Unclassified
SECURITY CLASSIFICATION OF THIS PAGE

REPORT DOCUMENTATION PAGE

1a. REPORT SECURITY CLASSIFICATION: Unclassified	1b. RESTRICTIVE MARKINGS: -
2a. SECURITY CLASSIFICATION AUTHORITY: -	3. DISTRIBUTION/AVAILABILITY OF REPORT: Approved for public release distribution unlimited
2b. DECLASSIFICATION/DOWNGRADING SCHEDULE: -	
4. PERFORMING ORGANIZATION REPORT NUMBER(S): Department of Anatomy and Neurobiology University of Tennessee, Memphis	5. MONITORING ORGANIZATION REPORT NUMBER(S): AFOSR-TR- 93 0671
6a. NAME OF PERFORMING ORGANIZATION: University of Tennessee, Memphis; 6b. OFFICE SYMBOL (If applicable): -	7a. NAME OF MONITORING ORGANIZATION: Air Force Office of Scientific Research/NL
6c. ADDRESS (City, State and ZIP Code): University of Tennessee, Memphis 875 Monroe Avenue, Memphis Tennessee 38163	7b. ADDRESS (City, State and Zip Code): Building 410 Bolling AFB, D. C. 20332-6448
8a. NAME OF FUNDING/SPONSORING ORGANIZATION: AFOSR; 8b. OFFICE SYMBOL (If applicable): NL	9. PROCUREMENT INSTRUMENT IDENTIFICATION NUMBER: USAF GR AFOSR 91-0333
8c. ADDRESS (City, State and ZIP Code): Building 410 Bolling AFB, D. C. 20332-6448	10. SOURCE OF FUNDING NOS.

PROGRAM ELEMENT NO.	PROJECT NO.	TASK NO.	WORK UNIT NO.
61102F	2312	A2	

11. TITLE (Include Security Classification): SOMATONSENSORY RESPONSIVENESS IN BEHAVING MONKEYS & HUMAN SUBJECTS

12. PERSONAL AUTHOR(S): Randall J. Nelson, Ph. D.

13a. TYPE OF REPORT	13b. TIME COVERED	14. DATE OF REPORT (Yr., Mo., Day)	15. PAGE COUNT
Annual Technical	FROM 7/1/92 TO 6/30/93	93, 07, 31	18

16. SUPPLEMENTARY NOTATION

17. COSATI CODES		
FIELD	GROUP	SUB. GR.

18. SUBJECT TERMS (Continue on reverse if necessary and identify by block number): Changes in sensory responsiveness; Response gating; Reaction times; Cortical neuronal responses; visual and vibratory cues; Monkeys; Humans

19. ABSTRACT (Continue on reverse if necessary and identify by block number)

Three research goals were accomplished during this second year. 1) Analysis of data indicated that sensory responsiveness of primary somatosensory (SI) cortical neurons that respond to vibratory go-cues for wrist movement with the greatest fidelity have their activity modulated just prior to movement onset. This observation fits with the hypothesis that prior to active movement, sensory inputs that are no longer behaviorally relevant are gated so as not to interfere with monitoring movement parameters by the primate CNS. 2) The preliminary results from the recordings from 249 task related sensorimotor cortical neurons indicate that when behavioral conditions become suddenly unpredictable, responsiveness to peripheral sensory and centrally-generated inputs is increased. This is tentatively being viewed as a release from the tonic attenuation that probably occurs during the performance of stereotypic behaviors. 3) Preliminary findings suggest that human subjects can alter wrist movements toward a positional target if vibratory abort-cues are presented early enough. Correct alterations in movement become more likely with increased practice. Final performance and the time necessary to achieve it range on the order of 4-6 days.

20. DISTRIBUTION/AVAILABILITY OF ABSTRACT	21. ABSTRACT SECURITY CLASSIFICATION
UNCLASSIFIED/UNLIMITED ☒ SAME AS RPT. ☐ DTIC USERS ☐	Unclassified

22a. NAME OF RESPONSIBLE INDIVIDUAL	22b. TELEPHONE NUMBER (Include Area Code)	22c. OFFICE SYMBOL
Genevieve Haddad, Ph. D.	202-767-5021	NL

DD FORM 1473, 83 APR — EDITION OF 1 JAN 73 IS OBSOLETE.

Unclassified
SECURITY CLASSIFICATION OF THIS PAGE

Research Objectives

Three research goals were accomplished during this second year of USAF grant AFOSR 91-0333. 1) Further analysis of data indicated that sensory responsiveness of primary somatosensory (SI) cortical neurons that respond to vibratory go-cues for wrist movement with the greatest fidelity have their activity modulated just prior to movement onset. This observation fits with the hypothesis that prior to active movement, sensory inputs that are no longer behaviorally relevant are gated so as not to interfere with monitoring movement parameters by the primate CNS. 2) The preliminary results from the recordings from 249 task related sensorimotor cortical neurons indicate that when behavioral conditions become suddenly unpredictable, responsiveness to peripheral sensory and centrally-generated inputs is increased. This is tenatively being viewed as a release from the tonic attenuation that probably occurs during the performance of stereotypic behaviors. 3) Preliminary findings suggest that human subjects can alter wrist movements toward a positional target if vibratory abort-cues are presented early enough. Correct alterations in movement become more likely with increased practice. Final performance and the time necessary to achieve it range on the order of 4-6 days. The neurophysiological experiments suggest that the responsiveness of SI neurons is profoundly influenced by behavioral conditions. The human psychophysical experiments suggest that the addition of vibratory abort-cues in addition to visual indicators may have performance benefits even in more complex control systems.

Status of Current Research - Statement of Work

Each study involving awake, behaving monkey neurophysiological recording used a behavioral paradigm that had many features in common. The basic paradigm and then the variations used in the individual studies will be described.

Experimental Design and Methods - Animals.

Behavioral Paradigm

The experiments were conducted with four adult male Rhesus monkeys (*Macaca mulatta*, 8-11 kg) that were trained to make wrist flexion and extension movements in response to visual and vibratory cues. During the experiments, each monkey was seated in a Plexiglas® primate chair with his right hand resting in a prone position upon a manipulandum attached at its proximal end to the axle of a brushless DC torque motor. This device permitted only wrist flexion or extension movements. The animal initiated each trial by centering his wrist and maintaining that position until given a cue to make a wrist movement. A load of 0.07 Newton-meters, which assisted extension movements, was applied continuously to the manipulandum, so that the monkey had to actively center its wrist and hold that position in order to initiate a trial.

Each monkey viewed a visual display, placed 35mm in front of him at eye level, that indicated his current wrist position. The display consisted of a centrally placed, red light-emitting diode (LED) that was bounded above and below by a vertical row of smaller, yellow LEDs. The central LED was illuminated when the monkey moved his wrist to mid-position, whereas illumination of each successive LED from the center corresponded to 1° differences in angular wrist deflection from the center. After the animal maintained its wrist in centered position for an interval of 0.5, 1.0, 1.5, or 2.0s (pseudo-randomly selected), either a visual or a vibratory cue was presented. During vibratory cued trials, the signal to move ("go-cue") was a palmar vibratory stimulus achieved by driving the

torque motor with a low-amplitude sine wave at either 27, 57, or 127Hz (<0.057°, or <100μm peak-to-peak measured 10cm distal to the coupling of the handle to the torque motor). This signal, which was applied to the same hand that the monkey used to perform the wrist movements, remained on until the animal moved the manipulandum at least 5° from the centered position. The presence of a load assisting extension movements assured that the manipulandum remained in contact with the animal's hand even during wrist movements made away from the side of stimulation. Two of the monkeys also performed visually cued trials during which the signal to move was a shift in position of the illuminated lamp away from center in a direction opposite that of the desired movement and by an amount that normally would correspond to 5°of wrist movement. Each animal learned to respond to this go-cue by making a movement of at least 5° back toward the center of the display. Like the vibratory cues, the visual cues remained on until the monkey moved his wrist at least 5° in the appropriate direction. Fruit juice reward was given after the successful completion of each trial.

Presentation of the visual and vibratory cues was alternated pseudo-randomly within a block of 160 trials each. Normally, three blocks of trials were performed, one for each of the three vibratory frequencies. Within each block of trials, the required movement direction alternated between flexion and extension in groups of 10 trials each. The appropriate movement direction was signalled by a small red LED that was located at the periphery of the visual display. This LED was illuminated continuously during each group of extension trials and remained unlit during each group of flexion trials. Likewise, the modality of the go-cue (visual vs. vibratory) was indicated by a green LED that was illuminated at the start of each visually cued trial and remained unlit for vibratory cued trials.

Surgical procedures

To permit chronic single-unit recording, a stainless steel recording chamber was implanted under aseptic conditions over the hemisphere contralateral to the hand used to perform the behavioral task. Each monkey was sedated with Ketamine (10 mg/kg) and then maintained on halothane and nitrous oxide anesthesia. A craniotomy was performed at approximately A+14.5mm. The recording chamber then was fixed to the skull at a lateral angle of 8° from vertical. The chamber and two small aluminum bars that later were used to permit head immobilization were secured to the skull using surgical cement (Howmedica Surgical Simplex P). After the incision was closed, local antibiotics were applied (Furazone and bacitracin-neomycin-polymyxin ointment). The chamber was filled with sterile saline and a bacteriostatic antibiotic (chloramphenicol, 0.8 mg), and was sealed with a removable translucent acrylic plate. The animal was given butorphonal (0.01 mg/kg/12hr) to provide analgesia for two days after the surgery. For the duration of the study, the recording chamber was flushed daily with sterile saline, and chloramphenicol (0.8 mg) was added to the chamber solution after daily recordings were completed. Animal care was provided in accordance with the *NIH Guide for Care and Use of Laboratory Animals.*

Electrophysiological Recording and Data Collection

Training was resumed one week after the surgery to permit the animals to adapt to performing the behavioral task with their heads restrained. When the animals again performed the task reliably, daily recording sessions were begun. Glass-coated, platinum-iridium microelectrodes (0.7-2.0MΩ at 1Khz) were used to isolate single units from the somatosensory cortex using conventional extracellular recording techniques. The electrodes were lowered transdurally using a hydraulic microdrive with adaptor (Narishige MO-95B). The neuronal activity was amplified and filtered (500Hz-10Khz), and single-unit discharges were detected with a window discriminator. For recording of EMG activity,

multi-unit EMG responses were obtained via needle electrodes, and this activity was also amplified and counted using a window discriminator. An on-line program operating on a PDP-11/23+ microcomputer was used to collect and store the neuronal activity in real-time, the time of onset of task related cues, and other significant behavioral events, with a temporal resolution of 0.1ms. Transducer output indicating current wrist position was digitally sampled every 10ms. The computer also controlled the behavioral task, including the presentation of stimuli, the pseudo-randomization of the hold period duration and trigger stimulus type, and sequencing of the movement direction requests.

Experimental Studies

1) *Sensory Cortical Neuron Responsiveness Synchronized to Vibratory Stimuli.*

Goals of the Study-

Primary somatosensory cortical (SI) neurons exhibit characteristic patterns of activity prior to initiation of voluntary movements. It is believed that premovement activity in SI neurons may result from centrally-generated as well as peripheral inputs. We examined premovement activity patterns for a group of SI neurons that represent somatosensory peripheral stimuli in a most faithful way. These neurons were characterized by entrainment of their activity to vibrotactile stimuli (i.e., by a very close temporal correlation between the stimuli and the neurons responses to them). We hypothesized that, for selected neurons, activity patterns of central and peripheral origin can be distinguished. It was expected that central input, if any, would introduce an asynchronous component into the vibration-entrained neuronal firing.

Brief Description of Methods-

Monkeys made wrist flexion and extension movements in response to sinusoidal vibration (27, 57 or 127 Hz) of their palms. Vibration remained on until the animal moved at least 5° from the initial hold (center) position. The activity of 55 extracellularly recorded SI neurons (areas 3a, 3b, 1, 2 respectively: 10, 13, 28, 4) was vibration-entrained (Figure 1). The temporal relationship between the vibratory stimuli and neuronal firing was described by the mean phase (MP) of spikes with respect to the vibratory cycle. The degree of entrainment was quantified as synchronicity (Sync), which was derived from the standard deviation (SD) of the phase and expressed in units scaled between the SD for non-entrained firing and the SD for a constant response phase. Mean firing rate (MFR) was derived from the number of spikes per vibratory cycle. More complete descriptions of the behavioral paradigm, the electrophysiological recording procedures and methods of data analysis can be found in Appendix 1. This work has been submitted and is currently being review for publication in The Journal of Neurophysiology.

General Results-

Typically, during the hold phase of the paradigm preceding vibration onset, neurons with either cutaneous or deep receptive fields (RFs) exhibited background activity. The background firing rate was, on the average, larger for units with deep RFs (mean=30.2 spike/s) than for units with cutaneous RFs (mean=21.5 spike/s).

After a transitory burst in response to vibration onset, the studied neurons responded to the ongoing vibration in a steady-state manner. During this period of stabilized response, which was usually about 100 ms in duration, neuronal firing was entrained to the vibratory stimulus. For some neurons, MFR of the stabilized response was not substantially different from background MFR. Thus, the characteristics of peripheral input were coded by the temporal firing pattern rather than by

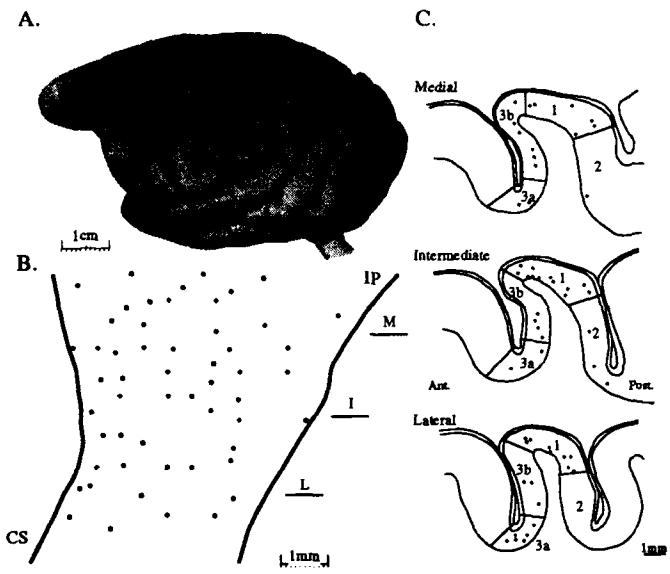


Figure 1. A. A digitized view of the dorsolateral surface of the brain of the most extensively studied monkey. The brain has been tilted 30° in the coronal and sagittal planes. Central sulcus (CS) and intraparietal sulcus (IP) are marked. B. A composite estimate of the recording area with the circles indicating penetrations in which neurons with vibration-entrained activity were located. The activity of 55 extracellularly recorded SI neurons (areas 3a, 3b, 1, 2 respectively: 10, 13, 28, 4) was vibration-entrained. The representative parasagittal sections indicating the location of neurons in three planes (medial [M], intermediate [I] and lateral [L]) are shown in C. The location of each neuron was marked after scaling and fitting the reconstructions of sections from individual animals to the composite sections taken from the most extensively studied monkey.

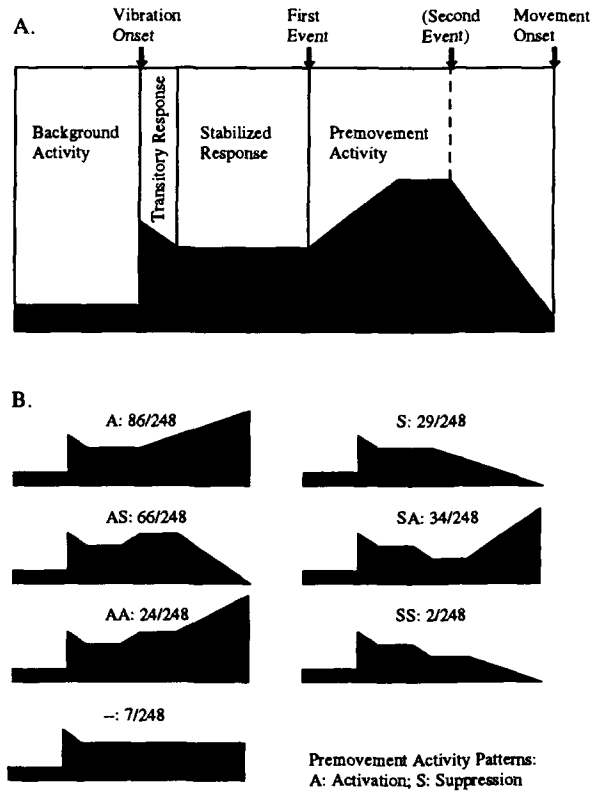


Figure 2. A. Schematic illustration of different epochs of neuronal activity in this reaction time paradigm. Background firing preceded the vibratory stimulus onset. After a transitory response to the stimulus onset, a stabilized response to vibration was observed. Then premovement activity occured (one or two events of mean firing rate change). B. Different types of premovement activity and the number of cases for which they were observed.

MFR. For neurons with deep RFs at all tested vibratory frequencies, and for neurons with cutaneous RFs at 27 and 57 Hz, MFRs were not significantly different (mean=46.4 spike/s). At 127 Hz, for neurons with cutaneous RFs, MFR decreased (mean=19.4 spike/s).

For the majority of cells, the pattern of stabilized response was modulated prior to movement onset (Figure 2). Cases of MFR increase (premovement activation) and of MFR decrease (premovement suppression) were observed. Also, two premovement changes in MFR often were observed (two-event cases). For these two-event cases, early and late MFR changes could be distinquished. In many cases, premovement changes of MFR began before EMG onset, suggesting that this modulation results from centrally-generated inputs rather than from movement-associated peripheral reafference.

Premovement activation was accompanied by shifts of mean phase towards earlier responses to the ongoing vibratory stimulus, and by a decrease of response Sync. The correlations of the onset of MFR increases with these shifts in MP and Sync were statistically significant. The desynchronization was more profound at the lower vibratory frequency (27 Hz) when compared to higher ones (57 and 127 Hz). However, MP shifts were more prominent at the higher vibratory frequencies. We suggest

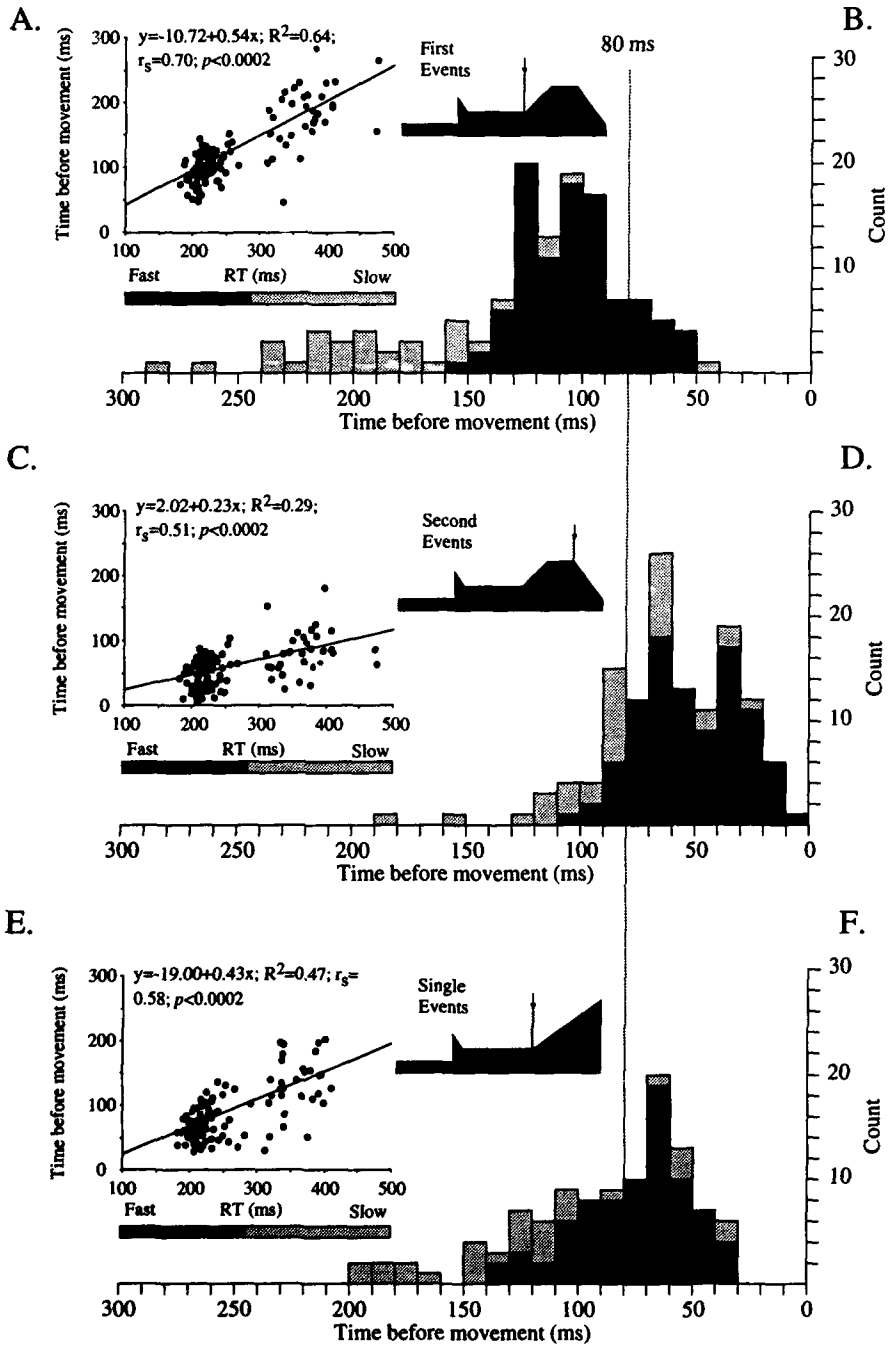


Figure 3. Results of statistical analyses of onsets of mean firing rate changes during premovement activity. A & B. Onsets for first events in two-event premovement activity cases. C & D. Onsets for second events. E & F. Onsets for single-event cases. Relationship of premovement activity onsets and reaction times is shown in panels A, C, E. Correlation between these onsets and reaction times (RTs) is statistically significant (Spearman rank analysis). According to average RTs, the results from individual monkeys were split into two groups: fast and slow. In panels B, D, F, onset histograms for these groups are shown. The majority of the first events took place earlier than 80 ms prior to movement onset (an estimation of the EMG onset) (B). Most of the second events occured later than 80 ms before movement onset (D). Approximately an equal number of the single events took place prior to and after the 80 ms boundary (F).

that, during premovement activation, an asynchronous signal is integrated with the periodic peripheral input. This asynchronous signal may make neurons more likely to discharge and to do so earlier with respect to the vibratory input. The asynchronous component may also disrupt the vibration-entrained activity pattern. Thus, differences in MP and Sync changes at different vibratory frequencies probably reflect the interaction between the temporal properties of these inputs.

Premovement suppression was not associated with consistent shifts of MP and Sync. The cases of premovement suppression were, on average, characterized by larger MFR during stabilized responses than the cases of premovement activation (e.g., at the vibratory frequency of 57 Hz, for one-event

patterns, mean value of MFR during stabilized responses for cases of suppression was 56.2 spike/s, and for activation it was 32.0 spike/s).

The onset times of premovement changes in MFR, MP and Sync were compared with reaction times for each animal (Figure 3). For animals with longer reaction times, premovement events occurred earlier relative to movement onset. Such relationship is unlikely for peripherally-induced events. The dependence of premovement modulation onset time upon the reaction time was more prominent for earlier activity changes than for later ones.

The variability of the firing characteristics associated with the direction of the subsequent movement was estimated (Figure 4). This was done for the activity during the stabilized response period and the later premovement period by examining the flexion-extension activity differences. For the stabilized response period, these difference values (for MFR, MP, but not for Sync) were significantly larger for neurons with cutaneous RFs. For the premovement period, modulation patterns substantially varied depending on movement direction. These premovement patterns were classified as reciprocal or symmetrical with respect to movement direction. For two-event cases, early events were more often symmetrical than late events.

Brief Conclusions-

From these data we conclude that the activity patterns of SI neurons that most faithfully represent the sensory periphery are modulated prior to voluntary movements. We suggest that inputs of central origin contribute to this premovement modulation. Presumably, the role of the central inputs may be to prepare the sensory cortical areas for changes in activity (reafference) that results from voluntary movement.

2) *Sensory Cortical Neuron Responsiveness During The "Unpredictable Task".*

Goals of the Study-

We are currently conducting experiments designed to test the hypothesis that variations in expectation alter the sensory responsiveness and the magnitude of premovement activity exhibited by SI cortical neurons. The paradigm being used is a superset of task normally used. By using an unpredictable reward schedule for correct task performance, we have created a condition under which monkeys sometimes are not reinforced for seemingly appropriate movements. Several types of results are thought to be possible. In trials immediately following correct but unrewarded performance ("after trials"), both sensory responsiveness and premovement activity may be either enhanced or suppressed. We wish to describe these changes quantitatively as well as qualitatively.

Brief Description of Methods-

Three monkeys were trained to make wrist flexion and extension movements in response to vibratory and/or visual go-cues. We have recorded or are currently recording from two of them. Each monkey first held a centered wrist position and awaited the trial's go-cues. Upon receipt of that cue, he made ballistic wrist flexion or extension movements, in blocks of ten. Using a pseudo-random reward schedule, we created a condition in which behavioral outcome could not be reliably predicted. Approximately 75% of the trials in which the monkey performed correctly were rewarded. The other 25% were not. The activity patterns of 249 task-related neurons have been recorded during this year. Histological confirmation of the neurons' locations awaits the termination of these ongoing experiments. A total of 85/249 were vibratory responsive, exhibiting sustained or transient changes inneuronal activity associated with stimulus presentation. A total of 149/249 exhibited premovement

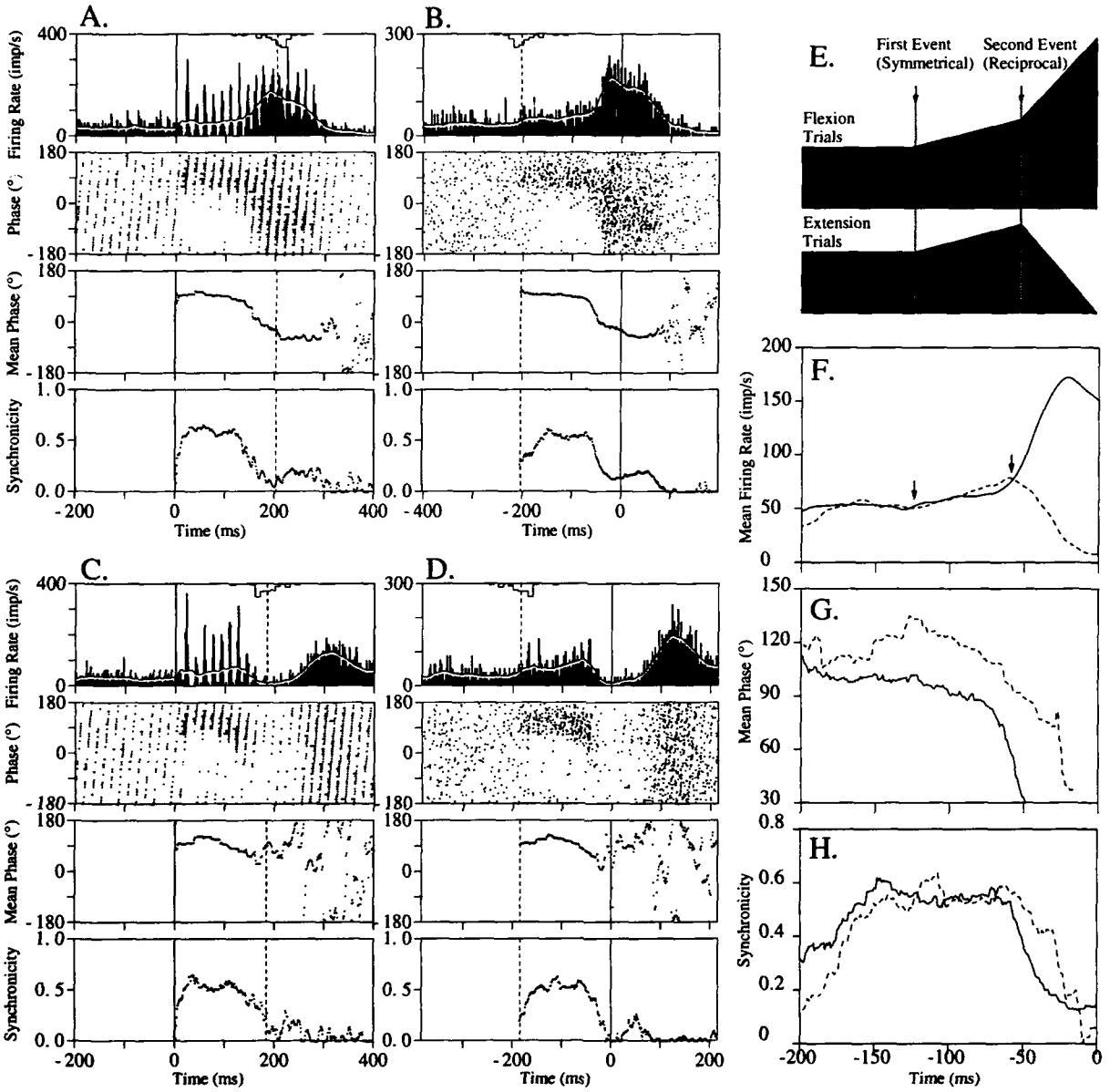


Figure 4. Variability of premovement activity patterns with respect to intended direction of movement.. The activity of an area 1 neuron during flexions (A & B) and extensions (C & D) made in response to 57 Hz vibration is illustrated. This neuron was activated during palpation of flexor carpi ulnaris and during passive flexions in the third metacarpo-phalangeal joint. An AA pattern was observed during flexions, and an AS pattern was observed during extensions (see Fig. 2B). Histograms (bin width =2 ms) of activity and raster displays aligned on vibration onset (A&C) and on movement onset (B&D). Mean firing rate traces are superimposed upon the histograms. In rasters, movement onset (A&C) and vibration onset (B&D) are shown by darker marks. Distribution histograms for these onsets are displayed in top panels. Periodic pattern of vibration-entrained activity is visible in A&C. However, this pattern is not evident in movement-aligned display (B&D). The activity change associated with the first event that occured 120 ms prior to movement onset, was symmetrical with respect to movement direction, whereas that for the second event (60 ms prior to movement onset) was reciprocal (E & F). F. Superimposed traces of mean firing rate. G. Superimposed traces of mean phase. H. Superimposed traces of synchronicity.

activity. Of these, 17 showed reciprocal, 27 exhibited unidirectional and 75 had nondirectional premovement activity patterns.

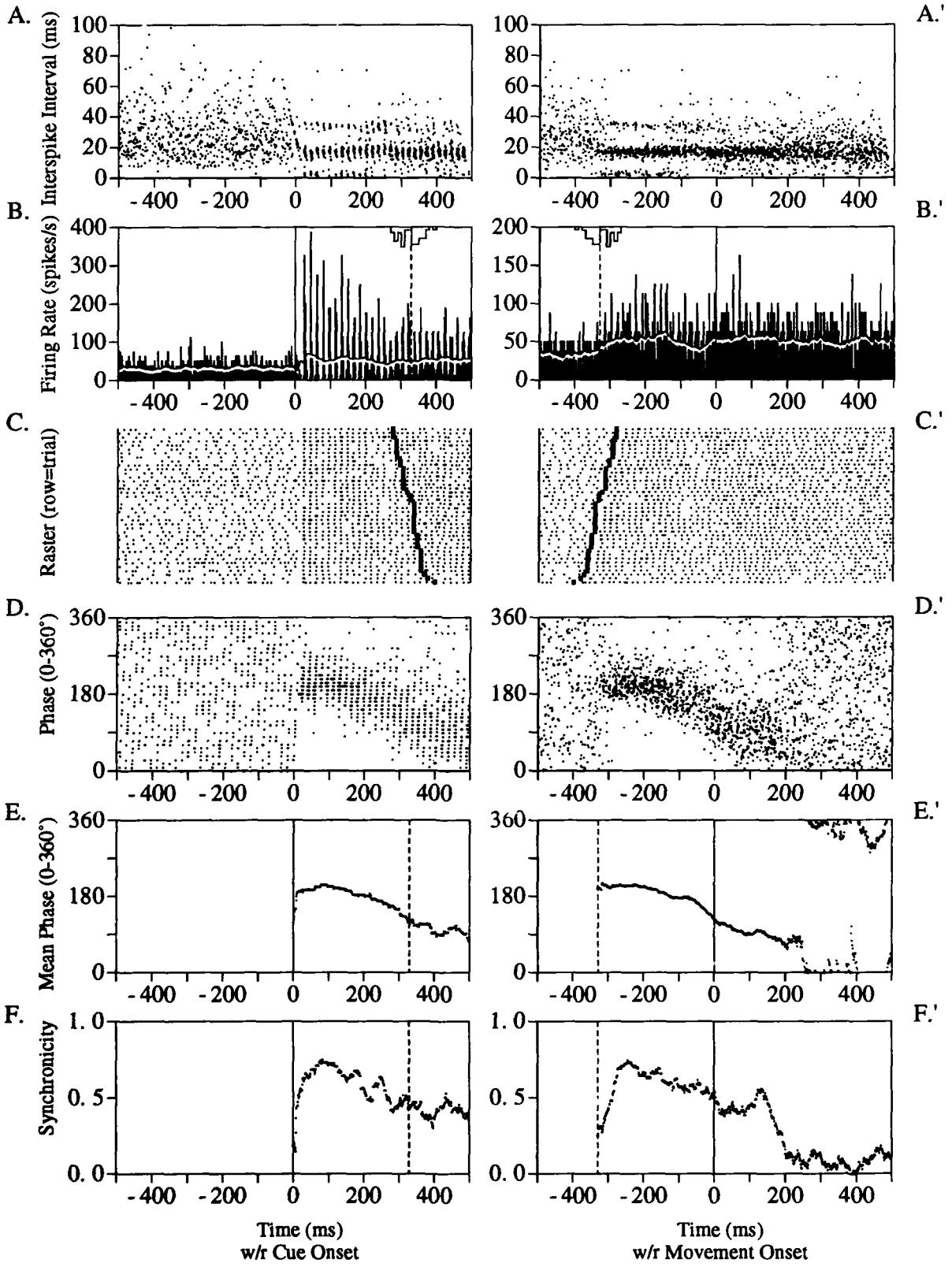


Figure 5. Displays of the parameters, as a function of "behavioral time", centered on vibration onset (left; regular) or movement onset (right; prime). All records are from trials that followed a rewarded trial (regular trials). A. Interspike intervals (ISI) constructed by plotting ISI of the nth and nth+1 spike. Rhythmic firing appears as horizontal bands. B. Histograms showing instantaneous and mean firing rates. Entrainment may occur without significant increases in mean firing rate. C. Rasters in which each dot represents a spike and each row represents a single trial. (conventions as in figure 4). D. Phase plots which preserve the temporal relationship of spikes to the vibratory stimulus period when trials are "re-aligned" on movement onset. E. Mean phase for the spikes occurring after stimulus onset. F. Synchronicity, a measure of how well the firing pattern is entrained to the frequency of the peripheral vibratory stimulus, scaled from zero (random firing) to 1.0 (perfectly entrained).

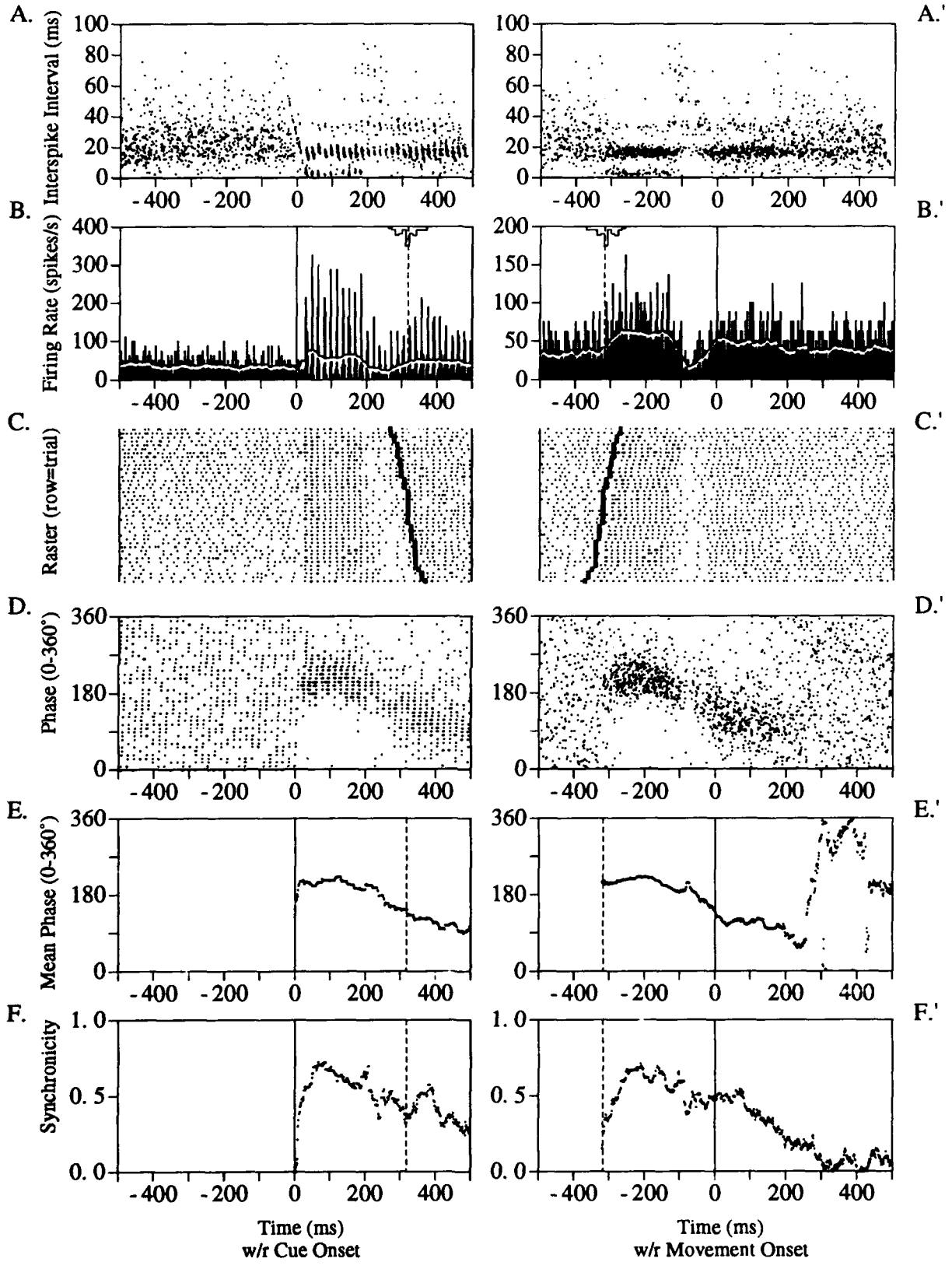


Figure 6. Conventions as in figure 5. Activity of the same neuron except that records show firing associated with trials that immediately followed withholding of reward for correct behavior (after trials). This and the previous figure were constructed from peri-event records associated with vibratory-cued wrist extension movments. This neuron had a cutaneous receptive field on the palm of the hand. It was recorded 1.29mm from the cortical surface and thus was probably an area 1 neuron. Histological verification awaits completion of these on-going experiments.

General Results-

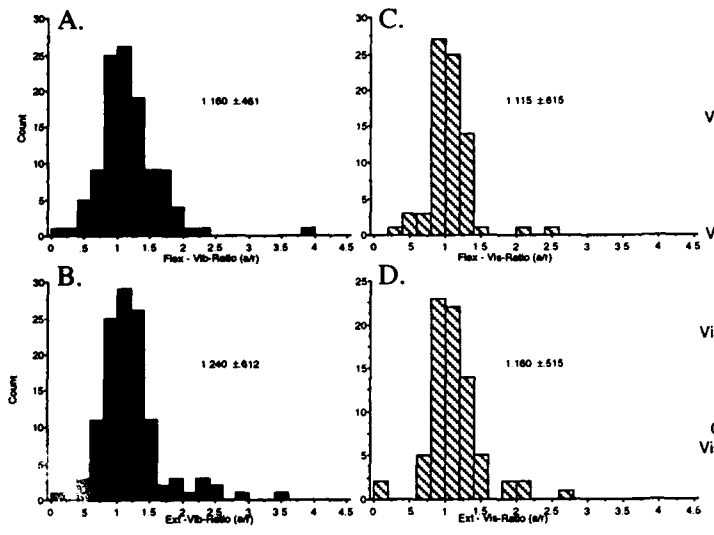
Neuronal activity during rewarded trials (Figure 5) was compared with that for after trials (Figure 6) for instances in which the monkey made similar wrist movements. In many cases, qualitative differences in the activity patterns of these SI cortical neurons during regular (rewarded) and after trials were readily noticeable. For example, compare the activity occurring ~100ms before movement onset in Figure 5&6. For the initial quantitative examination, we calculated the premovement activity (PMA) magnitudes and the onset times of these magnitude changes for all neurons. Using a modified version of the Kolmogorov-Smirnov test (p=.01) for determining significant differences in the frequency distribution of populations, we selected a maximum of 119 neurons which 1) had significant changes in PMA magnitude that 2) occurred between 70-250ms before movement onset. Figure 7E shows results that indicate that PMA magnitude and onset for the regular and the after trials appear to be distributed in two statistically different populations. In panels A-D of this figure, the distribution of the enhancement indices (EIs; after trials PMA magnitude / regular trial PMA magnitude) are presented.

From these initial analysis, we can make several tentative conclusion which serve as working hypotheses to guide subsequent experiments First, regardless of whether trials were triggered by visual or vibratory cues, PMA onsets occurred earlier in regular as compared with after trials. This was especially true for extension trials compared with flexion trials. Said in another way, PMA changes occur nearer movement onset when the behavioral conditions are less predictable. Second, PMA magnitudes are greater during after trials than during regular trials. This is suggested by the fact that the mean EIs are greater than unity and indicate that PMA may be, on average, 11-24% greater in after trials. The broad distribution of these EIs may be explicable once we have histological confirmation of the cortical location of each neuron and can related the activity to this location and to the type of peripheral receptive field which each neuron has. Third, previous analysis of a small sample of vibratory-responsive neurons (n=17) indicate that these sensorimotor cortical neurons tend to be more responsive to peripheral stimuli in after trials as compared with regular trials. We are in the process of conducting a similar analysis on the additional 85 vibratory responsive neurons from which we have recently recorded. Initial impressions are that the tentative observations stated above will be confirmed with these additional data.

Brief Conclusions-

As we have stated earlier, when the behavioral outcome is predictable (i.e., when the monkey has previously been rewarded for performing correctly) both sensory responsiveness and PMA in SI neurons are at some baseline level. In trials which follow the withholding of the reward for correct performance, the outcome is unpredictable. When behavioral conditions become unpredictable, PMA (which, depending upon the time of its occurrence in relationship to EMG onset may reflect either central or peripheral inputs, and sensory responsiveness) appear to be enhanced. However, decreased predictability is associated with later PMA onset timing, perhaps because of behavioral uncertainty.

These data are open to at least two types of interpretations. We have previously argued that the role of PMA may be to gate the response of other SI neurons that do not play an important part in the upcoming movement. We have also argued that PMA may reflect a corollary discharge from primary motor cortex (MI) since neurons in SI areas receiving direct MI projections tend to show PMA while those in areas without direct MI projections do not. MI stimulation is known to alter SI neuronal responsiveness to cutaneous and proprioceptive inputs. Finally we have observed, for the 17 completely analyzed sensory-responsiveness neurons, that vibratory stimulus-related responses are



E.

		DF:	Mean R - A:	Paired t value:	Prob. (2-tail):
PMA VibTrials	Flex	110	-1.315	-1.349	.1798
	Ext	119	-2.946	-4.010	***.0001***
	Total	230	-2.169	-3.573	***.0004***
PMA Onset VibTrials	Flex	110	7.658	1.419	.1588
	Ext	119	11.008	2.909	***.0043***
	Total	230	9.398	2.893	***.0042***
PMA Vis.Trials	Flex	76	-1.257	-1.853	.0678
	Ext	76	-2.329	-2.449	***.0166***
	Total	153	-1.793	-3.072	***.0025***
PMA Onset Vis.Trials	Flex	76	2.272	.577	.5655
	Ext	76	10.701	3.008	***.0036***
	Total	153	6.487	2.4325	***.0161***

A= After Trials value; R=Regular Trials value
Paired *t-test*.

Figure 7. The distributions of the ratio of the magnitude of the premovement activity during after trials as compared with during regular trials (Enhancement Index; EI). The mean change in premovement activity during the after trials was ~ 11-24%. A) vibratory-cued flexion trials; B) vibratory-cued extension trials; C) visually-cued flexion trials; D) visually-cued extension trials. E) The results of paired t-tests conducted to determine the relationship between PMA onset times and PMA magnitude as a function of movement direction. Bold values indicate significant mean differences.

greater in the after trials. This last observation would appear to indicate that during conditions of predictable behavioral outcome, the responsiveness of sensorimotor cortical neurons is attenuated. When conditions become unpredictable, this attenuation appears to be removed. The observation that PMA is, in general, greater in the after trials would seem to be in keeping with this if it is hypothesized that some general mechanism results in the decrease of activity of these neurons in response to both peripheral and centrally-generated inputs. One possible role for an increase in PMA might then be to actually increase the suppression of activity of other neurons that do not convey important information about the subsequent movements, as stated above. The other interpretation is that the neurons in question are themselves the behaviorally important ones and that increased PMA actually reflects increased information transfer regarding behaviorally important events. These two roles are not mutually exclusive and probably occur simultaneously.

Regardless of which interpretation is favored it appears that sensory gating is dependent upon whether there is a reasonable expectation that attenuating some inputs and strengthening others may actually improve performance by removing potentially competitive sources of information coming from the periphery. Further experimentation will determine if cortical location and RF type are important factors determining the effects of reward predictability upon neuronal responsiveness in SI.

3) Efficacy of Vibratory Abort Cues in Arresting Previously Triggered Wrist Movements

Goals of the Study-

The main objective of this study was to determine the efficacy of abort cues presented at various times prior to wrist movement. It was designed to determine if previously cued wrist movements could be altered by somatosensory signals presented prior to movement. Our working hypothesis is that abort signals presented nearer movement onset must be of greater amplitude to be detected and that abort signal presentation after some crucial point in time may result in the original movement being executed, even though the subjects will indicate that they detected the abort signal either verbally or by

making compound movements. In addition, we would predict that the amplitude of the abort cues presented in complexly cued trials would need to be comparatively larger than in visual only trials. This prediction is based upon theories of the nature and occurrence of changes in somatosensory responsiveness to peripheral stimuli that occur prior to movement onset. Finally, we sought to determine if the performance benefit of using vibratory go-cues (i.e., shorter reaction times [RTs]) was maintained for this task. As an initial study, we have conducted the following experiments in which the time of the presentation of abort cues relative to go-cue onset was varied, and their frequency of occurrence was unpredictable. In these experiments, abort cue magnitude was not varied.

Brief Description of Methods-

Seven adult volunteers performed the paradigm described below. They were asked to perform the task with their right hand. All had normal or corrected-to-normal vision and normal hearing. These subjects received no compensation for participating in this study.

Subjects were seated in a specially designed chair in a quiet, moderately lit (5 foot-candles) room and viewed a display panel placed 50cm directly in front of them at eye level. This display contains 31 light-emitting diodes (LEDs). The subject's right hand rested on a flat aluminum handle coupled at one end to the axle of a brushless DC torque motor while the forearm was supported by an arm rest.

Each trial was initiated when the subject centered the handle so the central LED was illuminated. The handle had a 0.12Nm load assisting extension. At the start of each trial, an instruction LED was sometimes lit. It was located in the upper left corner of the visual display (8.3° of visual angle from the center). The presence or absence of illumination of this LED instructed the subject about the direction of the required movement (a red LED; on-extension; off-flexion). This LED also warned the subject that a trial had started. The subject maintained a centered wrist position for a randomly chosen period (0.5-2.0sec). If the subject maintained a steady position within ± 0.5° (each lamp = 1°) of center, the current wrist position was designated as the start position for analysis and a go-cue was presented.

Two "go-cues" were used to indicate that a movement should begin. The first (visual cue) consisted of illuminating a target LED on the visual display. The second (combined cue) consisted of the target *and* a vibratory stimulus delivered to the palm of the hand that was to be moved. Vibratory components consisted of vibrating the handle by driving the torque motor with a low-amplitude sine wave at 57Hz or 127Hz (see below). Visual targets consisted of the illumination of the target lamp at 4°, 8° or 12° from center (± 1.7°, ± 3.4°, or ± 5.1° of visual angle). Targets were presented randomly often requiring movement in the direction opposite that from the previous trial. Either cue (combined or target only) remained on until the subject moved to the target. Occasionally (1 in 4 trials; pseudo-randomly determined), subjects received a 127Hz vibratory "abort signal". This was accomplished by adding a 127Hz vibratory signal at various times after go-cue onset. The randomly presented abort signals were presented at 50, 100, 150 or 200ms after stimulus onset. Human movements in response to vibratory stimuli normally have reaction times of approximately 250-350ms in a task that is identical except that abort cues are not presented. Subjects were instructed to move in the direction opposite that originally requested if these signals were detected. Their behavior served as a confirmation that the signal was detected. Subjects heard a beep if that trial's movement was made in the appropriate direction. This beep informed the subject that the trial was successful and also served as a signal to recenter the handle to begin the next trial. On the first training day each subject was instructed to make the wrist flexion and extension movements as quickly as possible without sacrificing movement accuracy. The speed and amplitudes of these targeted movements were not restricted other than by

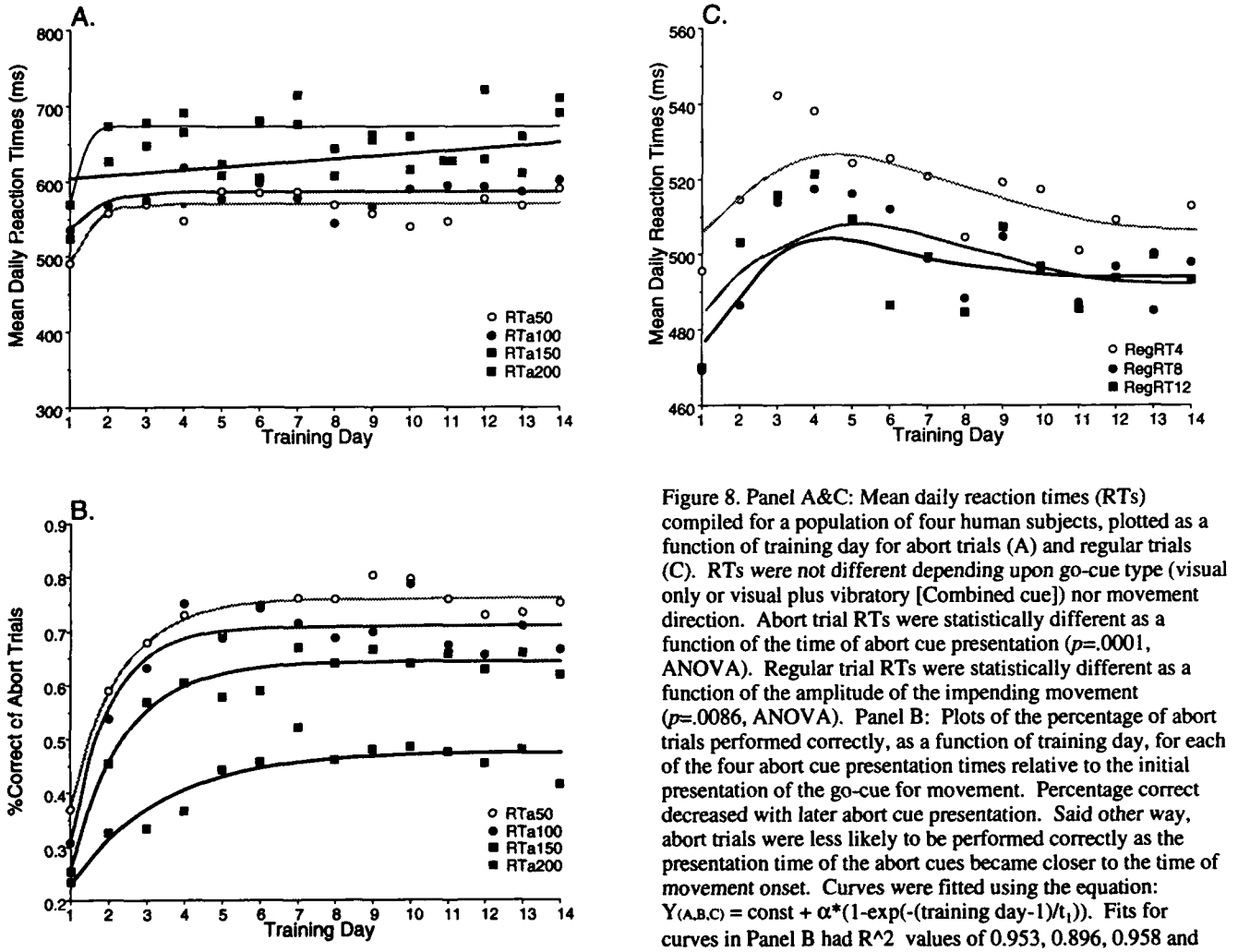


Figure 8. Panel A&C: Mean daily reaction times (RTs) compiled for a population of four human subjects, plotted as a function of training day for abort trials (A) and regular trials (C). RTs were not different depending upon go-cue type (visual only or visual plus vibratory [Combined cue]) nor movement direction. Abort trial RTs were statistically different as a function of the time of abort cue presentation (p=.0001, ANOVA). Regular trial RTs were statistically different as a function of the amplitude of the impending movement (p=.0086, ANOVA). Panel B: Plots of the percentage of abort trials performed correctly, as a function of training day, for each of the four abort cue presentation times relative to the initial presentation of the go-cue for movement. Percentage correct decreased with later abort cue presentation. Said other way, abort trials were less likely to be performed correctly as the presentation time of the abort cues became closer to the time of movement onset. Curves were fitted using the equation: $Y_{(A,B,C)} = \text{const} + \alpha*(1-\exp(-(\text{training day}-1)/t_1))$. Fits for curves in Panel B had R^2 values of 0.953, 0.896, 0.958 and 0.857 for abort times of 50, 100, 150 and 200ms, respectively. Fits for curves in Panel A had R^2 values of 0.622, 0.372, 0.038 and 0.456 for RTs for trials with aborts given at 50, 100, 150 and 200ms, respectively. Data in Panel C could not be fit reliably and so curves were drawn using a Distance-Weighted Least Squares algorithm with tension set to 0.15. All three groups of parameters were significantly different as a function of training day.

stops in the apparatus at ± 30° of angular deflection from center. However, a trial was considered to be a failure if the subject "overshot" the target by <1.5° in an attempt to acquire that target. The total duration of daily experimental sessions was about 35-40min. An on-line program operating on a PDP-11/23+ microcomputer was used to control the behavioral paradigms for these experiments and to record the time from stimulus presentation to movement onset (RT; reaction time) and the time from movement onset until the handle position coincided with the target (MT; movement time).

General Results-

To date we have complete analysis on the reaction times of five of the seven subjects that have participated in these experiments. Two subject are still completing their rounds of 14 days of performance assessment. The data from one subject was not included because this subject failed to master the paradigm even after 14 days of practice. For these ongoing experiments, we have initially examined two types of parameters, 1) the mean daily RTs and, 2) the percentage of correctly performed abort trials. Since it was unclear whether RTs would vary with the impending movement

direction and amplitude, go-cue type (visual or combined), or the delay between initial go-cue and the abort signal, several runs of analysis of variance (ANOVA) were conducted. It was found that significant variation in regular trial RTs occurred with the amplitude of the impending movement. RTs during abort trials and the percentage of abort trials correctly performed varied significantly with the time of abort cue presentation relative to the initial go-cue. Each of these three parameters varied significantly with training day.

Mean daily RTs for the four subjects were averaged and plotted as a function of training day (Figure 8C) for rewarded (or regular) trials. In addition, a similar plot was constructed for the RTs of the abort trials (Figure 8A). Finally, the percentage of correctly performed abort trials as a function of training day was plotted for the pooled data from the population (Figure 8B).

It appears that this population of subjects performed the task in a different manner from the performance of subjects on a similar task which lacked abort trials (unpublished observations). That is, combined cue trial RTs were not significantly different from RTs for trials in which the visual target alone was presented. The percentage of correctly performed abort trials initially was very low. In short, it appears that the subjects initially were performing the task as if the abort trials were not present.

With increased practice, subjects seemed to adopt a different performance strategy. Although additional training resulted in increases in the percentage of abort trials correctly performed, RTs became longer until they were ~60ms greater than initial levels.. With further practice, RTs for both types of trials decreased slightly, but were still above initial levels. The percentage of correctly performed abort trials rose steadily during the first 5 training days for trials representing abort cue presentation at each of the four presentation times. After Day 6 there was essentially no further improvement in performance as measured by the percentage of abort trials correctly performed. At this point, relatively consistent RTs were established for both visual and combined cue regular trials, although there continued to be great variance in the the RTs of individual subjects, as well as the population as a whole, as a function of training day.

Upon initial inspection, the percentage of correctly performed abort trials appears to vary inversely with onset of the abort cues relative to movement onset. RTs for individual trials and for individual subjects vary. Therefore, it is impossible to present abort cues at fitted times relative to movement onset. It is possible, however, to choose presentation times for these cues relative to the onset of the initial go-cues and to infer from this strategy what might be occurring as abort cues are presented closer to movement onset. From this reasoning, it appears that movements stand a better chance of being altered if the abort signals are presented earlier in the epoch between initial go-cue presentation and movement onset. In addition, subjects appear to reach stable performance levels earlier for trials in which the abort cues are presented further away from the time of onset of the impending movement. Time constants for the attainment of stable performance are currently being calculated for each subject and will be presented after complete analysis of the data from subjects that have yet to complete the full number of sessions.

Brief Conclusions-

These results suggest that wrist movements can be altered up until a certain point before movement onset, after which, vibratory abort signals may be ineffective, presumably because sensory responsiveness may be gated before active movement. Abort signals of a fixed amplitude are more effective in altering previously requested movement if they are presented as early as possible before

movement onset. It will be important in future studies to 1) present fixed amplitude abort cues even later relative to initial go-cue onset to determine if there is a point at which abort signals are no longer perceived, 2) vary the amplitude of the abort signals as a function of time from initial go-cue onset to determine if stronger signals can become more effective in alterning movements and presumably overcoming the peripheral sensory responsiveness decreases that have been demonstrated to occur prior to active wrist movement, and 3) determine if fine control of wrist position suffers from the presentation of vibratory abort cues at various amplitudes and times.

General Statement

The overall goal of the research conducted by this laboratory continues to be to understand the role that behavioral contingencies play in regulating the responsiveness of neurons that are involved in the control of wrist movement. Advances in this understanding make two contributions; the first to our general understanding of how the primate nervous system functions and the second to practical applications for device control.

We have chosen to study SI neurons because of our expertise with these neurons and because of their pivotal position in sensorimotor integration that ultimately results in controlled, goal-oriented behavior. It was previously thought that the responsiveness of SI neurons to peripheral and central inputs was essentially unaltered by behavioral contingencies. Findings from this laboratory and others have suggested that SI neurons undergo sometimes profound and sometimes subtle changes in responsiveness to both peripheral and central inputs. These findings have implications for the understanding of motor control because SI neurons provide direct or indirect inputs concerning limb position and muscle tension to other cortical regions such as posterior parietal, motor, premotor and supplementary motor cortices, as well as to the basal ganglia. All of these structures have been implicated in the control of movement. The demonstration of changes in the responsiveness in SI neurons then implies that the regions mentioned above may receive "pre-processed" information that differs depending upon the behavioral conditions present at any given time. Clearly, to understand motor control, the factors that influence it must be understood, and thus an understanding of the contributions which SI makes to this control are of great importance.

The practical application of this understanding may lead to more efficient design of control systems which utilize changes in wrist position. The results of human psychophysical experiments suggest that the wrist position changes controlling target acquisition may be altered before movements are actually made if vibratory abort cues are presented as early as possible. This may have performance advantages in that movement that are initially warranted and then become either unnecessary or detrimental may be arrested. Caution is warranted and further studies are needed, however, because it has been established that vibratory stimuli can adversely effect wrist position control if the signals are of great enough amplitude. By modeling human RT performance, predictions can be made about an individual's capacity for behavioral improvement and the time course of that improvement.

Status of Future Research

We will continue to record from monkeys who are being trained to perform the "Unexpected Failure" Paradigm during Year 03 of this grant. We currently are recording from one and have another monkey trained to perform this task.

We have an additional set of human psychophysical experiments planned. We will randomly

introduce an "abort signal" at increasing longer times from go-cue onset and at varying amplitudes, to determine if pre-planned wrist movements can be aborted given the presentation of additional sensory information. This will be done to determine when in the movement initiation and execution cycle the movements are committed and unalterable and whether there is any difference in this timing as a function of the type of go-cue (visual only or visual plus vibration) used.

List of Publications

Manuscripts

T.W. Gardiner and **R.J. Nelson**. Striatal neuronal activity during the initiation and execution of hand movements made in response to visual and vibratory cues. Exp Brain Res. 92:15-26, 1992.

(Note: This manuscript includes a comparison of premovement activity onset times and magnitudes of sensorimotor cortical neurons and has direct relationship to our continuing work toward the understanding of sensory gating during active movement. See General Statement).

Presentations of Supported Work

M.A. Lebedev and **R.J. Nelson**. The Activity of Vibratory Responsive Monkey Primary Somatosensory Cortical Neurons is Modulated Prior to Hand Movements. Neuroscience Abst. 18:503, 1992

Submitted Manuscripts

M.A. Lebedev, J.M. Denton and **R.J. Nelson**. Premovement activity patterns of monkey primary somatosensory cortical neurons responding to vibrotactile go-cues by entrained firing. (*Submitted* J. Neurophysiol.)

Manuscripts in Preparation

R.J. Nelson and E.D. Thomas. Reaction times and movement times for visually-cued and combined vibratory- and visually-cued hand movements. (*In preparation* for Perception and Psychophysics)

Submitted Abstracts

R.J. Nelson, E.D. Thomas and J.M. Denton. Reaction times differ for hand movements made to visual targets alone compared with targets and vibratory go-cues. Abst. Soc. Neurosci. (Submitted).

M.A. Lebedev and **R.J. Nelson**.Modulation of rhythmic firing of monkey primary somatosensory cortical (SI) and neostriatal (NS) neurons during active hand movements. Abst. Soc. Neurosci. (Submitted).

Associated Personnel

John M. Denton continues to be employed as a Research Assistant. He has, over the three years, proved to be important in the studies conducted under this grant. He now has expertise in data analysis and behavioral training of monkeys.

Michael A. Lebedev joined the laboratory this two years ago as a graduate student following his arrival from Moscow, Russia. He brings to the laboratory an extensive background in mathematics and physics. He is largely responsible for the phase analysis of the vibratory responsive neurons described herein and will present this work at this year's Annual Meeting of the Society for Neuroscience. He is truly a remarkable individual and an asset to the laboratory. Beginning July 1, 1992, he received 50% of his support for funds of AFOSR 91-0333. The other 50% of his support

comes from an award by the Center of Excellence in Neuroscience at the University of Tennessee, Memphis.

Erica D. Thomas, a graduate of Christian Brothers University, has worked in the laboratory since the summer of 1991. She has been responsible for analyzing data from human subjects as they performed the psychophysical experiments outlined above. She has been diligent in analyzing the data from these rather time consuming experiments and has been able to show some very interesting results with regard to what parameters affect reaction and movement times during hand movements toward a target.

Interactions

1992 Society for Neuroscience Annual Meeting, Anaheim, CA Oct. 25-30.

1993 Winter Conference on Brain Research, Whistler, BC, Canada Jan. 25-Feb. 1

New Discoveries

None.