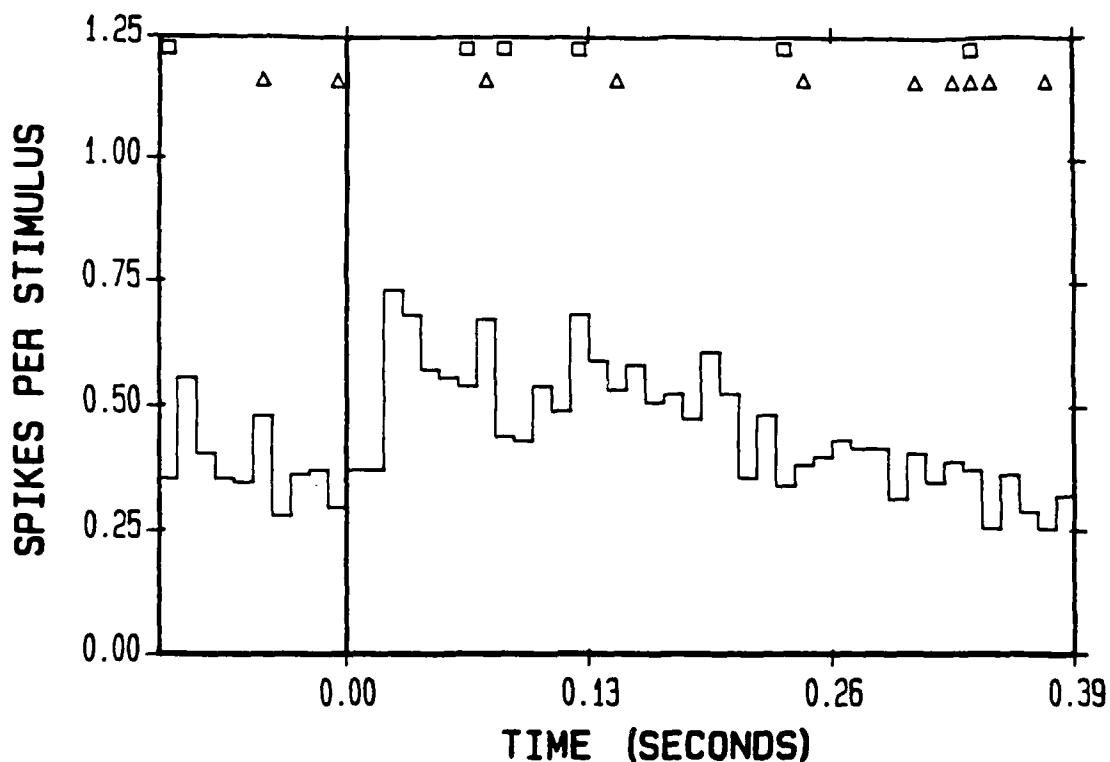


FIGURE 2

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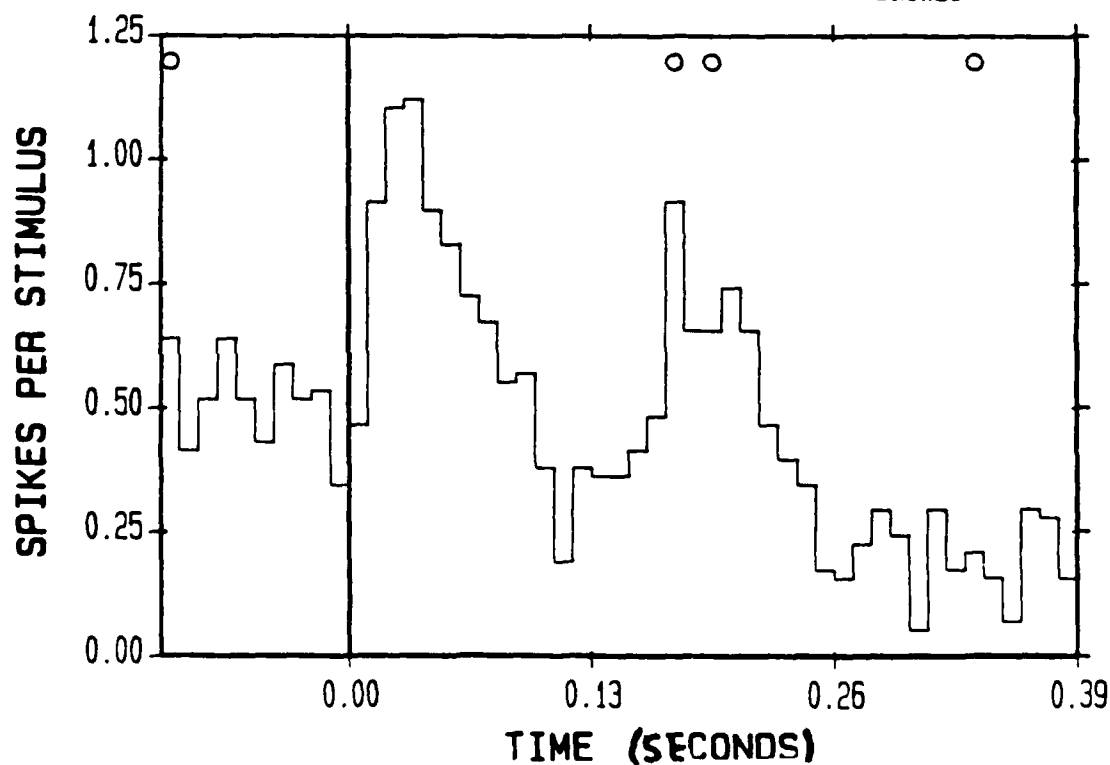


FIGURE 3

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