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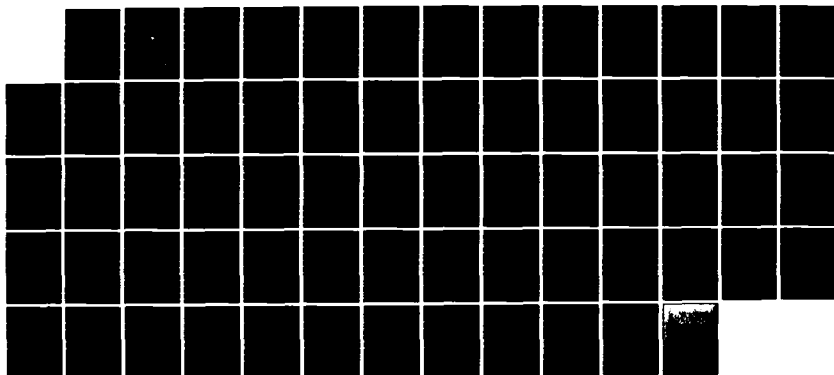
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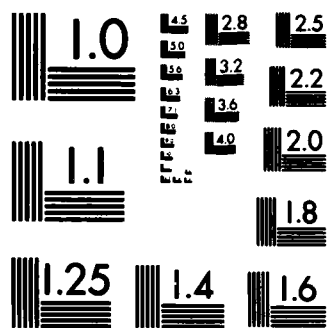
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EFFECTS OF IMPACT ACCELERATION ON
SOMATOSENSORY EVOKED POTENTIALS

Michael D. Berger, Ph.D.

and

Marc S. Weiss, Ph.D.



April, 1983

NAVAL BIODYNAMICS LABORATORY
New Orleans, Louisiana

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some of the measures of CNS function which may provide the basis for establishing such criteria.

The experiments reported here are part of an on-going program to test the neurophysiological effects of indirect or inertial head-neck impact acceleration. In these experiments, eight unanesthetized Rhesus monkeys, with torsos restrained in a seated position, and with head and neck free to move, were subjected to peak sled accelerations in the -X direction ranging from 42 m/s² to 963 m/s². Recordings of somatosensory evoked potentials (SEP's) were made using recording electrodes chronically implanted over the somatosensory cortex, and over the cervico-medullary junction. Electrical pulse stimuli were delivered at a rate of 5 Hz through spinal electrodes located at L1-L2. SEP's were recorded prior to impact, through the impact event, and subsequent to impact. Qualitative analyses were performed on both cervical and cortical SEP's, and extensive quantitative analysis was performed on cervical SEP's. The results of these analyses indicate that neurophysiological indices of injury may include: increases in latencies of the cervical SEP peaks exceeding 2.5%; large changes in the amplitude of the cervical SEP; changes in ripples on the cortical primary SEP; and substantial and persistent changes in the surface-positive cortical primary SEP. In particular, analysis of shifts in latency of the cervical SEP suggests the possibility of an injury threshold in the vicinity of 700 - 800 m/s². Smaller shifts in latency occurring near 600 m/s² may indicate a pre-injury condition.

Quantitative measures of neurophysiological function are useful in assessing the effects of inertial forces acting on the CNS through the freely moving head and neck. Continued investigation and extension of these measurement techniques is recommended.

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April 1983

Bureau of Medicine and Surgery
Work Unit M0097-PN.001-5004

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SUMMARY PAGE

PROBLEM

In order to test and evaluate impact protection devices, an impact-injury model for restrained humans in a crash environment must be developed. Disruption of the functioning of the central nervous system (CNS) is an important consequence of impact injury involving the head and neck, and is an important consideration in the development of a useful impact-injury model. Ultimately, neurophysiological criteria for functional injury of the CNS are desired. The main purpose of the experiments reported here is to identify some of the measures of CNS function which may provide the basis for establishing such criteria.

FINDINGS

The experiments reported here are part of an on-going program to test the neurophysiological effects of indirect or inertial head-neck impact acceleration. In these experiments, eight unanesthetized Rhesus monkeys, with torsos restrained in a seated position, and with head and neck free to move, were subjected to peak sled accelerations in the -X direction ranging from 42 m/s^2 to 963 m/s^2 . Recordings of somatosensory evoked potentials (SEP's) were made using recording electrodes chronically implanted over the somatosensory cortex, and over the cervico-medullary junction. Electrical pulse stimuli were delivered at a rate of 5 Hz through spinal electrodes located at L1-L2. SEP's were recorded prior to impact, through the impact event, and subsequent to impact. Qualitative analyses were performed on both cervical and cortical SEP's, and extensive quantitative analysis was performed on cervical SEP's. The results of these analyses indicate that neurophysiological indices of injury may include: increases in latencies of the cervical SEP peaks exceeding 2.5%; large changes in the amplitude of the cervical SEP; changes in ripples on the cortical primary SEP; and substantial and persistent changes in the surface-positive cortical primary SEP. In particular, analysis of shifts in latency of the cervical SEP suggests the possibility of an injury threshold in the vicinity of $700 - 800 \text{ m/s}^2$. Smaller shifts in latency occurring near 600 m/s^2 may indicate a pre-injury condition.

RECOMMENDATIONS

Quantitative measures of neurophysiological function are useful in assessing the effects of inertial forces acting on the CNS through the freely moving head and neck. Continued investigation and extension of these measurement techniques is recommended.

ACKNOWLEDGEMENTS

This research was sponsored by the Naval Medical Research and Development Command and the Biophysics Program of the Office of Naval Research, and was performed under Navy work unit No. M0097-PN.001-5004. A project as complex as the one discussed here would not be possible without the dedicated cooperation of a large number of skilled people. The following list is incomplete, and is in no particular order. From the Naval Biodynamics Laboratory: Mr. L. Lustick provided valuable discussion on the mathematical procedures; Mr. G. Williamson provided administrative services in expediting computer operations; Mr. W. Anderson designed and programmed the hardware and software required for the specialized digitization procedures; Dr. E. Jessop, with the assistance of the NBDL veterinary staff, provided excellent clinical maintenance and evaluation of the subjects, as well as supervision of the electrode implantation procedures and associated logistics; Mr. A. Prell provided excellent photographic and artistic services; Mr. S. Morrill maintained and operated the physiological data acquisition system; Dr. D. Thomas provided overall project coordination, and valuable contributions to the experimental design; Dr. C. Ewing provided leadership and direction without which this work never would have been done. From the Medical College of Wisconsin: Dr. P. Walsh performed the neurosurgery; Dr. J. Myklebust performed the electrophysiological aspects of the electrode implantation. From the Texas Research Institute for Mental Science: Dr. B. Saltzberg and Mr. W. Burton supplied the CSTRIP program and some material on non-linear regression, as well as valuable discussion. From the Slidell Computer Complex, numerous staff members provided valuable assistance in dealing with the administrative and technical problems involved in inter-machine communication and analysis of a huge amount of data. In this regard, special thanks are due to Mr. F. Lovato and Mr. C. Johnson.

ANIMAL CARE

The animals used in this study were handled in accordance with the Guide for the Care of Laboratory Animals, prepared by the Committee on Care and Use of Laboratory Animals of the Institute of Laboratory Animal Resources, National Research Council.

TRADE NAMES

Trade names of materials or products of non-government organizations are cited where essential for precision in describing research procedures or evaluation of results. Their use does not constitute official endorsement or approval of the use of such commercial hardware or software.

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I. INTRODUCTION

Impact injury involving the head and neck disrupts the normal functioning of the central nervous system (CNS) to an extent dependent upon the severity and nature of the trauma. The often temporary CNS dysfunction, which results from head and neck trauma (identified clinically as "concussion"), is of special interest in the development of a useful injury model. The pioneering work of Denny-Brown and Russell (5) was the first thorough attempt to identify the physiological concomitants of direct head injury and led to numerous subsequent investigations (e.g., 7, 12, 13, 31). These studies shared the following features: (a) the impact blow was delivered directly to the head which was free to move, (b) anesthetized animals (monkey, dog, cat) were subjects, (c) basic vital functions and EEG were monitored. Generally, the results followed a typical pattern, similar to the one described by Denny-Brown and Russell (5) and Williams and Denny-Brown (33). Severe, but non-fatal, blows resulted in a loss of corneal reflex, rise in blood pressure, fall in heart rate, drop in EEG amplitude and frequency, sometimes followed by development of slow waves. These effects could occur in the absence of any apparent brain pathology and have been well reviewed (6, 21, 30).

In the decade following these reports, two important extensions to these basic findings were made. Foltz and Schmidt (8), using unanesthetized monkeys, stimulated the sciatic nerve and recorded evoked potentials (EP's) from the reticular formation (RF) and the medial lemniscus. In six out of eight monkeys receiving severe direct head impacts, the lemniscal response persisted while the RF response was abolished. This first use of the EP in a head injury study indicated that the non-specific brainstem gray matter was functionally more sensitive to impact than the sensory specific ascending pathway. Subsequently, Friede (9) demonstrated that in the cat, both cervical stretch and a blow to the head produced the same loss of reflexes as well as the same neuropathology at the C₁ level of the spinal cord. This, again, suggested that the lower brainstem might be the vulnerable site in CNS impact dysfunction.

More recently, Ommaya and his co-workers (10, 15, 18) subjected both the unanesthetized monkey and chimpanzee to non-impact head acceleration while stimulating the median nerve and recording the somatosensory EP's at the cortex. The EP amplitude was more sensitive to head acceleration than the EEG. This occurred in animals that were rendered unconscious (loss of muscle tone, insensitivity to painful stimuli) as well as in some that remained conscious. The duration and intensity of the EP effect appeared to parallel the duration of the unconsciousness, but no relationship to the intensity of acceleration was reported.

These earlier results provided the background for the effort begun in late 1974 when the Naval Biodynamics Laboratory (then the Naval Aerospace Medical Research Laboratory, Detachment #1) undertook the first of many experiments designed to test the neurophysiological effects of indirect or inertial head acceleration. In these

experiments the restrained torso is accelerated, with the freely moving head and neck receiving the "indirect" acceleration through the skeletal and soft tissue anatomy. Results from the early experiments (2, 32) indicated that the cortical somatosensory EP showed a decrement in amplitude and an increase in latency following non-lethal impact. These changes appeared to be greater with increased peak acceleration. This confirmed the utility of neurophysiological measures in assessing the effects of inertial forces on the functioning of the brain. Ultimately, neurophysiological criteria for functional injury to the CNS are desired. The main purpose of the experiments reported here is to identify those measures of CNS function which can be the basis for establishing such criteria.

II. METHODS

II-A. Experimental Procedure

The adult Rhesus (Macacca Mulatta, ca. 10 Kg) was selected as the animal model and the somatosensory system as the pathway for testing CNS function. All the experiments were designed to use unanesthetized animals, restrained in a sitting, upright position, with head and neck freely moveable. The restraint system consisted of a nylon suit which covered the entire body except for the head and neck. Straps sewn to the suit firmly restrained the subject to a fiberglass chair which was molded to the shape of the subject's back. The subject was seated on a 410 kg sled which was accelerated by a HYGE system with a one meter stroke. Peak sled accelerations ranged from 42 to 963 m/s². The subject was oriented so that he was accelerated in the -X (24, 25) direction. The sled was decelerated by friction (2 to 3 m/s²) over a distance of up to 213 meters. Precise inertial data were obtained from an array of transducers rigidly mounted to the monkey's skull. Physiological data included EKG, respiration, and cervical and cortical EP activity; the exact configuration occasionally varied. Average heart rate was computed by hand from EKG strip chart records.

The eight monkeys used as subjects for these 22 experiments were prepared surgically with chronic in-dwelling electrodes using procedures previously described (28, 29). Briefly, strip disc electrodes were implanted epidurally over the dorsal spinal cord at L₁ - L₂ and over the cervico-medullary (CV) junction. Bilaterally, subdural electrodes were implanted over the primary somatosensory cortex (SX). Three months were allowed for recovery from implantation surgery.

Constant current monophasic pulses at a nominal rate of 5 Hz were delivered to one pair of lumbar electrodes. The stimulus intensity ranged from 0.3 to 3.0 ma among animals and was selected for each animal as the highest intensity consistent with the apparent comfort of the subject. Large, but sub-maximal EP's were recorded from the CV and SX electrodes through a telemetering system with an overall bandpass of 30 to 1500 Hz for CV and 10 to 1500 Hz for SX. Table 1 details the parameters used for each experiment.

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TABLE 1 SUMMARY OF EXPERIMENTAL PARAMETERS

Experiment	Date	-Gx Sled Peak 2 (m/s ²)	Subject	Stimulus Intensity (mA)	Cortical Recording	Amplifier		Low Frequency		Comment
						Gain (X1000) Cerv. Cort.	Cerv. Cort.	Cutoff (Hz) Cerv. Cort.	Cerv. Cort.	
LX3008	19578	208	AR0761	.75	left	80	20	30	1	
LX3009	19578	796	AR0761	.75	left	80	20	30	1	
LX3010	19578	963	AR0761	.75	left	80	20	30	1	
LX3017	20078	209	AR0761	.75		80	20	30	1	*
LX3018	20078	589	AR0761	.75		80	20	30	1	*
LX3019	20078	416	AR0761	.75		80	20	30	1	*
LX3020	20078	206	AR0761	.75		80	20	30	1	*
LX3027	28478	102	AR4114	.3	left	120	60	50	10	
LX3028	28478	407	AR4114	.3	left	120	30	50	10	
LX3183	06679	103	AR8824	.75	right	20	20	50	10	
LX3184	06679	611	AR8824	.75	right	20	20	50	10	
LX3185	07179	100	AR8857	1.25	right	40	20	50	10	
LX3186	79	810	AR8857	1.25	right	40	20	50	10	
LX3691	24180	99	AR0012	1.5	right	80	8	30	10	
LX3693	24680	727	AR0012	1.5	right	80	8	30	10	
LX3694	24680	767	AR0012	1.5	right	80	8	30	10	
LX3695	24780	98	ARNA28	1.5	right	80	2.5	30	10	
LX3697	24880	441	ARNA28	1.5	right	80	2.5	30	10	
LX3698	980	435	ARNA28	1.5	right	80	2.5	30	10	*
LX3699	42	42	AR8872	4.0	right	40	10	30	10	
LX3701	25480	436	AR8872	3.0	right	40	10	30	10	
LX3702	25480	434	AR8872	3.0	right	40	10	30	10	
LX3703	25580	99	AR8802	2.0	right	40	8	30	10	
LX3705	25680	630	AR8802	2.0	right	40	8	30	10	
LX3706	25680	624	AR8802	2.0	right	40	8	30	10	
LX3707	26080	98	AR8790	2.5		20	10	30	10	*
LX3709	26180	860	AR8790	2.5		20	10	30	10	Fatal 10 min. post-impact. *
LX3710	26280	97	ARNA02	3.0		160	16	30	10	*
LX3713	26680	98	ARNA02	2.0	left	160	16	30	10	
LX3714	26680	598	ARNA02	2.0	left	160	16	30	10	
LX3715	26680	598	ARNA02	2.0	left	160	16	30	10	

Cortical amplifier failure at impact.

Fatal 10 min. post-impact. *

* Results not included.

EP data acquisition was initiated 30 to 45 minutes prior to impact, was continued through impact delivery, and was terminated 45 to 90 minutes after impact. There was a five to ten minute gap in data acquisition ending ten minutes prior to impact. The data were amplified on the sled, telemetered to nearby equipment and recorded on FM tape. The data were digitized off-line on a hybrid EAI PACER 600[®] computer at a sampling rate of at least 20 kHz. A software-hardware design was used which synchronized digitization with the stimuli. The digitized data were then processed on a UNIVAC 1100[®] series computer. Some of these data were also analyzed elsewhere (19).

II-B. Data Analysis

Qualitative analysis was performed on both cervical and cortical EP's. Starting at various times in relation to impact, average evoked potentials (AEP's) with N = 50 were computed from sequences of EP's. These AEP's were visually examined for effects related to impact.

Quantitative analysis was performed on cervical EP's only, and was used to determine the extent to which the impact produced shifts in latency of various peaks of the cervical AEP's. Fig. 1 is a flow diagram of the quantitative data analysis procedure. Two types of AEP's were computed: "test" and "baseline". Test AEP's were each computed with N = 10, and since the inter-stimulus interval was 0.2 seconds, each spanned an interval of two seconds. For each run, a sequence of test AEP's was computed starting two minutes pre-impact, and ending five minutes post-impact. A single baseline AEP was computed using the EP's occurring from two minutes pre-impact until impact. N was approximately 580.

Most of the cervical AEP peaks with latencies between 1.7 and 5.5 ms were subject to latency analysis. Peaks which proved too unstable for analysis were excluded. In order to determine the pre-impact latency of each peak, a simple peak detection algorithm was used. For each peak of the pre-impact test AEP, a latency interval was selected within which the peak appeared. The absolute maximum or minimum in this interval was determined and used as the peak latency. The result was discarded for that test AEP if the absolute extremum was at the beginning or end of the selected interval. For each peak, the median latency for all pre-impact AEP's was then computed and used as a baseline latency.

To determine shifts in latency produced by impact, an algorithm to compute normalized cross-correlation functions (NCCF's) was used. Computation of an NCCF may be thought of as a search for a selected portion of the baseline AEP in each of the test waves. This selected portion of the baseline AEP is called the "reference wave" and was that portion of the baseline AEP between two specified latency limits on either side of the peak of interest. To compute the NCCF, the reference wave was shifted along the test wave and Pearson's correlation coefficient was computed between the reference and test wave at each value of the shift. The NCCF is the correlation coefficient as a function of the amount of shift. To obtain the shift

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DATA ANALYSIS

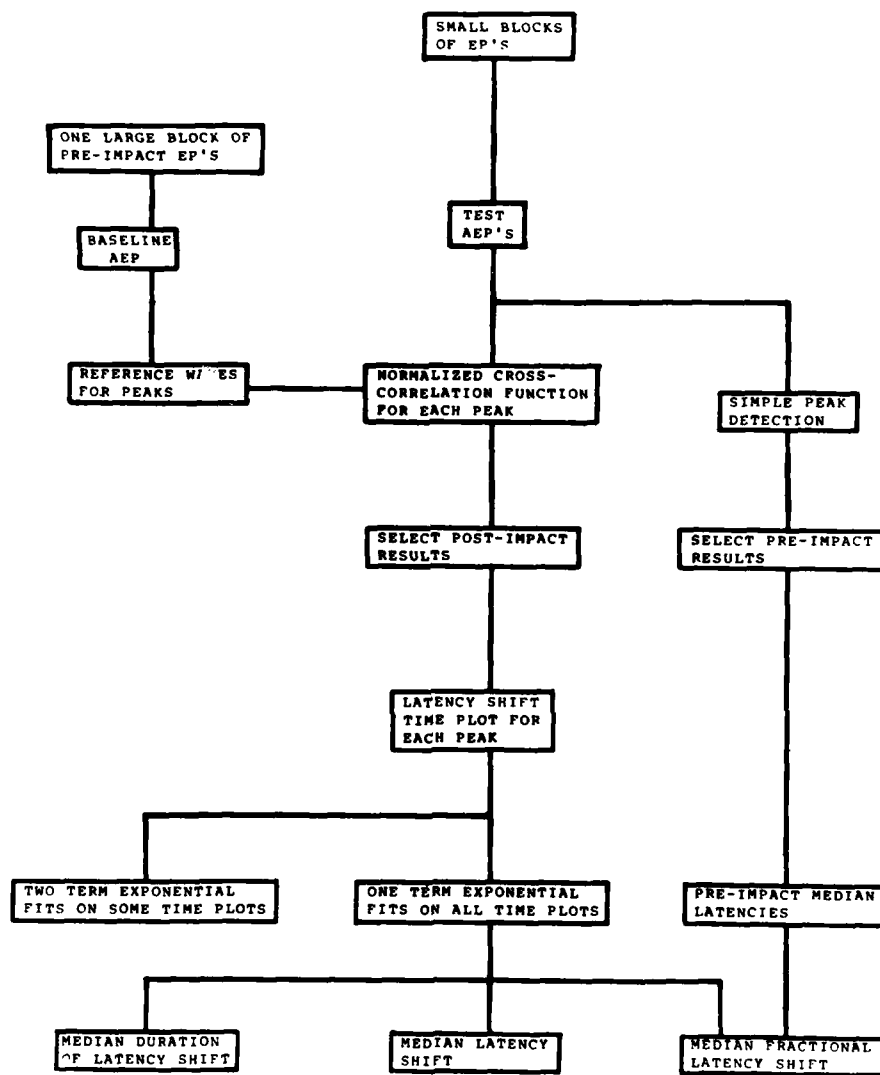


FIGURE 1

Flow diagram of the analysis procedure applied to cervical EP data from each experiment. There are two inputs: 1 - one large block of pre-impact EP's; 2 - numerous small blocks of EP's from both pre- and post-impact periods. There are four outputs: 1 - median duration of latency shift; 2 - median latency shift; 3 - median fractional latency shift; 4 - two-term exponential fits. The first three outputs are single values plotted in fig. 4. The last output consists of graphs illustrated in fig. 5, and regression coefficients given in table 3. The coefficients for one-term exponential regression are intermediate values in the flow diagram, and are given in table 2.

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in latency, each NCCF was scanned for the highest value of the correlation coefficient. The shift in latency (of reference wave with respect to test wave) at this maximum was taken as the shift in latency for the test AEP. If the maximum correlation coefficient occurred at either end of the range of shift in latency the corresponding data were discarded. The NCCF was applied to the pre-impact and post-impact test AEP's.

In both simple peak detection and NCCF computation, it was necessary to select a latency interval over which the AEP was searched. Selection of this interval was based on both physiological and technical considerations. The interval was made long enough so that shifts in latency known to be possible from extensive visual examination of AEP data would be detected. It was necessary, however, to keep the interval short enough to avoid confusion with adjacent peaks. Occasionally, these two requirements proved incompatible, in which case the peak was not used.

Both the simple peak detection and the NCCF procedures involved detection of an extremum over a sequence of points. In some cases, to increase the resolution of the measurements, quadratic interpolation was used. The best parabola (in the least-squares sense) was determined for an odd number of points centered at the previously determined extremum. The extremum of this parabola was then taken as the final result.

Shifts in latency for each peak were plotted as a function of time over the experiment, relative to impact (figs. 2, 3, 5). To compare shifts in latency, the magnitude of the effect of impact on the latency of each peak was represented by two variables. The first is the amplitude of the effect, i.e., a measure of the deviation of the shift in latency from its pre-impact value (not to be confused with the amplitude of the evoked potential). The second is the duration of the effect.

To estimate these two variables, first, values of shift in latency that resulted from failure of the NCCF to detect the selected peak were manually removed. Next, amplitude and duration were determined by regression of a one or two term exponential decay function on data from the first five post-impact minutes. In most instances, the initial effect of impact was an increase in latency, and in about 85% of these cases, single exponential regression was used. However, in the remaining 15%, the latency shifted to values well below the pre-impact baseline for a substantial portion of the first five post-impact minutes. In these cases, a large positive constant was added to the post-impact sequence of shifts in latency, and two term exponential regression was used. This generally resulted in one term with a time coefficient that was much longer than the five minute analysis interval, and could thus be considered essentially constant. The amplitude of the effect was then computed as the sum of the two exponential amplitude coefficients and minus constant added to the data. This final amplitude represented the initial post-impact displacement of the latency from the pre-impact baseline, and was, in this sense, comparable to the amplitudes from the one term analyses.

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The shorter of the two time coefficients was used to estimate duration, although it was not always comparable with those from the one term procedure.

Aside from determination of the amplitude and duration, one and two term exponential regressions were also used to determine whether the corresponding decay functions would provide a good representation of the time course of effects of impact. Only data from high level impacts were used for this purpose.

For exponential regression the method employed was a modification of the modified Gauss-Newton, least-squares method recommended by Metzler, et al. (17, pp. 3-9). Initial estimates of the exponential coefficients were usually obtained with a modified version of the program CSTRIP (20), but in some cases initial estimates were manually supplied.

In determining the least squares fit, the mean square deviation is expressed as a function of the exponential coefficients, and the absolute minimum of the mean square deviation is sought. The method used to locate the absolute minimum can sometimes be "trapped" in a relative minimum, and return an incorrect result. Generally, this was obvious from the plots. The situation can often be corrected by altering the starting values, or dropping a few data points. These methods were applied where appropriate. In other cases, the correct least squares solution did not involve only exponential decay. Instead, an exponential growth term with a short time coefficient appeared. Such results were excluded from consideration. Detailed consideration of some aspects of the data analysis appears in Appendix B.

III. RESULTS

Pre-impact and post-impact AEP's from all experiments analyzed appear in Appendix A, and are specified by experiment number. Each experiment number begins with the characters "LX". Constant latency cursors are provided to aid in the observation of shifts in latency. Unless otherwise indicated, the results reported here refer to data illustrated in Appendix A.

III-A. Cortical AEP's -- Description

The cortical recordings were bipolar. However, in many of the subjects the recording electrodes were selected so that the positive electrode was over the most active cortical region available, while the negative electrode was relatively inactive. It is therefore reasonable to speak of surface polarity of the signal as if the recordings were monopolar. The activity observed in the cortical recordings may be divided into four general categories:

- 1 - Cortical Slow Waves. A positive wave began at about 5 to 12 ms, peaked at about 9 to 11 ms, and was followed by a negative wave

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that peaked at about 15 to 24 ms. The positive wave was considered to be the first cortical response to the afferent volley. There was a substantial subject-to-subject variation in the amplitude of the cortical slow wave.

- 2 - Fast Ripples. These appeared on the rise and peak of the positive slow wave. They have been observed in numerous subjects in this and other studies after stimulation of either the dorsal columns or the median nerve of Rhesus. They appear to have a narrower spatial distribution than the cortical slow wave and under some conditions the cortical slow wave can change without apparent change in the ripples. These ripples may represent afferent activity in the thalamo-cortical radiations.
- 3 - Early Fast Activity. This appeared at practically any latency from about 1 ms. to the onset of the cortical slow wave, and may have been due, in part, to far field activity. In some subjects, an especially prominent and very stable diphasic spike was seen with about 3.4 ms latency after spinal stimulation. It appears that this fast spike is localized in the region of the primary somatosensory cortex. It may be an antidromic pyramidal tract response.
- 4 - Early Slow Wave. This was seen in a few of the cortical recordings with a peak latency of about 5 ms. This may be a far field response, possibly of thalamic origin.

III-B. Cervical AEP's -- Description

The cervical recordings were bipolar, and no significance is assigned to the polarity of the waves. The earliest peak in each subject ranged from 1.5 ms to 2.9 ms. Multiphasic fast activity of considerable amplitude typically lasted until about 5 to 6 ms, with many low amplitude ripples following. Narrow and wide "half-waves" can be described. The narrow half-waves were roughly .35 ms wide. The wide half-waves were typically two to three times as wide as the narrow half-waves, and often had either a double peak, or an inflection near the peak. This suggested that the wide half-waves consisted of two nearly overlapping narrow half-waves. Where a double peak was observed, high impact levels sometimes affected the two peaks differently, in keeping with the idea that two "components" were present. Each "component" may represent the activity of fibers with similar conduction velocities. Variation in the placement of the recording electrodes allows each "component" to appear with either polarity, resulting in a great variety of wave configurations.

III-C. Qualitative Effects of Impact -- Cervical AEP's

The cervical and cortical qualitative results were derived from visual inspection of the AEP's illustrated in Appendix A.

In five experiments on three subjects (subject AR0761,

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experiments LX3009, LX3010; subject AR8857, experiment LX3186; subject AR0012*, experiments LX3693, LX3694) the peak sled accelerations exceeded 700 m/s^2 ("high level impacts"). Cervical EP's were available in all of these experiments. In two subjects, each receiving two high level impacts, there were profound changes in the cervical AEP's. In one subject (subject AR0761; experiments LX3009, LX3010) the cervical AEP's were nearly or entirely obliterated by impact. At 796 m/s^2 (LX3009) the AEP waveshape remained distorted for at least 60 seconds. At 963 m/s^2 (LX3010) the pre-impact waveshape was certainly not restored at two minutes, and probably not at four minutes post-impact. In the other subject (subject AR0012, experiments LX3693, LX3694) in which strong effects were observed, the early portion of the cervical AEP (2.11 ms and earlier) was drastically reduced in amplitude, while a later major peak (3.44 ms) did not change, or possibly increased in amplitude. In the remaining experiment (subject AR8857, experiment LX3186, 810 m/s^2) there is no obvious effect in the cervical AEP. In the four experiments in which strong effects were observed, there were obvious increases in peak latencies observable as the AEP components became recognizable after impact. In LX3186 visual inspection showed no increase in latency, although quantitative analysis using AEP's with an N of 10 (see below) indicated unequivocally that there was a considerable increase in latency of short duration.

In five experiments on three subjects (subject AR8824, experiment LX3184; subject AR8802, experiments LX3705, LX3706; subject ARNA02, experiments LX3714, LX3715) the peak sled acceleration was approximately 600 m/s^2 ("middle level impact"). Cervical AEP's were available in all three subjects, although in one subject they were marginal (subject AR8824, experiment LX3184). There were no profound effects on the cervical AEP amplitude although some small amplitude effects can be observed (subject AR8802, experiments LX3705, LX3706). There was no apparent effect on waveshape with one noteworthy exception. This was the early portion of the cervical AEP in experiment LX3706, and will be discussed below. Some increases in peak latency can be seen in experiments LX3705 and LX3706.

The peak sled accelerations of the remaining experiments (see table 1) were below 440 m/s^2 ("low impact levels"). Substantial changes in cervical AEP's did not occur in these. There are occasional shifts in latency of the cervical AEP peaks, but these were small. No apparent AEP amplitude effects related to low level impact were noted by visual examination of these AEP's.

* Histological examination revealed old traumatic alterations in the cervico-medullary region of subject AR0012 (27). The results from this subject should therefore be considered tentative.

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CERVICAL AEP LATENCY SHIFT

POLY-EXPONENTIAL AND
LINEAR REGRESSION

RUN LX3009, 796 M/S,² PEAK 3.45 MS. N-50

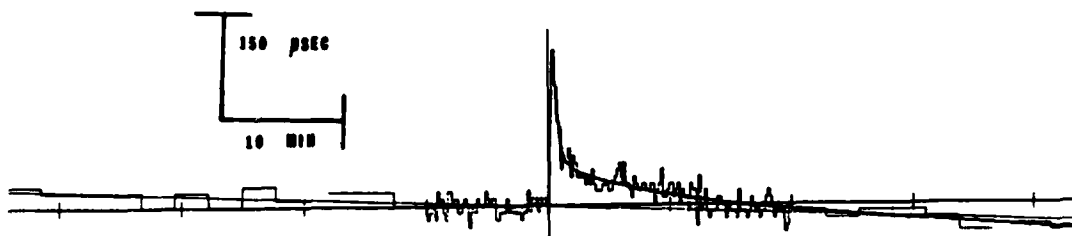


FIGURE 2

Linear and three-term exponential regression procedure applied to shifts of cervical AEP peaks measured by normalized cross-correlation for all of experiment LX3009. AEP's were computed with $N = 50$, and except in the region of impact, only every sixteenth EP was used. For the purpose of regression, the data were weighted by the actual time covered by the AEP (length of the horizontal line representing the data point). First, linear regression was applied to the pre-impact data resulting in a slope of $-35 \mu\text{s/hr}$ and a Y intercept of $-12 \mu\text{s}$. This was extrapolated into the post-impact period and subtracted from the data. Next, the constant $200 \mu\text{s}$ was added to the post-impact data. Finally, three-term exponential regression was applied resulting in the coefficients:

AMPL (μs):	214.	51.2	551.
TIME COEF (min):	-341.	-7.30	-.356

The first term has a value of $214 \mu\text{s}$ at impact, and $191 \mu\text{s}$ at 40 min. post-impact. Subtracting the $200 \mu\text{s}$ constant originally added to the data to the first term, the contribution of the first term ranges from $+14 \mu\text{s}$ at impact to $-9 \mu\text{s}$ at 40 min. post-impact. The long time coefficient of the first term means the first term is essentially constant with its amplitude range being within the range of experimental error. This term accounts for the drift below the linear regression line at the end of the experiment. The other two terms account for most of the curvature. The final weighted, post-impact RMS deviation was $10.9 \mu\text{s}$.

CERVICAL AEP LATENCY SHIFT

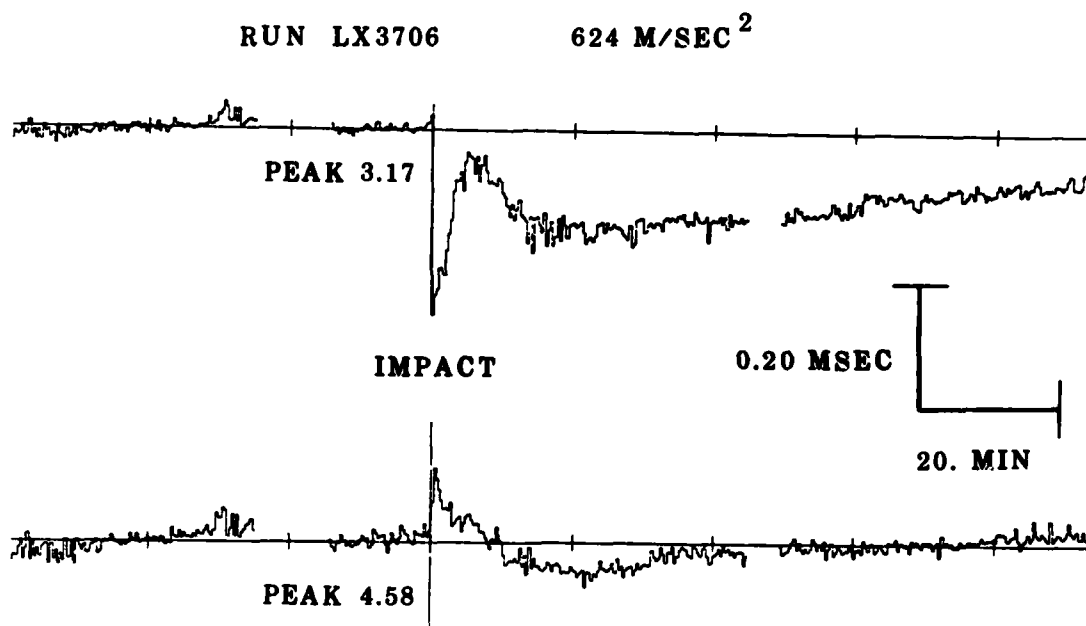


FIGURE 3

Plots of the shifts in latency at two peaks measured with NCCF's for all of experiment LX3706. AEP's were computed with $N = 100$. The increase in latency of the peak at 4.58 ms. induced by impact illustrates the most common finding. The substantial decrease in latency of the peak at 3.17 ms. is unusual and was caused by the impact-induced appearance of a new component that overwhelmed the original peak.

TABLE 2

ROW	SUBJ	ACCEL	LAT	AMP	TIME	LAT	AMP	TIME	LAT	AMP	TIME	LAT	AMP	TIME	LAT	AMP	TIME
		(m/s ²)	(ms)	(uV)	(min)	(ms)	(uV)	(min)	(ms)	(uV)	(min)	(ms)	(uV)	(min)	(ms)	(uV)	(min)
3183	8824	103	**	**	**	**	**	**	**	**	**	**	**	**	**	**	**
3185	8857	100	**	**	**	**	**	**	**	**	**	**	**	**	**	**	**
3491	0012	99	1.78	19	-73	2.13	31	-58	2.43	37	-43	2.68	5.8	(-1.4)	3.59	41	(-1.3)
3495	8628	98	1.73	0	(0)	2.03	25	(-7.3)	**	**	**	**	**	**	4.08	35	(-8.5)
3499	8872	42	2.08	-14	(-3.1)	2.53	30	(-140)	3.03	14	(-3.0)	3.13	14	(-13.1)	3.98	0	(-120.)
3703	8802	99	**	**	**	**	**	**	2.78	52	(-56)	3.58	20	(-5.4)	4.13	43	(-5.9)
3713	8802	98	**	**	**	2.48	0	(0)	2.88	23	(-23.)	3.48	32	(-280.)	3.93	48	(-1.1)
			**	**	**				3.08	35	-2.7	3.38	34	-1.3	3.78	45	-1.6
3008	0761	208	**	**	**	**	**	**	2.73	0.4	(-1.8)	3.50	5	-5.4	3.93	34	(-4.7)
3497	8628	441	1.83	0	(0)	2.17	0	(0)	**	**	**	3.20	0	(0)	4.04	0	(0)
3701	8872	436	2.23	14	(-3.1)	2.73	3	(+14)	3.23	62	-83	3.73	0	(0)	4.43	46	-2.3
3702	8872	434	2.18	-49	(-30)	2.68	-16	(-15.)	3.23	45	-5.9	3.68	25	(-4.5)	4.33	100	-4.8
3184	8824	611	**	**	**	**	**	**	**	**	**	3.49	90	-4.0	**	**	**
3705	8802	630	**	**	**	**	**	**	2.88	-570	-1.6	3.88	55	-1.3	4.28	54	-1.6
3706	8802	624	**	**	**	**	**	**	3.17	-350	-3.2	3.68	43	-82	4.18	120	-3.4
3714	8802	598	**	**	**	2.53	0	(0)	3.18	81	-1.8	3.48	81	-1.8	3.93	53	-2.4
3715	8802	598	**	**	**	**	**	**	2.85	49	-7.7	3.15	58	-1.4	3.90	30	(-3.55)
3493	0012	727	1.78	240	-1.4	2.08	310	-1.1	2.43	300	-1.3	3.43	270	-7.7	4.03	180	-1.6
3494	0012	767	1.78	180	-2.5	2.08	270	-2.1	2.73	210	-6.5	3.33	170	-3.0	3.93	200	-3.0
3186	8857	810	**	**	**	**	**	**	**	**	**	3.22	130	-23	3.58	110	-40
3009	0761	796	**	**	**	**	**	**	2.68	92	-4.7	3.45	270	-1.2	3.87	200	-2.2
3010	0761	963	**	**	**	**	**	**	2.62	300	-5.1	3.38	400	-3.1	3.78	400	-5.3
			**	**	**	**	**	**							**	**	**
															4.71	320	-4.5

Exponential regression coefficients from one-term (except *) exponential regression on impact-induced shifts in latency of various cervical AEP peaks measured with the NCCF. LAT are the pre-impact median latencies of each peak. AMP are the exponential amplitudes (shifts in latency extrapolated back to time of impact). TIME are the exponential time coefficients. A negative time coefficient indicates exponential decay. ACCEL are peak sled accelerations. An asterisk (*) indicates that a substantial number of latency measurements fell below the pre-impact median during the first five post-impact minutes. It was therefore necessary to add a constant to the data and use two-term exponential regression. The amplitude shown is the sum of the two exponential amplitudes, minus the added constant. This amplitude well represents the initial displacement due to impact, and may be compared with the other exponential amplitudes in the table. The time coefficient shown is the shorter of the two obtained, and will tend to be substantially shorter than this entry otherwise would have had. The longer time coefficient always was at least 20 minutes. A double asterisk (**) indicates that the peak was not available or was too unstable to analyze.

III-D. Qualitative Effects of Impact -- Cortical AEP's

Cortical AEP's were available in two of the three subjects receiving high level impacts (subject AR0761, experiments LX3009, LX3010; subject AR8857, experiment LX3186). The most consistent finding in these three experiments was that the ripples on the rise and peak of the positive cortical primary response were reduced by impact. It appeared that the amplitude of the ripples covaried with the amplitude of the cervical AEP. The cortical primary itself was affected in varying degrees by the impact, corresponding to the strength of the cervical effect.

Cortical AEP's were obtained from two of the subjects receiving middle level impacts (subject AR8802, experiments LX3705, LX3706; subject ARNA02, experiments LX3714, LX3715). Distinct ripples were not seen, and in one subject (AR8802) the cortical AEP amplitude was low. A substantial decrease in the amplitude of the cortical AEP occurred in the same subject in which cervical increases in latency were seen (subject AR8802, experiments LX3705, LX3706).

Substantial changes in cortical AEP's were not seen in the low level experiments. Cortical ripples, where present, were never altered. There were no apparent cortical AEP amplitude effects related to low level impact.

III-E. Quantitative Analysis of Cervical Shifts in Latency

The shifts in latency of several cervical EP peaks were analyzed using the NCCF and exponential regression procedures (see Appendix B for details). This analysis was done using AEP's with 10 EP's each, and spanning a seven minute time interval starting at two minutes pre-impact. The reason for this restricted analysis interval is illustrated in figs. 2 & 3. Fig. 2 illustrates a nearly linear decrease in latency over the entire course of the experiment, including the pre-impact period. Fig. 3, on the other hand, illustrates shifts in latency which exhibited an erratic, slow drift during the experiment. Such slow drifts were often seen, and made it possible to follow reliably the impact-induced shifts in latency for no more than about ten minutes after impact.

III-F. Amplitude and Duration of Shift in Latency

Table 2 summarizes the results of estimation of the amplitude and duration of shifts in latency produced by impact for all available cervical AEP peaks in the range 1.7 ms to 5.5 ms. The shifts were measured using the NCCF. Each peak is identified by its pre-impact median latency (LAT) in milliseconds obtained from AEP's computed using data collected during the two minutes immediately prior to impact. Alignment of comparable peaks into columns is only approximate across subjects. However, within subjects, the alignments are correct, and pre-impact latency differences within subjects represent actual shifts in latency between experiments.

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For each exponential regression, the exponential amplitude (AMP) is given in μ s of increase in latency, and the time coefficient (TIME) is given in minutes. A negative time coefficient indicates exponential decay.

For plotted data which had no visually apparent exponential patterns, there were two common outcomes of the exponential regression. First, a long time coefficient resulted and the exponential amplitude represented an estimate of the mean of the data. Second, a short time coefficient resulted and the exponential amplitude represented latency shifts in the early post-impact part of the data. Both types of results appear in the table. In each case, the time coefficient is meaningless. Such results were identified by visual examination of the graphs, and the corresponding time coefficients appear in parentheses. Where the exponential algorithm returned no useful result, and visual inspection of the graphs revealed no apparent effect due to impact, zeros were filled in.

Two points should be emphasized in regard to this table. First, the initial few post-impact points were generally discarded. Additionally, in high level impact experiments, for the first 10 to 60 seconds post-impact, the shifts in latency were very variable. This resulted in a substantial number of shifts in latency in this interval being considered outliers,* and being discarded. The exponential amplitudes represent extrapolation of the shifts in latency back to impact from the post-impact period, and do not represent actual observations of the shifts in latency. The actual values of the maximum shifts in latency that occurred as a result of impact are not known due to the severe distortion of the evoked potentials as well as the artifact produced by impact. The second point is that, the one-term exponential regression is used as a good means of providing objective comparison among experiments, and not as a model for the actual underlying process (see Appendix B).

The results in table 2 are summarized in fig. 4. For each experiment, a single median value computed from all of the peaks for that experiment is shown as a point in each of three plots. The computations for each plot were as follows:

4A - The median of the negative time coefficients that are meaningful (not in parentheses) and are not associated with negative exponential amplitudes.

4B - The median of non-negative exponential amplitudes.

* In general, an "outlier" is defined here as a data value that deviates enough from other data values so that it is likely to contain erroneous information. Operationally, the definition of "outlier" is embodied in the procedure that is used to exclude it. Such procedures will always imply assumptions about the nature of the data. (see Appendix B)

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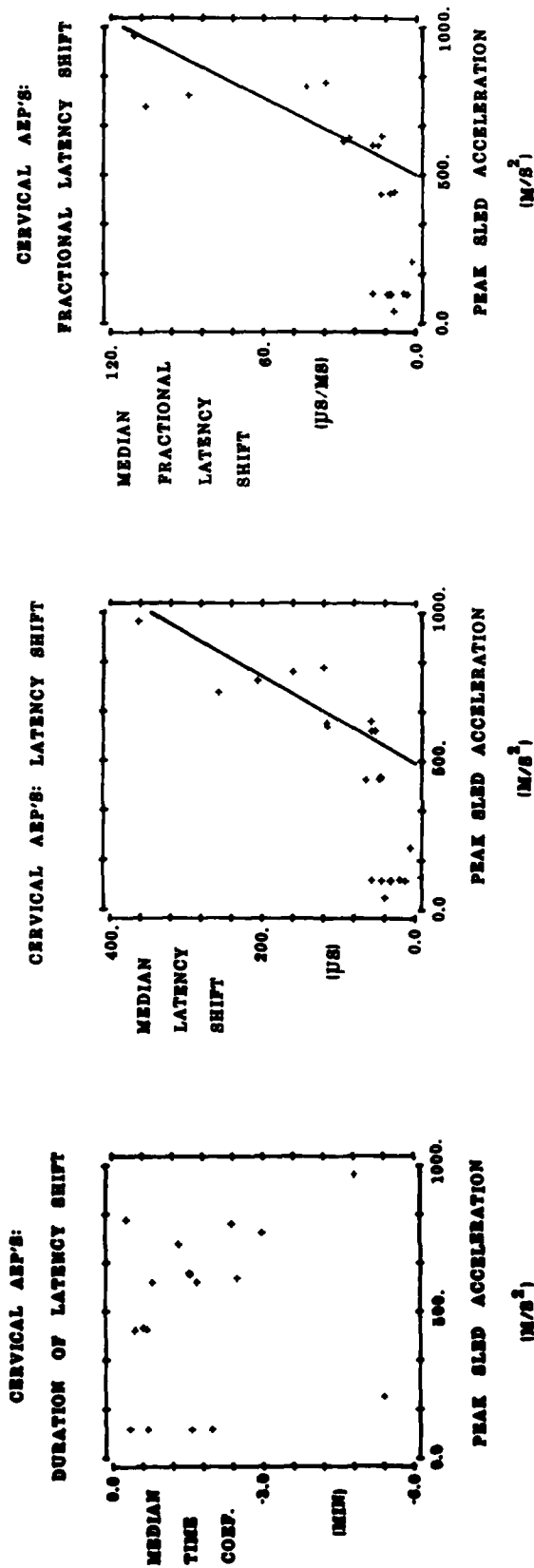


FIGURE 4

Plots of three values derived from one-term exponential regression on shifts of latency as a function of peak sled acceleration. The results from each experiment are represented by a single point on each plot. Each point is the median value for all peaks in table 2 for the experiment represented except the few with peaks with negative latency shifts. A - the median negative time coefficient representing the duration of the shift in latency excluding those in parentheses. B - the median initial latency shift. C - the median initial fractional shift in latency obtained by dividing the initial shift in latency for each peak by the pre-impact median latency for the peak before computing the plotted median. In B and C, linear regression was applied only to those points for peak sled accelerations greater than 500 m/s² with these results:

figure	slope	impact intercept
4B	$\frac{6.8 \mu s}{m/s^2}$	$\frac{490 m/s^2}{500 m/s^2}$
4C	$\frac{2.3 (\mu s/ms)}{(m/s^2)}$	

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- 4C - The median of non-negative exponential amplitudes each divided by the corresponding pre-impact median latency.

Fig. 4A shows that the median time coefficients were very variable even at low impact levels, and there was little if any relationship between the median time coefficient and impact level. Figs. 4B & 4C, on the other hand, show that there was a strong relationship between the exponential amplitudes (initial shift in latency) and impact level. At impact levels below about 500 m/s^2 , there were small positive median latency shifts (mean = $40 \text{ } \mu\text{s}$) and small positive median fractional latency shifts (mean = $9.3 \text{ } \mu\text{s/ms}$). At about 600 m/s^2 there was a tendency for shifts in latency following impact to exceed those at lower levels. Above 700 m/s^2 , impact produced increases in latency that exceeded those at lower levels. There are not enough data to determine the form of the functional relationship between impact and the initial shift in latency. As a first approximation to the curve at high impact levels, linear regression was applied to the results in figs. 4B and 4C, using only those values with impact levels above 500 m/s^2 . The results were:

<u>figure</u>	<u>slope</u>	<u>impact intercept</u>
4B	$6.8 \text{ } \mu\text{s}/(\text{m/s}^2)$	490 m/s^2
4C	$2.3 (\text{ } \mu\text{s/ms})/(\text{m/s}^2)$	500 m/s^2

III-G. Two-Term Exponential Fits.

Only in the high impact (727 m/s^2 and above) experiments were the data generally noise free enough to allow meaningful comparisons between one-term and two-term regression. The results are presented in table 3. For each peak, two pairs (exponential amplitude and time coefficient) of results are shown representing each of the two exponential terms. Also shown are the percent decreases in mean square deviation obtained with the two-term regression compared with the one-term regression. Substantial improvement is often obtained. This is illustrated in fig. 5, where the decrease in mean square deviation represents a clear improvement in the fit. As in the case of the single exponential results, the exponential amplitudes represent extrapolations.

III-H. Heart Rate Effects

For each experiment in table 2, the average heart rate was compared for two 20 second intervals: one immediately before, and one immediately after impact. The difference between these two rates ("relative bradycardia", 23) is plotted in fig. 6 as a function of peak sled acceleration. A linear regression using all of the data points is also plotted, and has a slope of $-0.14 (\text{beats/min})/(\text{m/s}^2)$. The impact intercept (zero change in heart rate) is 113 m/s^2 . The duration of the measured bradycardia did not exceed one minute except in experiment LX3184, where a slight relative bradycardia persisted for approximately 2.5 min. post-impact.

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TABLE 3

RUN	SUBJ	ACCEL (m/s ²)	LAT (ms)	%	AMP (μ s)	TIME (min)	AMP (μ s)	TIME (min)	LAT (ms)	%	AMP (μ s)	TIME (min)	AMP (μ s)	TIME (min)
3693	0012	727	1.78	17	250	-.23	170	-1.9	2.08	31	440	-.25	170	-1.7
3694	0012	767	1.78	15	230	-.48	92	-5.9	2.08	88	510	-.32	130	-5.1
3693	0012	727	2.43	3	260	-.90	62	-2.8	2.73	2	-0.0	1.0	240	-2.6
3694	0012	767	2.38	50	360	-.60	130	-12.	2.73	5	180	-.26	190	-7.6
3693	0012	727	3.43	0.2 *	150	-.40	210	-1.8	4.03		no double			
3694	0012	767	3.33	33	150	-.58	95	-6.9	3.93	33	190	-.34	130	-5.3
3009	0761	796	3.45	42	330	-.68	23	+30	3.87	7.2	230	-1.1	34	-110
3010	0761	963	3.38	61	560	-.98	100	-26	3.78	43	820	-.69	220	-42.
3009	0761	796	4.71	double	has short + time coef.				5.45	45	260	-.38	90	-6.2
3010	0761	963	4.71	49	860	-.69	160	-27.	5.34		no double			

Exponential regression coefficients from two-term (except *) exponential regression on impact-induced shifts in latency of various cervical AEP peaks measured with the NCCF. LAT are the pre-impact median latencies of each peak. AMP are the exponential amplitudes (shifts in latency extrapolated back to time of impact). TIME are the exponential time coefficients. A negative time coefficient indicates exponential decay. ACCEL are peak sled accelerations. The % are the percent improvement in mean square deviation over corresponding one-term exponential regression. The asterisk (*) indicates that as discussed in the table 2 caption, the latency curve fell below the pre-impact median in the first five minutes of the post-impact period. A three-term exponential regression was therefore used. In this case, however, the amplitudes of the two shorter terms were not adjusted. The "permanent" shift in latency was -50 μ s.

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CERVICAL AEP LATENCY SHIFT POLY-EXPONENTIAL REGRESSIONS (ON 132 OF 145 POST-IMPACT POINTS)

RUN LX3009, 796 M/S², PEAK 5.46 MS, N-10

ONE TERM, RMS DEV. = 31.9 μ S

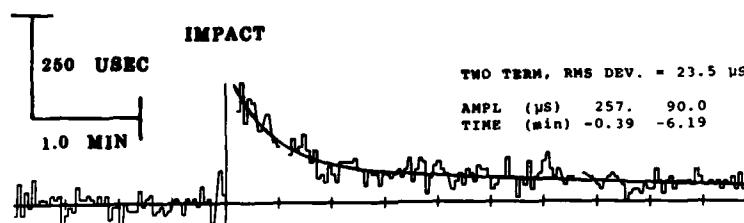
AMPL (μ S) 191.
TIME (min) -2.22



IMPACT

TWO TERM, RMS DEV. = 23.5 μ S

AMPL (μ S) 257. 90.0
TIME (min) -0.39 -6.19

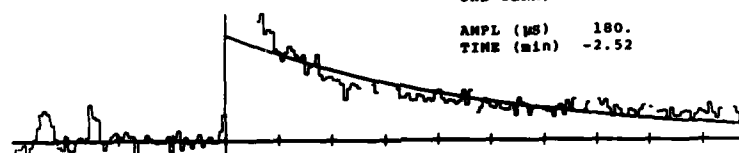


CERVICAL AEP LATENCY SHIFT POLY-EXPONENTIAL REGRESSIONS (ON 124 OF 151 POST-IMPACT POINTS)

RUN LX3694, 767 M/S², PEAK 1.77 MS, N-10

ONE TERM, RMS DEV. = 16.3 μ S

AMPL (μ S) 180.
TIME (min) -2.52



IMPACT

TWO TERM, RMS DEV. = 9.7 μ S

AMPL (μ S) 227. 92.0
TIME (min) -0.49 -5.60

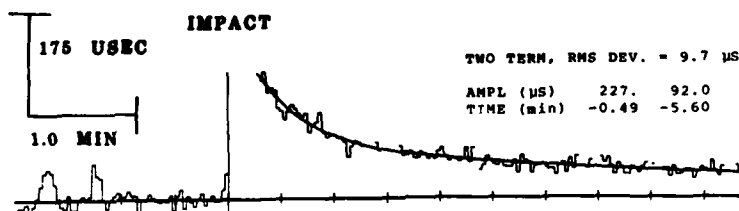


FIGURE 5

A and B are each plots of the shift in latency for one peak (indicated by the peak latency over the plot) in high impact experiments. Each is from a different subject. AEP's were computed with N = 10, and the interval shown ranges from 2 min. pre-impact to 5 min. post-impact. These are the parameters that were used for the quantitative analysis in this report. The shifts for each peak are illustrated twice, showing one and two term exponential regression curves. In each case the two term fit is substantially better than the one term fit. Pre-impact linear regression (Appendix B) was not used in these fits.

POST-IMPACT CHANGE IN HEART RATE

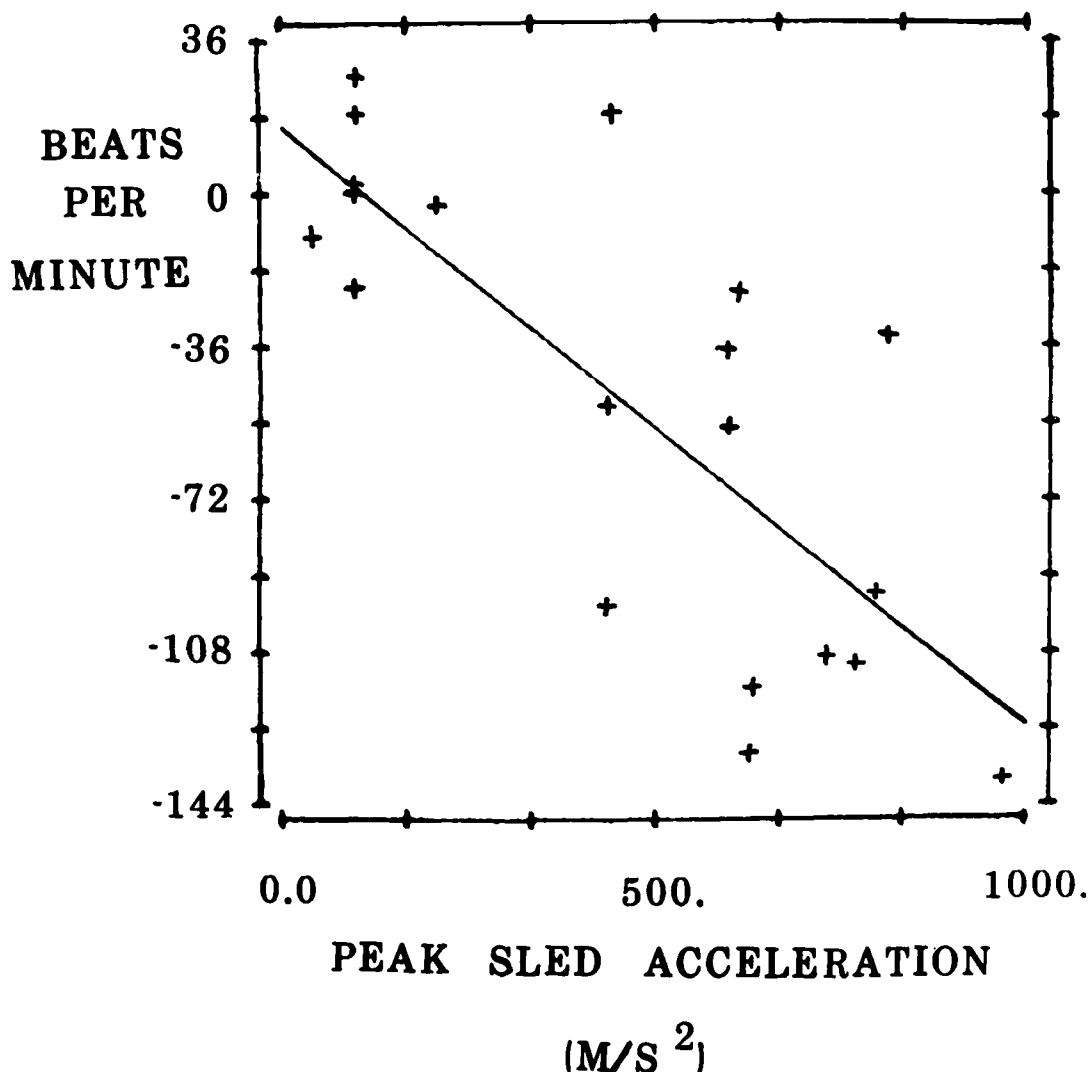


FIGURE 6

Change in heart rate plotted as a function of peak sled acceleration. Heart rate was computed from strip chart EKG records for the 20 seconds immediately preceding impact and for the 20 seconds immediately following impact. The change in heart rate is the post-impact rate subtracted from the pre-impact rate. The average pre-impact heart rate across experiments was 216 beats/min with a standard deviation of 27 beats/min. A linear regression is also plotted and has a slope of -0.14 (beats/min)/(m/s²) and an impact intercept of 113 m/s².

III-I. An Unusual Decrease in Latency

An unusual change occurred in experiment LX3706 (624 m/s^2). A substantial, long-lasting decrease in latency was seen. The significance of this result is seen in Appendix A, experiment LX3706. At the time of impact, an early EP component which previously had been present with low amplitudes, if at all, appeared with high amplitude. This additional component substantially distorted the peak at 3.17 milliseconds, resulting in the apparent decrease in the latency of the peak. The impact apparently lowered the stimulus threshold for this component. Fig. 3 (upper trace) presents the time course of the recovery of this effect over the entire experiment. The effect begins to decay at a rate consistent with the -3.2 minute time coefficient given in table 2, but at about five minutes post-impact, the trend reversed and the new early component again gained strength. Subsequently the shift in latency followed the variation in the peak at 4.58 milliseconds which was not comparably distorted. In the absence of such peak distortion, substantial decreases in latency as a consequence of impact have not been observed.

IV. DISCUSSION

IV-A. Amplitude and Duration of Shift in Latency

The one-term exponential regression was used to provide objective measures of the amplitude and duration of the shifts in latency of various peaks of the cervical EP's produced by impact. The data show that there is a positive relationship between the strength of impact and the increase in latency of the cervical AEP. The data are insufficient to determine the mathematical form of the relationship between impact strength and increase in latency. Linear regression was used as a first approximation to the high-impact portion of the curve (figs. 4B and 4C). The linear regression shows that there was no change in the shift in latency until 500 m/s^2 . This may be contrasted with the results of Weiss and Berger (32) who found that a complex measure of cortical EP's changed at all levels of impact. Further analysis of the cortical EP data from these experiments should provide additional information in this regard.

In most of the high level impact experiments (727 m/s^2 and higher), the cervical AEP was either substantially modified or virtually obliterated (Appendix A: subject AR0761, experiments LX3009, LX3010; subject AR0012, experiments LX3693, LX3694; but not subject AR8857, experiment LX3186). Under such conditions, the NCCF algorithm operates marginally, and the variability of the measurements of shifts in latency is high. For the purpose of exponential regression, many of these shifts in latency were considered outliers, and were eliminated. This leaves open two questions of considerable interest. First, what is the greatest latency shift that can actually be produced by impact? Second, does impact increase the variability of the latency? Extensive visual examination of the AEP's showed a low signal-to-noise ratio in much of the AEP data immediately following high level impact. Therefore, given the small number of relevant

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experiments, these issues cannot be resolved at present, but may be after additional experimentation.

IV-B. Two-Term Exponential Fits

The double exponential model provides an excellent fit to the shifts in latency for the first five post-impact minutes in high level impact experiments. However, numerous other models with four or fewer free coefficients are likely to fit these results at least as well. This, as well as the fact that the double exponential results rely on only four experiments on two subjects, leaves a double exponential hypothesis tentative.

This hypothesis is that high level impact produces two different increases in cervical EP latency, each decaying at its own rate. The two hypothetical effects may be differently related to impact. It should be noted that despite the possible inaccuracy of the longer time coefficients, the use of the two-term regression results in an increase in accuracy of the shorter time coefficient. This is because of the better fit to the early post-impact part of the curve in the two term fits. The shorter time coefficient ranges from -14 to -66 seconds, and the longer time coefficient from -102 seconds to very large negative values. Assuming the double exponential hypothesis is correct, time coefficient magnitudes up to about ten minutes are reliable.

Exponential amplitudes for changes in latency as high as 860 μ s were obtained with two-term regression in the high level impact experiments (table 3). However, the greatest shift in latency found by direct visual examination of cervical AEP's in these experiments was from 300 to 700 μ s. One possible explanation for this discrepancy is that immediately after impact the EP disappeared, and after some delay reappeared with an increased latency which then began to decay. Introduction of such a delay into the regression procedure would reduce the exponential amplitudes.

IV-C. Heart Rate Effects

The bradycardia observed after impact was also reported by Taylor and Rhein (23) in human subjects experiencing indirect head-neck acceleration. At a peak acceleration of 15g they found very slight decrements in heart rate after -X acceleration, and substantial decrements after +X acceleration. The results of our experiments using -X acceleration on Rhesus (fig. 6) suggest an inverse relationship between heart rate and peak sled acceleration. There is a lack of any apparent threshold, in contrast to the cervical AEP latency results (fig 4, B & C). The extent to which these cardiovascular effects are related to the measures of CNS function remains to be elucidated.

IV-D. Possible Temperature Effects

Stockard, et al. (22) report the relationship between the relative latencies of peaks of the auditory far field potentials and esophageal temperature in human patients undergoing anesthesia and induced hypothermia. Using their data from 37.1°C and 34.5°C, we computed a temperature dependence of $-38 (\mu\text{s/ms})/^{\circ}\text{C}$ ((microseconds of shift per millisecond peak latency) per degree centigrade). Marshall and Donchin (16) report the relationship between circadian variation of oral temperature and auditory far field potentials in normal human subjects. From their figure 1, and tabular data on "Latency to peaks" we computed a temperature dependence of $-30 \pm 7 (\mu\text{s/ms})/^{\circ}\text{C}$. If the cervical EP's were to exhibit comparable temperature dependencies, the slow drifts observed (figs. 2 & 3) could be due, at least in part, to changes in core temperature during the experiment. Further work is required to clarify this matter. The influence of core temperature may place an upper limit on the time interval over which the latency data can reliably be used to determine effects of impact. However, measurement of the sudden effects of impact* will not be contaminated over a five to ten minute interval, since the core temperature cannot change rapidly enough.

V. CONCLUSIONS

Decreases in the amplitude of cortical EP's have been observed as a result of direct impact (10, 15, 18) and indirect impact (3, 32). However, there is evidence that large amplitude changes resulting from cognitive factors may occur in primary EP's recorded from both the cortex and the lower brainstem (e.g., 1, 14). While shifts in EP latency under such conditions are less frequently reported, behavioral manipulations can result in changes in the peak latencies of visual primary cortical EP's (3), as well as auditory EP's recorded from the round window (11). The anatomic substrate for comparable effects in the somatosensory system is known to exist (e.g., 26). Thus, EP changes seen after impact may be assumed to be related to injury or precursors of injury only after serious consideration of these other factors. For the cervical EP's analyzed here, it is likely that there are no synapses between the stimulating and cervical recording sites, and that the observed shifts in latency result from changes in conduction velocities of spinal fiber groups. Consequently, considerations involving cognitive factors should not apply. However, since small increases in latency often occur at low levels of impact, the extent to which the observed changes are within the limits of the "healthy" operating range of the system must be considered. There is no simple way to deal with this problem, and therefore the approach taken at the Naval Biodynamics Laboratory is to evaluate the

* Note also that the reported temperature relationships would require a sudden decrease in temperature to account for the increase in latency resulting from impact.

relationship of each neurophysiological measure to the level of the impact. Conclusions concerning CNS dysfunction depend on the form of the relationship, as well as the injury threshold determined by clinical and neuropathological examination.

Three broad categories of changes in measures of CNS function may be distinguished: 1 - changes observed at clearly non-injurious low levels of impact (less than 200 m/s^2); 2 - changes that occur at intermediate levels of impact ($200 - 800 \text{ m/s}^2$); 3 - changes that occur at high levels of probably injurious impact (greater than 800 m/s^2). The first category of changes may be excluded from further consideration. This includes moderate changes in the amplitude of the cortical slow wave and shifts in the latencies of the cervical EP peaks less than $25 \text{ } \mu\text{s/ms}$ (microseconds shift per millisecond peak latency). The latter two categories, which may be of value as neurophysiological indices of injury include: shifts in the latencies of cervical EP peaks exceeding $25 \text{ } \mu\text{s/ms}$; large changes in the amplitude of the cervical EP; changes in the shape of the cervical EP (2); changes in the cortical EP ripples; and substantial and persistent changes in the cortical primary slow wave (19). In particular, the quantitative analysis of shifts in latency of the cervical EP peaks suggests that this may be a useful measure. The results of this analysis suggest the possibility of an injury threshold in the range of $700 - 800 \text{ m/s}^2$. The smaller shifts in latency that occur near 600 m/s^2 may indicate a pre-injury condition. This is an encouraging step towards identifying criteria for assessing injury to the CNS caused by indirect impact of the head.

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APPENDIX A. AEP's From All Experiments Analyzed

Each figure in this appendix shows cortical and cervical AEP's computed with $N = 50$ from a single experiment. The individual figures are referred to in the main text by experiment numbers, each of which begin with the characters "LX" (e.g., the first experiment number is LX3008). For each recording site, two pre-impact and five post-impact AEP's are arranged in a column. AEP's in the same row are taken from the same time epoch relative to impact. The time indicated in each row is the time, relative to impact, in seconds, of the stimulus resulting in the first EP of each of the two AEP's. The time of the stimulus is the beginning of the AEP. Selected constant latency cursors (vertical axes) are shown to aid in the observation of small shifts in latency. The number at the top of each cursor is the median latency (ms) of the peak from AEP's ($N = 50$) computed using the EP's from the two minutes immediately preceding impact.

Somatosensory Evoked Potentials

LX3008

CERVICAL

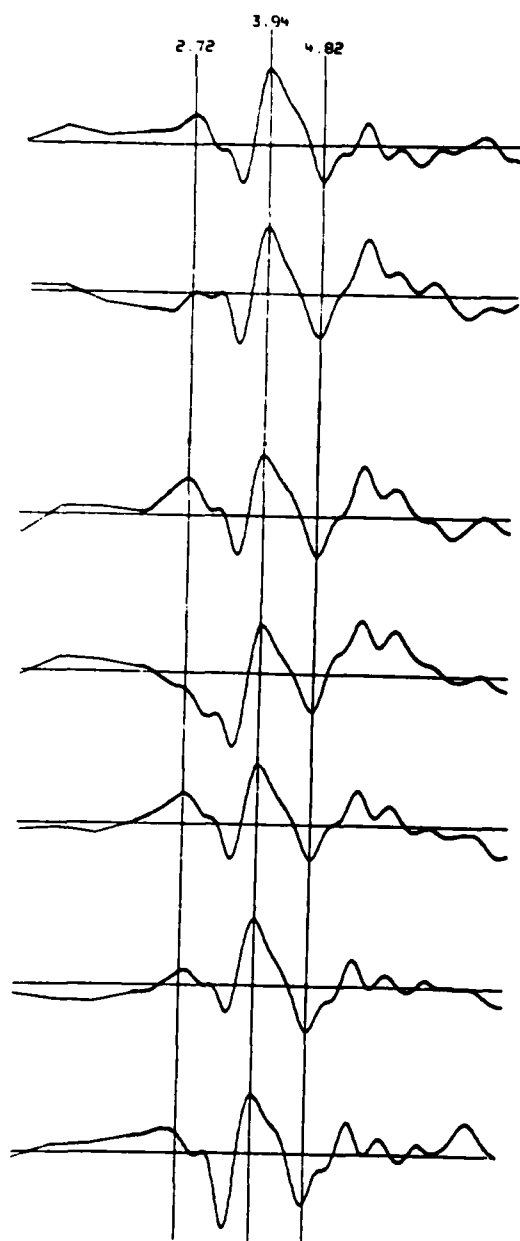
$\cdot G_X :$

208 M/S²

N: 50

CORTICAL

TIME
(SEC.)



IMPACT

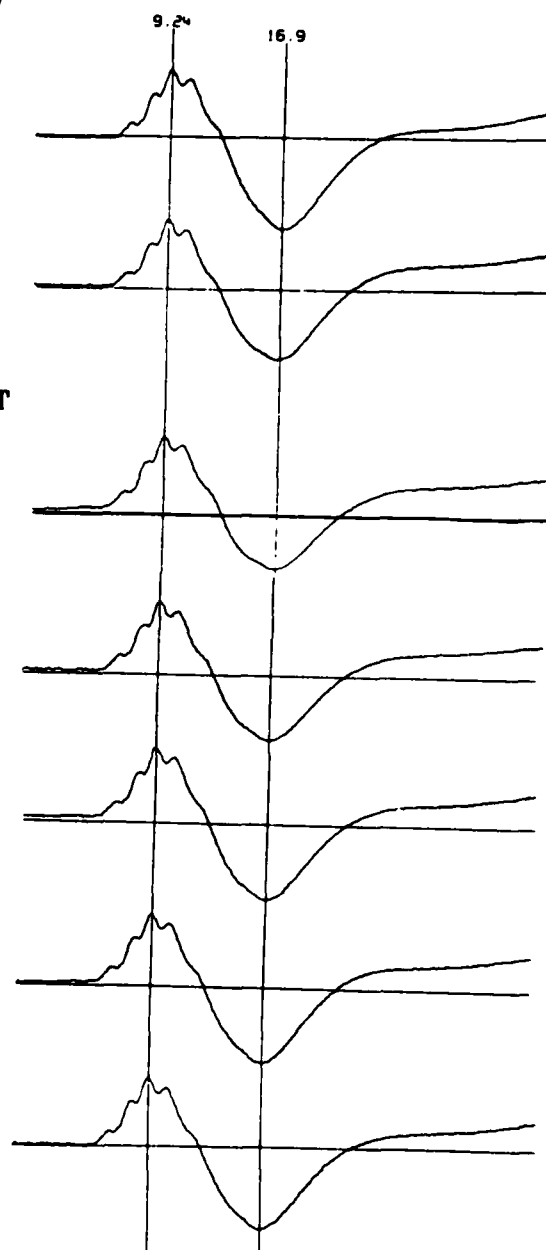
10

30

60

120

240



Somatosensory Evoked Potentials

LX3009

$-G_x$

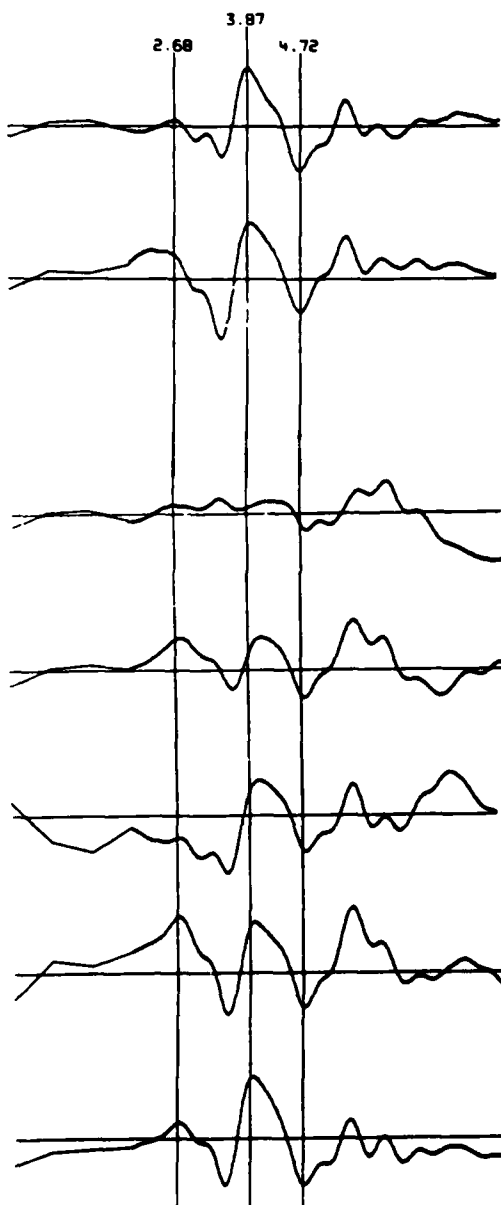
796 M/S²

CERVICAL

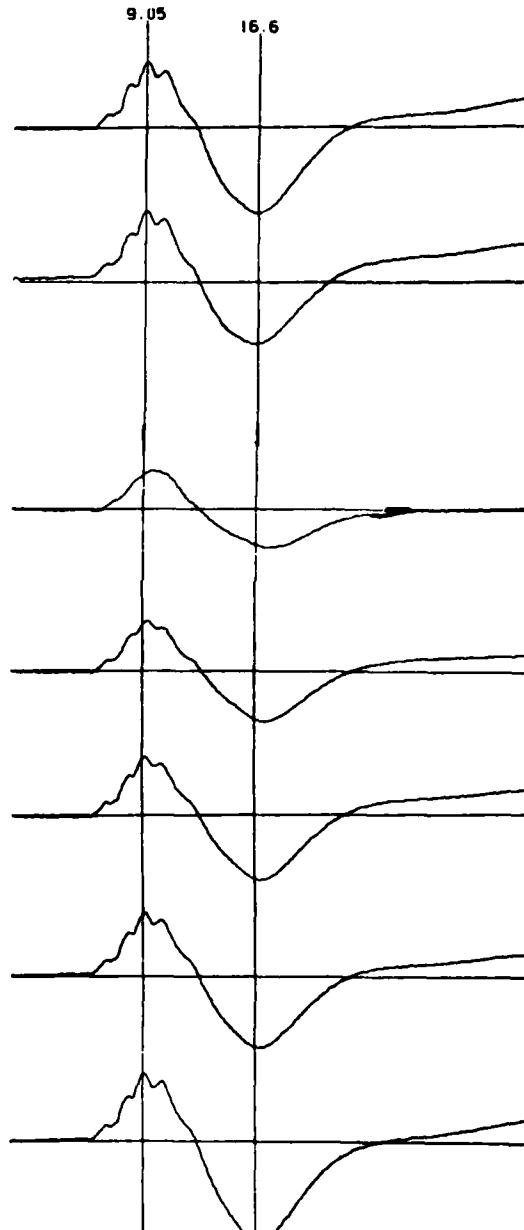
N: 50

CORTICAL

TIME
(SEC.)



30 μ V
2 MS



300 μ V
10 MS

Somatosensory Evoked Potentials

LX3010

-G_X

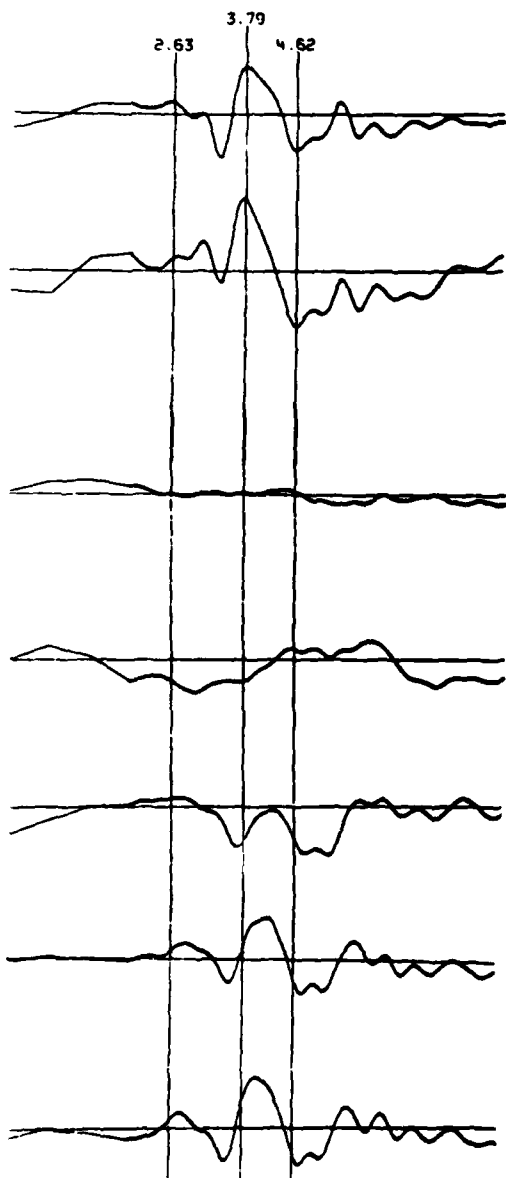
963 M/S²

CERVICAL

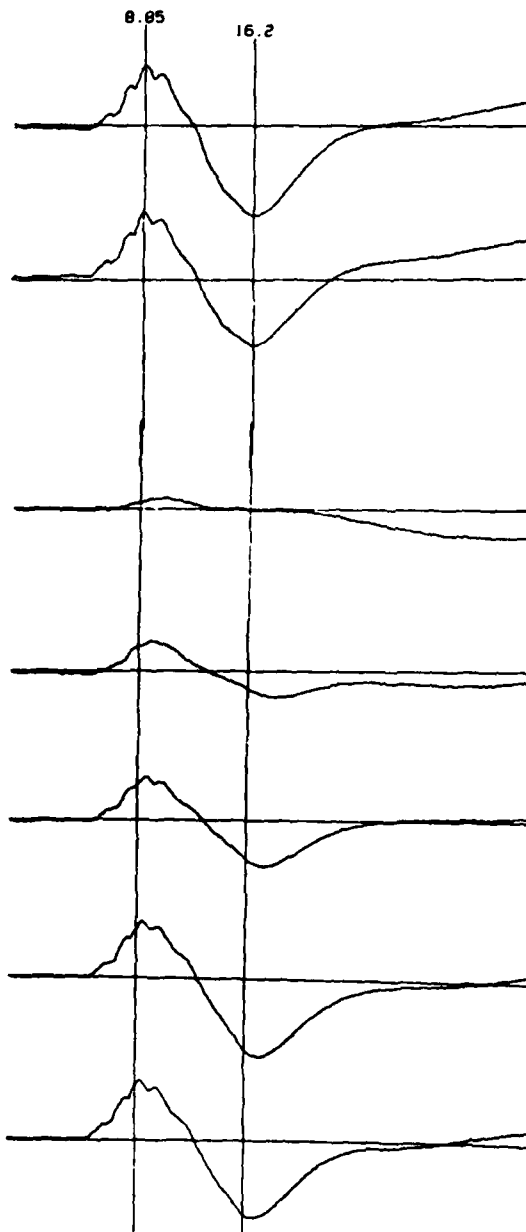
N: 50

CORTICAL

TIME
(SEC.)



30 μ V
2 MS



300 μ V
10 MS

Somatosensory Evoked Potentials

LX3027

$\dot{G}_X$: 102 M/S²

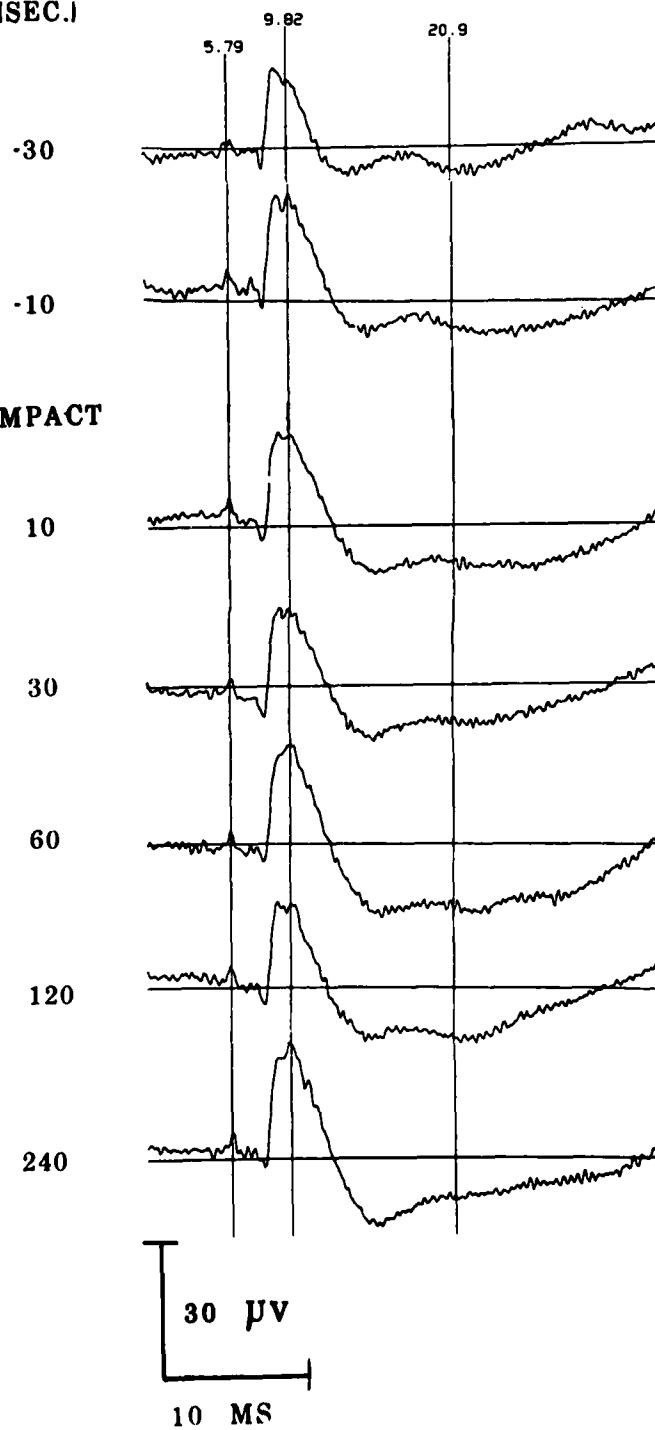
CERVICAL

N: 50

CORTICAL

TIME
(SEC.)

NOT YET ANALYSED BECAUSE
OF TECHNICAL PROBLEMS



Somatosensory Evoked Potentials

LX3028

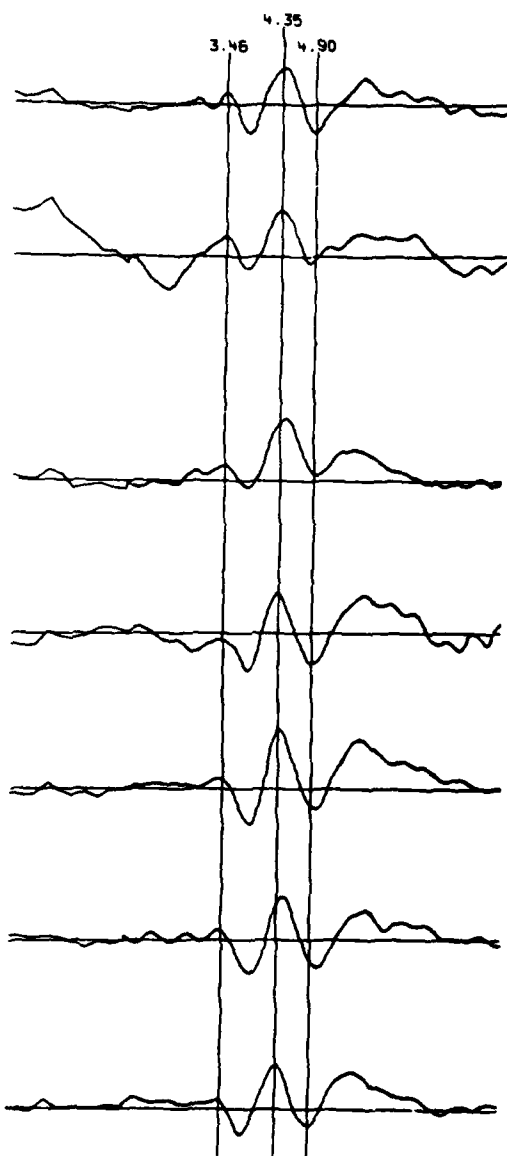
$-G_X$: 407 M/S²

CERVICAL

N: 50

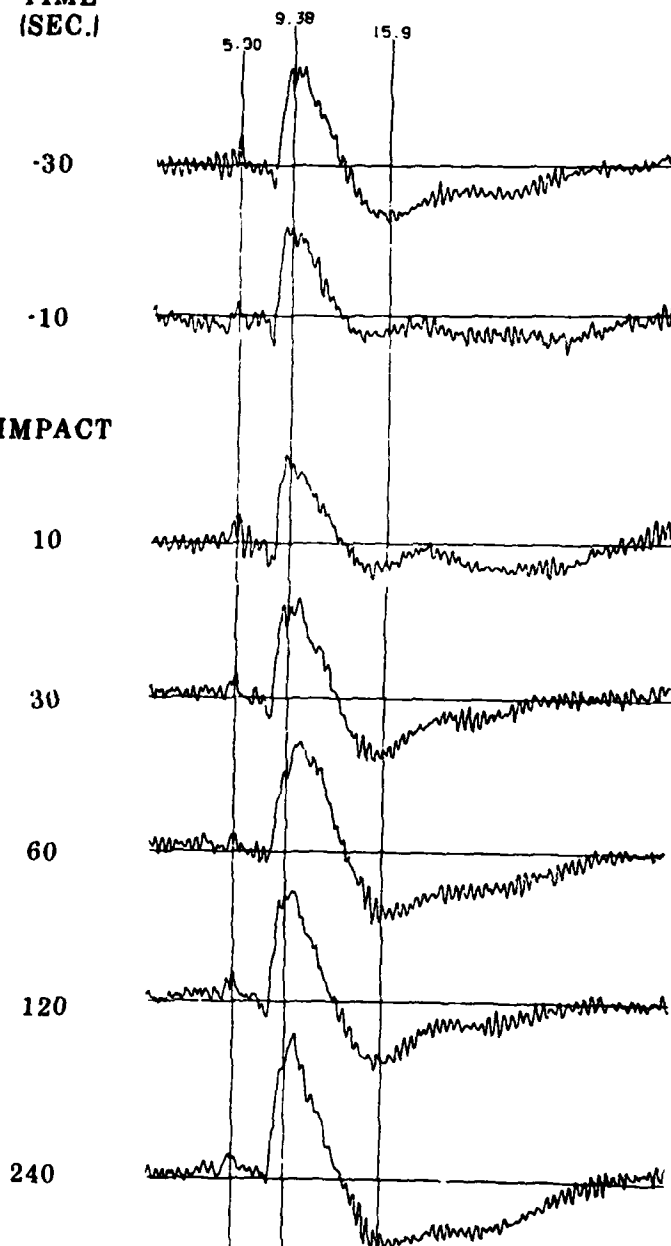
CORTICAL

TIME
(SEC.)



15 μ V
2 MS

IMPACT



30 μ V
10 MS

Somatosensory Evoked Potentials

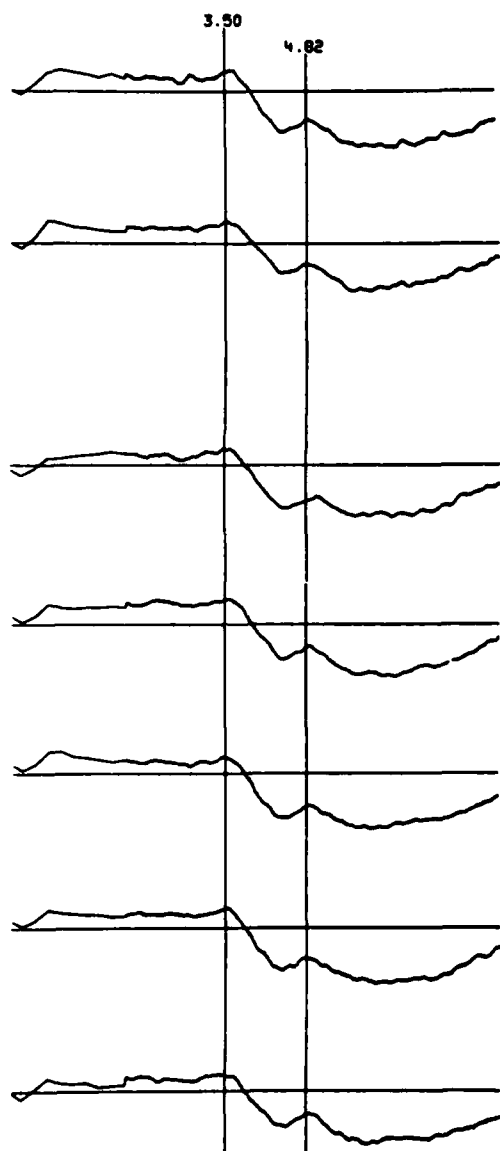
LX3183

$-G_X$: 103 M/S²

CERVICAL

N: 50

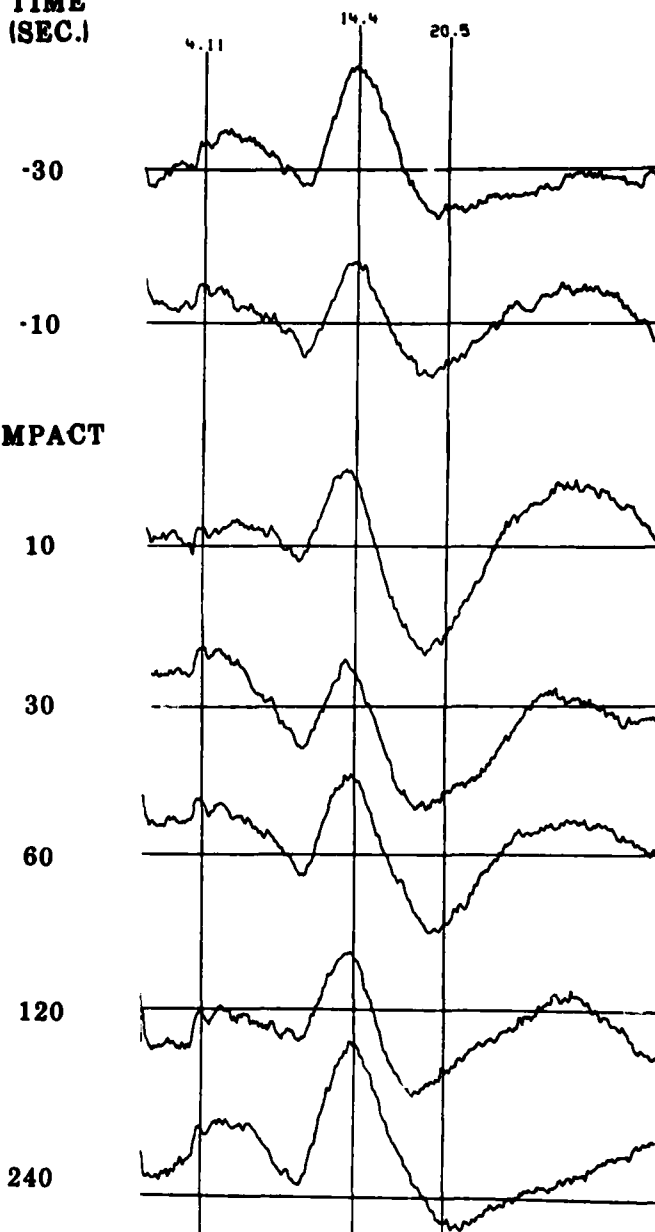
CORTICAL



30 μ V
2 MS

TIME
(SEC.)

IMPACT



15 μ V
10 MS

Somatosensory Evoked Potentials

LX3184

$-G_X$

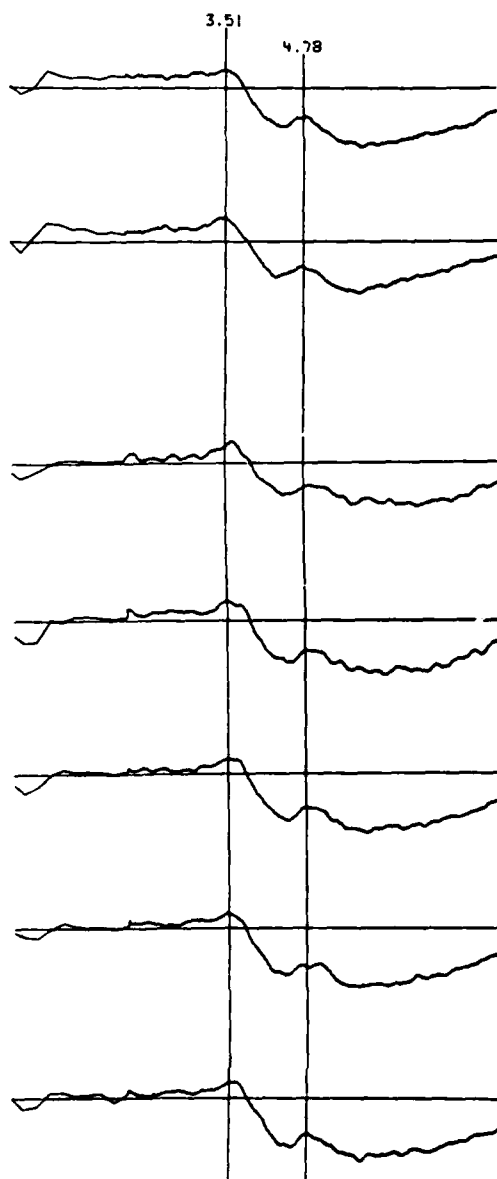
611 M/S²

CERVICAL

N: 50

CORTICAL

TIME
(SEC.)



AMPLIFIER FAILURE
AT IMPACT

IMPACT

30 μ V
2 MS

Somatosensory Evoked Potentials

LX3185

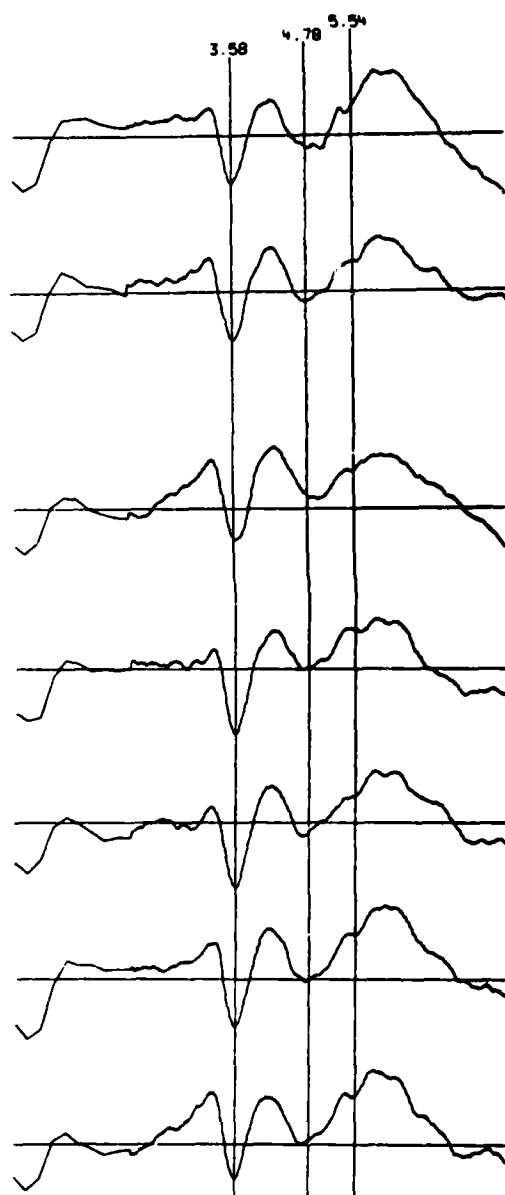
CERVICAL

N: 50

$-G_X$: 100 M/S²

CORTICAL

TIME
(SEC.)



-30

-10

IMPACT

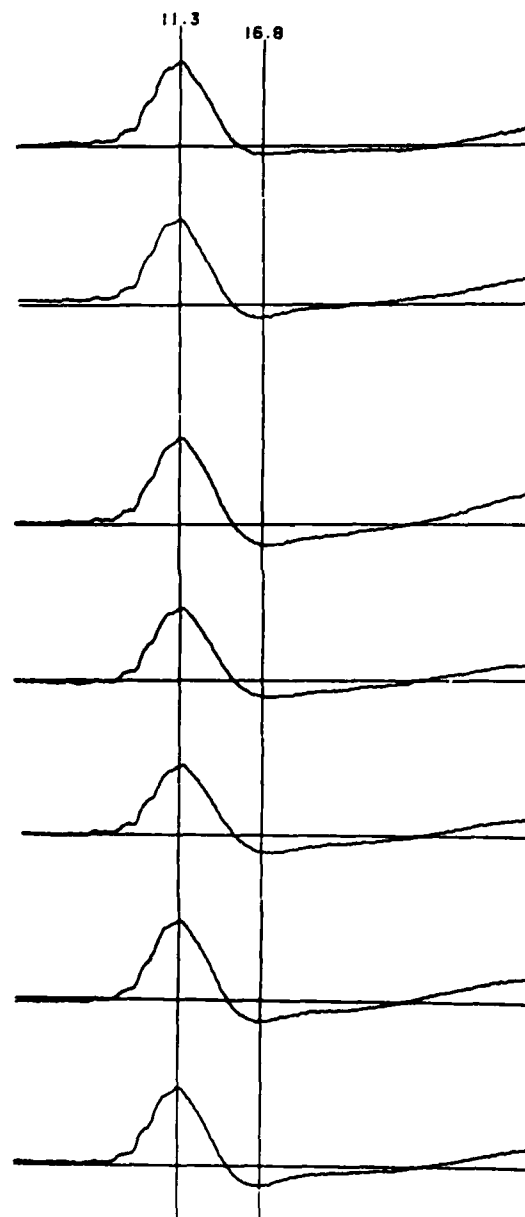
10

30

60

120

240



10 μ V
2 MS

100 μ V
10 MS

Somatosensory Evoked Potentials

LX3186

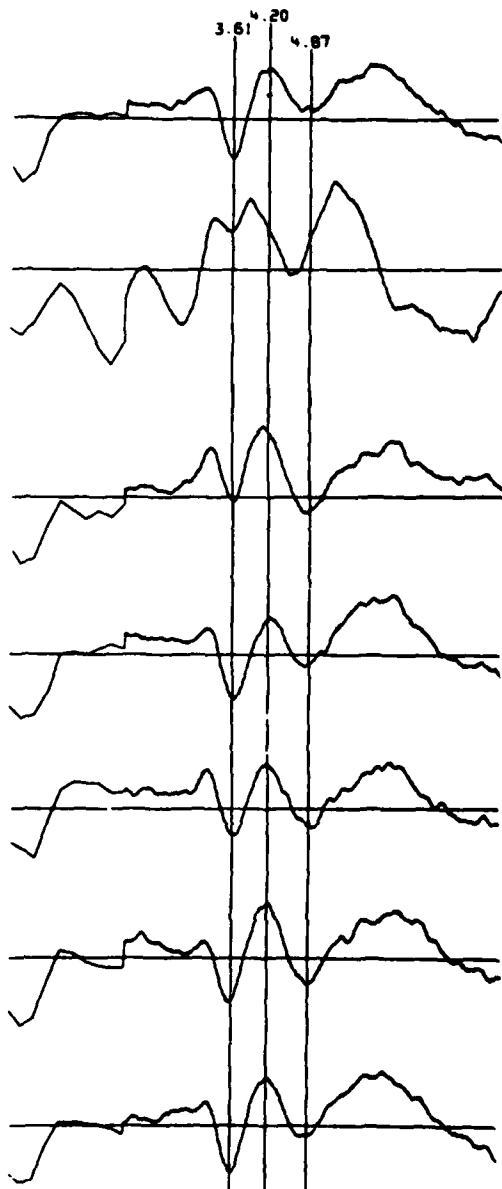
$-G_X$: 810 M/S²

CERVICAL

N: 50

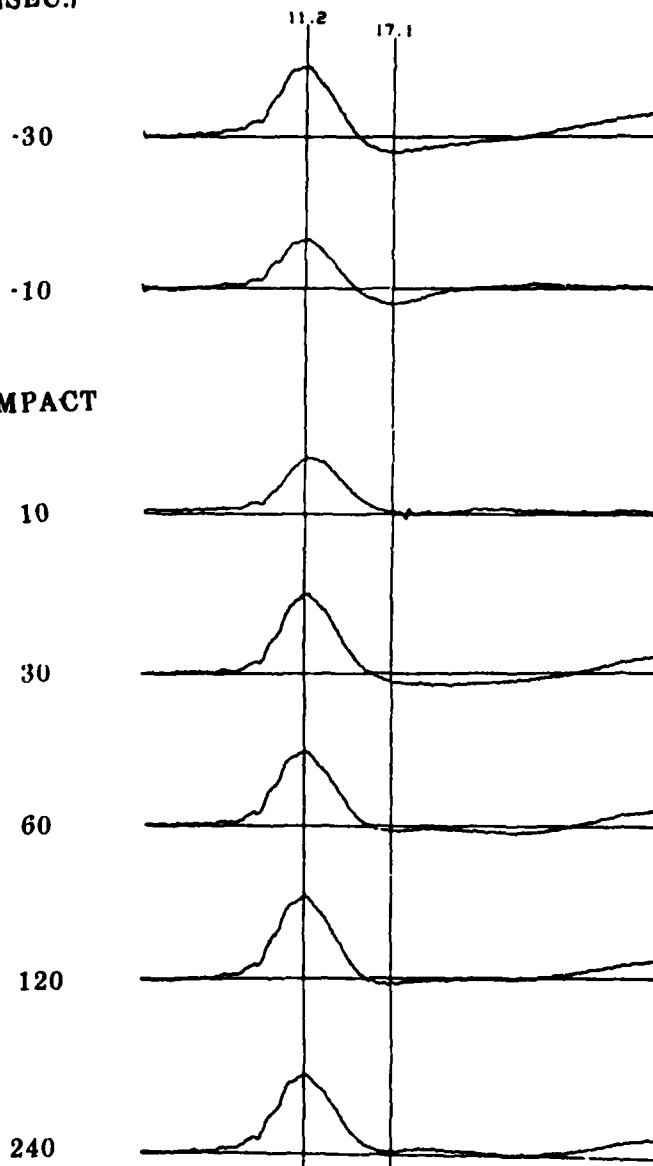
CORTICAL

TIME
(SEC.)



10 μ V
2 MS

IMPACT



100 μ V
10 MS

Somatosensory Evoked Potentials

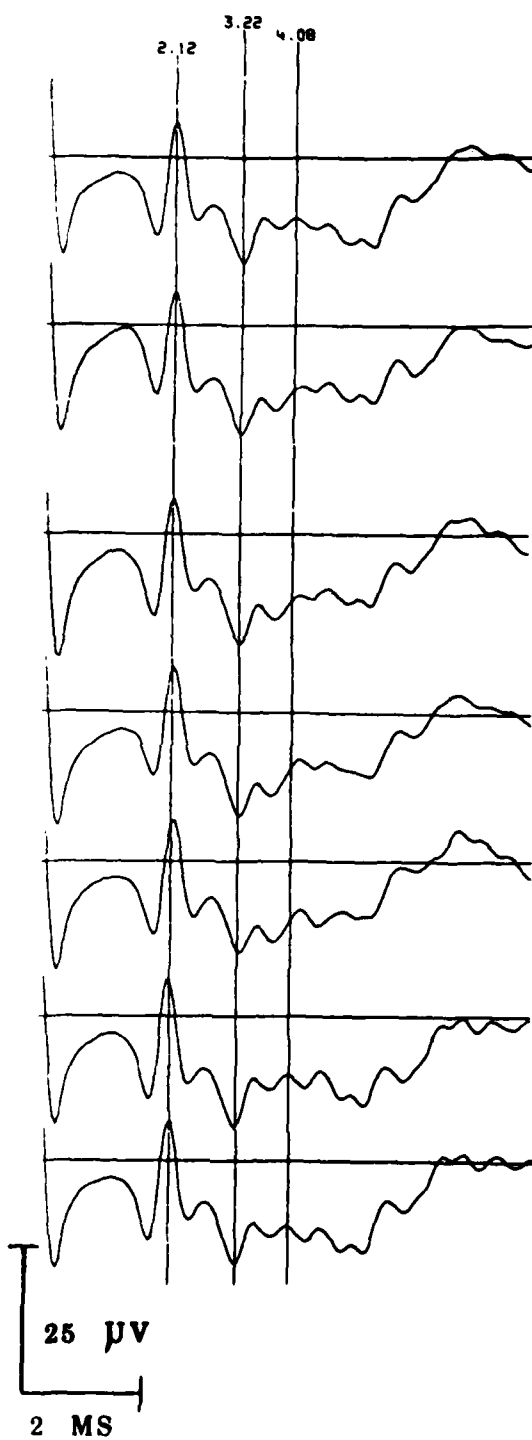
LX3691

G_X: 99 M/S²

CERVICAL

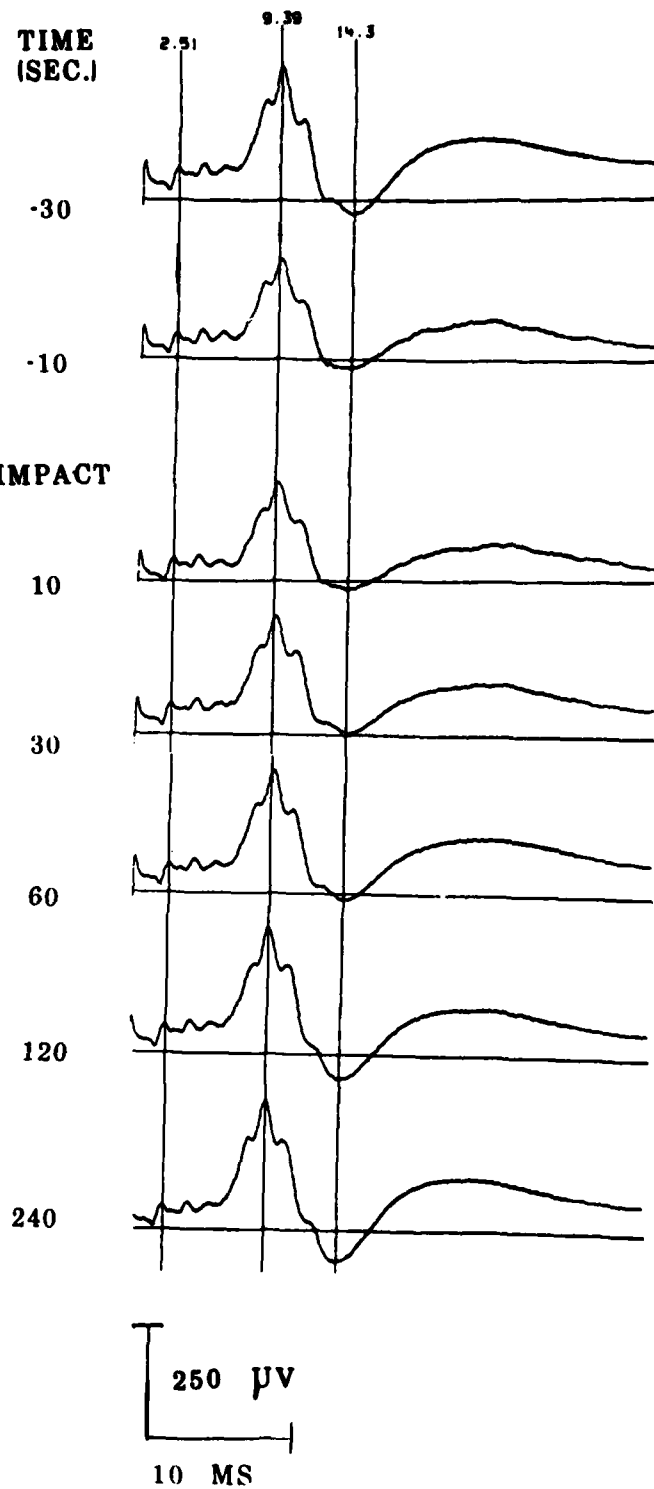
N: 50

CORTICAL



TIME
(SEC.)

IMPACT



Somatosensory Evoked Potentials

LX3693

$-G_X$:

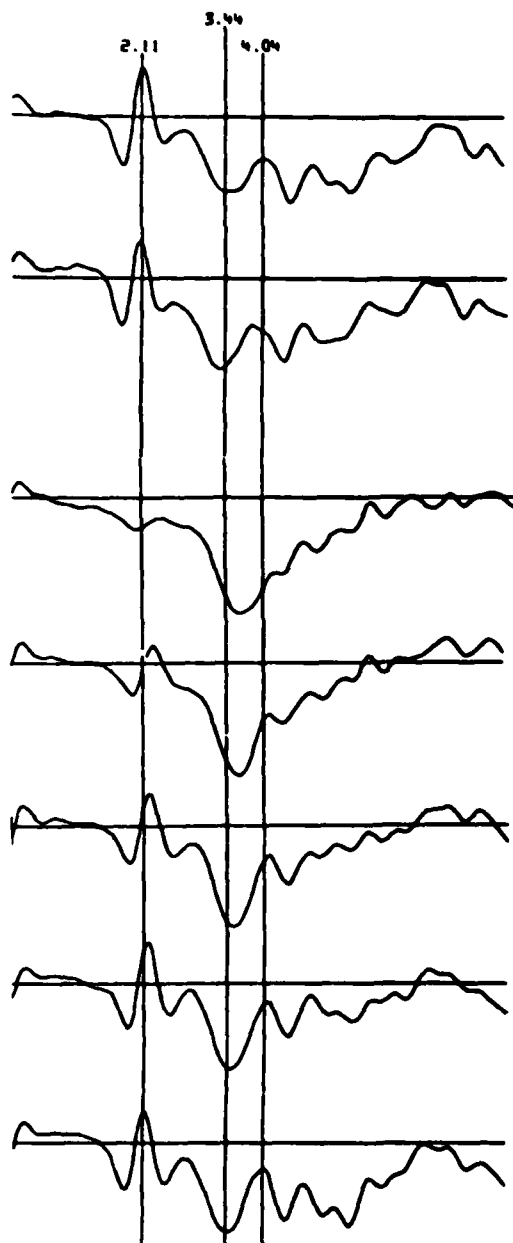
727 M/S²

CERVICAL

N: 50

CORTICAL

TIME
(SEC.)



UNEXPLAINED DISAPPEARANCE
OF CORTICAL EVOKED POTENTIALS
AFTER EXPERIMENT LX3691

IMPACT

10 μ V
2 MS

Somatosensory Evoked Potentials

LX3694

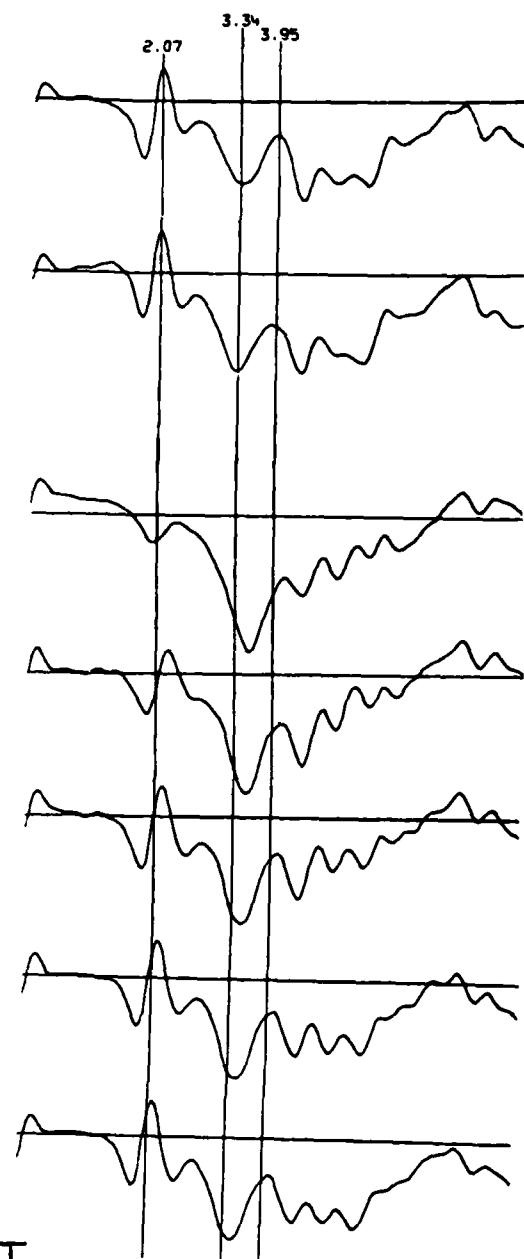
-G_X: 767 M/S²

CERVICAL

N: 50

CORTICAL

TIME
(SEC.)



UNEXPLAINED DISAPPEARANCE
OF CORTICAL EVOKED POTENTIALS
AFTER EXPERIMENT LX3691

-30

-10

IMPACT

10

30

60

120

240

10 µV
2 MS

Somatosensory Evoked Potentials

LX3695

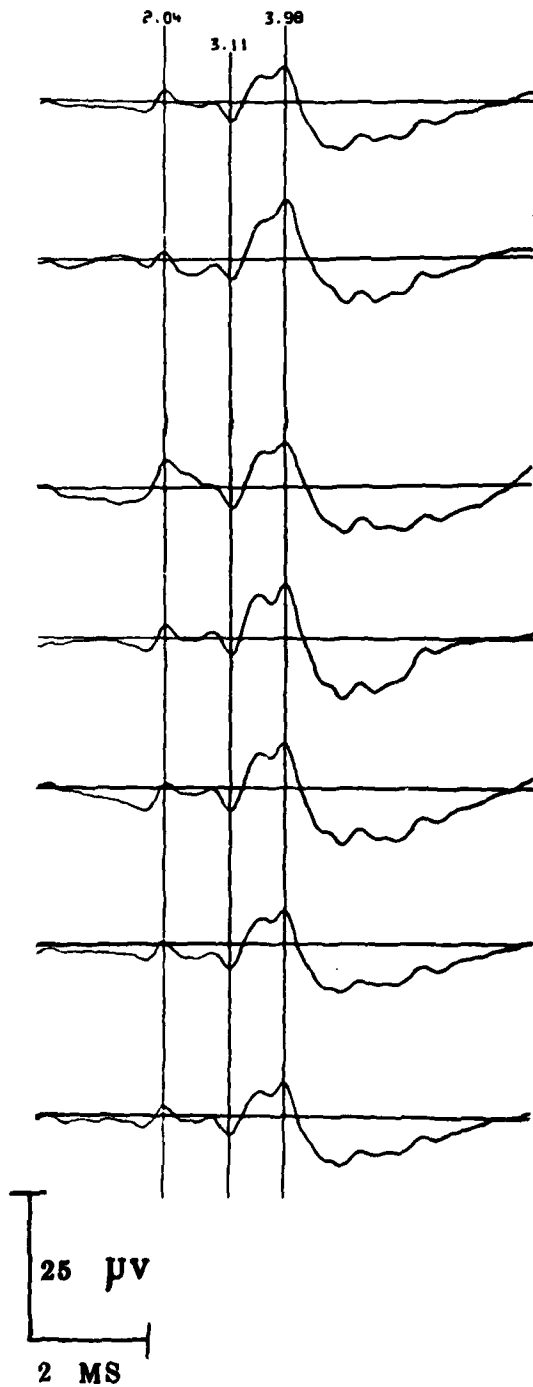
$-G_X$: 98 M/S²

CERVICAL

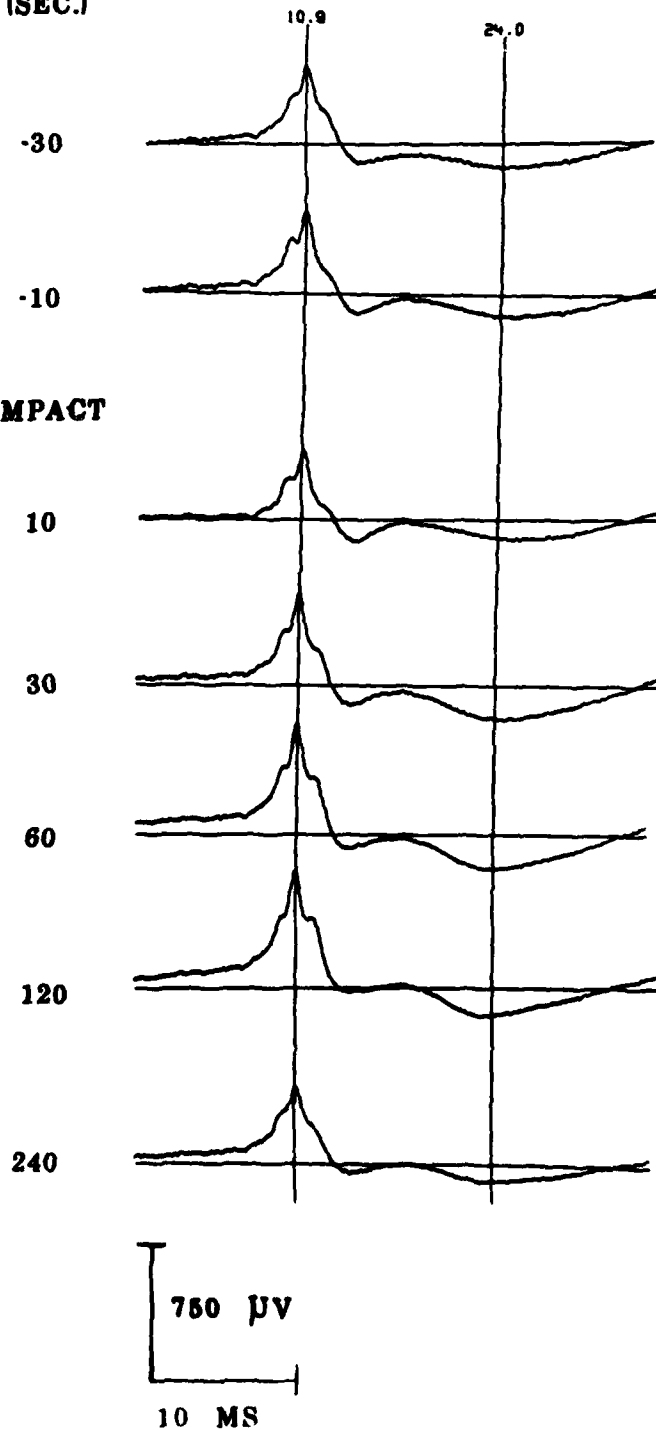
N: 50

CORTICAL

TIME
(SEC.)



IMPACT



Somatosensory Evoked Potentials

LX3697

CERVICAL

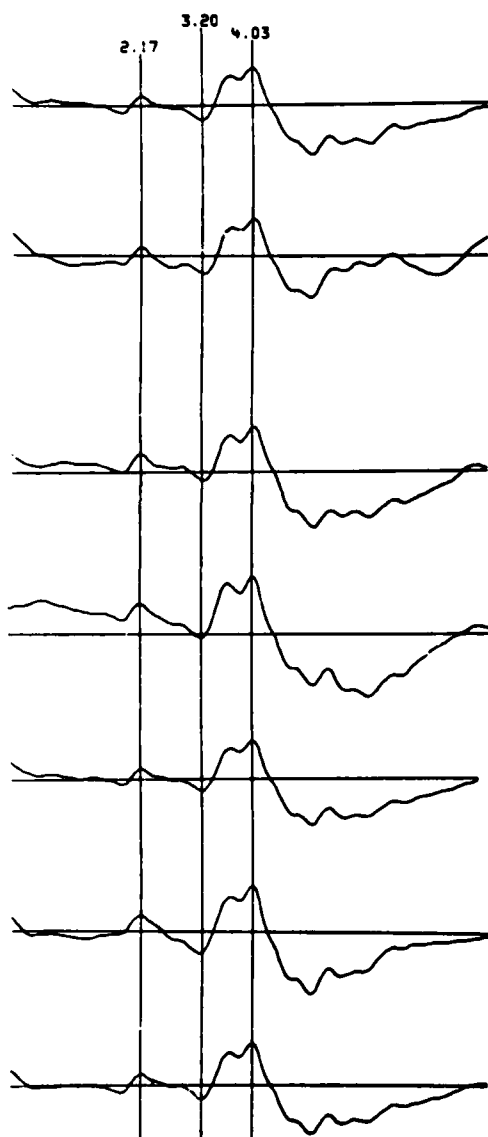
N: 50

$-G_X$

414 M/S²

CORTICAL

TIME
(SEC.)



-30

-10

IMPACT

10

30

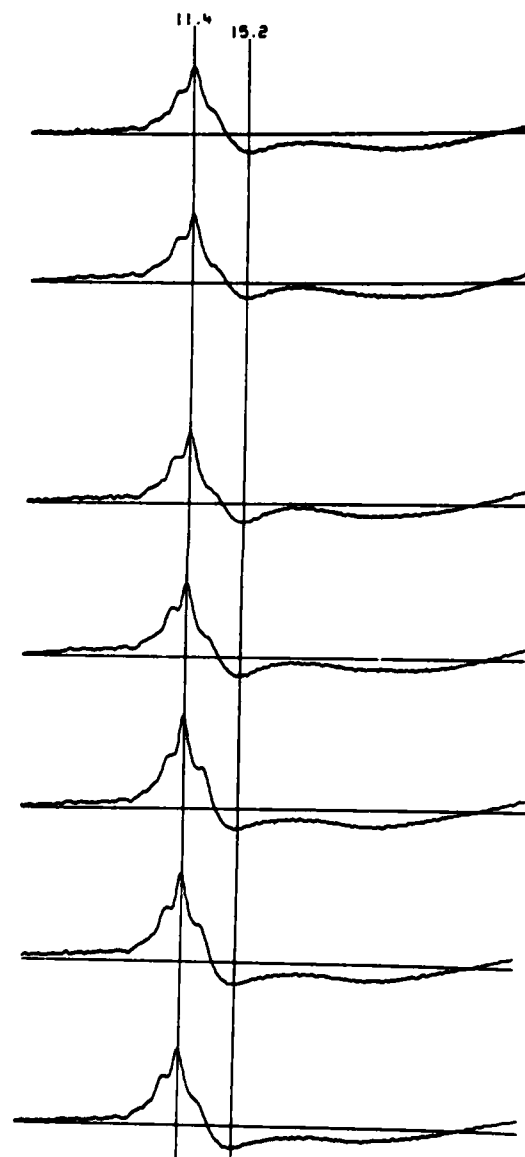
60

120

240

25 μ V

2 MS



750 μ V

10 MS

Somatosensory Evoked Potentials

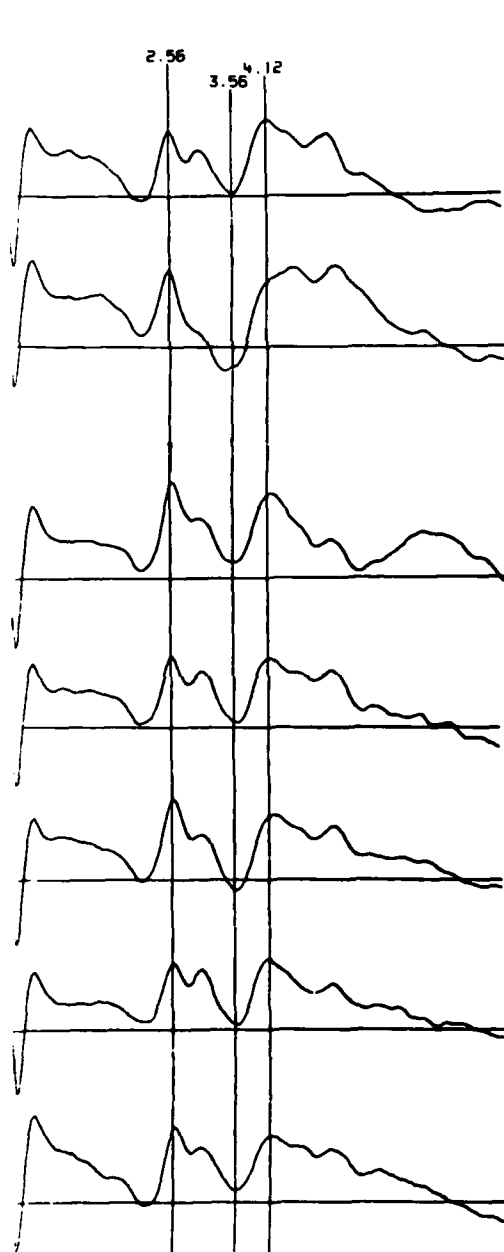
LX3699

-G_X : 42 M/S²

CERVICAL

N: 50

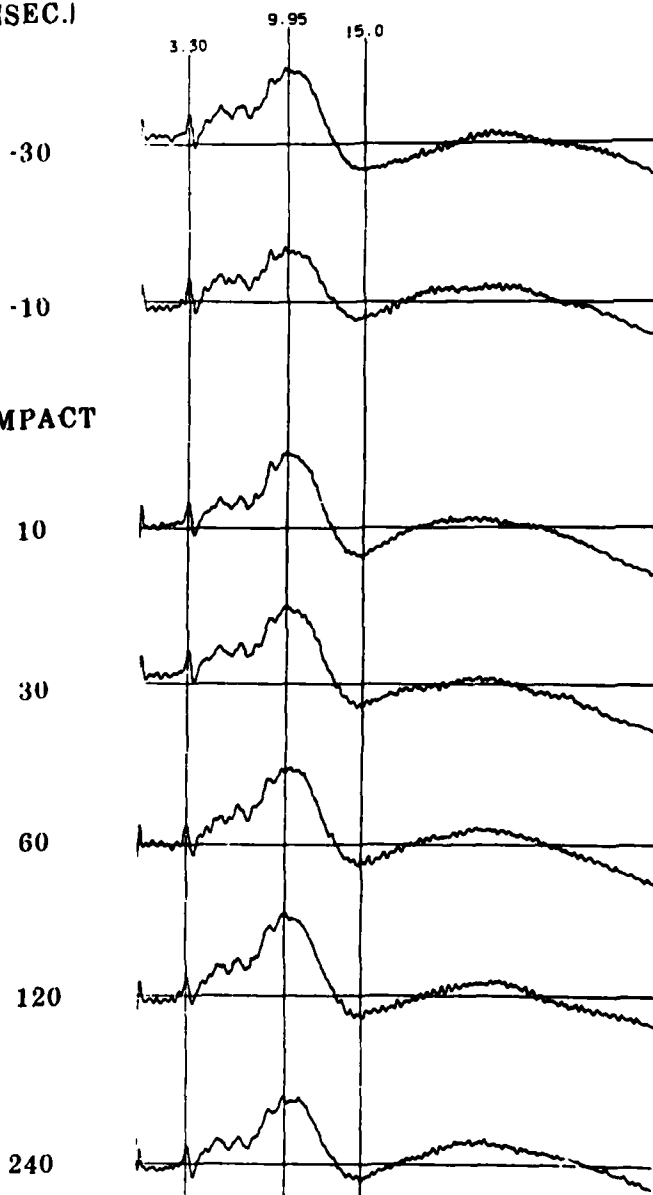
CORTICAL



10 μ V
2 MS

TIME (SEC.)

IMPACT



60 μ V
10 MS

Somatosensory Evoked Potentials

LX3701

$-G_X$

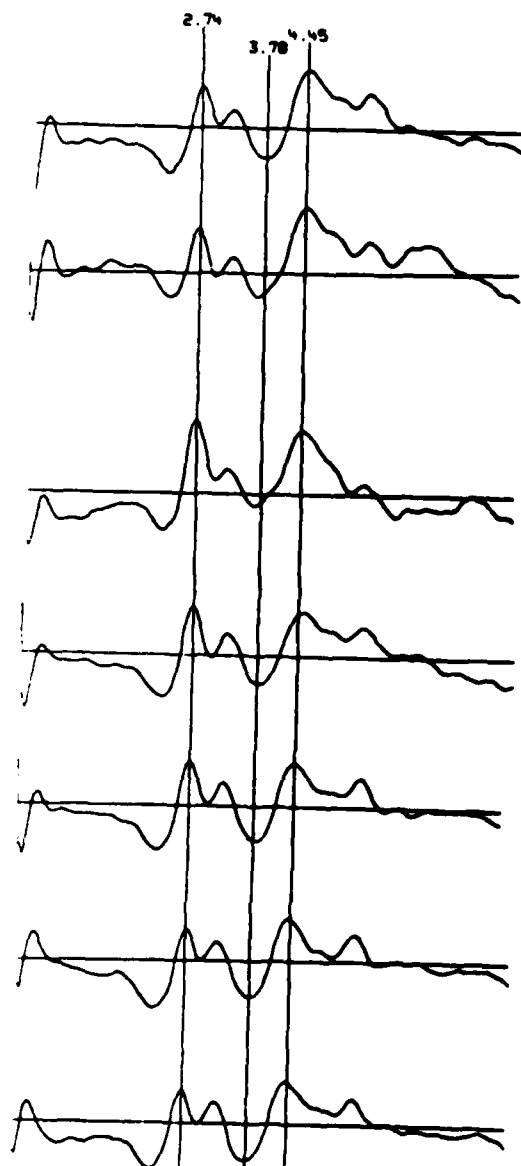
436 M/S²

CERVICAL

N: 50

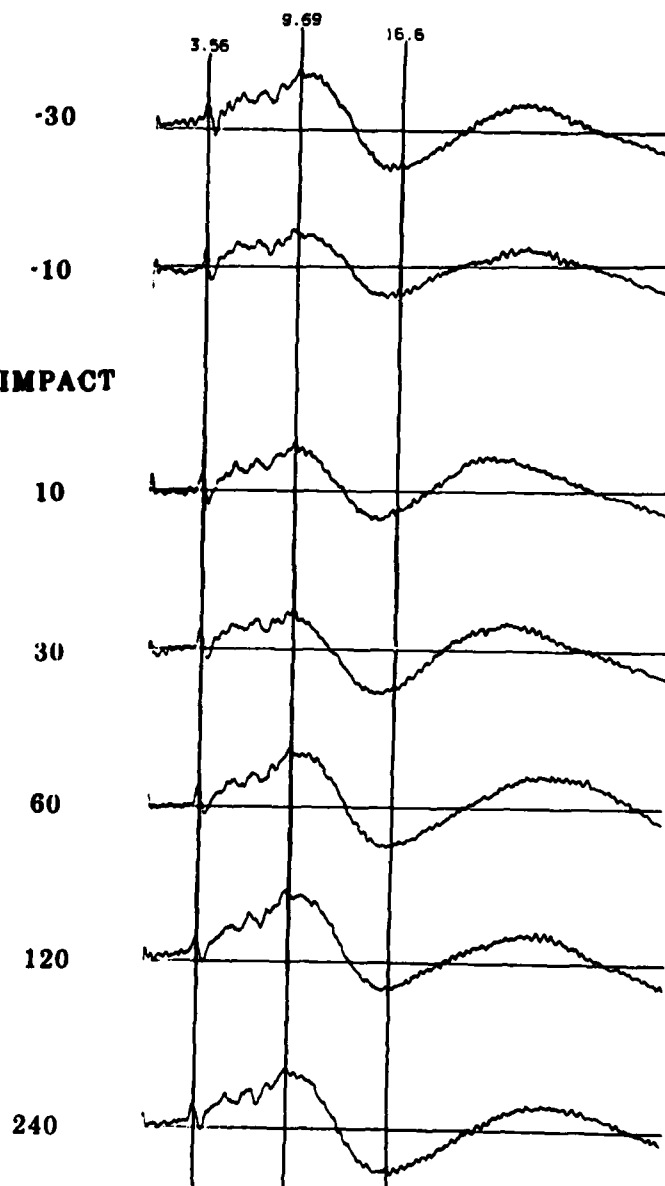
CORTICAL

TIME
(SEC.)



10 μ V
2 MS

IMPACT



60 μ V
10 MS

Somatosensory Evoked Potentials

LX3702

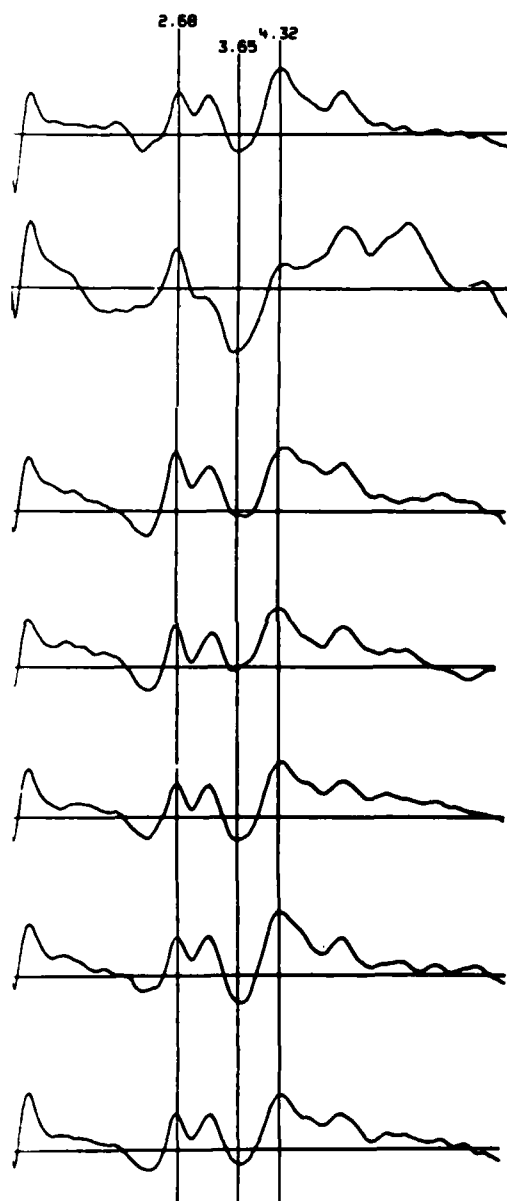
-G_X : 434 M/S²

CERVICAL

N: 50

CORTICAL

TIME
(SEC.)



IMPACT

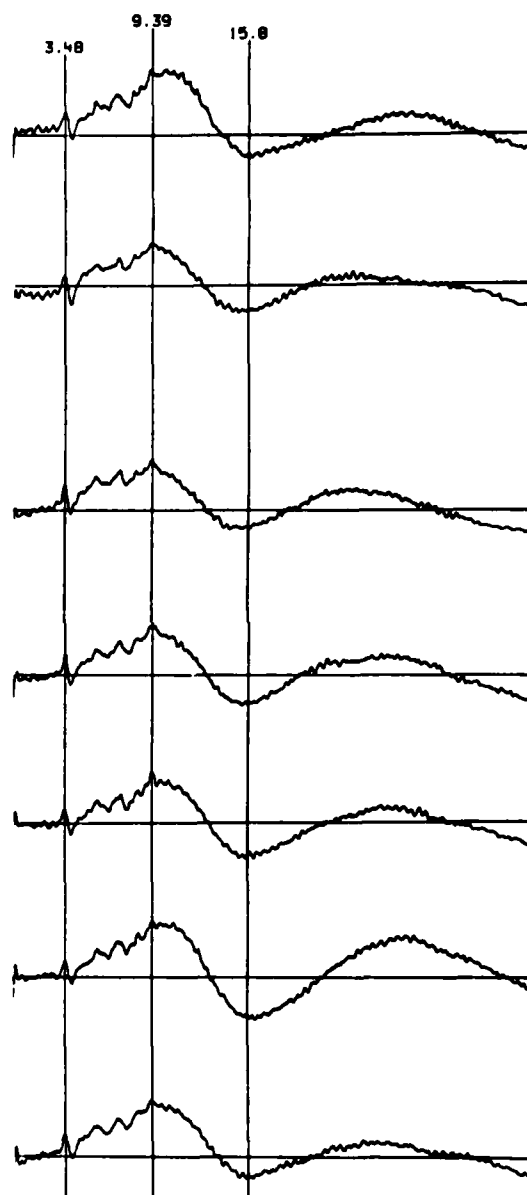
10

30

60

120

240



10 μ V
2 MS

60 μ V
10 MS

Somatosensory Evoked Potentials

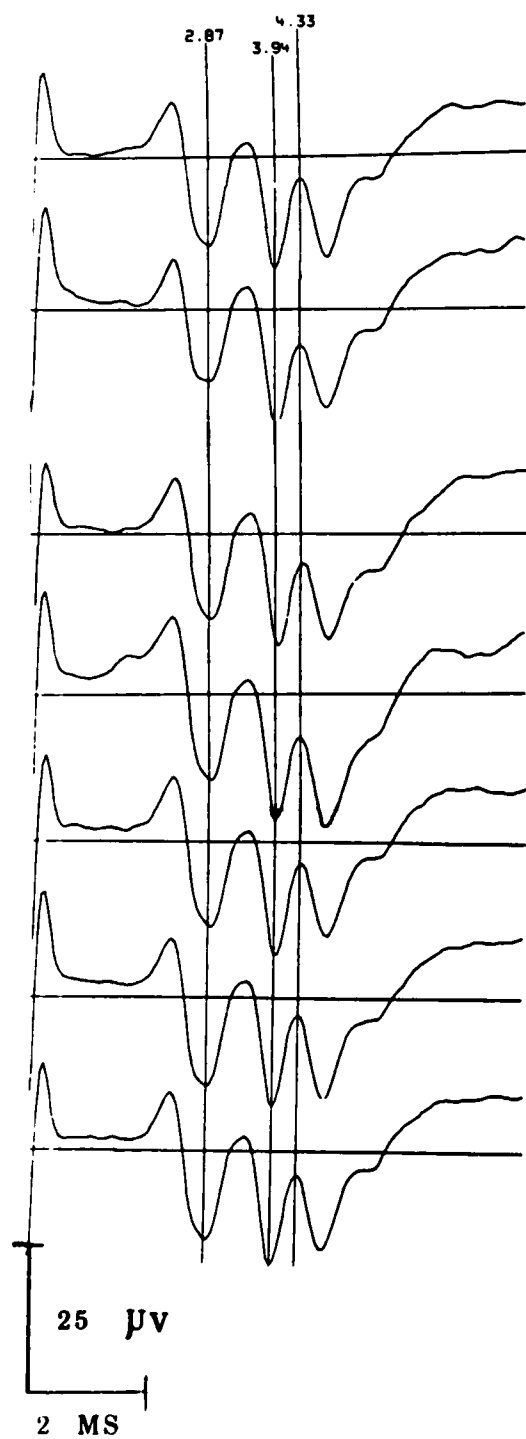
LX3703

CERVICAL

N: 50

$-G_X$: 99 M/S²

CORTICAL



TIME (SEC.)

IMPACT

-30

-10

10

30

60

120

240

3.29 10.7 14.9

75 µV

10 MS

Somatosensory Evoked Potentials

LX3705

CERVICAL

N: 50

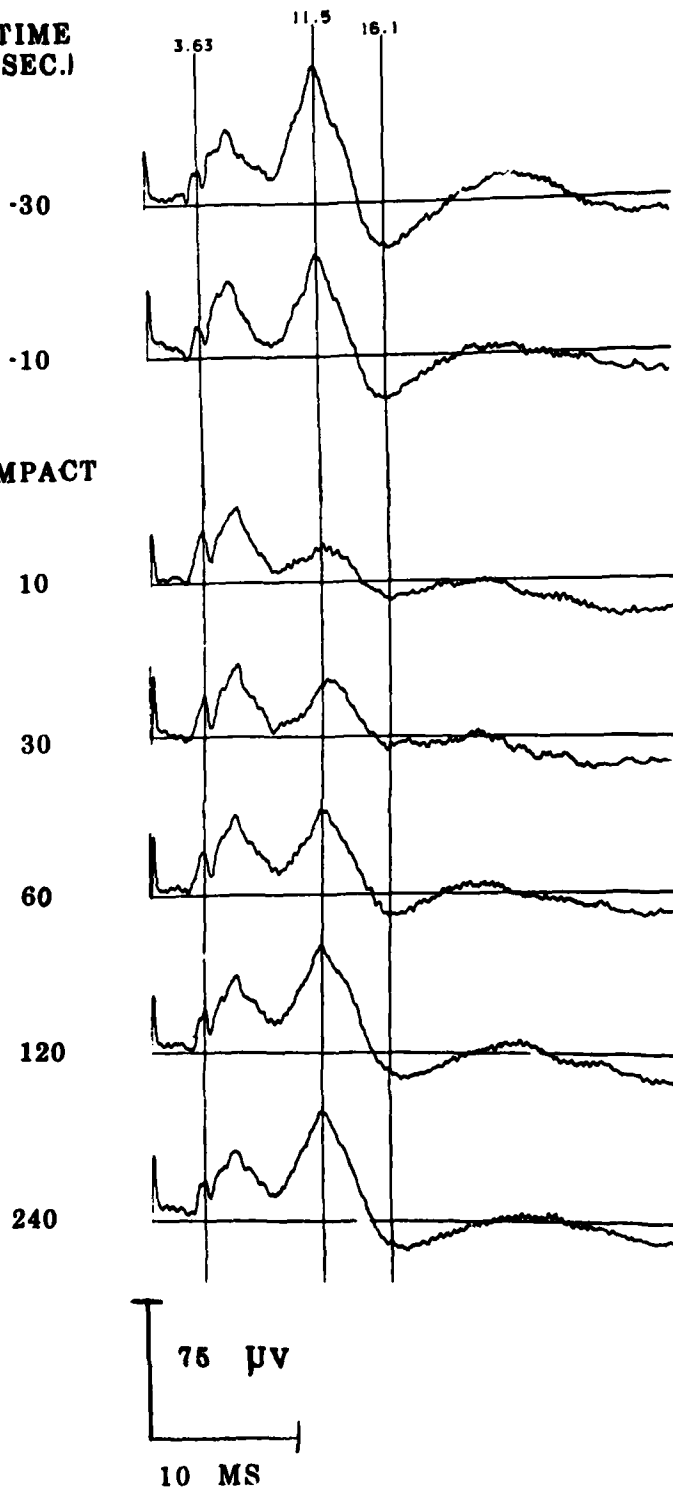
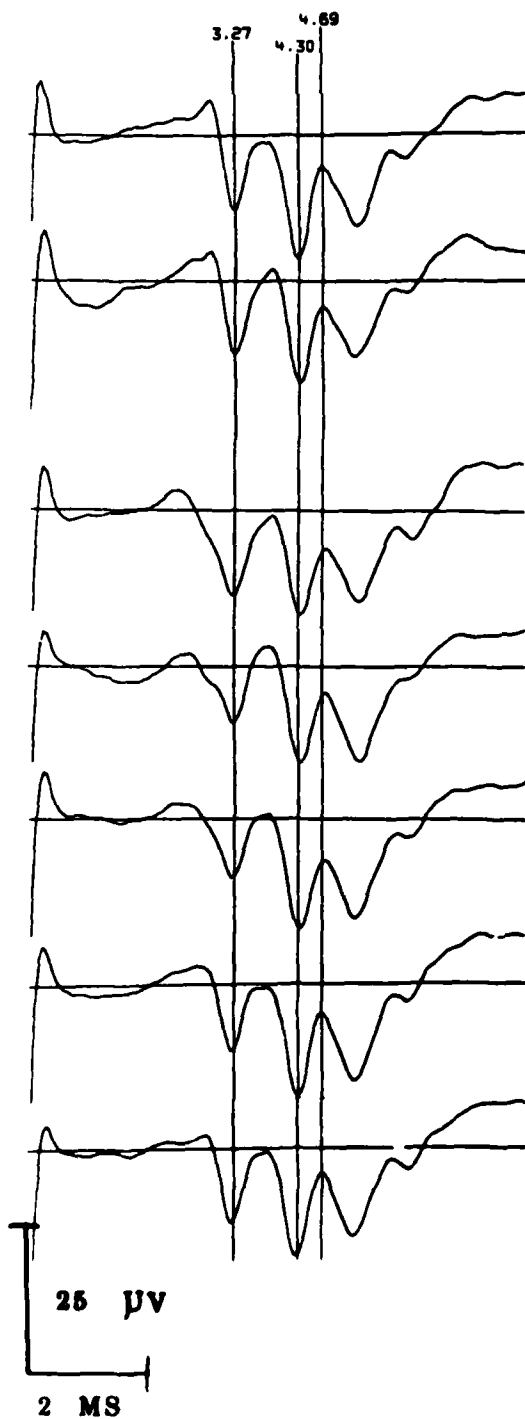
$-G_X$

630 M/S²

CORTICAL

TIME
(SEC.)

IMPACT



Somatosensory Evoked Potentials

LX3706

CERVICAL

N: 50

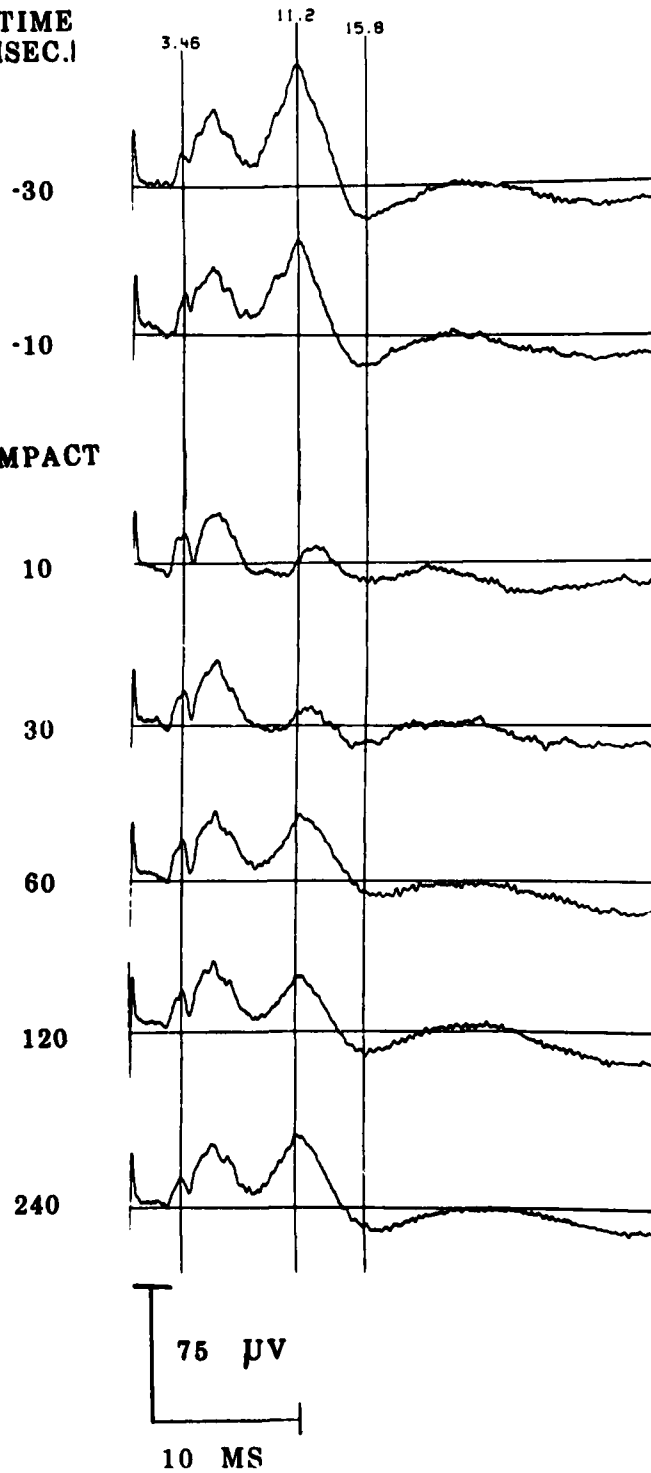
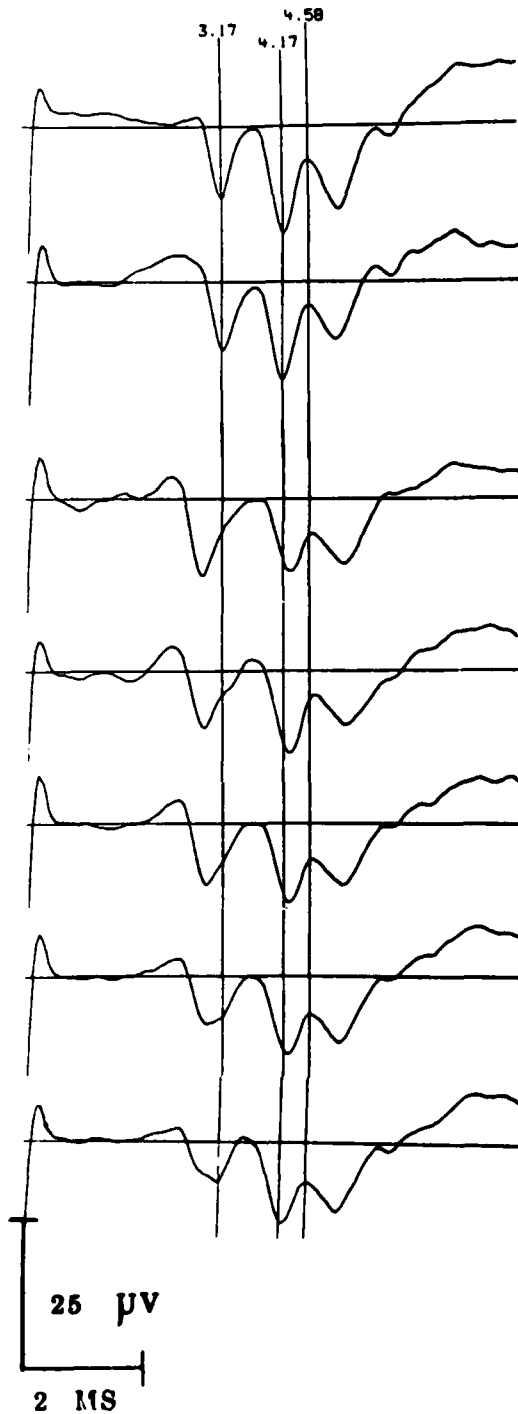
$-G_X$

624 M/S²

CORTICAL

TIME
(SEC.)

IMPACT



Somatosensory Evoked Potentials

LX3713

$\frac{G}{X}$

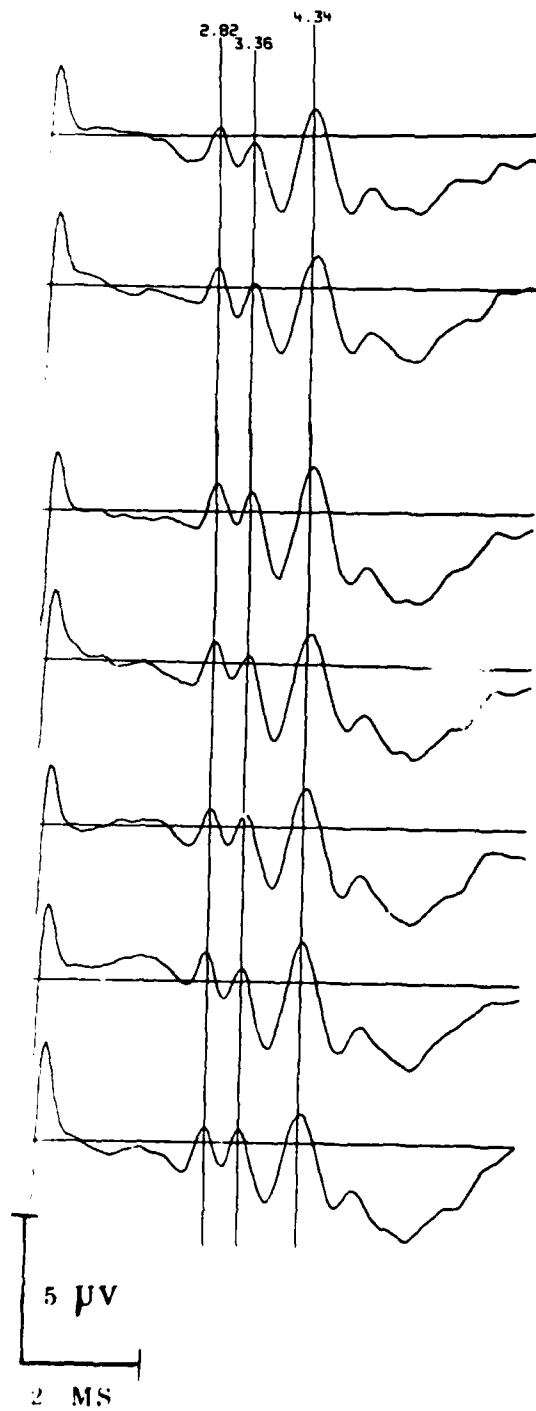
98 M/S²

CERVICAL

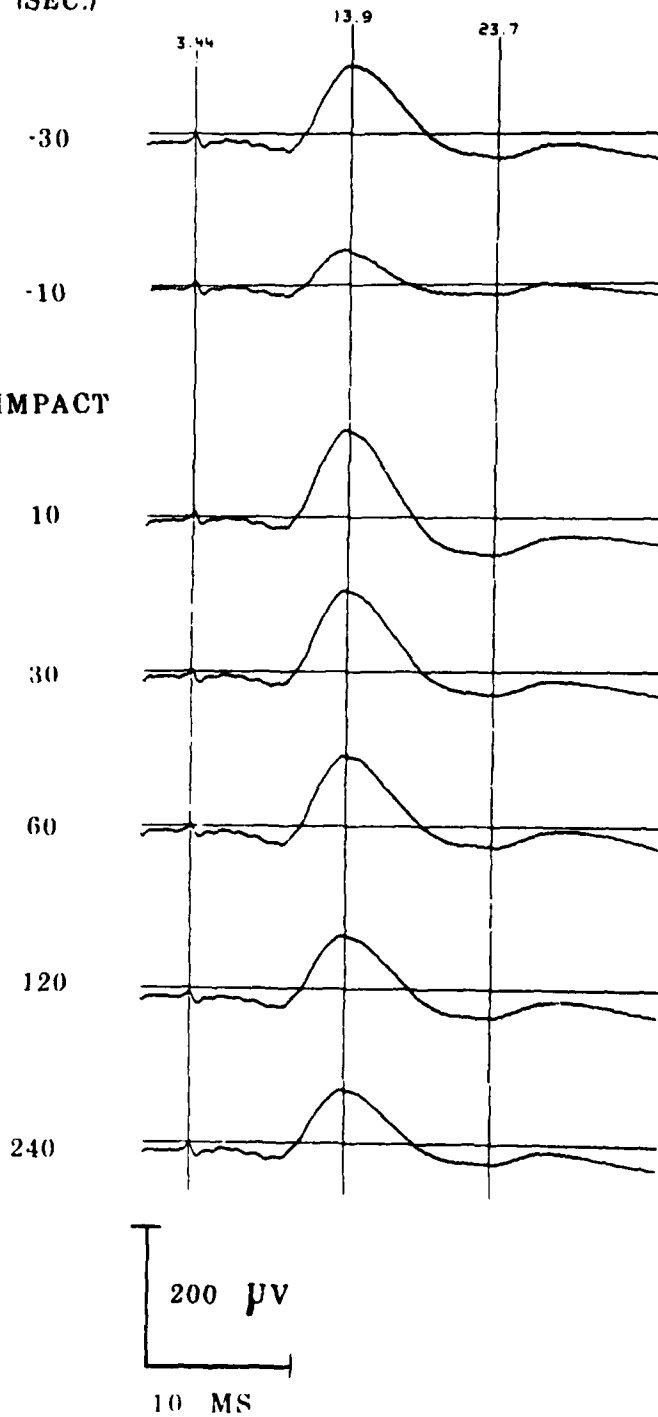
N: 50

CORTICAL

TIME
(SEC.)



IMPACT



Somatosensory Evoked Potentials

LX3714

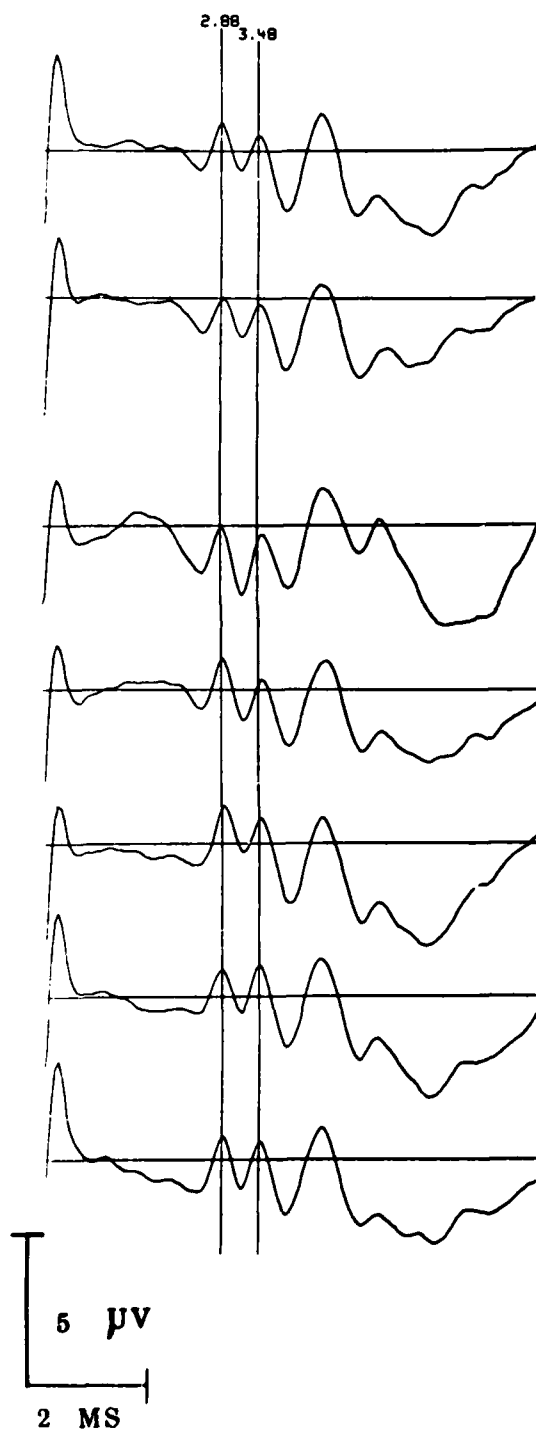
$-G_X$: 598 M/S²

CERVICAL

N: 50

CORTICAL

TIME
(SEC.)



-30

-10

IMPACT

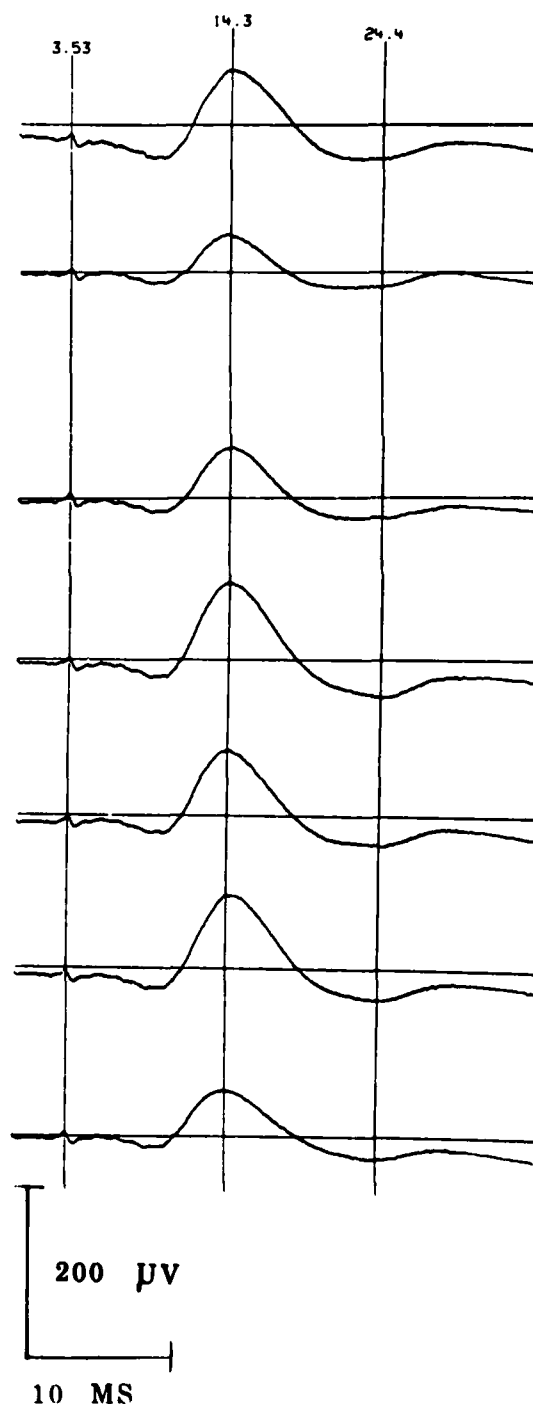
10

30

60

120

240



Somatosensory Evoked Potentials

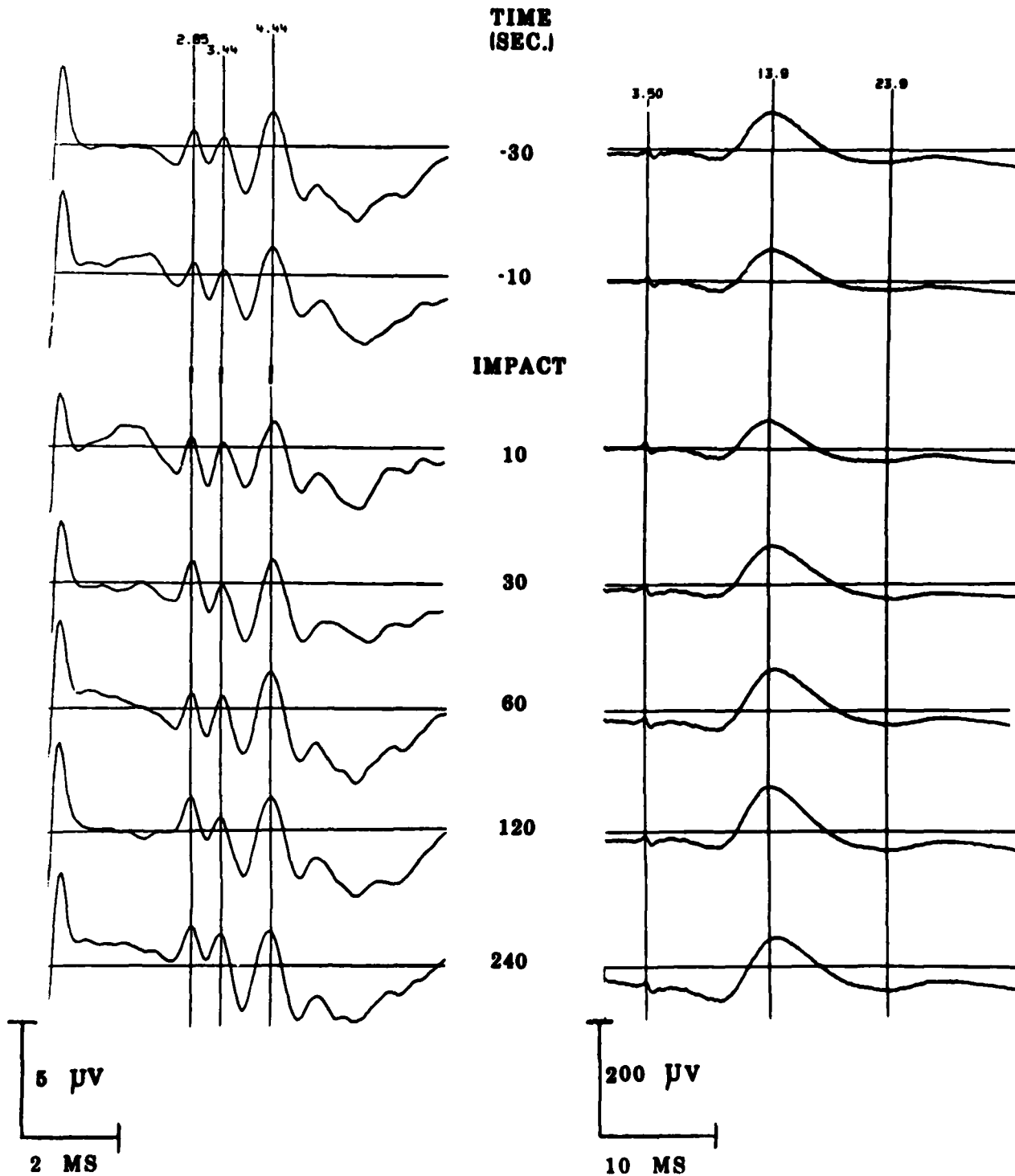
LX3715

$-G_X$: 598 M/S^2

CERVICAL

N: 50

CORTICAL



APPENDIX B. Concepts in EP Data Analysis

B-1. Data Space

All of the results of any of the experiments can be represented exactly by the position of a single point in a space containing a very large number of dimensions. For example, if the spectral properties of the EP data on a particular channel are such that 100 digital values are required to represent each EP, and there are 1,500 EP's on that channel in the experiment, then 150,000 dimensions would be required to represent that portion of the results. This is approximately the dimensionality for the five minutes of the post-impact cervical data analysed in this paper. The purpose of the data analysis is to reduce the dimensionality to a small number without excessive loss of the information that is crucial to the purpose of the experiment.

The data analysis procedure is a sequence of steps, each of which reduces the dimensionality by one or more orders of magnitude. At each step, a model is assumed, which if correct, will insure that the information loss in that step will not be catastrophic. The success of the analysis is critically dependent on the applicability of the model. For example, the first step in EP work is usually the computation of AEP's. The associated model includes the requirements that the important information is contained in that portion of the electrical activity that is synchronous with the stimulus, and that the time course of the important changes are such that they will be observable in the AEP's. Averaging is useful only to the extent that these are true. Averages were computed with $N = 10$, reducing the five minute dimensionality to 15,000.

The next step requires the reduction of the dimensionality of each AEP. Though the means for accomplishing this remains an active field of research, two approaches can be distinguished. In the first approach, the extent to which the dimensionality of the AEP can be reduced without loss of any appreciable amount of information is determined. In the second approach, information other than EP data is available. This information is generally in the form of different conditions under which the various EP's were acquired. In this case, the approach is to determine the extent to which the dimensionality of the AEP can be reduced, while selectively retaining information that is related to the different conditions.

In the present work, the second approach is taken. Conditions are assumed to be changing as a function of time at first discretely at the moment of impact, and continuously thereafter as a consequence of the sequelae to impact. Various algorithms are used to extract single scalar measures from each AEP. Scalar measures are accepted or rejected on the basis of computational stability in the face of the variability of the data, as well as the ability to distinguish the effects of impact. These scalar measures include measures of the latency and amplitude of various peaks, and quantitative representations of the waveshape of various portions of the AEP. Each scalar measure entails its own set of assumptions. In general, it is

assumed that different simply measurable aspects of the AEP will be differently related to impact, and represent different functional effects of impact. In the present report, only the latency shifts of peaks have been analysed in detail. This was not because other scalar measures are considered to lack information, but because of limitations of resources, as well as preliminary indication that there was important information in the latency shifts. The average number of peaks measured in each subject was about six, reducing the five minute dimensionality in each subject to 900. At this point, each of the six scalar measures (shifts in latency at the six peaks) could be plotted as a function of time allowing observation of the effects of impact, as well as qualitative comparisons of the strength and duration of the effects of impact among subjects and conditions. These observations may be considered to be subjective reductions of dimensionality. For more objective comparisons, further quantitative reduction of dimensionality was required.

B-11. Exponential Model for Reduction of Dimensionality

To reduce the dimensionality further, it was assumed that following impact, the essential* properties of the time course of each scalar measure could be represented by two variables. The first was the amplitude of the effect, i.e., a measure of the deviation of the the scalar measure from its pre-impact value (not to be confused with the amplitude of the evoked potential). The second was the duration of the effect. At this point, any of a large number of additional assumptions could be made to allow computation of the variables. It was assumed here that the essential effect of impact was instantaneous, and after impact it decayed exponentially to the pre-impact level. The amplitudes and durations were usually determined by regression of a single exponential decay curve on each scalar measure from the first five post-impact minutes. In most instances, this is all that was necessary. In some cases, however, a substantial portion of the plot of the scalar measure fell below the pre-impact baseline in the first five post-impact minutes, even though the initial effect was an increase in the scalar measure. In these cases, the single exponential decay model was grossly inadequate, and a step function, with the step occurring at the time of impact was added. Using two-term exponential regression the effect of the step was minimized and a single amplitude and duration could still be computed in most cases.

Assuming six peaks per subject, the five minute dimensionality for each subject was now 12. The dimensionality was finally reduced to two by computing the medians of the amplitude and duration across

* It is important that it is only assumed that the essential properties of the scalar measures can be represented by the two variables. It is not assumed that all, or even most of the details of the time course can be so represented.

peaks for each subject. With two values per subject, it was a simple matter to construct scatter diagrams for observation of the final experimental result.

B-iii. Exponential Model for Curve Fitting

Aside from determination of the amplitude and duration, it was also interesting to ask whether exponential decay would be a good model for the detailed effects of impact. It was immediately apparent that at lower impact levels, the measures were too variable to provide an answer. Therefore, only data from high level impact were used for this purpose, and after preliminary work, it was found necessary to consider a model somewhat more complex than exponential decay alone. An example in which this model fits the data reasonably well is shown in fig. 2. The complete model is as follows:

- 1 - Linear baseline shift. It was assumed that in the absence of impact, the scalar measure may be changing at a constant rate with time. It was further assumed that impact would not alter the process responsible for this change. This assumption was based on the observation that in some experiments, some of the measures appeared to change in an approximately linear fashion during the experiment. This was most commonly observed with measures of latency, which tended to decrease during the experiment. In some cases, peak latencies tended to decrease during an entire day in which there were several experiments. For example, experiments LX3008, LX3009, and LX3010 were all run on the same day (table 1). LX3008 and LX3010 were separated by about 4 hours. From table 2 it was computed that the average (across the four peaks) change in the pre-impact median latencies was $-34 \mu\text{s/ms}$ between experiments LX3008 and LX3010.
- 2 - Impact-induced shift with poly-exponential decay. It was assumed that impact would produce an instantaneous shift that decayed back to baseline according to a poly-exponential function decay (the sum of several simple exponential decay terms). The simplest assumption for a process that appears to be decaying with time toward an asymptote is that the decay is a single exponential one.* Some of the plots of the scalar measures as a function of time suggested this possibility.

* This amounts to assuming that the rate of decay at any given time (relative to impact) is proportional to the remaining strength (amplitude) of the effect at that time. The constant of proportionality is the reciprocal of the time coefficient of the decay. This simple description is applicable to a large number of physical, chemical, and physiological processes. For example, Brown and Brown (4) report that changes in cardiovascular measurements produced by a direct occipital blow in Rhesus returned to normal with an exponential time course.

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However, in some cases it appeared that partial recovery took place quite rapidly, while part of the effect of impact took a much longer time to recover, suggesting the poly-exponential model.

- 3 - Impact-induced "permanent" shift. It was assumed that the impact would produce an instantaneous change in the measure persisting unchanged for the duration of the experiment. In practice, it was found that in the least noisy data, once the magnitude of a time coefficient exceeded several times the duration of the interval analyzed, it became impossible to distinguish a slow decay from a permanent shift.
- 4 - Residual noise. This is the variation not accounted for by the above three parts.

The model can be represented by the following equation:

$$y = St + B + h(t)D + \sum_{i=1}^N h(t)a_i \exp(t/T_i) + E(t)$$

where:

- y is the value of the measure,
- t is time relative to impact,
- S is the slope of the linear baseline shift,
- B is the amplitude value of the baseline instantaneously prior to impact,
- D is the "permanent" shift induced by impact,
- N is the number of exponential terms,
- a_i are the exponential amplitudes,
- T_i are the exponential time coefficients,
- $h(t)$ is the unit step function with value zero for t less than zero, and unity for t greater than or equal to zero,
- $E(t)$ is the noise.

B-iv. Regression Procedures for Curve Fitting

The linear baseline shift parameters, S and B , were determined by applying simple linear regression to the pre-impact data. The linear equation was extrapolated into the post-impact region, and values

computed from the linear equation were subtracted from the data. The residual was then subjected to poly-exponential regression, providing estimates of the a_1 and T_1 .

The poly-exponential regression was also applied to the residual to estimate the "permanent" shift due to impact, D . This was done by using an additional exponential term in the regression procedure. If there were a "permanent" change in the measure, the extra exponential term would have a time coefficient (T) of either sign that was very long in relation to the duration of the analysis interval. The sign of the amplitude of this term depended on the direction of the permanent shift. For all values of t during the analysis interval, t/T is close to zero and $\exp(t/T)$ is close to unity irrespective of the sign of T . The corresponding amplitude is thus an estimate of D , the "permanent" shift induced by impact. In practice, the regression algorithm did not always produce a term with a long time coefficient, especially if the "permanent" displacement was small or non-existent, or if the "permanent" shift was in the same direction as the exponential decay. Rather, it used the additional term to fit some detail of curvature, which usually resulted in substantial distortion of the other coefficients. However, the algorithm could often be induced to provide the term with a long time coefficient by simply adding a constant value to all of the data. The permanent shift, D , was then the difference between the added constant and the amplitude of the exponential term with the long time coefficient. If, in fact, there were no "permanent" shift at impact, this difference would be very small.

B-v. The Distribution of the Latency Shifts -- Outliers

Generally, when a particular type of result is to be derived from a given data set, some identifiable subsets of the available information are more reliable than others. Therefore, various statistical procedures have been developed which selectively use information that has a high probability of being reliable. A common example is the use of the median to estimate central tendency. In this case, only part of the available information is used; the actual magnitudes of most of the data values are discarded. The elimination of outliers provides another example. In the current analysis, both of these procedures are combined, resulting in a substantial improvement of the reliability of the estimates of the amplitude and duration of the observed effects.

Poly-exponential regression is very sensitive to outliers. This sensitivity arises from two sources. First, the squaring in the mean square deviation criterion amplifies the affect of outliers. Second, there are strong correlations among the regression coefficients which allow relatively small changes in the data to affect the coefficients sufficiently so that the essential character of the result is changed. This often happens without an appreciable change in the mean square deviation. The problem is especially acute if more than one exponential term is used. Using poly-exponential regression, however, it is possible to devise a procedure that eliminates outliers.

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Before selecting outliers, some understanding of the distribution of the data is necessary. Assume, for the moment, that there is no impact, and that the time series of evoked potential vectors is stationary. In the case of latency measurements (either by simple peak detection or normalized cross-correlation) the distribution of the measurements may be considered as the sum of three distributions as follows:

- 1 - Correct detection of the target peak. The distributions of the target latency measurements are assumed to resemble normal distributions. In the absence of experimental manipulation, in all cases where the cervical EP is clearly present, it was found that the latencies for the various peaks are very stable over short periods of time. The standard deviations of the latency distributions are of the order of 50 microseconds or less.
- 2 - Absence of the Evoked Potential. Due either to artifact, or to true physiological absence of the EP, the expected distribution of the latency measurements is rectangular over the latency range of the peak search. Since the peak is generally not found in the middle of the range, this rectangular distribution is asymmetric with respect to the mean of the distribution of target detections. A typical width of the search range, and thus the width of the rectangular distribution, is 500 to 1000 μ s.
- 3 - Detection of an incorrect peak. This distribution will depend on the latencies of available incorrect peaks. Often, there is one extra peak in the search interval. The resulting distribution is severely asymmetric with respect to the theoretical mean of the correct target distribution. Rarely, two extra peaks are present. The distribution still results in asymmetry, because the peaks do not occur at regular intervals, and are not detected with equal probability. The smallest intervals between peaks in the cervical data are of the order of 300 μ s.

Thus, the observed distribution has excessively large and asymmetric tails, as compared with the target distribution. It is clear that because of the large, asymmetric contributions of the two "error" distributions, the mean of the observed distribution will not be a good estimate of the target mean. The median will provide a substantially better estimate of the target mean if more than 50% of the peak detections are target peak detections.

Because of the non-stationarity due to impact, the above considerations cannot be directly applied, but the following procedure may be used to eliminate outliers from the post-impact data if the number of outliers is not too great:

- 1 - Compute a least-squares poly-exponential regression using the entire data set.

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- 2 - Subtract the poly-exponential function from the data leaving a "residual".
- 3 - Discard outliers relative to the median of the residual using some predetermined criterion.
- 4 - Recompute the poly-exponential regression using the remaining data.

In this procedure, it is assumed that the post-impact data may be considered to be the sum of a continuation of the stationary pre-impact time series and the effect of impact on the time series. The short term stability of the data are assumed to be unchanged by the impact except for this additive effect. It is further assumed that the initial poly-exponential regression is close enough to the actual effect of impact so that the data in the tails of the residual distribution can be considered outliers. Since the "error" distributions are much wider than the target distribution, a very rough initial fit will accomplish this, as was judged by examination of graphs of the initial regression and the associated residual.

Procedures for objective elimination of outliers are in the planning stage. In the current analysis, outliers were removed subjectively after exhaustive examination of the graphic results of initial poly-exponential regressions. Sometimes the procedure was iterated several times. The final results (tables 2 & 3, figs. 4 & 5) were obtained using the following guidelines:

- 1 - Any coefficient resulting from a few data points was eliminated, generally by discarding the data points. Thus no time coefficients with magnitudes less than 10 seconds are reported.
- 2 - Where the data were clearly multimodal, all data outside of the main mode were discarded.
- 3 - Where the data were highly variable, but not clearly multimodal, no coefficients were computed.
- 4 - Where shifts in latency were small and no apparent pattern was seen, various procedures were used to produce a regression that would represent most of the plot. The time coefficients in such cases are meaningless.
- 5 - Positive time coefficients indicating exponential growth were considered meaningless in the current context. Unless they were so large that the contribution of the term was essentially constant over the time interval under study, they were eliminated by various means.
- 6 - The first few points after impact were eliminated. The exponential amplitudes therefore represent values that are extrapolated back from post-impact data.

- 7 - Last, but possibly most significant, data were discarded if they indicated shifts in latency larger than any seen in clearly resolved AEP's under comparable conditions. This was especially important in high level impact experiments. It is considered that there is some uncertainty regarding the magnitude of the largest shifts in latency occurring under these conditions.

B-vi. Measurement of Duration -- Comparison With Other Methods

In past work the duration has been emphasized, using "threshold crossing" procedures (19, 32). These measure the time between impact and the first value of the scalar measure to return to some threshold level, such as the pre-impact median, or one standard deviation from the pre-impact grand mean. With moderately noisy data such as ours, this simple procedure may be misleading unless some sort of smoothing is applied to the data before measuring the time to threshold crossing. However, if the noise is of such a nature that outliers are frequent, the smoothing procedure can be further improved by incorporating a method that selectively discards outliers. The exponential regression method, as used here, is a smoothing procedure of this type.

Any procedure for discarding outliers during the non-stationary period following impact must involve assumptions about the effect of impact. The exponential model implies that except at the instant of impact, there are no sudden changes. Other models may be used to exclude outliers, and it is likely that many would do at least as well as the exponential decay model. The final results should be relatively insensitive to the choice of the model for the same reason that the exponential model works even if the exponential coefficients are known only approximately: the error distributions are much wider than the target distributions.

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