CORTICAL POTENTIALS ASSOCIATED WITH VOLUNTARY HAND MOVEMENTS IN THE MONKEY (MACACA MULATTA)

by

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A dissertation submitted to the Graduate Faculty in Psychology in partial fulfillment of the requirements for the degree of Doctor of Philosophy, The City University of New York.

1975

This manuscript has been read and accepted for the Graduate Faculty in Psychology in satisfaction of the dissertation requirement for the degree of Doctor of Philosophy.

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ACKNOWLEDGMENTS

I wish to gratefully acknowledge my many friends and colleagues for their assistance and encouragement in this project.

Julie Wong wrote the computer programs; Chester Freeman solved many of the recurrent electronic problems and assisted in the design and construction of the behavioral equipment; Arthur Pickoff participated in the early surgical procedures and in the development of the implantation technique; Linda Peterson typed and assisted in the proof-reading and spelling of the text.

Doreen Berman, Gad Hakerem, and Jerome Engel reviewed the manuscript and provided valuable suggestions for its improvement.

Joseph Bossom taught me the care, handling and training of monkeys and under his guidance I began my interest in the motor system.

I am indebted to my sponsor, Jack Orbach, for his assistance, advice and support in all phases of this project. Dr. Orbach's teaching ability was an important stimulus in my early training as a neuroscientist.

Finally, I wish to express my deepest gratitude to Herbert Vaughan, in whose laboratory this study was conceived and undertaken. Dr. Vaughan taught me electrophysiology, and stimulated

my reading and thinking along the lines which led to this study. In addition, he assisted in the design, running, interpretation and writing of this project.

This research was supported in part by NIMH Grant MH 06723, NIH Grant HD 01799, and Grant GB 35596 from the National Science Foundation.

ABSTRACT

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Motor potentials (MP) associated with self-paced voluntary movements were recorded from chronic epidural and intracortical electrodes in four monkeys. The epidural distributions of each component were mapped and related to the points of intracortical polarity inversion which indicated the location of component sources. Somatosensory evoked responses (SER) elicited by forearm electrical stimulation were also recorded at each electrode location.

The contralateral epidural motor potentials comprised four major components, two of which preceded the electromyographically defined onset of movement. The antecedent components were surface negative and were generated in the hand area of the precentral gyrus. The components which followed the onset of contraction were surface positive and were generated in specific areas of the pre- and post-central gyrus. The morphology, timing and distribution of the potentials corresponded to those recorded from the scalp of man by Vaughan, Costa and Gilden (1968).

The present study identified two long latency motor potential components (P3 and P4) which have not been previously described.

Afferent - efferent interactions within cortex were assessed by comparing the locations and depth of the MP component sources to those of the SER.

The timing and sources of the gross motor potentials found in this study were compared to previously reported cortical unit activity associated with voluntary movement and the functional significance of the components was discussed.

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Chapter I

INTRODUCTION

The function of specific areas of the cerebral cortex in the initiation and control of voluntary movements has been the subject of extensive examination for more than 125 years. Early investigators were limited to the available techniques of clinical observation, selective ablation and electrical stimulation. Based on data from these procedures a discrete portion of the cortical mantle was identified as the motor area in several species and this region was considered to represent the highest level of organization within the mammalian motor system. In primates, the motor cortex was localized in the precentral gyrus and was thought to function solely to initiate and guide willed movements through its control of the corticospinal tract.

Within the last decade, advances in computer technology and in the use of microelectrodes have permitted investigators to examine the neuroelectric concomitants of specific motor acts and of sensory phenomena in unanesthetized preparations. Electrophysiological data have indicated that there is extensive integration of sensory and motor function within cortical and subcortical areas. It has been demonstrated that the precentral gyrus receives auditory, tactile and kinesthetic information (Brooks and Stoney, 1971) while the postcentral region and many subcortical nuclei display phasic changes in activity which

consistently antecede the occurrence of a voluntary movement (Evarts, 1973).

These findings have led several physiologists (Asanuma and Rosen, 1972 b; Evarts, 1973; Goldring, Aras and Weber, 1970; and Towe, 1973) to question the classical definition of motor cortex. It has been suggested that the cortex may only serve as a sensory integrator to add speed to "extra-pyramidal" motor control. At the present time our concepts of cortical motor function are perhaps less well defined than at any previous time in the history of this work. This is partially due to the introduction of electrophysiological data but also reflects a modern assault on the long-standing and often over-simple notions of "cortical supremacy".

The difficulty of resolving these issues has been underscored by the recent lesion studies which have indicated that in higher primates, portions of the cortex are differentially involved in the control of specific types of movements. Although an extensive repertoire of movements remains following cortical insult or ablation, fine control of the distal musculature is uniquely dependent on the integrity of precentral gyrus (Denny-Brown, 1966). Movements of the hands and fingers apparently constitute a functionally important portion of the motor behavior of both man and monkey and the fine control of these movements has evolved in concert with the expansion of cortex in these species. An eval-

uation of the cortical motor potentials associated with hand movements in the monkey may be especially valuable for an understanding of cortical motor function in man. This data must however be integrated with the findings of previous studies which have utilized stimulation, sensory evoked potentials and single unit recordings to examine cortical motor function.

A. Organization of Motor Cortex, as Defined by Electrical Stimulation

Electrical stimulation of the exposed surface of the cerebral cortex has provided an effective method for studying the efferent organization of the cerebral cortex. Localized movements were first elicited utilizing this means by Fritsch and Hitzig in 1870. Extension and elaboration of these studies in experimental animals (Ferrier, 1874; Franz, 1915; Horsley, 1886; and Sherrington, 1893) and in man (Forster, 1936; Penfield and Boldrey, 1937; and Penfield and Jasper, 1954) have resulted in the identification of motor cortex as a restricted region from which movements were elicited by relatively low levels of electrical stimulation, and have demonstrated somatotopic efferent representation within these cortical motor areas. The evoked movements were generally limited to contralateral muscles and ranged in magnitude from the displacement of a single digit to the massive contraction of many muscles.

Woolsey and his co-workers have painstakingly examined the

various movements which could be elicited by discrete cortical stimulation in a variety of mammals (Woolsey, 1958). They reported that the most distal portion of the limbs were represented posteriorly within the motor cortex, while the proximal and axial musculature were situated more anteriorly within this zone. In addition, in primates, the leg areas are located medially, the face area laterally and the arm area is found to lie between them substantially overlapping both (Woolsey, Settlage, Meyer, Spencer, Pinto-Hamuy, and Travis, 1951). The relative size of the cortical representation of a body part is roughly proportional to the dexterity of that portion of the body (von Bonin, 1960; Welker and Seidenstein, 1959).

In primates, the electrically excitable motor cortex is generally believed to occupy the precentral gyrus and anterior bank of the central sulcus. It is evident however that the application of high intensities of stimulation elicit discrete movements when applied to tissue anterior to the precentral gyrus (Penfield and Welch, 1951; Woolsey et al., 1951) or to the postcentral gyrus and even more caudal parietal areas (Kennard and McCulloch, 1943; Vogt and Vogt, 1919; Woolsey, 1958). Stimulation at these sites results in overt movements even following ablation of the precentral gyrus.It is therefore apparent that there is motor representation in areas traditionally labeled sensory or association cortex. Woolsey, in his more recent

work, stated the complementary position that abundant afferents are projected to the classically defined motor areas of cortex and has suggested that these regions should more properly be referred to as motor sensory zones (Woolsey, 1965).

Investigators have emphasized the lability of movements and thresholds obtained by means of cortical stimulation (Franz, 1915; von Bonin, 1960). Phillips and colleagues (Landgren, Phillips and Porter, 1962; Phillips, 1956) have dealt with this problem by utilizing a response restricted to a single muscle and by simultaneously monitoring the activity of spinal motor neurons. Based primarily on the variability of the evoked movements, Phillips held the position that there was no fine grained anatomical mosaic at the head of the corticospinal outflow (Phillips, 1966).

Stimulation of the surface of the cerebral cortex has been termed a "blunderbuss" method (Liddell, 1953) because selective activation of functionally meaningful groups of neurons is not possible. It has been demonstrated that surface stimulation, at intensities sufficient to elicit movement, influences cortical cells up to 7 mm from the site of excitation (Horn, Phillips and Porter, 1962) and that such stimuli undoubtedly result in the co-activation of alpha and gamma motor neurons (Vedel and Mouillac-Boudevin, 1970). The variability of movements which has been reported in the cortical stimulation literature may therefore

be due to spread of current resulting in diffuse physiological effects.

The recent development of microelectrode technique for intracortical stimulation has led investigators to stimulate a limited number of corticofugal neurons in the depths of the cortical motor areas of unanesthetized animals. The threshold for evoking a contraction of the contralateral distal arm musculature is in the order of 100 times lower in the depths of the cortex than on the surface. Contractions can be produced with stimulating currents of 1.5 - 3 μa, which has been calculated to excite as few as three to eight cortical neurons (Porter, 1972).

Microstimulation at various depths within the hand area of the precentral gyrus in monkeys elicits a series of different movements, i.e., flexion, extension, abduction, adduction of a single digit, especially the thumb (Asanuma and Rosen, 1972a). Histological reconstruction of the sites of stimulation reveals that neurons are oriented radially according to function forming a columnar organization in gray matter. The average diameter of an efferent column is about one mm and there is frequently spatial overlap betwen columns which produce opposite movements (Asanuma and Rosen, 1972a). Within an efferent column, the stimulus intensity required to elicit a movement is lowest in the fifth lamina.

The functional differentiation of efferent zones was found

to be more complex in the cortical motor areas of the monkey than in comparable areas of the cat. Although it had previously been demonstrated that the cat, like the monkey, has efferent columns (Asanuma and Sakata, 1967), the number of zones and the specificity of the movements that they elicited were more limited in the cat relative to the monkey. In addition, intensity required to elicit movements was considerably higher and there was less overlap of efferent zones in feline cortical motor areas (Asanuma and Rosen, 1972a).

The effects of intracortical stimulation are thought to be the result of pyramidal tract discharges on spinal alpha motor neurons (Asanuma and Sakata, 1967). Asanuma, Stoney and Abzug (1968) reported that a group of spinal interneurons located in the ventrolateral portion of the dorsal horn in the cat mediates the transmission of corticospinal outflow to the motor neurons following cortical microstimulation. In primates, pyramidal fibers project monosynaptically and polysynaptically to hindlimb and forelimb spinal units (Phillips, 1969) and thus, cortical stimulation exerts an influence on alpha motor neurons both directly and indirectly. It is unlikely that the activation of these pathways by direct electrical stimulation yields direct information regarding their normal involvement in the control of self-initiated movements.

B. Afferent Projections to Motor Cortex

A great deal has been learned regarding the nature and organization of peripheral inputs to motor sensory cortex since the early work of Adrian and Moruzzi (1939) which demonstrated short latency activation of pyramidal tract neurons by peripheral stimulation. It is now established that the precentral cortex of the monkey receives a wide variety of sensory input (Albe-Fessard, Derome and Gallouin, 1969; Fetz and Baker, 1969) and that many of these afferents are independent of the somatosensory cortical areas (Gardner and Morin, 1953; Rosen and Asanuma, 1972).

Brooks, Rudomin and Slayman (1961a, b) examined 500 single units in the motor cortex of paralyzed cats and found that 60% were activated by superficial receptors while 30% responded to stimulation of deep receptors and 10% were unresponsive to peripheral stimulation. In primates, the motor cortex was found to be less sensitive to tactile stimulation which influenced only 45% of the precentral cells examined (Rosen and Asanuma, 1972). The cells which could be driven by peripheral input in the monkey displayed small and fixed receptor fields and none showed the wide and labile fields which sometimes characterize cat units. Asanuma and Rosen (1972a) recorded cortical potentials evoked by stimulation of the superficial radial nerve and found that their precentral distribution was maximal overlying the hand and wrist

areas. The latency of the responses was equal on either side of the central sulcus.

A cortical projection of group Ia afferents from muscle spindles was demonstrated in the cat through the recording of a short latency evoked potential in Brodmann's area 3a and 4y following weak stimulation of forelimb muscle nerves or short pulls on the tendons of forelimb muscles (Oscarsson and Rosen, 1963). Group Ia afferents are shown to be responsible for these potentials by the close correspondence between the amplitude of the cortical response and the amplitude of the Ia volley recorded from the dorsal funiculus. Procedures which depress muscle spindle activity also reduce the recorded cortical evoked potentials (Oscarsson and Rosen, 1966).

Fast conducting muscle spindle afferents have also been reported to reach the primate motor sensory cortex. Lamarre and Liebeskind (1965) reported cortical evoked potentials in both precentral and postcentral cortex following hindlimb stimulation of monkeys at strengths which were sub-threshold for eliciting activity in group II fibers of the peripheral nerve. The latency of the precentral evoked response was 1.0 msec longer than that recorded in the postcentral area. Recent studies (Phillips, Powell and Wiesendanger, 1970; Rosen and Asanuma, 1972) have confirmed the projection of Ia afferents to motor sensory cortex but have demonstrated that these

afferents are confined to Brodmann's area 3a which is adjacent to, but separate from, the low threshold precentral efferent zones.

Flexor reflex afferents have been defined as myelinated fibers which are capable of evoking a flexion reflex in the spinal preparation, and include high threshold cutaneous afferents, groups II and III muscle afferents and high threshold joint afferents (Wall, 1970).

Flexor reflex afferents constitute a major source of input to cerebral motor centers, particularly the cerebellum (Oscarsson, 1967; 1971) and the motor areas of cortex (Grampp and Oscarsson, 1968; Oscarsson, 1971). Asanuma and Rosen (1972a) recorded precentral evoked potentials resulting from group II muscle afferent volleys (stimulation of deep radial nerve). The distribution of evoked potentials was similar to those found for cutaneous afferents and the latency of the response was shorter in the depths of the central sulcus than in either bank.

Albe-Fessard and Liebeskind (1966) examined 137 pre-Rolandic cells which responded to natural peripheral stimulation in monkeys under chloralose anesthesia. Approximately 65% of the cells were driven by various movements of the limbs while slightly more than 15% were responsive to deep pressure and 11% were activated by tapping. The type of receptor which was responsible for this input to motor cortex was determined by dissection of the skin and muscle. The vast majority of the units were driven

by receptors located in the muscles themselves.

Classically defined areas of motor cortex receive auditory and visual as well as cutaneous and proprioceptive information in a variety of species when tested under chloralose anesthesia. In the cat, pericruciate units respond to visual and auditory stimuli (Buser and Imbert, 1961; Teyler, Shaw and Thompson, 1972). However, in the squirrel monkey, precentral cells respond to auditory signals but not to visual stimuli (Goldring, Aras, Weber, 1970). Goldring used transcortical recordings (Goldring et al., 1970) and microelectrode analysis (Goldring and Ratcheson, 1972) to assess sensory input to the hand area of motor cortex in human subjects. He reported that in man the motor cortex did not respond to auditory clicks or ipsilateral somatosensory stimulation, both of which were adequate stimuli for the motor cortex of cats and squirrel monkeys. Goldring concluded that "in man the function of processing diverse sensory input from the periphery, a function characterizing the motor cortex of cats and to a lesser extent that of the macaque, has been relegated elsewhere" (Goldring and Ratcheson, 1972).

The vast majority of studies concerning motor cortex afferents have been undertaken utilizing anesthetized, immobilized or at least restrained preparations. In a recent review, Brooks and Stoney (1971) warned against overemphasizing input characteristics of motor cortical neurons that were obtained

under such static conditions. It is likely that the afferent receptor fields undergo changes in size and excitability as a function of limb position and motor outflow. Collaterals of pyramidal tract fibers project back onto cortex and have been found to influence the ventral lateral nucleus, the dorsal column nuclei and other subcortical centers involved in relaying sensory information to the cortex (Marchiafava, 1968). Due to the activity of these collaterals the sensory information which reaches the level of the motor cortex may be very different during the performance of a movement than that which is discerned in static testing procedures. Coquery (1971) has reported in fact that somesthetic evoked potentials are increased for the 200 msec preceding a movement and decreased during and following the contraction in humans.

C. Intracortical Afferent - Efferent Interactions

Several investigators (Asanuma and Rosen, 1972b; Asanuma, Stoney and Abzug, 1968; Sakata and Miyamoto, 1968; Stoney, Thompson and Asanuma, 1968) have examined the input - output relations of the cortical motor areas by using a single microelectrode to first record sensory unit activity and then to evoke a movement at that cortical site. It has been shown, in unanesthetized cats, that most single neurons receive simple inputs but that each efferent colony receives convergent afferents from various peripheral receptors. A colony of cells in the motor

cortex receives cutaneous and group II and III muscle afferents from the same area of a limb to which it projects its motor outflow. In over 90% of the cases, stimulation at a site where cells are uniquely activated by passive movement of a joint results in a motor effect which involves that particular joint (Asanuma et al., 1968). As previously stated group I afferents do not directly influence cortical efferent zones from which movements can be elicited with low threshold stimulation.

Close input - output coupling, where the peripheral receptor field and the area of motor response overlap, have also been reported for the primate motor cortex (Rosen and Asanuma, 1972). The authors elaborated their previous findings in the cat by demonstrating that in the monkey the skin regions that project to an efferent colony lie in the direction of movement which results from the excitation of that colony. Thus, efferent zones causing dorsiflexion have their tactile receptor fields in the dorsal surface of the hand. It is unlikely that these afferents directly initiate movement since they terminate almost exclusively on superficial cortical layers which display relatively high thresholds for movements. Asanuma and Rosen (1972b) examined the intracortical dynamics of afferent - efferent coupling by placing separate recording and stimulating electrodes in the same efferent column. They reported that activation of cortical cells in layers II and III resulted in polysynaptic EPSPs in the cortico-fugal neurons located in the fifth lamina of the same column.

This arrangement provides positive feedback from peripheral afferents to the efferent zones of the motor cortex during the performance of a movement (Asanuma and Rosen, 1972b). A similar positive feedback organization for joint and muscle afferents allows the efferent colonies to monitor joint displacement and changes in the length and tension of muscles which develop as a result of the motor outflow.

The basic findings reported by Asanuma and his colleagues have recently been questioned by Doetsch and Gardner (1972). They observed that in both precentral and postcentral cortex there was loose input - output coupling with little overlap between peripheral receptor fields for an efferent zone and the movements produced by stimulation of that colony. These discrepant findings may reflect differences in experimental procedures. Doetsch and Gardner used much higher stimulus intensities (averaging 1.4 ma) and anesthetized rather than tranquilized preparations.

Intracortical stimulation and sensory evoked potential studies have provided important contributions to an outline of the functional organization of the cortical motor areas. These studies have however examined the motor system in acute, non-moving preparations and have consequently provided no information as to the timing and pattern of activity which accompanies voluntary movements. This information must be empirically

obtained in situations where subjects are free to initiate and guide their own efferent outflow.

D. Cortical Unit Activity Associated with Voluntary Movements

Neurophysiologists have long recognized the necessity of examining the electrophysiological correlates of movement but have lacked the ability to record from unanesthetized preparations and to stabilize the electrodes during movements to avoid artifacts. These difficulties were overcome with the development of a miniaturized microelectrode system which could be directly mounted on a monkey's skull and with the widespread use of surgically introduced skull bolts to maintain a fixed head position in behaving animals (Evarts, 1974).

Evarts (1965; 1966; 1968; 1969; 1972; 1973; and 1974) utilized these technological advances to explore the relationship between cortical cellular activity and the various aspects of operantly conditioned movements in monkeys. He reported that contralateral arm movements were preceded by changes in the discharge rate of pyramidal tract neurons in the precentral gyrus (Evarts, 1966). Individual cells were found to either increase or decrease their activity but neurons having the highest conduction velocities tended to display phasic increases in discharge frequency occurring between 70 and 100 msec prior to the EMG monitored contraction. The responding units were identified as pyramidal on the basis of their short latency

antidromic response to medullary pyramidal tract stimulation. In a reaction time task there was a positive correlation between the frequency of unit activity and the speed of muscular contraction. Although most of the precentral units were exclusively associated with contralateral movements, a number of ipsilateral motor cells were also identified.

Evarts contrasted the activity of pre- and post-central neurons during the performance of repetitive wrist extensions (Evarts, 1972; 1974). He reported that discharges of precentral cells preceded those of the postcentral gyrus by an average of 60 - 80 msec. Most postcentral units were activated only during and following the movements and the phasic discharge of these cells was almost entirely confined to within 100 msec of the onset of contraction. In each study a small portion of the postcentral cells responded prior to the EMG. Evarts' findings have been confirmed in studies which have indicated that both pyramidal and non-pyramidal neurons on either side of the central sulcus vary their discharge rate as a function of the initiation and control of movements (Fetz, 1969; Fetz and Finocchio, 1971; Luschei, Johnson and Glickstein, 1968; Porter, Lewis and Horne, 1971).

A major advance in our understanding of the relationship between cortical unit activity and motor performance was achieved through experiments in which Evarts was able to associate the

same wrist displacement with a number of different force conditions by adding loads to the response lever. The majority of pyramidal neurons investigated were primarily related to the force and change of force with time of the movement and only minimally related to the position of the limb (Evarts, 1968). This conclusion was strengthened by the subsequent demonstration that many cortical units responded during the maintenance of a fixed wrist position against a changing force (Evarts, 1969). Luschei, Garthwaite and Armstrong (1971) were not able to confirm these observations, on the basis of recordings from the cortical face area of conscious monkeys performing conditioned jaw movements. Although the authors were able to identify precentral units which responded approximately 50 msec prior to the motor response they reported no clear relationship between the cellular firing pattern and the force of the jaw movements.

Fetz and Finocchio (1971) used differential reinforcement to demonstrate that the activity of precentral neurons could readily be dissociated from the motor response to which it was originally related. Bursts of cortical unit activity could be conditioned in less than 50 trials to occur in the absence of any overt muscle contraction. Conversely the animal could be trained to perform the specific movement without displaying activity in the sampled cortical cells. These findings indicate that considerable flexibility exists in the coupling of cortical

unit discharge to the consequent motor performance.

Units in the dorsolateral prefrontal cortex have also been examined in relation to volitional movements in the monkey (Kubota and Niki, 1971). Several neurons bordering the principal sulcus were reported to increase their spike activity 200 - 300 msec prior to a reaching movement and to maintain their firing level during the motor performance. Some units in this study were reported to alter their discharge frequency as early as 600 msec before the contraction. Responding units were located in both hemispheres even though the movements were limited to a single limb.

Although the analysis of cortical unit activity associated with voluntary movements is still in its infancy, several new techniques for data accumulation and interpretation have been proposed. Humphrey, Schmidt and Thompson (1970) have advocated the simultaneous recording of activity from a set of cortical neurons during conditioned muscular contractions. They report that the position, velocity, force and change of force of a contracting muscle can be more accurately predicted on the basis of information obtained from groups of cells (3 - 8) than from the more commonly utilized single cell samples. Their data was particularly accurate for force but less reliable for displacement and velocity measurements. Porter and Muir (1971) and Porter (1972) have emphasized the analysis of the temporal pattern

of impulses within the naturally occurring burst of cortical unit activity associated with a voluntary movement. They report that sequences which contain increasing intervals between spikes are highly correlated with powerful excitation of motor neurons and feel that the interval ordering may serve as a precentral code for the timing and force of a muscular contraction.

Single unit electrophysiological studies share several limitations inherent in the microelectrode technique. Among these are the small sample size, sampling bias with the larger units being more likely isolated for recording and the impossibility of obtaining the same population of cells for repeated observations in different animals or on different occasions.

E. Cortical Motor Potentials

Within five years of the work of Fritsch and Hitzig, Caton (1875) had reported that changes in EEG were related to the voluntary movements of experimental animals. In humans, Jasper and Penfield (1949) found that the rolandic EEG rhythms could be suppressed by hand movements. Bates (1951) superimposed EEG tracings in relation to the onset of EMG and detected a cortical potential beginning between 20 and 40 msec after the onset of movement but failed to find any activity which anteceded the contraction. The early experiments were severely limited by the necessity of examining raw EEG.

The advent of computer averaging and of prestimulus data storage enabled investigators to detect small but consistent changes in brain activity which were associated with voluntary movements.

Phasic neurogenic potentials which preceded the motor response in a simple reaction time task by an interval appropriate for the corticospinal transmission time to the muscle, were detected overlying the central region of the brain by Vaughan, Costa and Gilden (1965) using averaging combined with the subtraction of the sensory evoked response. Scalp recorded potentials associated with self-paced voluntary movements (MP) were identified by Gilden et al. (1966) and by Kornhuber and Deecke (1965) by averaging with respect to the onset of movement. According to Vaughan, Costa and Ritter (1968) the MP waveform consisted of three major components: a slow negative shift beginning 0.5 - 2.0 seconds before contraction, N1 (the readiness potential of Kornhuber and Deecke); an abrupt negativity, N2, beginning between 50 and 100 msec prior to movement and which is occasionally preceded by a small positive wavelet, P1; and a complex late positive wave which outlasts the contraction, P2.

An analysis of the distributions of the scalp MPs (Vaughan et al., 1968) demonstrated that all components were maximal overlying the contralateral rolandic cortex and that they displayed a somatotopic distribution for foot, hand and face

movements consistent with the data on motor cortex representation derived by electrical stimulation. Deecke, Scheid and Kornhuber (1969) failed to confirm the distribution reported by Vaughan and colleagues and reported that only the phasic negativity was differentially largest over the contralateral precentral cortex and concluding that it alone should be considered a "motor potential".

These conclusions were modified on the basis of subsequent topographical studies (Deecke et al.,1973) which utilized more accurate triggering procedures and a larger number of trials and determined that both the readiness potential and the N2 component were largest overlying the contralateral precentral cortex. In the later study, the author stresses the importance of the small positivity preceding the N2 component which is termed the premotion positivity (PMP). The PMP was postulated to represent the expression of the initiation of movement and was reported bilaterally distributed over the parietal cortex.

A recent study of the scalp MP in man (Gerbrandt, Goff and Smith, 1973) reported that the phasic negativity began after the onset of movement. The authors suggest that the N2 component may have a sensory origin and could reflect the polarity inversion of positive activity generated in the postcentral gyrus. On the basis of their observed timing and distribution of cortical activity they state that there is no evidence that any of the cortical "motor potentials" are generated by neurons

concerned with efferent processes.

Few studies have attempted to record gross cortical motor potentials in behaving infrahuman primates. Vaughan, Gross and Bossom (1970) reported a similar configuration of the cortical response associated with a wrist extension in both man and monkey. They sought to define the extent to which somesthetic feedback contributed to the waveform of the cortical motor potential by recording the cortical responses in operantly conditioned deafferented monkeys. The general morphology of the MP was not altered by deafferentation suggesting that kinesthetic feedback may not ordinarily reach the precentral cortex during the performance of well trained repetitive movements. The authors did not map the cortex however and were thus unable to determine the effect of feedback on the surrounding cortical areas. Although the waveshape of the cortical activity remained constant, deafferentation introduced a longer delay between the onset of brain and muscle activity. This finding has been confirmed using the functional deafferentation of hand digits with anesthetic agents (Lewis, Porter and Horne,1971).

Two recent publications have been concerned with slow cortical potentials associated with voluntary movements. Rebert (1972) reported that "contingent negative variation like" slow potentials could be recorded from motor and pre-motor cortical areas of monkeys trained to bar press to obtain juice. The response

was largest overlying the frontal cortex anterior to Brodmann's area 4. Donchin, Otto, Gerbrandt and Pribram (1971) investigated the interval between the warning signal and the movement in a reaction time task. They reported a prominent positive - negative - positive wave which was associated with key pressing and which was maximal in the postcentral cortex of the monkey.

F. Objectives of the Present Study

Although it has been repeatedly demonstrated that the neuroelectric activity of portions of the cerebral cortex is associated with voluntary movements in both man and macaque, only a glimpse of the complex cortical activity involved in the initiation and control of even the simplest movement has so far been provided. The studies of the MP undertaken to date have resulted in unresolved conflicts regarding the timing and distribution of the individual components and regarding which, if any, of the potentials are related to efferent discharges and which reflect afferent processing. In addition, there is almost no information as to the interaction of distinct areas of cortex in the control of discrete movements and only speculation as to the location and geometry of the generators of motor potential components.

The specific aims of the present study are:

1. To characterize the morphology and timing of the epidural motor potential in the monkey. The relationship between this

finding and those reported from the scalp of humans will be discussed and evaluated.

2. To provide isopotential maps detailing the epidural amplitude distribution of each component of the motor potential along medial - lateral and anterior - posterior dimensions.

3. To determine the source of each component of the motor potential by locating the site and depth of its transcortical polarity inversion.

4. To examine differences in the waveform and distribution of the cortical motor potential between homologous areas on ipsilateral and contralateral hemispheres.

5. To relate the distribution and sources of individual motor potential components to those of the somatosensory evoked potential and to the location of electrically excitable motor cortex defined by direct application of stimulation.

Chapter II

METHOD

A. Subjects

Four adult male macaques (M. mulatta) weighing approximately 3.0 kg at the time of their implantation were employed in the present studies. The first two subjects were utilized primarily to develop implantation and recording techniques which were fully applied in the final two preparations; monkey G and monkey R.

B. Training

Each subject was adapted to the restraining chair, during which time he was handled and fed by the experimenter. The monkeys were then trained to perform a series of self-paced extensions of the right wrist at two second intervals. The movements are termed self-paced due to the absence of any external signal prior to the initiation of the movement. The reinforcement consisted of a small piece of apple which was delivered manually by the experimenter following a variable ratio schedule which had as its mean eight "correct" movements. The timing and amplitude of contraction of several muscles were monitored by recording and displaying the EMG on a dual channel storage oscilloscope (Tektronix R564B). A movement was considered correct only if, 1) the extensor EMG amplitude fell between 100 - 150 μv, 2) the EMG burst lasted for no longer than 150 msec, and 3) the baseline EMG between movements remained

below 10 μv. After four months of conditioning, each monkey precisely executed the desired movement as indicated by the stability of the EMG pattern within and across experimental sessions (see Figure 4).

C. Electrodes

Two types of electrodes were implanted in each monkey: fixed epidural electrodes, which were positioned at surgery; and individually moveable depth electrodes, which were subsequently introduced during the recording sessions.

The epidural electrodes consisted of 20 mm lengths of 20 gauge stainless steel tubing. The tubing was insulated with Insul-x (E 33) except on the inferior surface which contacted dura. Each epidural tube served as a recording electrode as well as a guide for the insertion of intracortical depth electrodes. During implantation the epidural tubes were sealed with removable 26 gauge plugs which filled the entire length of the lumen. The plugs protected the exposed dura and prevented dried blood from filling the tubes. The resistance of the epidural electrodes was approximately 25,000 ohms.

Depth electrodes were fabricated from 0.25 mm stainless steel wire which was electrolytically sharpened and coated with Insul-x except for 0.5 mm at the tip. The resistance of the depth electrodes was slightly under 50,000 ohms.

Forearm EMG was recorded using Grass Gold Cup electrodes.

D. Implantation

The epidural implantations were performed under Nembutal anesthesia utilizing aseptic technique. The animals were positioned in a stereotaxic instrument and the skin was widely resected over the dorsal surface of the calvarium. At predetermined locations a series of small holes were drilled perpendicularly through the exposed skull without damaging the underlying dura. These holes were of such dimension that epidural electrodes could be inserted and come to rest directly on the dura due to gravity. Forty-five epidural electrodes were implanted over the fronto-parietal region in monkey G and 57 electrodes were similarly arrayed in monkey R (Figure 1). Two-thirds of the electrodes were implanted on the hemisphere contralateral to the moving arm and one-third were placed ipsilaterally.

Four stainless steel bolts, with flattened heads to fit between the skull and dura, were "keyed" into the skull and fastened in place with stainless steel nuts. A single dental screw (Dentatus RRL #18) was screwed into the bone overlying the left occipital lobe to serve as a reference. The entire array of epidural electrodes and the dental screw were embedded in a mound of self-curing dental acrylic and thus secured to the skull and skull bolts. Two Plexiglas bars were placed along the anterior and posterior margins of the acrylic and their positions were determined. Stereotaxic ear bars could be inserted into drilled holes in the Plexiglas.

Figure 1: Position of 36 epidural electrodes implanted on the hemisphere contralateral to the moving hand. Note that the markings on the dura have been transferred to the surface of the fixed cortex. The dots were added for purposes of illustration.

This permitted the monkey's head to be restrained during recording sessions and also allowed depth electrodes to be positioned accurately without the necessity of placing the monkey's head in the ear bars under general anesthesia.

E. Recording Apparatus and Procedure

1. EMG and EEG:

Each recording session lasted approximately three hours during which time the monkey's head was restrained and its trained limb was tied into a fitted and cushioned plastic splint (Figure 2). The EMG was recorded from two marked positions, 2.5 cm apart, on the surface of the extensor carpi radialis muscle of the trained forearm. On several occasions the EMG was simultaneously recorded from the untrained arm to demonstrate the absence of time-locked activity in this limb. White noise (approximately 30 db) was maintained throughout recording sessions to mask any sound which may have resulted from the movements.

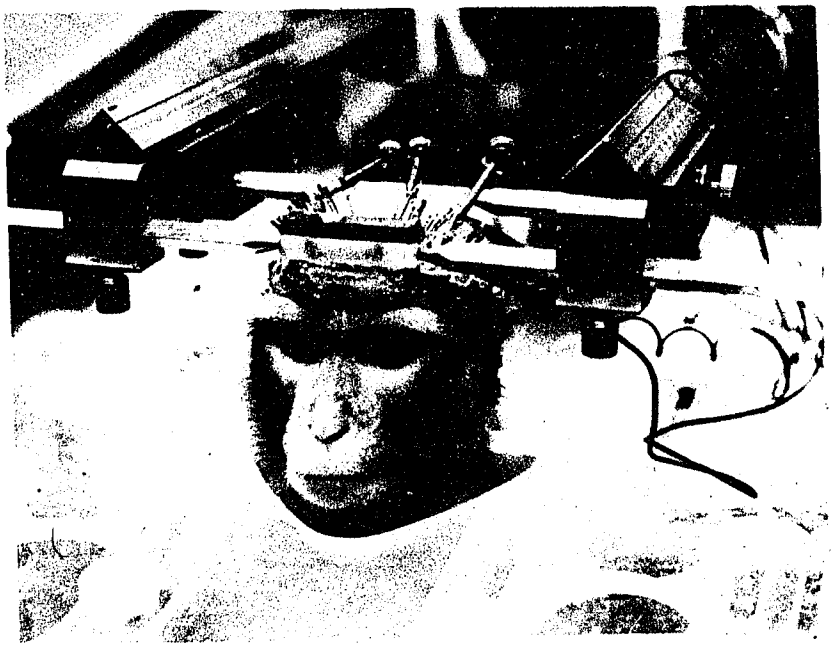
All EEG recordings were monopolar and were referenced to the occipital screw. The lack of activity of the reference site was assessed by employing it as the active lead referenced to the earlobe or to the posterior scalp. This recording configuration failed to reveal any activity which was time-locked to a voluntary movement or to forearm stimulation.

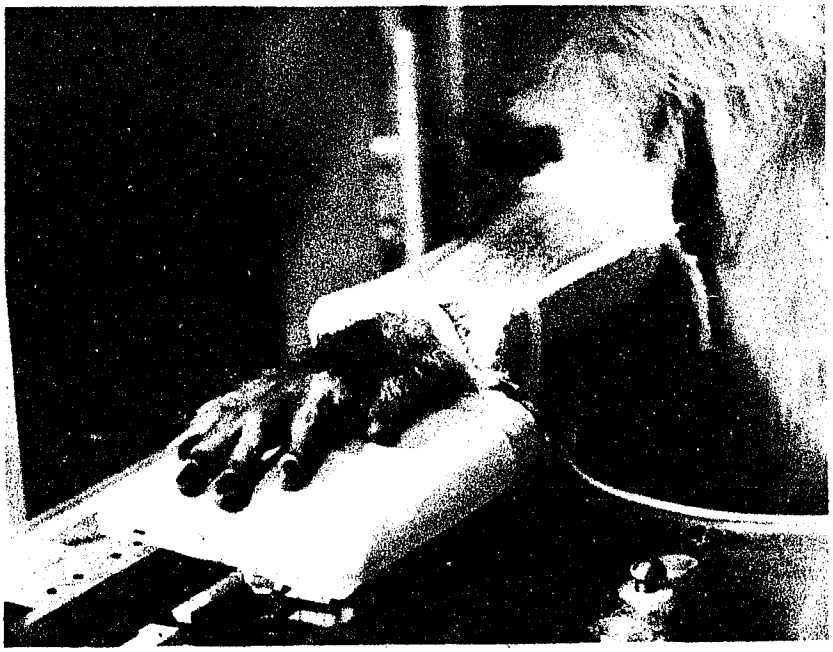
2. Recording Apparatus:

The equipment for recording and data analysis is depicted

Figure 2: Restraint of head and arm used during all recording. Animals were maintained in this apparatus for periods up to three hours. EMG electrodes are not shown on the forearm in this illustration.

R





in Figure 3. Brain potentials were amplified by four Tektronix 3A9 and two Tektronix 26A2 differential amplifiers set for a gain of 5K and a frequency response down 3 db at .1 and 300 Hz. The technical specifications of the two types of amplifiers were equivalent over the recording range. As the low frequency response is an important parameter for the recording of slow wave phenomena found in the MP, an empirical estimate of the time constant of the electrodes and amplifiers using the above setting was obtained by recording square current pulses in a saline bath. The epidural and depth electrodes in series with the amplifiers, were found to have a time constant of approximately 500 msec, which is shorter than that found for the amplifiers alone. This finding indicates that the capacitance of the stainless steel electrodes introduces a limit on the low frequency response of the system.

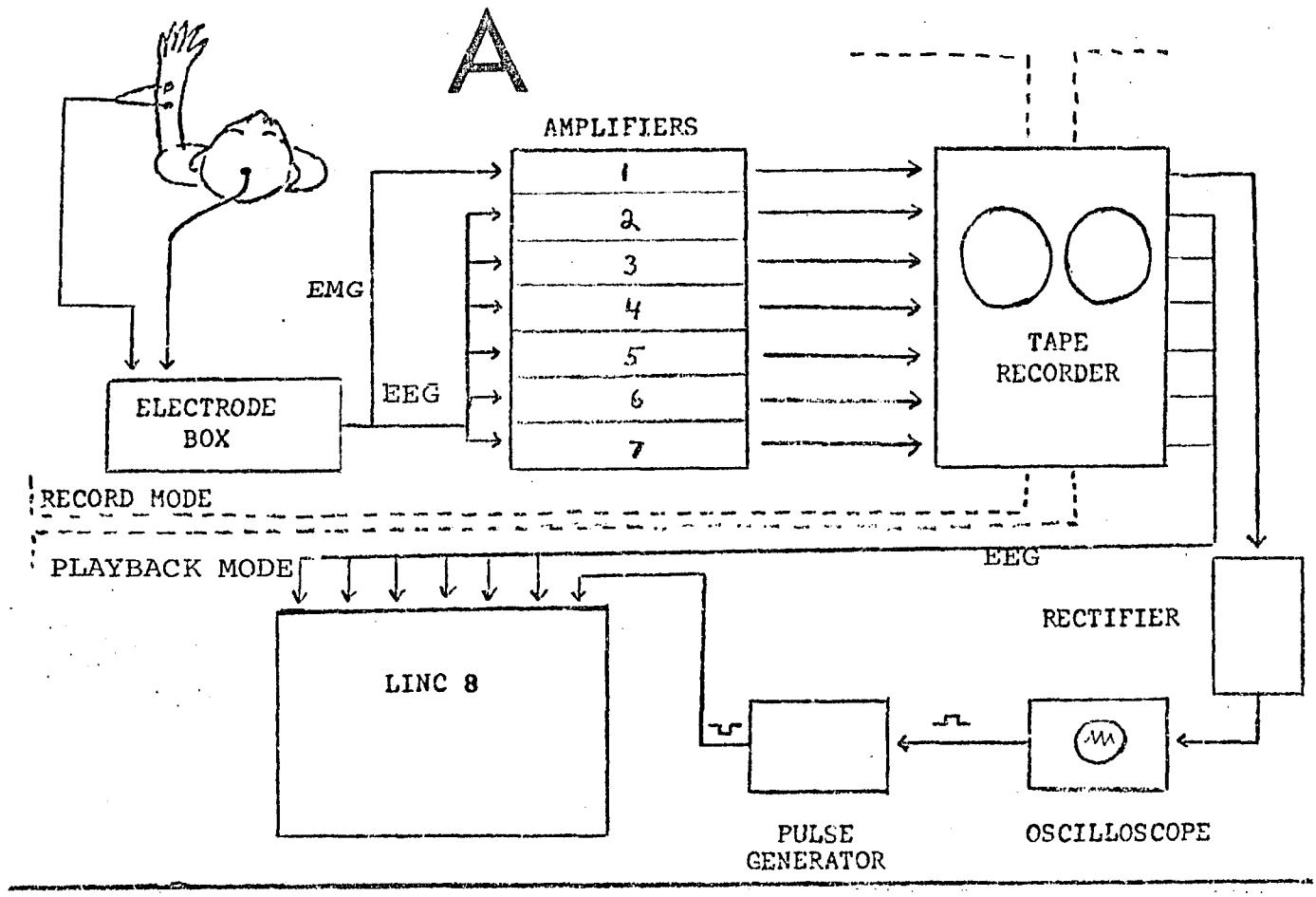
It was possible to increase the time constant using DC recordings and in each subject epidural MPs were recorded in the DC mode to better assess the true amplitude of the slow wave phenomena. This mode of recording was impractical and therefore not used due to excessive baseline drift which required frequent manual resetting of the amplifier DC level.

Muscle activity was amplified by a Tektronix 26A2 differential amplifier set for a gain of 5K and a band-pass of 10 to 10,000 Hz. EEG and EMG were continuously monitored on all channels during recording to insure their quality. The amplified data was recorded

Figure 3: Block diagram of the recording and data processing equipment.

A.) Motor potentials

B.) Somatosensory evoked potentials


A
AMPLIFIERS
1
2
3
4
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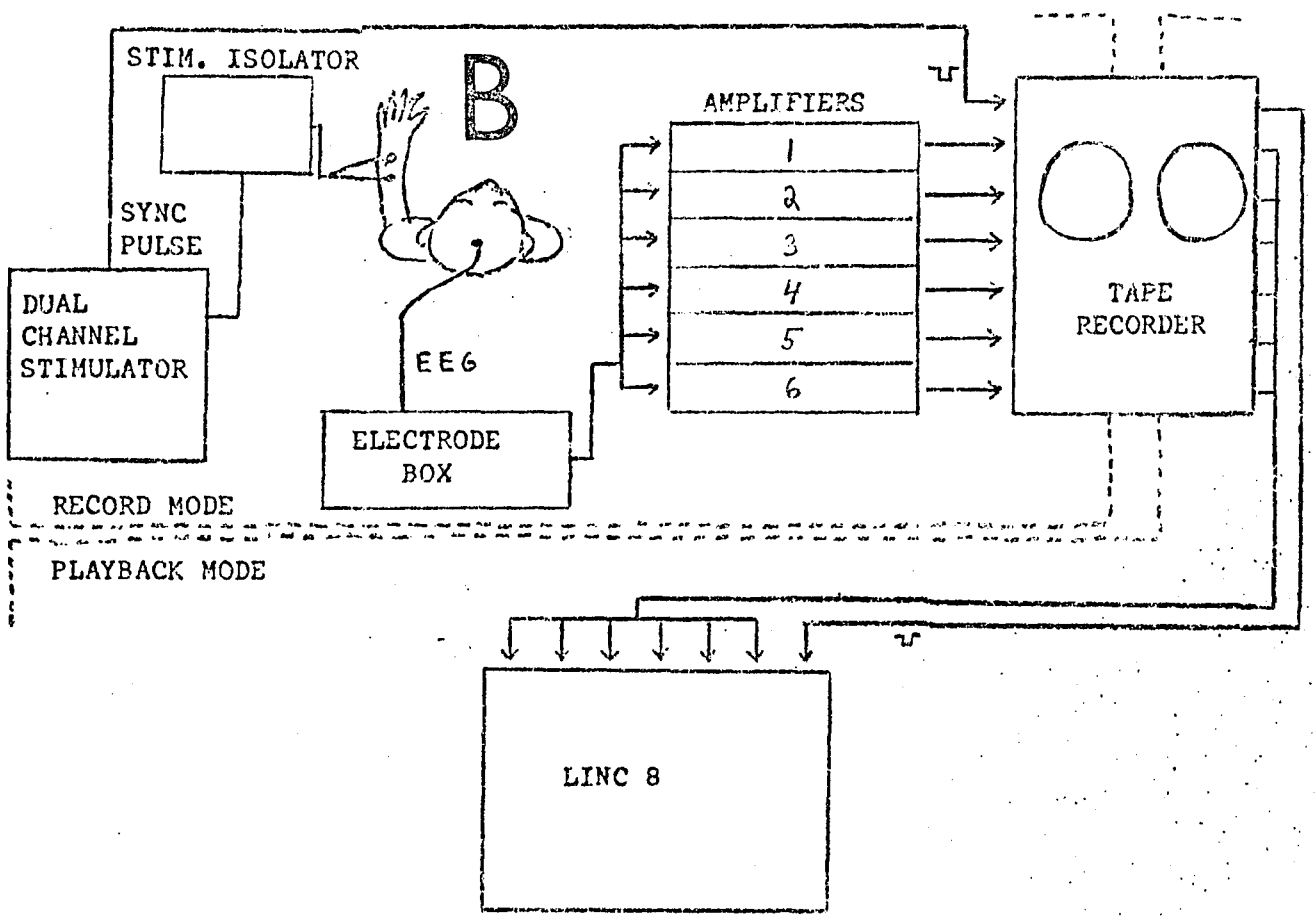
6
7
EMG
EEG
ELECTRODE BOX
TAPE RECORDER
RECORD MODE
PLAYBACK MODE
EEG
RECTIFIER
LINC 8
PULSE GENERATOR
OSCILLOSCOPE


STIM. ISOLATOR
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DUAL CHANNEL STIMULATOR
EEG
ELECTRODE BOX
TAPE RECORDER
RECORD MODE
PLAYBACK MODE
LINC 8

at 7 ips on half inch magnetic tape (Audiotape 3661R) employing a seven channel Mnemotron FM tape recorder, with a frequency response of DC to 2,500 Hz.

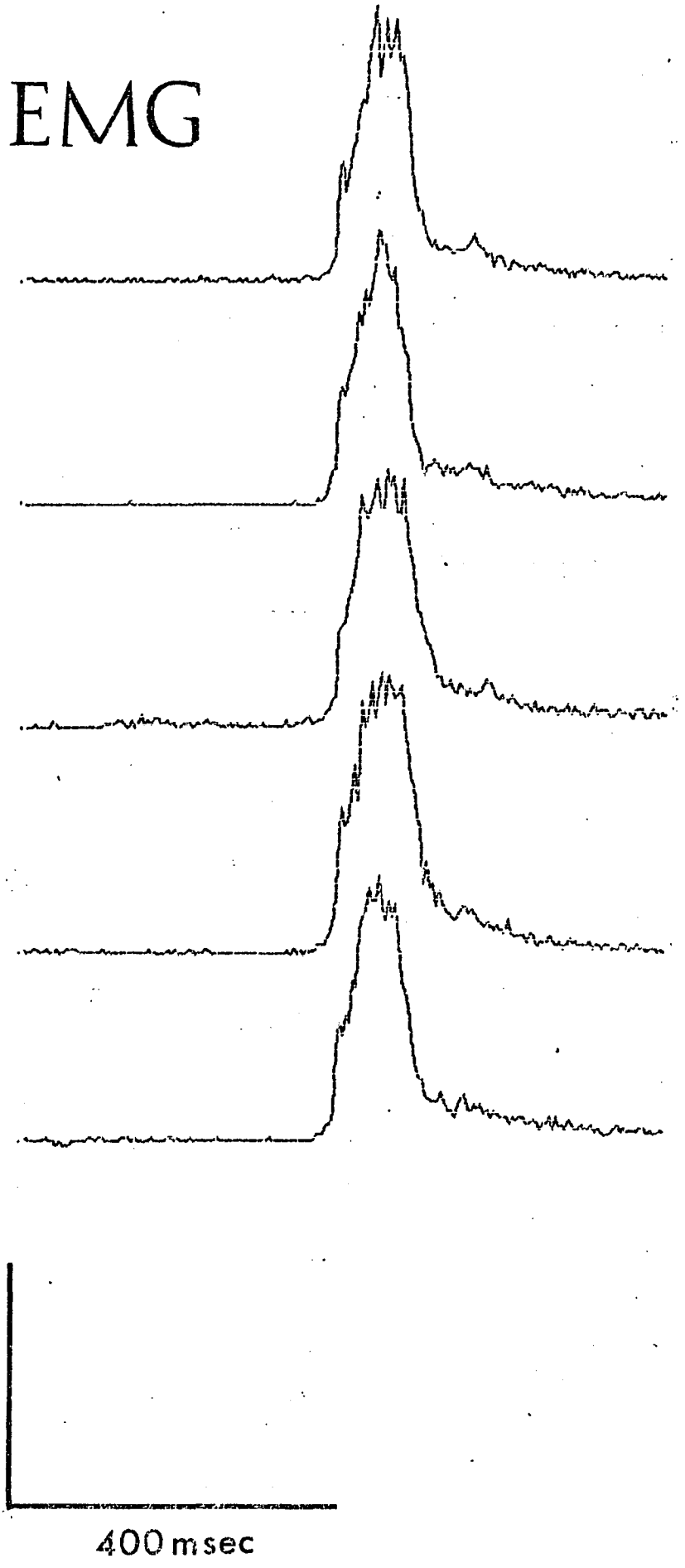
3. Averaging Procedure:

MPs were averaged using a Linc 8 computer, which could be employed on-line when desired. The onset of each EMG burst triggered an oscilloscope and the gate out of the scope in turn triggered a pulse generator (Tektronix 161) which provided a synchronization signal for averaging procedures. The triggering sensitivity of the oscilloscope was set as close to the baseline EMG as possible without resulting in false triggers due to small fluctuations in the baseline activity. The EMG bursts which triggered the computer were rectified and averaged and thus, the triggering sensitivity and consistency could be monitored by examining the rising phase of the averaged EMG. An example of the obtained consistency in EMG triggering is presented in Figure 4.

The computer was programmed to sample seven channels of analog data and to convert this information to digital form at a sampling interval of 1.0 msec. A preselected epoch of data was held in memory and continuously updated by adding new samples while discarding the earliest sample. Upon receiving the trigger pulse the stored data was held for averaging and an additional record was then stored for a specified period after the trigger. Typically the epoch included 500 msec both before and after the

Figure 4: Rectified averaged EMG recorded during five successive motor potential runs in monkey R. Note the similarity between runs in the slope of the rising phase, amplitude and duration of the responses.

R



onset of muscle contraction. Thus, each epoch contained 1,000 data points. Each epoch was added to the data obtained on previous trials and the total was divided by the number of trials to provide the averaged MP. The mean values of the waveform were stored in digitized form on magnetic tape and a computer program was used to determine the standard deviation of each point on the epoch across runs and thus the standard error of the MPs.

4. Epidural MPs:

In all cases epidural MPs were recorded prior to penetration of the dura. An individual run was comprised of either 100 or 200 wrist extension movements and the runs were repeated a sufficient number of times to record the MP from every epidural electrode on three occasions. The order of recording from epidural electrodes was randomized across runs. An epidural recording from the contralateral arm area was common to all MP runs and was used to monitor the stability of the averaged cortical activity within and across experimental sessions. This electrode will be referred to in the remainder of the text as the monitor electrode. The averaged EMG was also utilized to determine the stability of movement strength and speed. If either potential did not fall within accepted limits ($\pm$ 15%), the entire run was discarded and repeated. Using this criterion, 18 percent of the averages were discarded. An examination of the waveforms in the rejected runs showed that no consistently different pattern of activity had been removed from the data.

5. Intracortical MPs:

Following the completion of the epidural recordings, laminar studies of the MP were undertaken. Plugs were removed from a total of 22 guides which were selected on the basis of their epidural activity. The underlying dura at these sites was pierced with a sharpened probe in order to minimize depression of the cortex by the dura during penetration and advancement of the recording electrode. The depth electrodes were oriented along the angle of the guides and lowered to a depth of 5.0 mm below the dural surface using a mechanical stereotaxic microdrive. MPs were recorded at steps of 500 u or 333 u as the electrode was retracted through the cortex. All records from a given electrode pass were obtained in a single session which lasted approximately three hours. At the end of each session the electrode was repositioned at a depth of 5.0 mm and fixed in place. This electrode along with the overlying epidural guide provided a stationary transcortical electrode pair from which additional recordings could be taken.

Cortical locations at the extreme boundaries of the epidural arrays were not accessible to laminar analysis because the stereotaxic microdrive could not be properly positioned. At these sites fixed depth electrodes of a predetermined length were positioned by hand without prior intracortical recordings.

6. Somatosensory Evoked Responses (SER):

SERs were recorded from every fixed epidural and transcortical

electrode as well as from each position of the moveable depth electrodes. Recording conditions were identical to those described for MP recordings. After habituation to the experimental situation the monkeys appeared relaxed throughout the period of peripheral stimulation. The somatosensory stimuli consisted of a series of 0.5 msec, 2.0 ma constant current square pulses, at an ISI of 600 msec, delivered to the trained arm through the EMG electrodes. The intensity of stimulation was sufficient to result in a brief contraction of the extensor musculature. Pulses were isolated from ground by means of a stimulus isolation unit (Isopulsar PC-3). Evoked potentials were obtained by averaging the cortical response following either 100 or 200 stimuli using the Linc 8 computer. In one monkey, epidural and depth SERs were recorded in both the awake and anesthetized state (sodium pentobarbital, 30 mg/kg body weight) to determine which, if any, of the components were resistant to anesthesia.

F. Stimulation Procedure

After all recordings had been taken, a motor map was defined by the direct application of electrical stimulation through each of the fixed electrodes, using the occipital screw as a current return. Each stimulus consisted of a train of ten 0.5 msec square pulses with an intra-train ISI of 3.0 msec. A constant current pulse generator (Ortex 4710 Dual Channel Stimulator) was the source of stimulation which ranged from 100 ua to 5.0 ma. A mimimum delay

of one minute was employed between the presentation of each train. Cortical stimulation began at intensities which were below movement threshold and was gradually increased in strength until the first overt contraction was detected. The muscle group involved, as well as the direction of movement was determined by the observations of at least two experimenters. Stimulation studies were undertaken in both the anesthetized and unanesthetized state in one monkey.

G. Histology

At the end of each experiment the animal was painlessly sacrificed with an overdose of Nembutal and perfused with formalin. By injecting one percent methylene blue into the lumen of the epidural tubes, the locations of the electrodes were marked on the dura. The superior surface of the skull and the acrylic mound were then removed together and a dural flap was cut which encompassed the positions of all epidural electrodes (see Figure 1). The location of a given electrode was determined on the dura and the relationship of that electrode to the underlying cortical sulcal pattern was directly observed by replacing the flap. This procedure was repeated a sufficient number of times to locate each electrode on the surface of the cortex. The fixed brains were removed and blocks were taken for histological examination. The tissue was sectioned on a freezing microtome and stained with cresyl violet to permit reconstruction of the depth electrode tracks.

H. Data Analysis

Cortical MPs and SERs were examined with reference to three major questions: 1) the timing of the activity; 2) the epidural amplitude distribution of each component, and; 3) the anatomical location of the cortical sources.

1. Timing:

The timing of the MP components was determined in relation to the onset of muscle contraction defined as the rising phase of the averaged rectified EMG, while the timing of the SER components were referenced to the onset of peripheral stimulation. The peak latencies of the components were determined for each monkey and the mean latency and range of the components were computed across monkeys. This procedure provided an estimate of individual differences in timing as well as indicating the temporal pattern which is characteristic of the species.

2. Epidural Distribution:

Epidural isopotential maps were plotted for both MP and SER components in monkey R and monkey G. Components were identified by their constant latency and polarity and were measured from baseline voltage to peak voltage. The baseline was taken to be the mean value of the activity for 100 msec preceding the onset of N1. The amplitude values which were assigned to each epidural recording site represented the mean of the three runs recorded at that placement. The location of maximal amplitude for a given component was

determined and the amplitude of that component at all other recording sites was expressed as a percentage of this value. The isopotential maps consisted of a series of contour lines which depict a percentage level in the amplitude distribution of a component on one hemisphere. Since the electrodes represented discrete sampling points in a continuous field, an accurate location of the isopotential lines often required interpolation between adjacent amplitude measurements. In these cases the interpolation was not linear but was rather based on a graphic determination of the slope of amplitude decrement in both anterior-posterior and medial-lateral planes.

The isopotential maps provide information as to the epidural site of maximal activity, the extent of the distributions and the orientation of the epidural fields which can be directly compared to the human scalp distribution data. It is however, important to recognize that adjacent components temporally overlap and algebraically sum and so result in erroneous measurements of absolute amplitude and in distortions of distributions. In addition, surface maps do not provide enough information to determine the relative contribution of surface versus sulcal cortex in the generation of a particular component. For these reasons epidural amplitude distribution data was supplemented with more detailed direct intracortical recordings to define the active sources of the MP and SER components.

3. Sources:

The intracortical sources were defined by determining the location and extent of the surface cortical areas which displayed transcortical polarity inversions for a particular component. This technique is based upon the dipolar characteristics of the electrical fields which are generated by various cortical regions (e.g., somatosensory cortex, Stohr and Goldring, 1969; auditory cortex, Arezzo, Pickoff and Vaughan, 1975). Dipolar sources are characteristic of tissue in which the neurons are radially oriented, such as the pyramidal cells in the cerebral cortex. The nature of the extracellular fields established by these sources has recently been reviewed by Hubbard, Llinas and Quastel (1969). When cortical tissue is activated current flows from the sources located deep in the cortex to sinks near the cortical surface. The isopotential lines are perpendicular to the current flow and result in the differentiation of an inferior and superior field. These fields are separated by a zero potential plane that passes through the center of the dipole.

In the present study, the areas of surface cortex which displayed transcortical polarity inversions were subsequently studied by intracortical recordings. This study provided information as to the depth below the dura at which inversions of specific components occurred. Histological examination of the sectioned tissue determined the angle of the electrode pass and the thickness

of the cortex so that depth recordings could be associated with the cortical layers at which they were taken. The location of component sources within the cortex occupying the banks of the central, arcuate and intraparietal sulci was determined by examining the activity of depth electrodes which were found to pass through or near the boundaries of this tissue.

Chapter III

RESULTS

A. Motor Potentials (MP)

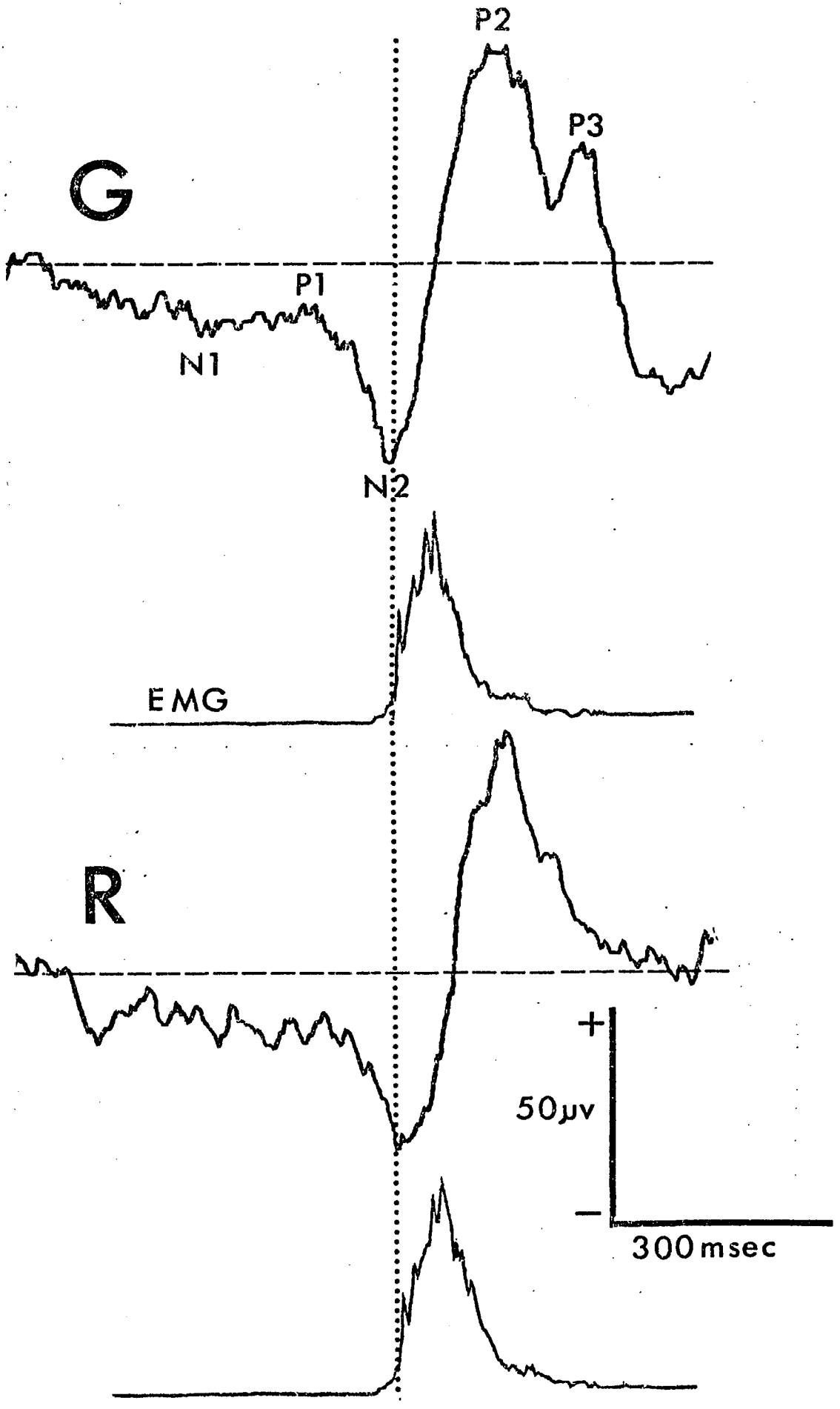
1. Epidural Morphology:

a. Contralateral Hemisphere:

Averaged epidural MPs were recorded in each subject over extensive areas of the dorso-lateral surface of the cerebral hemispheres and were largest overlying the cortex contralateral to the moving hand. Within this area, the MP waveshape was complex, comprising five identifiable components. These differed in their distributions and loci of maximum amplitude, resulting in a varied MP morphology at different recording sites. The following descriptions apply to MPs recorded from the immediate perirolandic area overlying the pre- and post-central gyri. The components are designated by their polarity and by the order of their occurrence as N1, P1, N2, P2 and P3 (Figure 5).

The first component of the MP consisted of a slow negative shift N1, which began as much as 500 to 600 msec before EMG onset. Due to the limited low frequency response of the recording system the amplitude of this slow potential shift was smaller than was seen in the limited DC recordings. A phasic negativity, N2, began at a mean of 90 msec (range 85 - 110) prior to the onset of muscle contraction and reached a peak before the maximal EMG response. In recordings overlying the contralateral

Figure 5: Epidural MPs recorded over contralateral precentral gyrus. Each potential is averaged across 200 hand movements. The rectified and averaged EMG is displayed below the individual MPs. Monkey G and monkey R.


P2
P3
G
P1
N1
N2
EMG
R
+
50μv
−
300msec

hand area of precentral cortex, N2 attained an amplitude of 33 μv in monkey G and 48 μv in monkey R. Over this region N1 and N2 were clearly differentiated, but at more peripheral locations these components could not be individually identified as there was no discrete change in the slope of the antecedent negativity. Occasionally N2 was preceded by a small positive deflection, P1, which peaked at a mean of 100 msec (range 93 - 109) before the movement. Although P1 was not detected on all runs, when it was present it occurred at a reliable latency and was therefore identified as a component of the epidural MP.

N2 was followed by a large positive wave which displayed two peaks. The first, P2, occurred at a mean of 150 msec (range 132 - 173) after the onset of muscle contraction, while the second, P3*, occurred at 265 msec (range 250 - 300) following EMG onset. P2 attained a peak amplitude of 58 μv in monkey G and 76 μv in monkey R, while P3 at its locus of maximum amplitude was 35 μv and 33 μv in monkeys G and R respectively. P3 was consistently larger, relative to the earlier components and was more clearly differentiated in monkey G than in monkey R. In monkey R, P3 often appeared only as an inflection in the falling phase of P2.

*Note that the designation of the long latency component of the MP as P3 does not imply that it is functionally related to the P3 phenomena in sensory evoked potentials.

The contralateral MP was completed by a slow return to baseline which was sometimes not reached until 600 msec following the onset of movement. In monkey G, P3 was occasionally followed by negativity and in these instances the final return to baseline had a positive slope.

b. Ipsilateral Hemisphere:

Potentials recorded ipsilateral to movement differed in waveform from those recorded from homologous contralateral sites. Antecedent potentials (N1 and N2) were present only over a small area of the precentral gyrus immediately anterior to the central sulcus. This activity consisted of a small negative wave which began approximately 100 msec prior to the movement and which had a maximal amplitude of 12 μv in monkey G (waveform A in Figure 6) and 16 μv in monkey R.

The most characteristic ipsilateral MP waveshape consisted of a broad positive component followed by a long-lasting negativity (waveform B in Figure 6). The positivity began in virtual synchrony with the onset of the averaged EMG and peaked at or within 100 msec following the maximal muscle contraction. The ipsilateral P2 component was largest overlying the central region where its amplitude was 36 and 47 percent of the homologous contralateral components in monkeys G and R respectively. Overlying Brodmann's area 5 of the postcentral gyrus, the ipsilateral MP contained a positive component which corresponded in timing to the

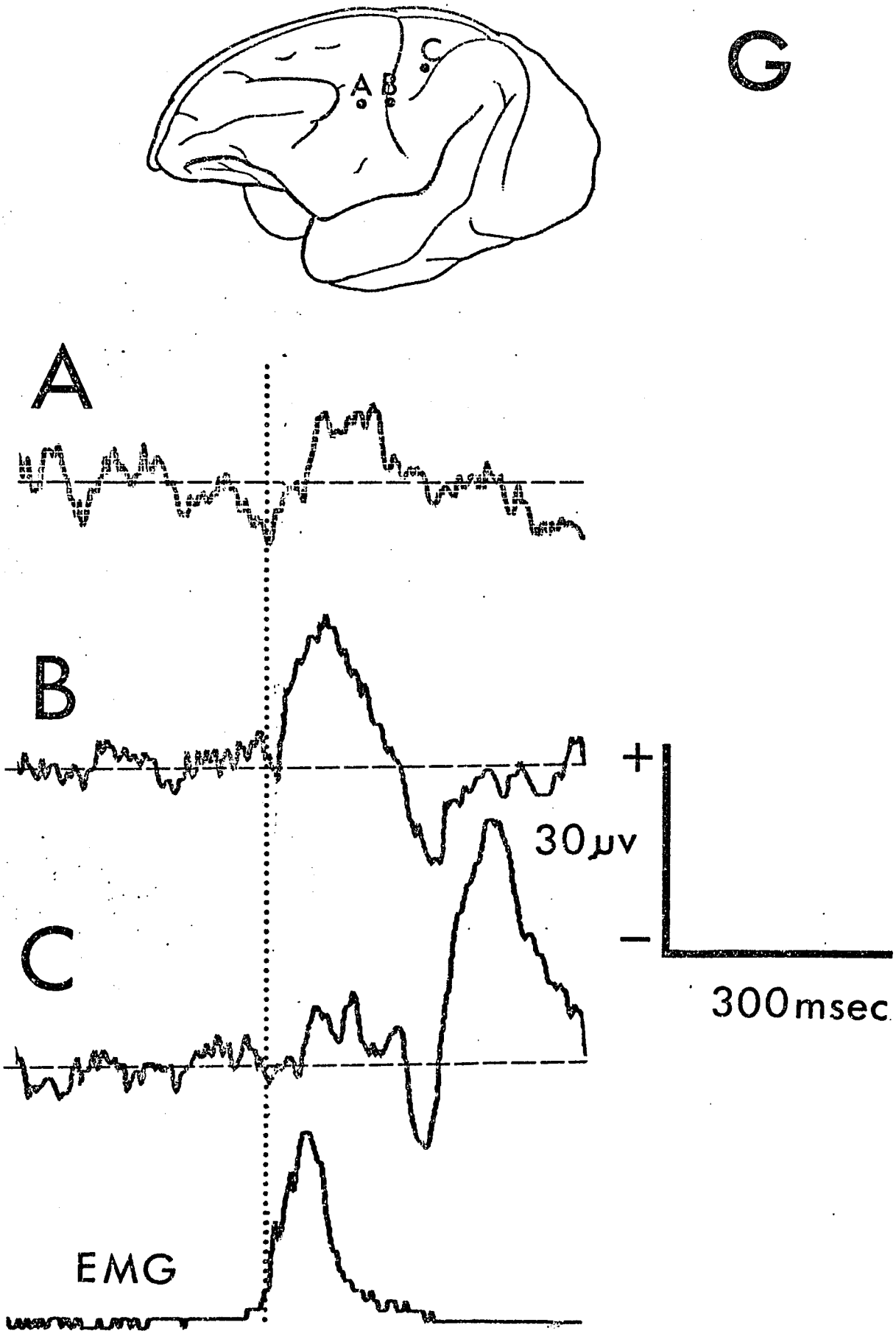
Figure 6: Ipsilateral epidural MPs recorded at three locations:

A.) Overlying the precentral gyrus

B.) Overlying the central sulcus

C.) Overlying the medial portion of the postcentral gyrus

Monkey G.


G
A
B
C
A
B
C
+
30μv
−
300msec
EMG

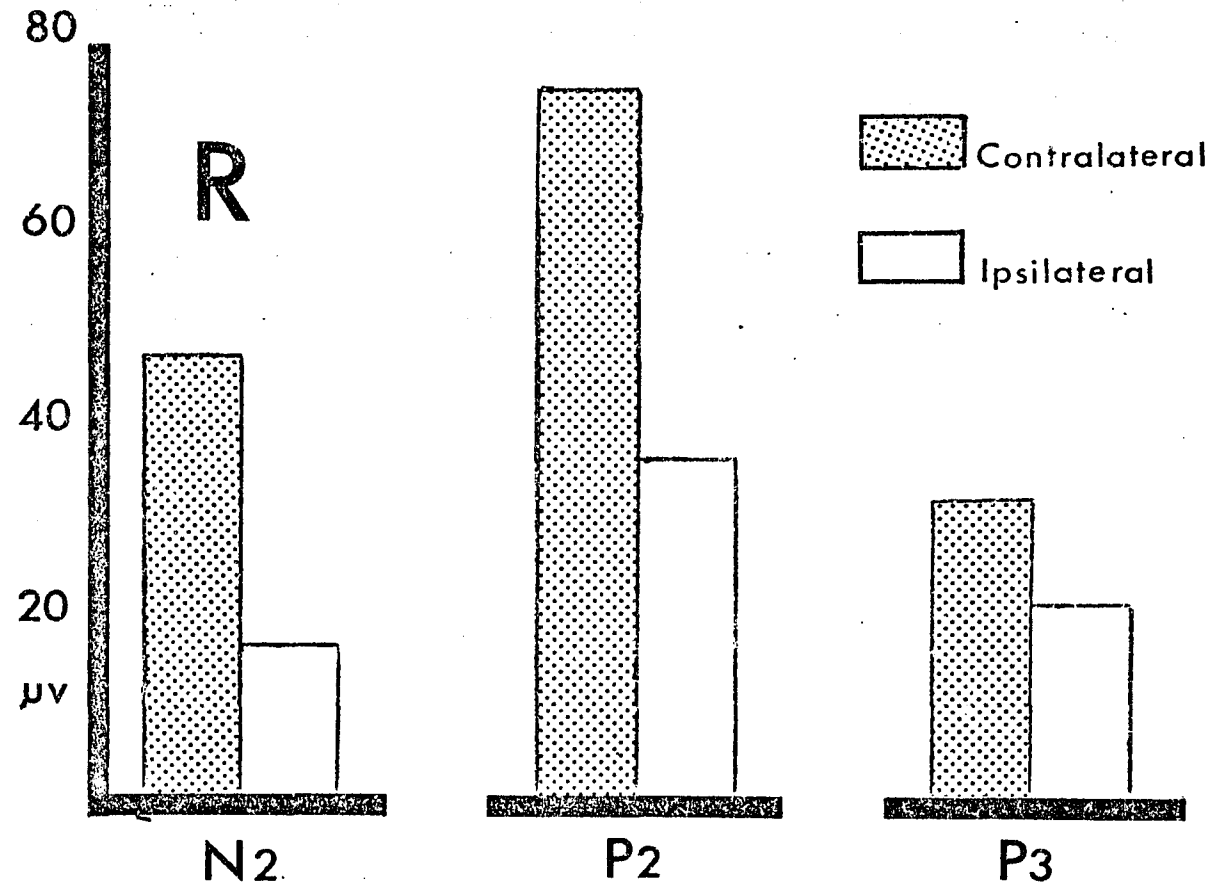
contralateral P3 activity (waveform C in Figure 6). In monkey G, P3 attained a maximum ipsilateral amplitude which was equal to that recorded overlying the contralateral hemisphere. In monkey R, however, the ipsilateral P3 was at its maximum only 70 percent of the largest contralateral P3 recording. In Figure 7, the maximum amplitude of N2, P2 and P3 contralateral to the movements are compared with the corresponding ipsilateral data in both monkeys.

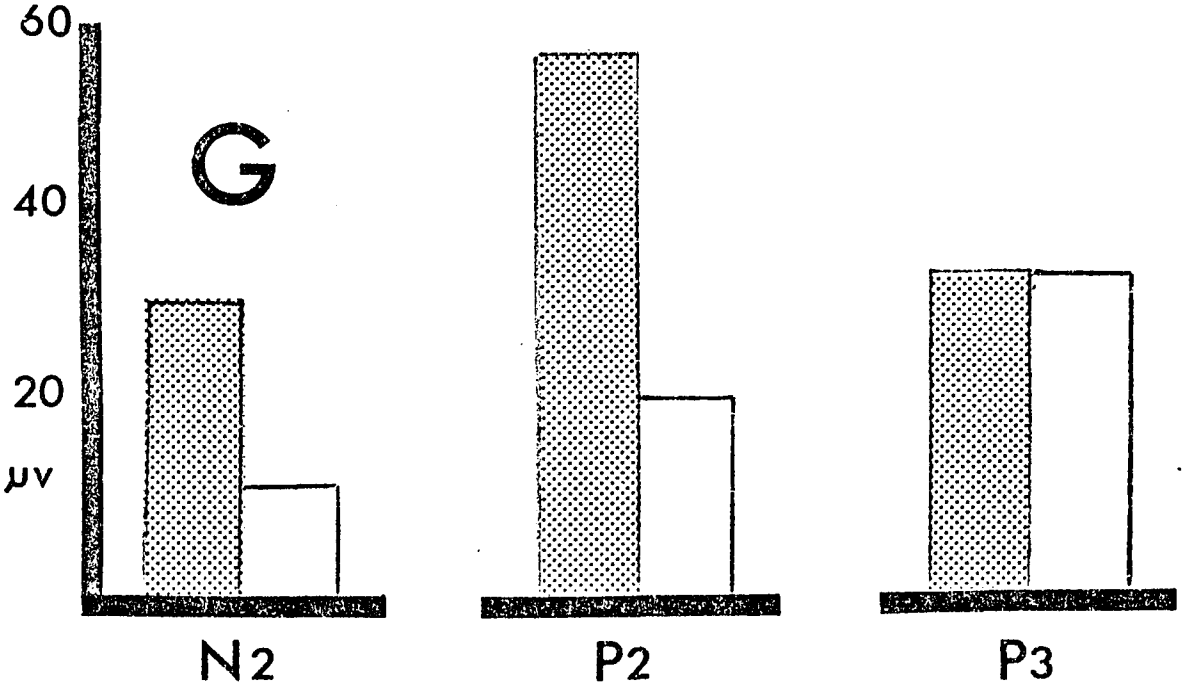
2. Reliability of the Epidural MPs:

The reliability of the MPs was an important consideration in the present study in that the amplitude distributions of specific components were derived from averaged MPs recorded in a large number of runs obtained over a four month period. Thus, it was necessary to assess the magnitude of random, and any systematic variations in the MP data over the entire duration of the recording period. The variability present in the MPs recorded at a single site had two sources. The first was the background EEG, assumed to be random and unrelated to the movement. The second source of variability was related to variations in the characteristics of the movements and to unknown variations in the cortical processes underlying the MPs.

On single sweeps the N2 - P2 excursion of the epidural MP, recorded at its site of maximum amplitude, was approximately equal in size to the low frequency components of the EEG. At all other locations the MPs were smaller than the background activity and

Figure 7: Histograms of the largest amplitude of the contralateral and ipsilateral N2, P2 and P3 components of the MP.


80
60
40
20
μv
R
Contralateral
Ipsilateral
N2
P2
P3


60
40
20
μv
G
N2
P2
P3

were virtually undetectable without averaging. Averaging increases the signal to noise ratio of the time locked activity by a factor equivalent to the square root of N (see review by Vaughan, 1974). As the number of samples is increased from one to 200, the relative contribution of the EEG is progressively reduced and the MP becomes more clearly defined (Figure 8). With an N of 200, the ratio of the MP to residual EEG is increased 14:1. The residual EEG is assumed to be equal in amplitude over the brain, while the amplitude of the MP varies. Thus, the contribution of the EEG to the total waveform was proportionally greater at locations where the MPs were smaller. Due to the random properties of the EEG the averaged potentials at these sites were more variable.

The effect of the variability which was present in the MPs themselves was reduced by utilizing data from runs when the activity of the monitor electrode fell within a preselected amplitude range. In each monkey the monitor electrode was located at the approximate level of the 50 percent isopotential line of the epidural N2 and P2 distributions. Because this was the smallest isopotential level mapped, examining the variability of the MP waveform at the monitor electrode yielded a conservative estimate of the consistency of this data.

The variability which remained in the MPs following averaging and data selection was monitored over the four month period in which recordings were taken from each monkey. Figure 9 compares

Figure 8: MPs recorded from a single contralateral electrode averaged across an N of 1, 10, 50 and 200 sweeps. Note the increase in the size of the MP relative to the residual EEG as a function of the number of sweeps averaged. Monkey R.

G

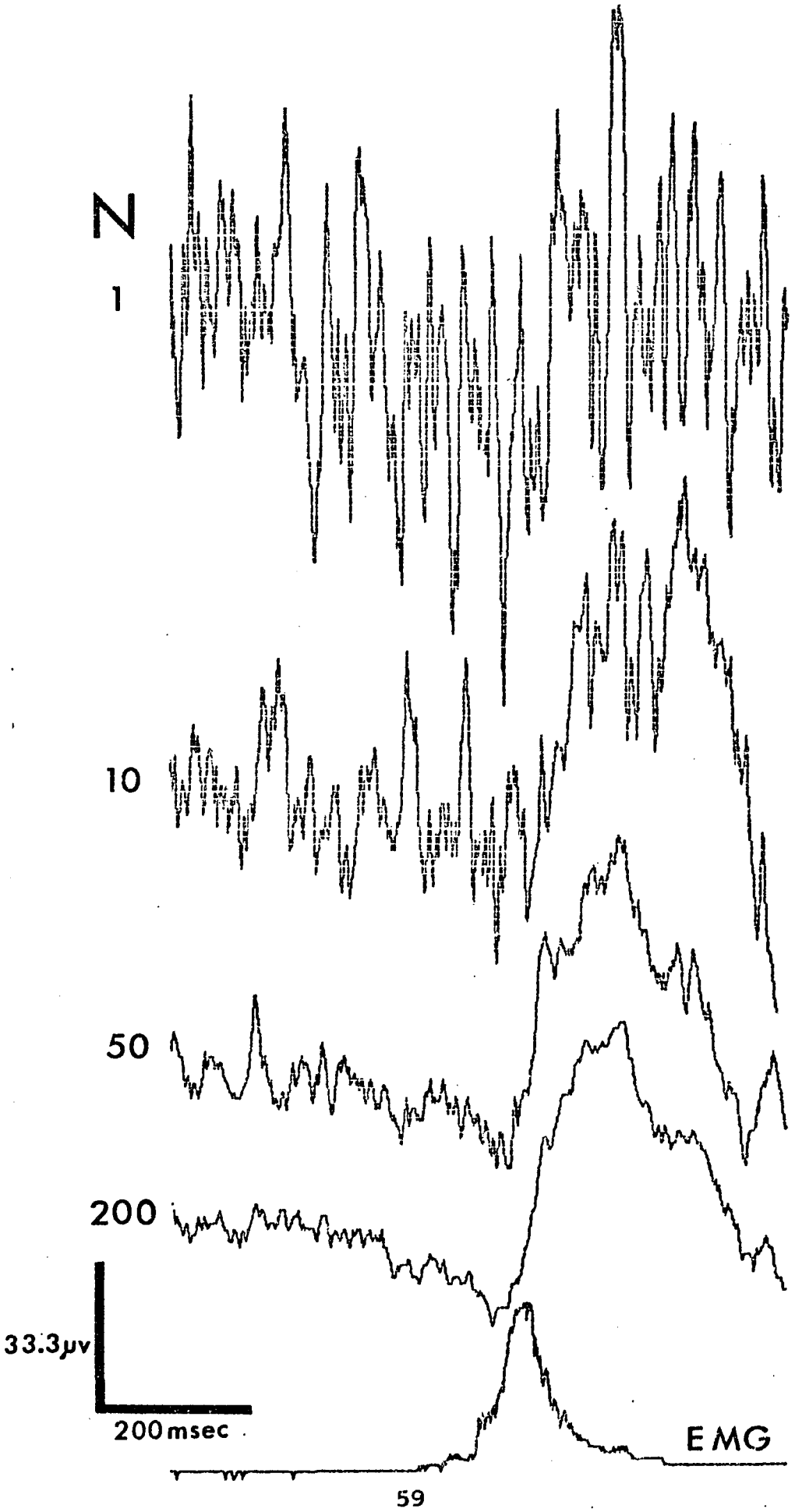
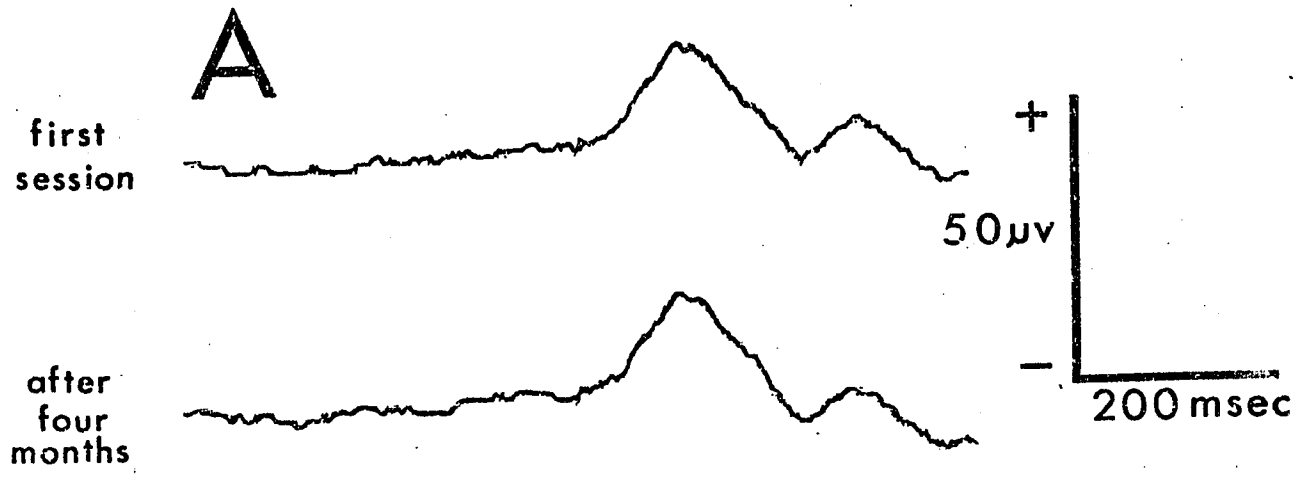


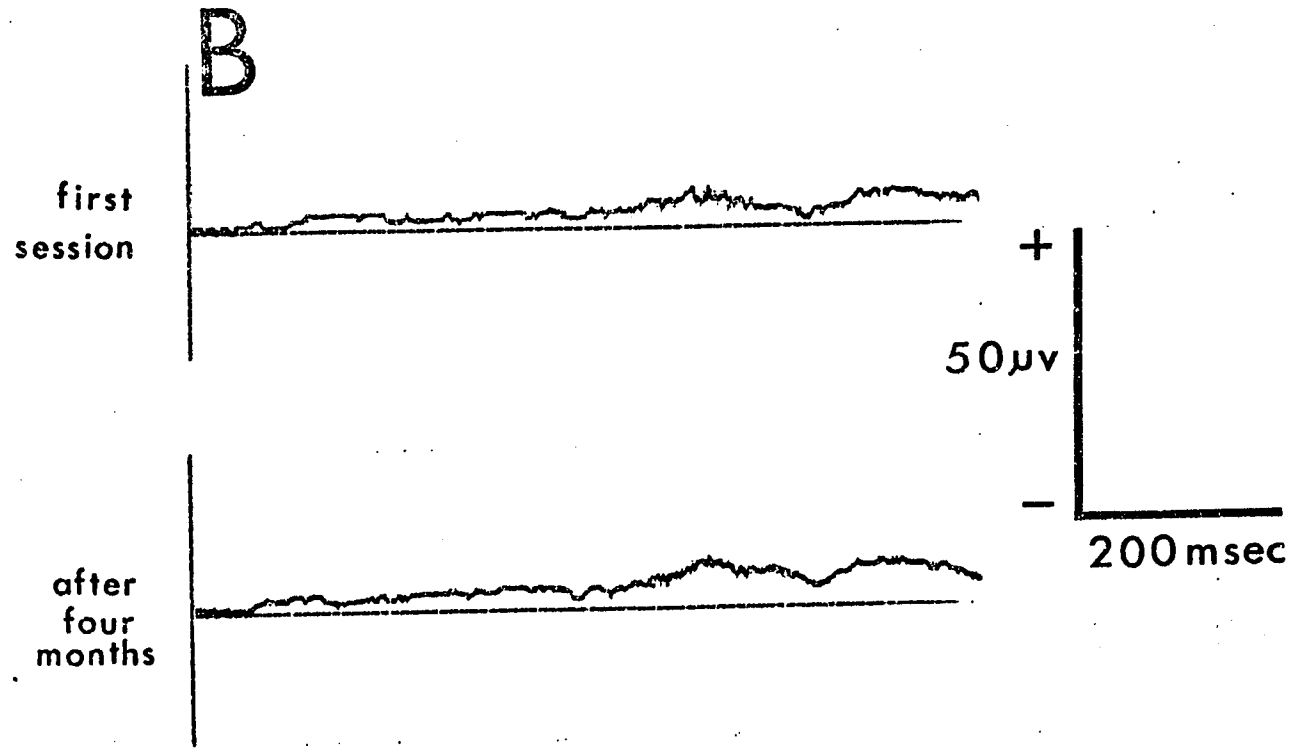
Figure 9:

A.) A comparison of the grand means of ten averaged MPs recorded at the monitor electrode on the first recording session and after a period of four months.

B.) A comparison of the standard deviation of the MPs used in calculating the grand means illustrated above.

Monkey G.


A
first session
after four months
+
50μv
−
200 msec


B
first session
after four months
+
50μv
−
200 msec

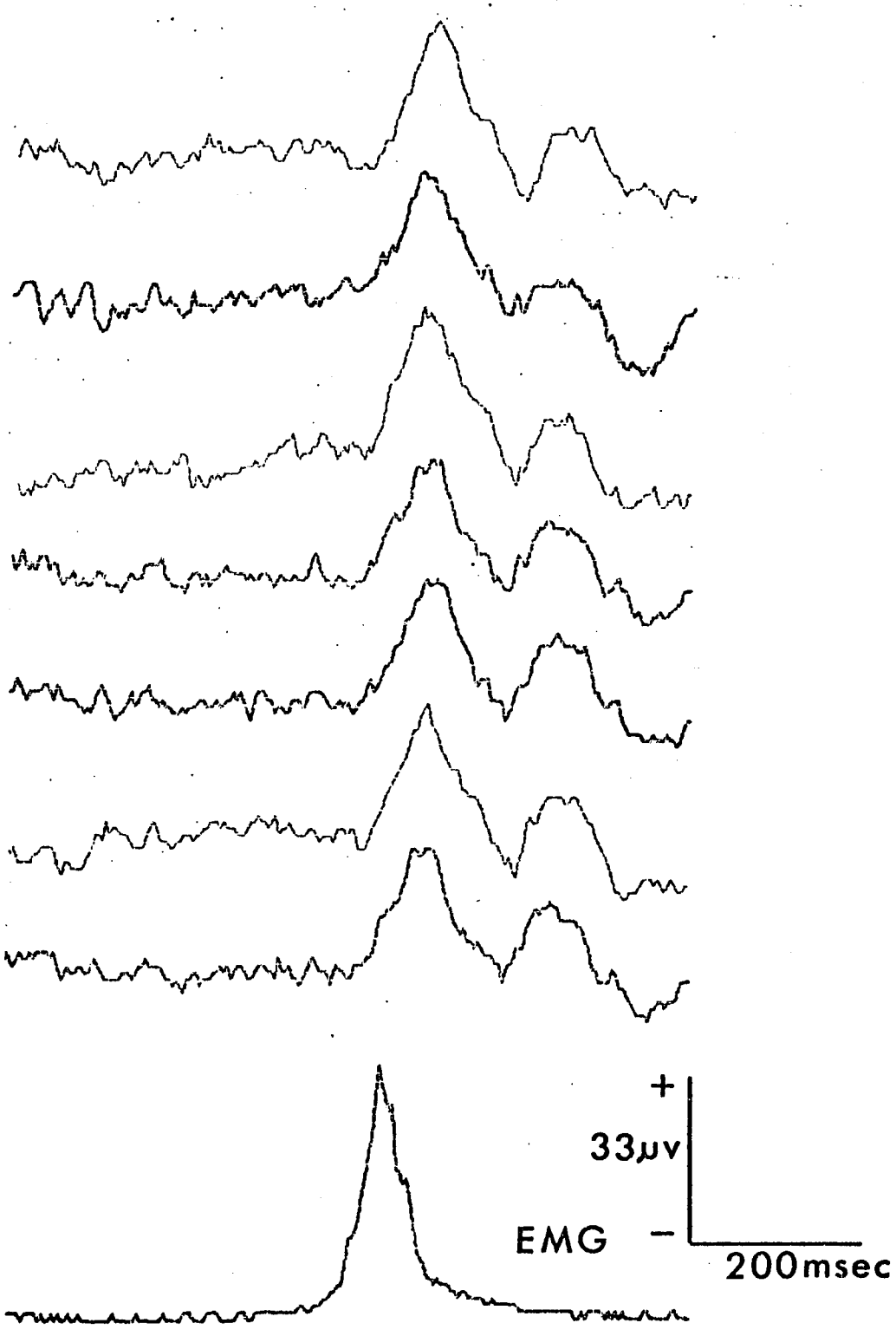
the standard deviation and grand mean of ten averaged MP waveforms recorded from the monitor electrode on the first recording session in monkey G with similar data recorded on the final session of that monkey. The data used in these computations was not preselected within the specified variability limits required for the amplitude mapping. The mean and variability of the averaged MPs remained stable across the four month recording period in both monkeys. This finding demonstrated that selection of data did not result in the elimination of any changes over time in the averaged MPs.

The standard deviation of at least ten ensemble averages serves as an estimate of the standard error of the mean. In both sets of data this was below 4.0 μv at most ordinates. Since the mean values can be considered to be normally distributed according to the Central Limit Theorem, there is less than a five percent chance that a given point on the epoch will deviate more than two standard error units from the population mean.

The reproducability of the averaged MP provides a direct demonstration of its reliability. Figure 10 depicts MPs recorded from the monitor electrode in monkey G on seven different sessions. Although these waveforms obviously do not represent a statistically meaningful sample they demonstrate the degree of replication of amplitude and morphology which was usually present in the averaged waveforms.

Figure 10: A comparison of the MPs recorded at the monitor electrode on seven different sessions. Note the similarity in the waveshape and amplitude of the potentials. Monkey G.

G



Epidural MPs recorded from the ipsilateral hemisphere were somewhat more variable than their contralateral counterparts. On runs when the contralateral activity fell within the accepted limits of plus or minus 15 percent, the simultaneously recorded ipsilateral MPs often displayed amplitude fluctuations up to 30 percent. The variability was characteristic of all ipsilateral recording sites and is partially attributable to the relatively small size of the ipsilateral MPs and to the consequent greater contribution of the residual EEG fluctuations. However, at some locations ipsilateral MP components attained amplitudes equal to or greater than those recorded at the contralateral monitor electrode, yet the waveform variability at these sites was still relatively higher than that of the contralateral MP. Thus, the interhemispheric differences in variability must reflect in part, differences in the processes underlying the MPs themselves.

3. Epidural Distributions:

a. Contralateral Hemisphere:

Epidural isopotential amplitude distributions were plotted for the N2, P2 and P3 components of the contralateral MP (Figure 11 and Figure 12). The isopotential maps demonstrate that, although there was considerable overlap in the distributions of the components, their sites of maximal amplitude and the extent of their fields differed. This finding precludes the possibility that all components of the contralateral MP was generated by a

Figure 11: Contralateral epidural amplitude distributions for N2, P2 and P3 components of the MP. Isopotential lines represent 90, 80, 65 and 50 percent of the maximal baseline to peak voltage of each component. The distributions are incomplete as electrode placements did not include posterior areas. Potentials on the right of the figure were recorded in or near the maxima of the distributions. Monkey G.

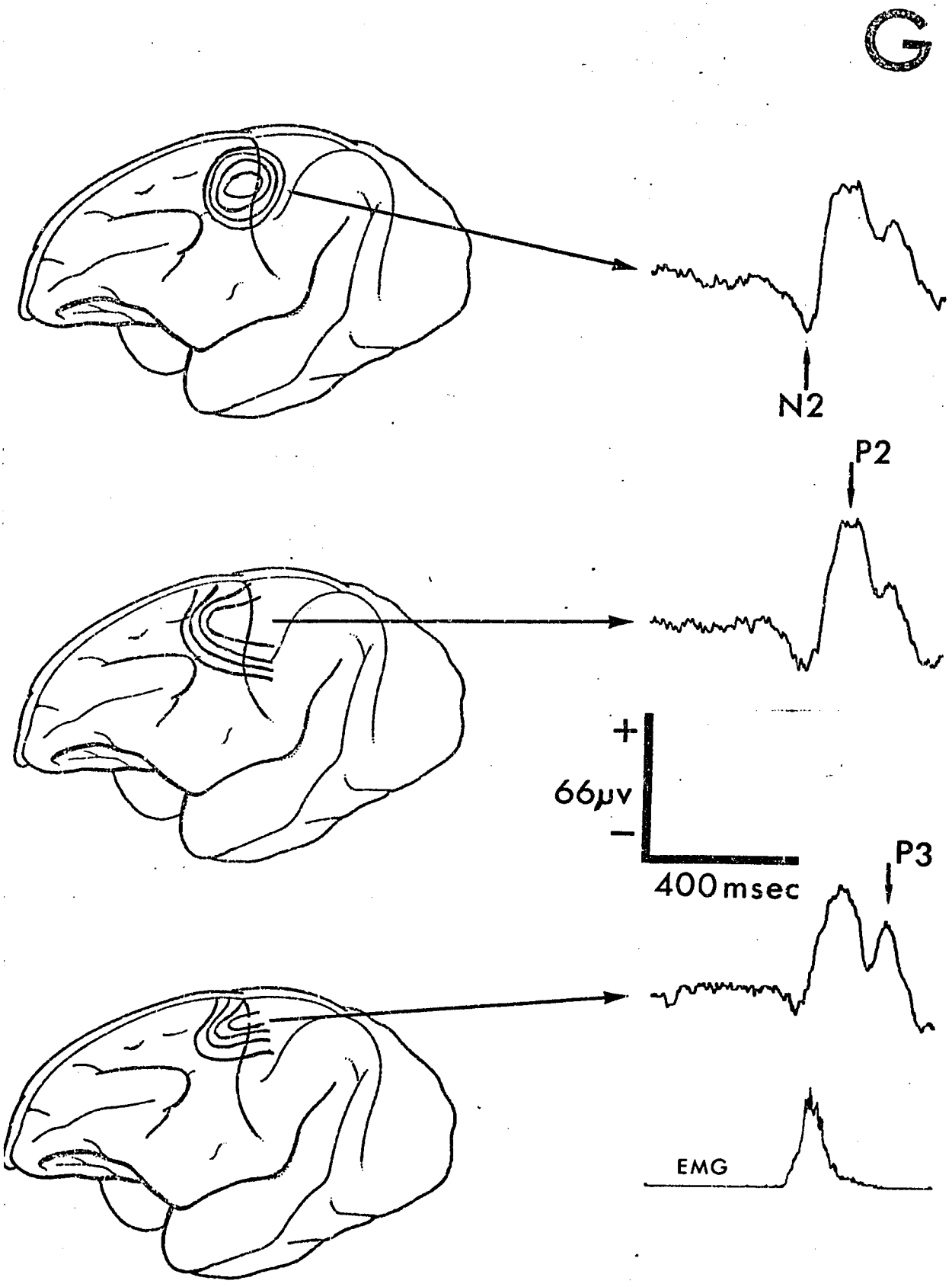
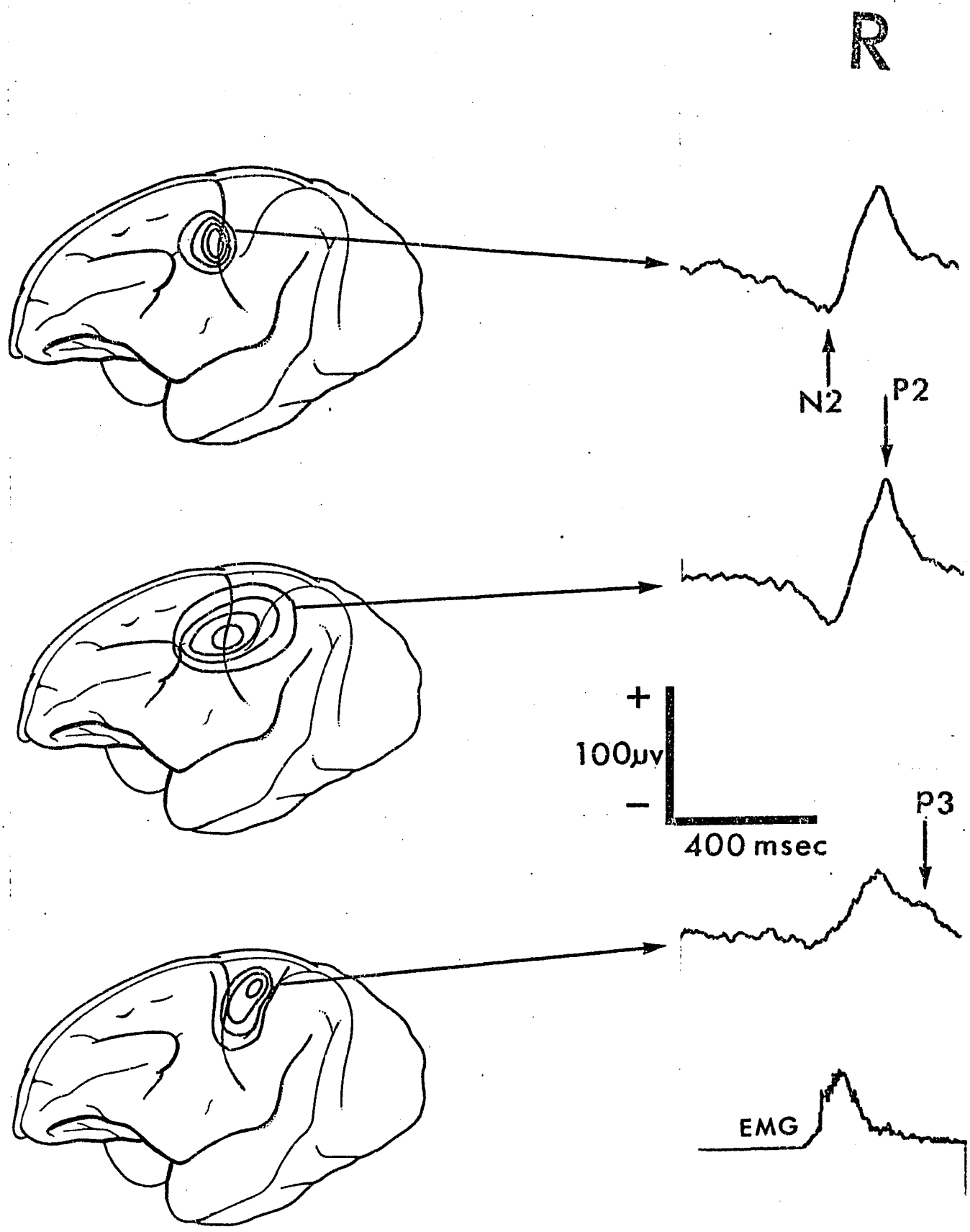

G
N2
P2
+
66μv
−
400msec
P3
EMG

Figure 12: Contralateral epidural amplitude distributions for the N2, P2 and P3 components of the MP. Isopotential lines represent 90, 80, 65 and 50 percent of maximal baseline to peak voltage of each component. Monkey R.


R
N2
P2
+
100μv
−
400 msec
P3
EMG

single source and indicates that the MP represents the composite of activity from anatomically disparate areas. Similar distributions of the individual components were found in both monkeys, although the isopotential maps were incomplete in monkey G due to absence of electrodes over the posterior portion of the P2 and P3 fields.

In each monkey the distribution of the N2 component was circumscribed and maximal over the precentral gyrus. In contrast, P2 displayed a more widespread field with amplitudes exceeding 75 percent of maximum over both pre- and post-central gyri. A comparison of the contralateral N2 and P2 fields contained in Figures 11 and 12 reveals that the distributions extensively overlapped and that they were centered overlying approximately the same cortical areas. The distributions of the two components were, however, considerably different in spatial extent particularly in the posterior dimension. The 50 percent isopotential line of the N2 distribution was entirely enclosed within the boundaries of the 50 percent contour of the P2 field. Due to the difficulty in detecting N1 and to instrumental reduction in its amplitude, this component was not isopotentially mapped. N1 was at its largest within the same precentral area as was the N2 potential. In each monkey, P3 was distributed in a small area centered over the posterior and superior region of the postcentral gyrus.

b. Ipsilateral Hemisphere:

Isopotential amplitude maps were not calculated for any of the components of the ipsilateral MP due to the variability of these potentials and because the activity was present at too few locations to permit the necessary interpolation. The distributions of the ipsilateral MP components can be grossly evaluated by examining Figure 6. Ipsilateral potentials were centered over cortical areas similar to those associated with the corresponding contralateral activity. The ipsilateral fields were however, relatively smaller. Thus, while P2 was maximally recorded overlying the central sulcus on both hemispheres, its ipsilateral distribution was significantly constricted in the anterior - posterior dimension compared to the corresponding contralateral activity. The relatively focussed nature of the ipsilateral potentials was most evident for the antecedent components, with N2 detected in only two adjacent ipsilateral electrodes in the precentral gyrus of monkey G.

Figure 6 illustrates that MPs recorded at nearby ipsilateral sites presented very different waveforms indicating little overlap in the dural distributions of specific components. This is in sharp contrast to the contralateral situation where MPs had a similar morphology, differing only in the relative amplitude of the components, over extensive areas of the dura (Figures 11 and 12).

4. Identification of Contralateral Sources:

a. Surface Cortex:

All components of the contralateral MP, with the exception of P1, inverted in polarity from surface to subcortex within regions underlying the maxima of their epidural response (Figure 13). The P1 component, which was inconsistently recorded on the dura, was not detected in the intracortical recordings and the origin of this activity is therefore in doubt. The location of the sites of transcortical inversion for N2, P2 and P3 are shown in Figure 14. The data pertaining to N1 are not presented in this figure for reasons outlined in previous sections. However, the areas of surface cortex displaying polarity inversions for N1 and N2 appear to be virtually identical.

Inversions of the contralateral antecedent potentials occurred at surface locations anterior to the central sulcus and posterior to the arcuate sulcus. Thus, the area of surface cortex involved in the generation of N1 and N2 was restricted to a precentral zone corresponding to the central portion of Brodmann's area 4. P2 inverted in polarity over an extensive area of the surface cortex ranging from the arcuate to the intraparietal sulcus and from the midsagittal sulcus to the approximate level of the temporal lobe. A limited region of the parietal lobe, occupying the posterior portion of the postcentral gyrus bordering the intraparietal sulcus, was identified as the source of the P3 component.

Figure 13: Contralateral MPs recorded from the dura and from a depth of 5mm below the dura at the indicated locations. Monkey G.

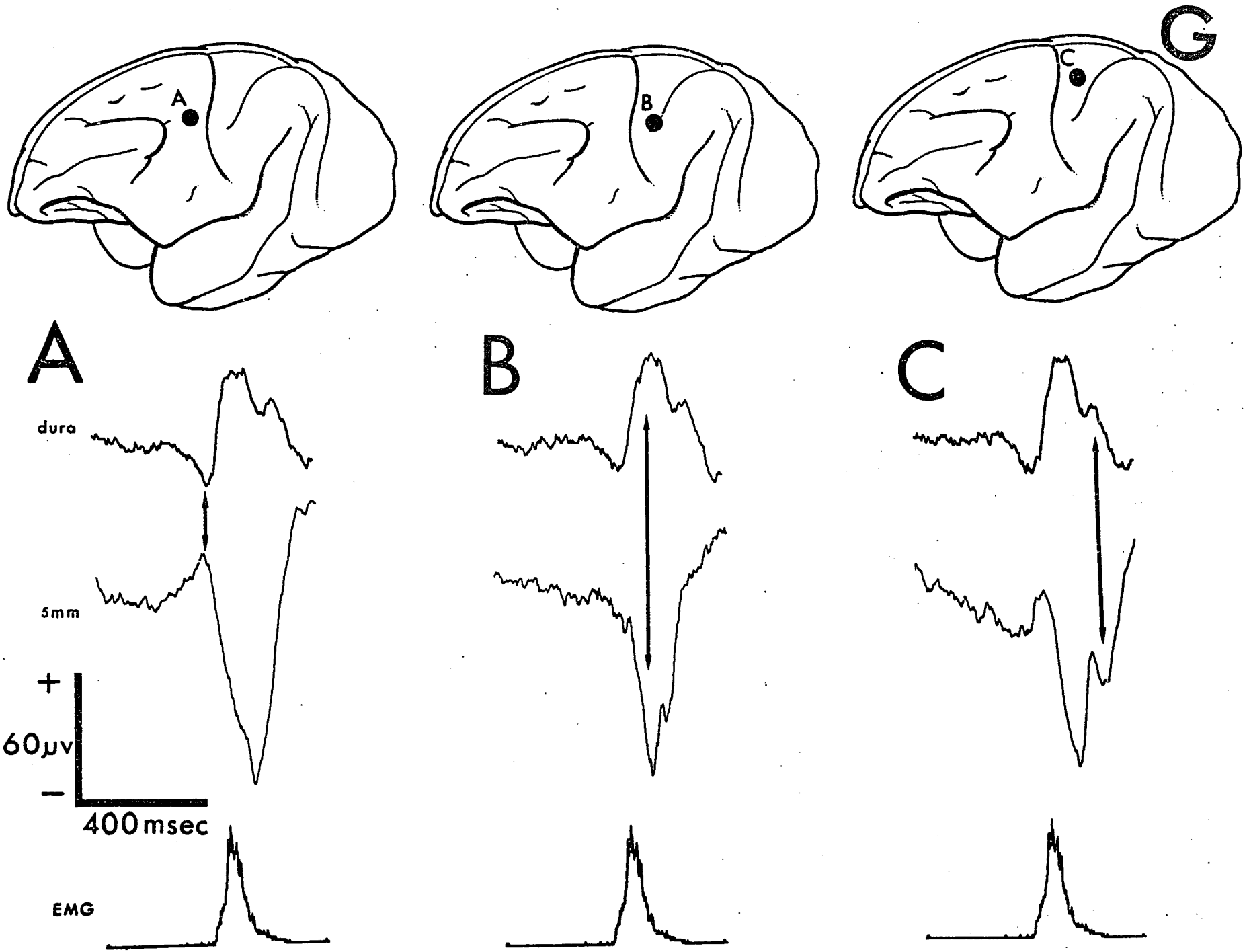
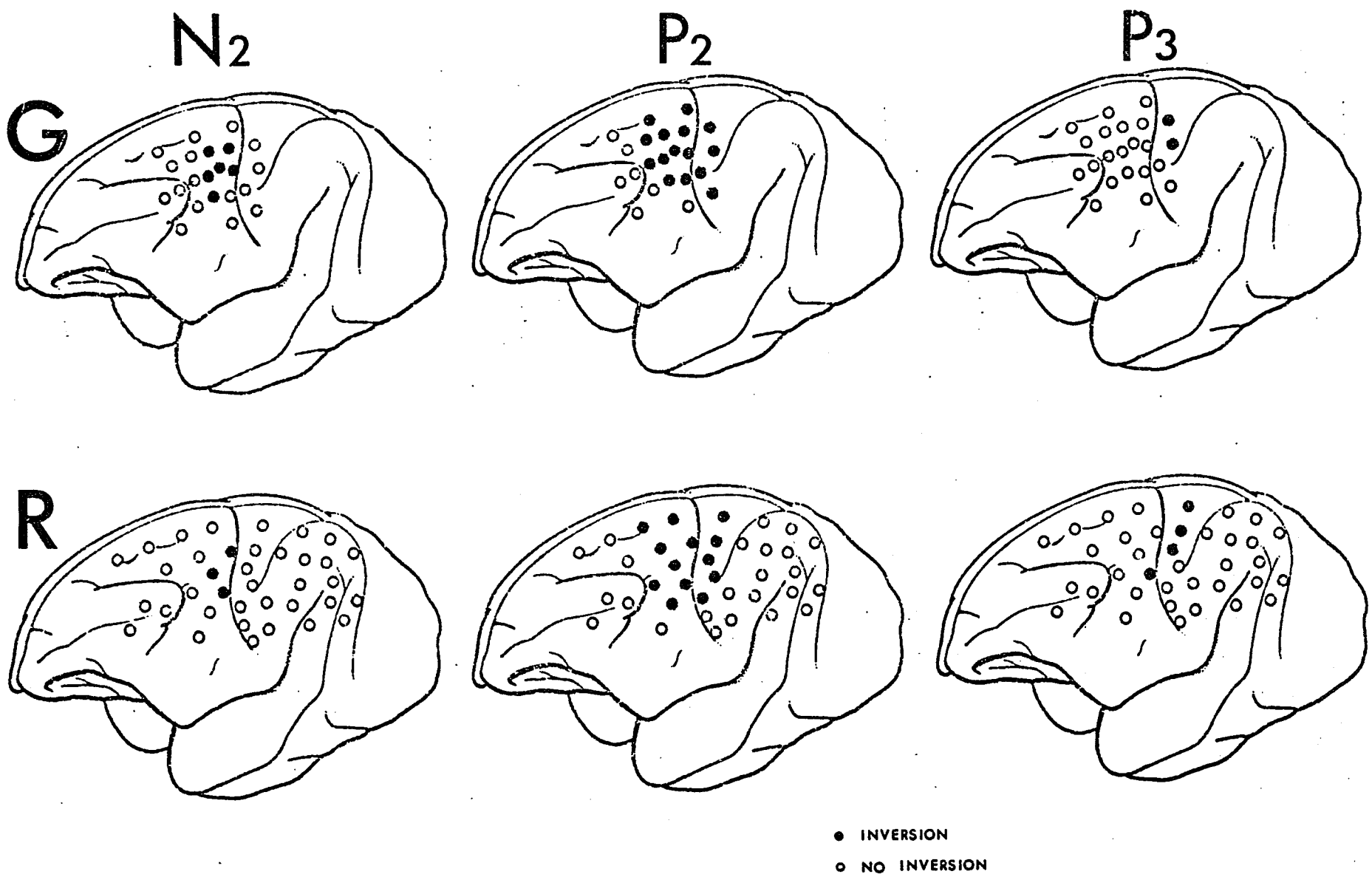

A
B
C
G
A
dura
5mm
+
60μv
−
400msec
EMG
B
C

Figure 14: Contralateral sites which yielded evidence of active response in the underlying surface cortex. Loci showing transcortical polarity inversions of the component indicated by the arrows are depicted as solid circles, and placements which revealed only volume conducted activity are indicated by the open circles. Monkey G and monkey R.


N2
P2
P3
G
R
● INVERSION
o NO INVERSION

The P2 generator was found to enclose completely the surface source of N1, N2 and P3 within its boundaries, but there was only a single electrode which demonstrated an overlap in the sources of N2 and P3.

A comparison of Figures 11 and 12 with Figure 14, reveals a correspondence in extent and location between the areas of surface cortex which displayed polarity inversions of an MP component and the center of the epidural distribution of that component.

b. Sulcal Cortex:

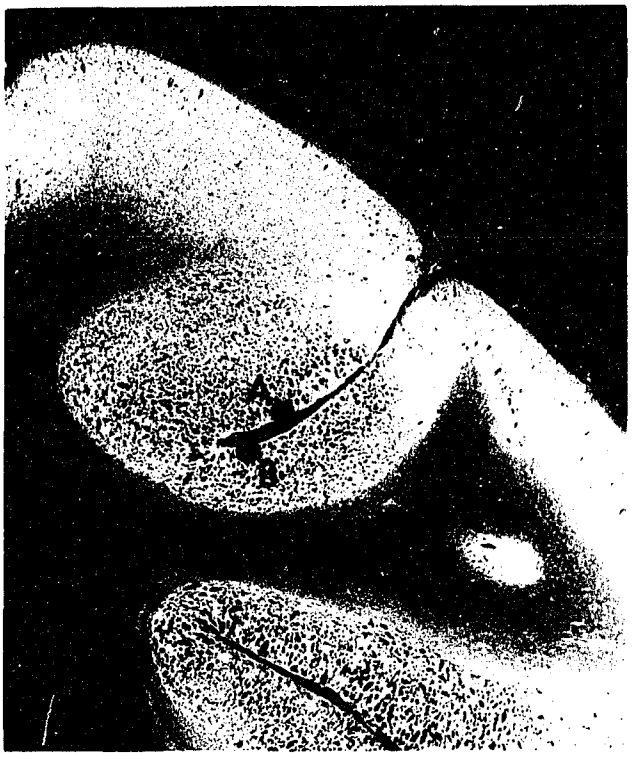
The identification of sources within the cortex occupying the banks of the various sulci, was made difficult by the limited number of electrodes which passed near this cortex and by the angles at which these electrodes (positioned perpendicular to the surface cortex) approached this buried tissue. The situation was further complicated by the presence of volume conducted activity from the inferior field of the surface cortex which because of its orientation influenced all depth recordings.

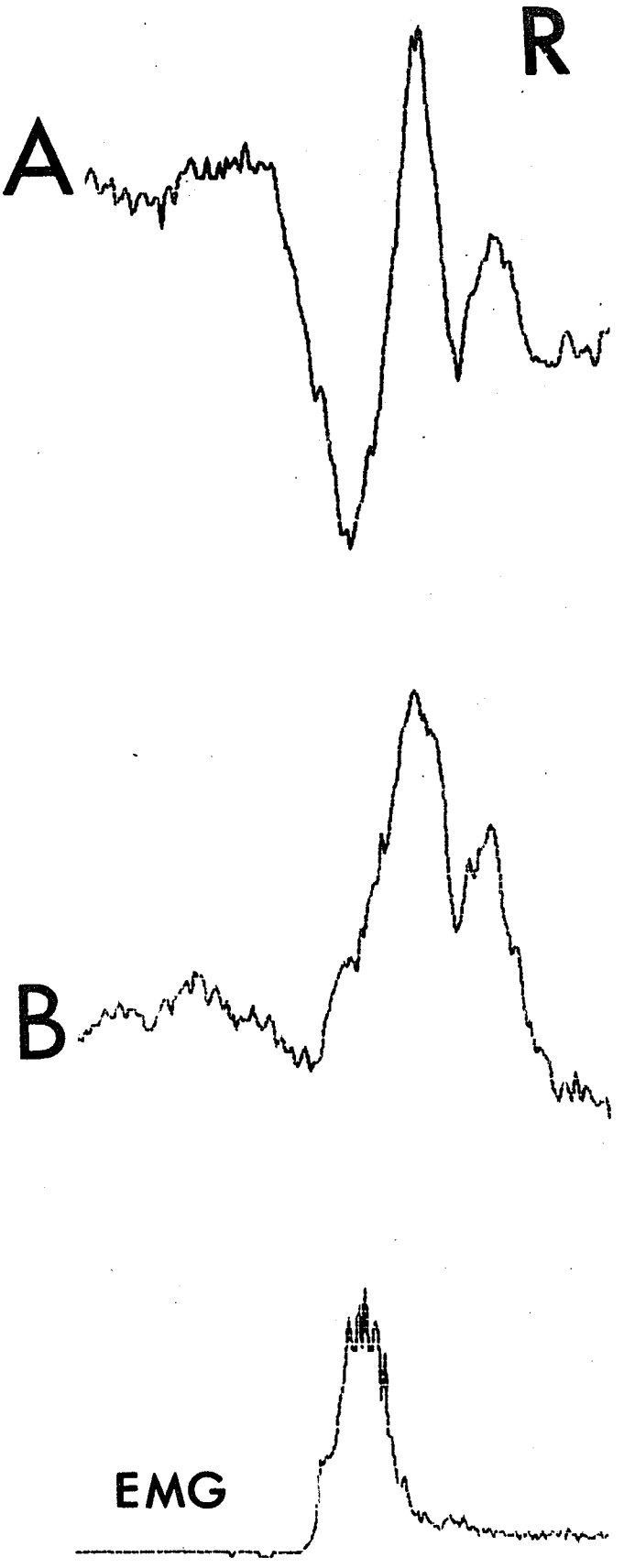
Although it was not feasible, with the present recording procedures, to provide a detailed description of the MP generators within the fissures, evidence was obtained indicating that sources were present in the cortex forming the central sulcus and Brodmann's area 3a. A large amplitude N2 component was detected on the superior surface of the cortex occupying the anterior bank of the central sulcus (waveform A in figure 15) and a P2 component was detected

overlying Brodmann's area 3a (waveform B in figure 15). The polarity and timing of these depth components were the same as those recorded at the dura. The possibility that this depth activity represented volume conduction of components from surface cortex was ruled out because of their large amplitude, the absence of activity of a similar polarity and timing in the surrounding tissue and location of the recordings which was below the superior field of the surface cortex. It must be concluded that depth MPs were in part generated within the banks of the central sulcus and that this activity summed with the inferior field of the surface sources. The interaction of these perpendicular generators could account for the complex morphology and for the distorted distributions of the depth MPs which were recorded in the immediate vicinity of the central sulcus.

An examination of the MPs recorded at 5 mm below the dura posterior to the central sulcus revealed activity which was not present in the overlying surface cortex (Figure 13). This activity consisted primarily of an early negative shift which corresponded to the dural N1 and N2 potentials and a positivity which had the same latency as the dural P2 component. The amplitude of these potentials decreased at more posterior electrode placements. Based on their polarity, timing and distribution, these components are believed to be volume conducted activity generated in the anterior bank of the central sulcus and projected posteriorly and inferiorly.

Figure 15: MPs recorded from two indicated sites in the depths of the contralateral central sulcus. Waveform A was recorded on the cortex forming the anterior bank of the central sulcus while waveform B was recorded on Brodmann's area 3a. Monkey R.


A
B

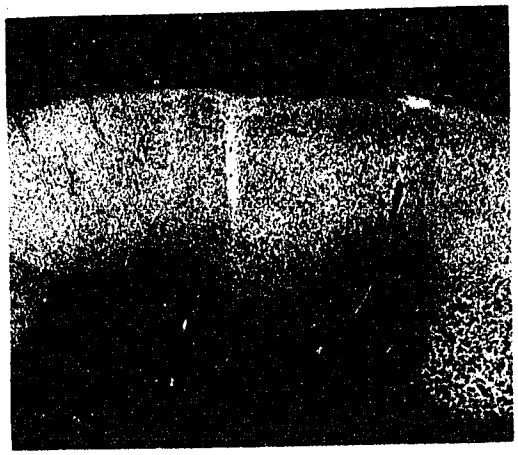

R
A
B
+
66uv
−
300MSEC
EMG

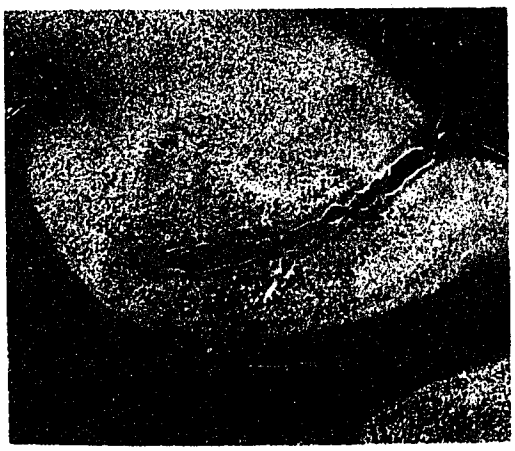
Depth recordings from the cortex forming the posterior bank of the central sulcus revealed a previously unidentified MP component (P4) which occurred between 300 and 400 msec following EMG onset and which represents the longest latency cortical activity associated with a voluntary movement (Figure 16). This component was positive on the superior surface of this cortex and was negative in the depth. Due to the orientation of the cortex forming the central sulcus, P4 was projected in the anterior - posterior direction so that its influence on epidural recordings was limited. The P4 component was only detected in the immediate vicinity of Brodmann's area 3, but the precise boundaries of the active tissue and the depth of intracortical inversion remain undefined because of an insufficient number of electrode passes in this region.

5. Intracortical Laminar Studies:

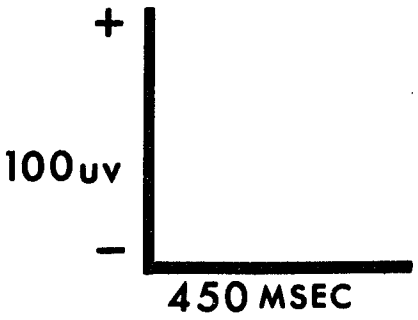
Laminar studies utilizing 22 electrodes were undertaken in preselected cortical areas to determine the intracortical pattern of MP fields with the intent of more precisely defining their sites of generation. Although the intracortical MPs were often extremely complex, several reliable patterns of activity were identified, each of which was characteristic of a particular cortical area. The following section describes the potentials recorded in a series of intracortical laminar passes and relates them to the corresponding cortical architecture. In those instances in which the entire depth pass could not be traced on a single coronal section the path of the

Figure 16: MPs recorded at a depth of 7.0 mm below contralateral dura. Waveform A was recorded at a depth placement in the precentral gyrus. Waveform B was detected on the inferior surface of the cortex forming the posterior bank of the central sulcus. Note the inversion of the long latency potentials which terminate each response. Monkey R.






R
A
B


+
100uv
−
450 MSEC


EMG

electrode was determined by examining serial sections.

Figure 17 shows the typical MPs recorded from an electrode passed through precentral cortex underlying the epidural maximum of the contralateral N2 distribution. As the electrode was moved through the cortex, N1, N2 and P2 traversed a zero potential point and appeared below that level as the approximate inversion of the corresponding surface potential. N1 and N2 were fully inverted below the approximate level of the fourth cortical lamina, while P2 inverted at a somewhat higher level within the cortex.

A second category of laminar findings was characteristic of recordings from electrodes in the anterior portion of the precentral gyrus (Brodmann's area 6) and in the zones of Brodmann's area 4 which surrounded the generators of the N1 and N2 components described above. At these locations there was a transcortical inversion of P2 with no inversion of N1, N2 or P3. Although N2 did not invert, it steadily increased in amplitude to reach a maximum within the lower cortical lamina and then decreased in size beneath the cortex (Figure 18). It is unlikely that N2 in these areas was volume conducted from the cortex forming the central sulcus since nearby electrodes which were closer to the fissure failed to reveal a negative component at this latency. Furthermore, the tissue within the arcuate sulcus did not appear to be a likely source of this potential since neither the dural nor the depth recordings anterior to the arcuate sulcus revealed consistent

Figure 17: MPs recorded from various intracortical locations.

A.) The point at which the electrode entered the precentral cortex.

B.) The electrode track and depth of recording.

C.) The coronal section containing the critical area.

Monkey G.

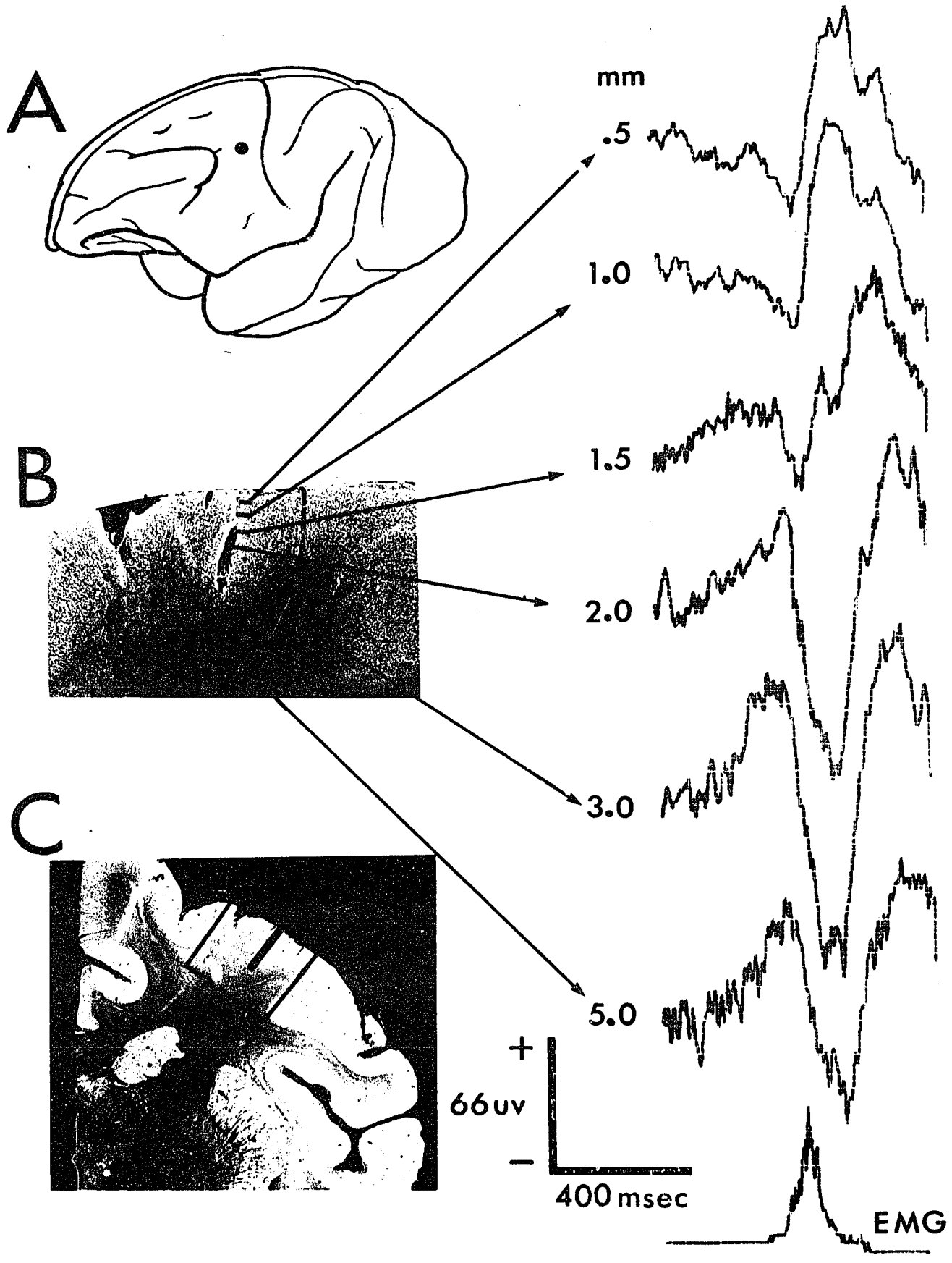
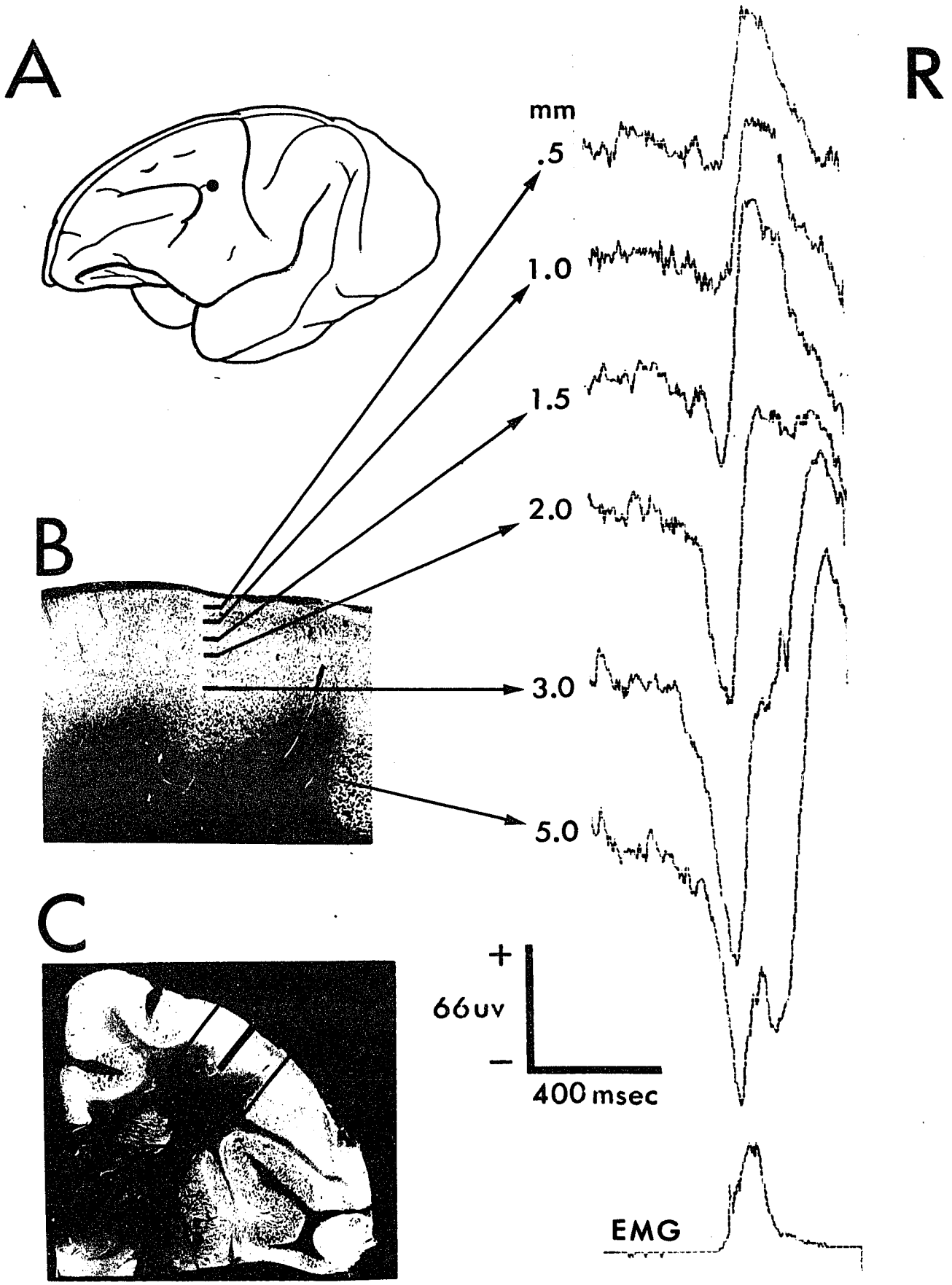

A
B
C
mm
.5
1.0
1.5
2.0
3.0
5.0
+
66uv
−
400 msec
EMG

Figure 18: MPs recorded from a depth electrode passing through cortex in the anterior portion of the precentral gyrus (Brodmann's area 6). Monkey R.


A
R
mm
.5
1.0
1.5
2.0
3.0
5.0
B
C
+
66uv
−
400 msec
EMG

MP components. The MPs recorded in the depths of the lateral portion of the precentral gyrus were influenced by the long latency positivity believed to be generated in the posterior bank of the central sulcus (Figure 18).

A third pattern of intracortical activity was recorded underlying the center of the contralateral P3 epidural distribution. This region was characterized by an inversion of both P2 and P3 with no inversion of N1 or N2. As seen in Figure 19, P3 inverted between 0.5 and 1.0 mm below the dural surface while P2 inverted at a depth between 1.0 and 1.5 mm. The lower traces in Figure 19 were recorded in the white matter of the postcentral gyrus and are presumed to reflect a complex interaction of components generated in both banks of the central sulcus and in the overlying surface cortex.

The final pattern of contralateral intracortical activity was recorded at all electrode placements posterior to the intraparietal sulcus. The MPs from this region consisted mainly of P2 and were similar in size and morphology at all cortical depths (Figure 20). An anterior - posterior gradient was present in that electrodes at the more posterior locations displayed smaller MPs throughout the cortex than those which were closer to the postcentral gyrus. The distribution of activity indicated that it was volume conducted from the infolding of the postcentral P2 generator which forms the anterior bank of the intraparietal sulcus.

Figure 19: MPs recorded from a depth electrode passing through the cortex of the medial portion of the postcentral gyrus (Brodmann's area 5). Monkey G.

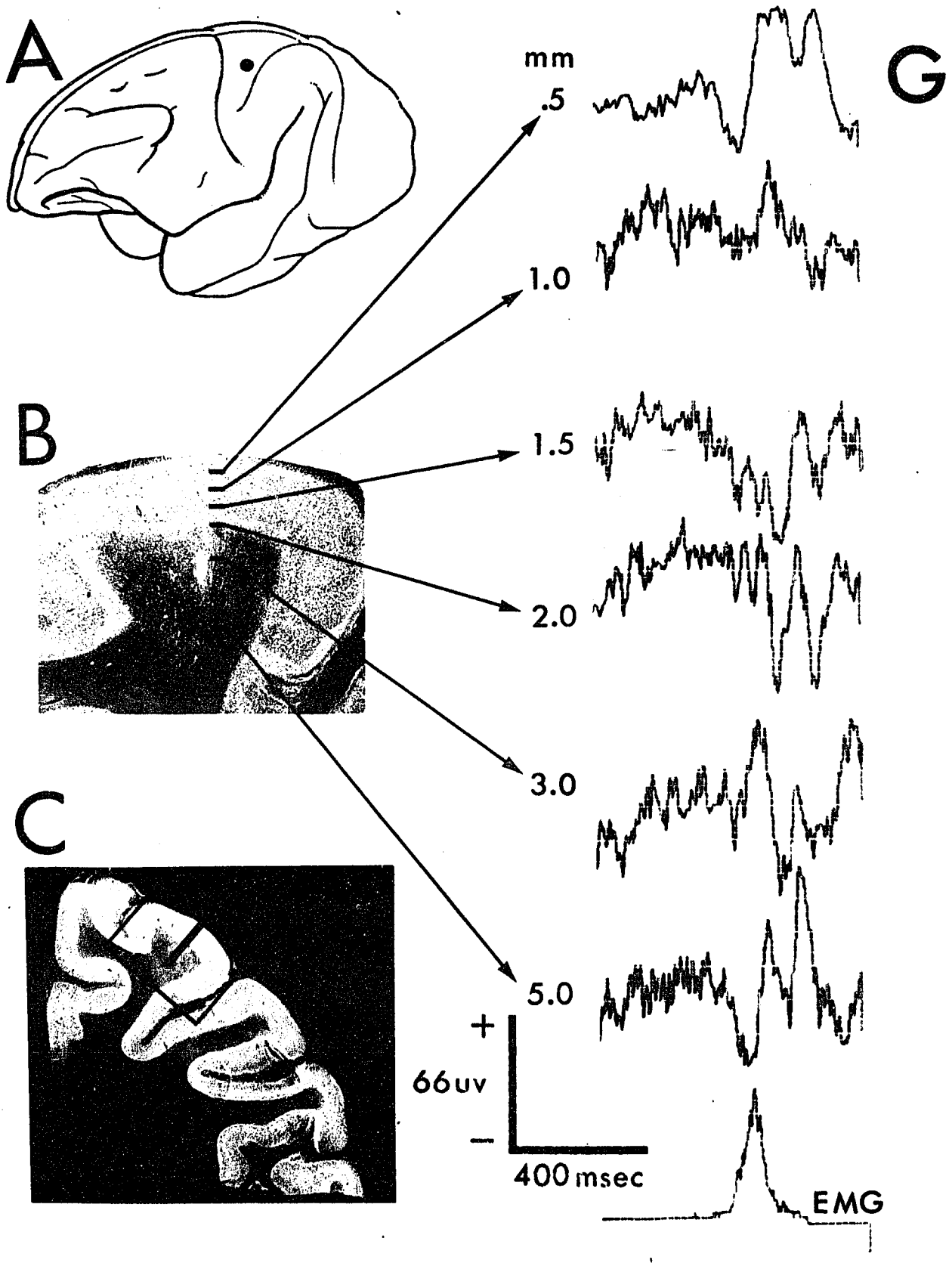

A
B
C
G
mm
.5
1.0
1.5
2.0
3.0
5.0
+
66uv
−
400 msec
EMG

Figure 20: MPs recorded from a depth electrode passing through the cortex posterior to the intraparietal sulcus. Monkey R.

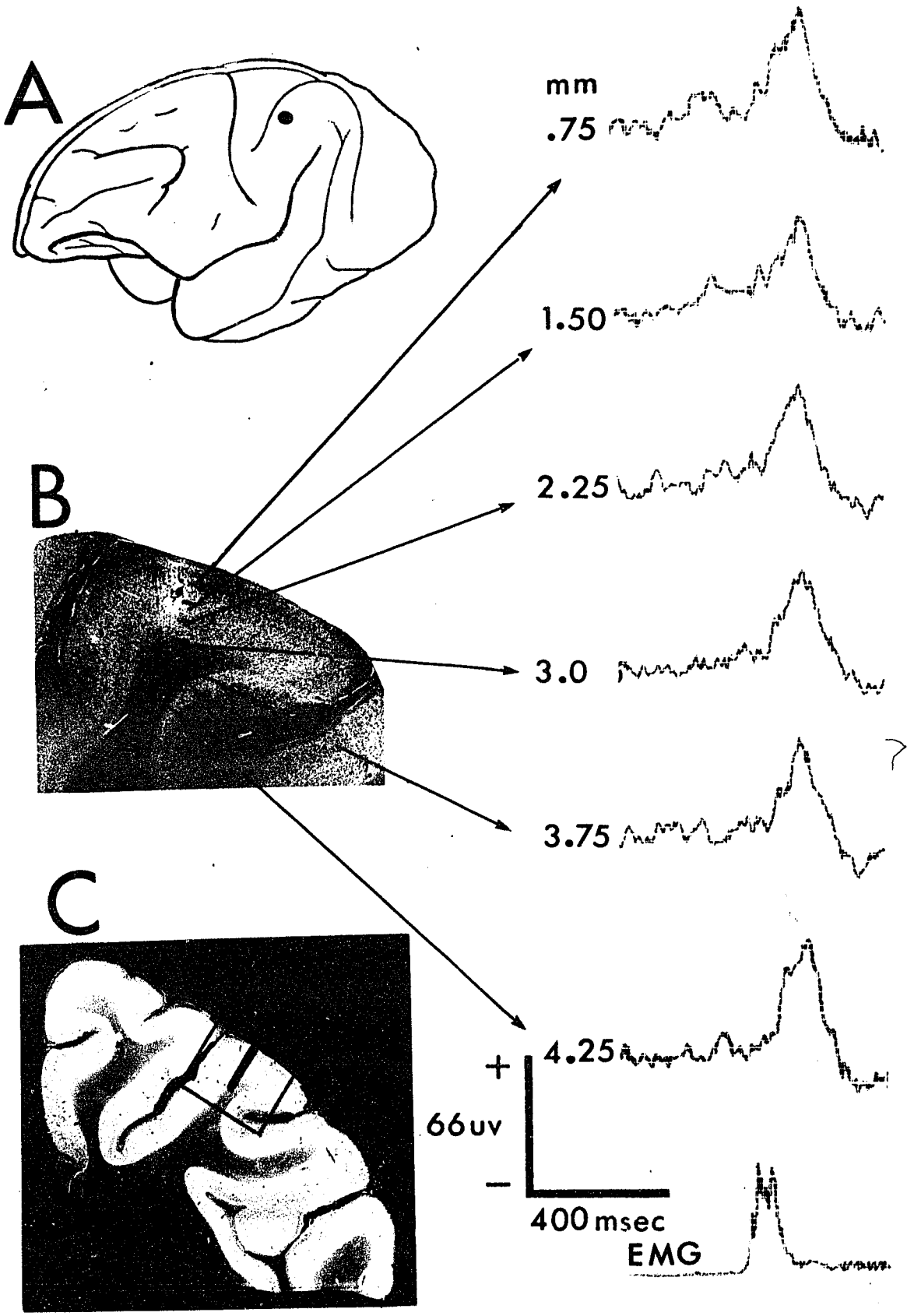

A
B
C
R
mm
.75
1.50
2.25
3.0
3.75
4.25
+
66uv
−
400 msec
EMG

Figure 21 depicts MPs recorded from an electrode which entered the contralateral posterior precentral gyrus on monkey R, immediately adjacent to the central sulcus and which paralleled this fissure. Recordings from this site displayed inversions of the four major components of the MP and permitted a direct comparison of the intracortical levels of component genesis. Analysis of Figure 21 reveals that P2 and P3 inverted at a more superficial level of cortex than did N1 and N2. In the recordings from this electrode it is difficult to correlate the level of inversion with specific cortical lamina because the electrode track passes into the cortex of the anterior bank of the central sulcus. It is clear, however, that at a depth of 2.0 mm both P2 and P3 had already inverted and were recorded as negative potentials while the antecedent potentials had just reached the level at which the inversion takes place.

The depth at which individual components inverted varied for different electrode sites as a function of cortical thickness and the angle of electrode penetration. The relative depth of component inversions was, however, a reliable finding, present in both monkeys.

6. Ipsilateral Sources:

Transcortical examination of the origins of the ipsilateral MPs reveal that each of the components inverted in polarity across ipsilateral surface cortex (Figure 22) and that they therefore did

Figure 21: MPs recorded from a depth electrode passing through the cortex immediately anterior to the central sulcus. Note that the lower portion of the electrode enters the cortex forming the anterior bank of the central sulcus. Monkey R.

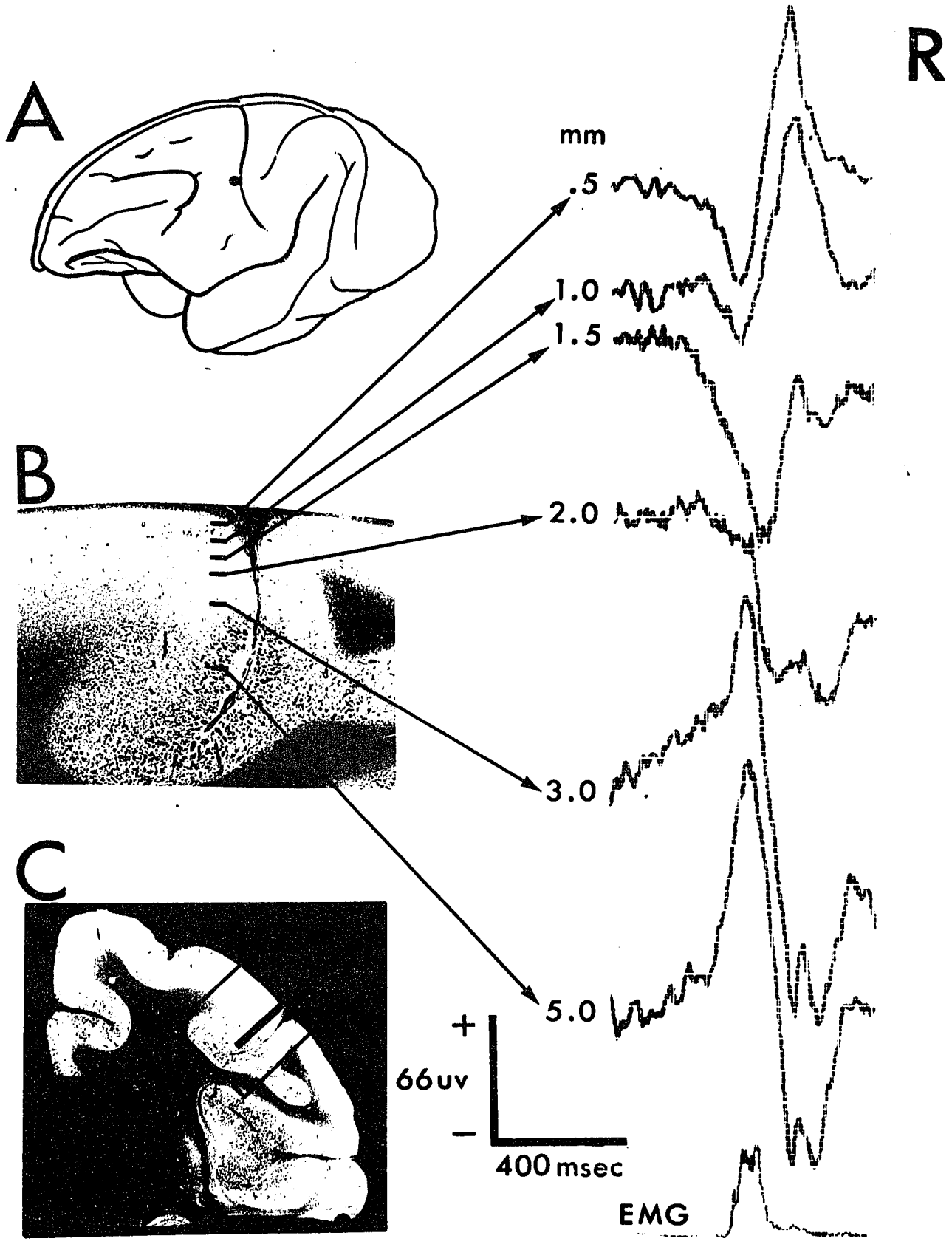
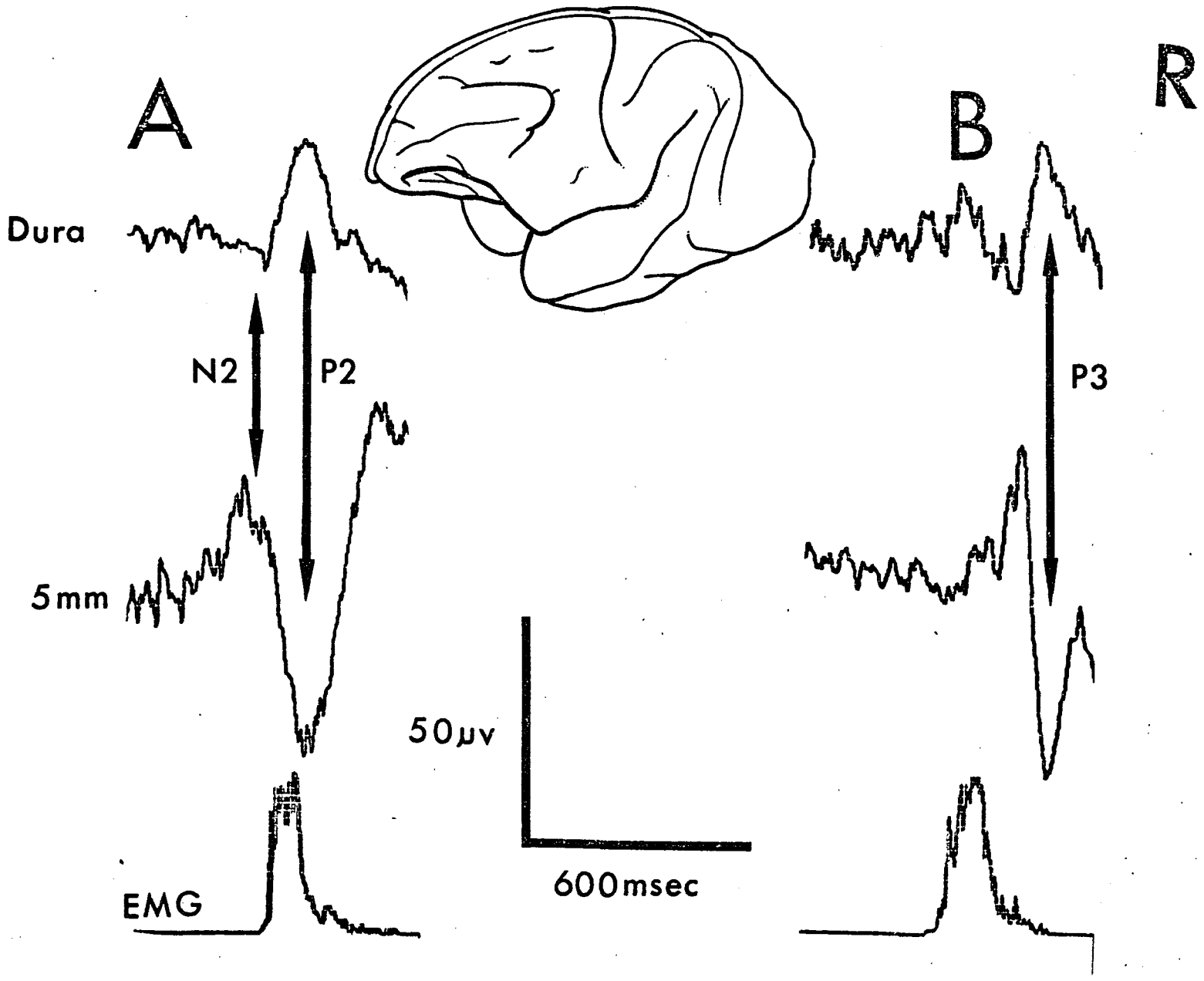

A
B
C
R
mm
.5
1.0
1.5
2.0
3.0
5.0
+
66uv
−
400 msec
EMG

Figure 22: Transcortical ipsilateral MPs recorded at the indicated locations. Monkey R.


A
B
R
Dura
N2
P2
P3
5mm
50µv
600msec
EMG

not represent passive interhemispheric spread of contralateral activity. Each component of the ipsilateral MP was generated in a cortical region comparable to the contralateral source of that component, but the extent of the ipsilateral N1, N2 and P2 generators was smaller. Only a single electrode (in monkey G) demonstrated an inversion of ipsilateral antecedent activity while in the same monkey the ipsilateral region of inversion for P2 was less than one-half that of the contralateral hemisphere. In contrast, the ipsilateral source of P3 is about the same size as the contralateral source of this activity and the amplitude of the inverted potential at that latency is larger than that recorded at any contralateral site.

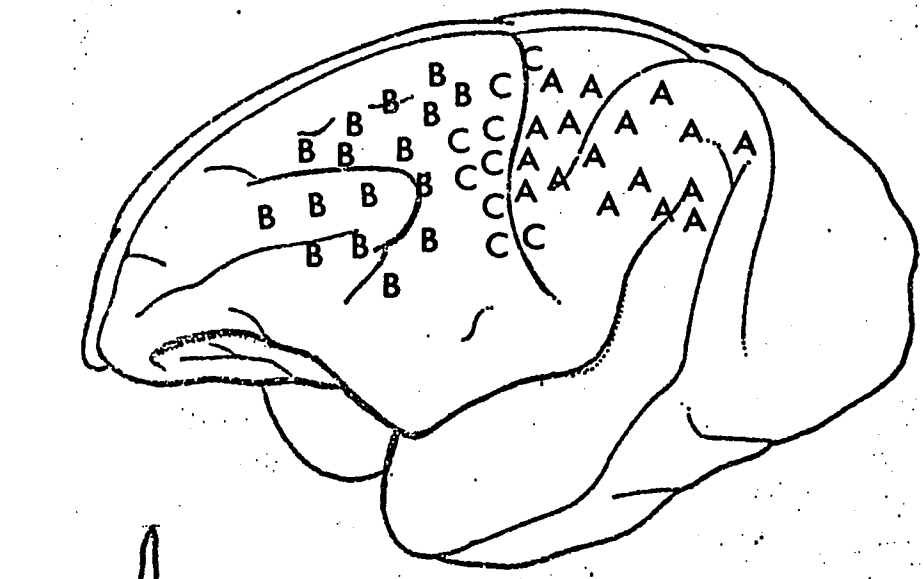
B. Somatosensory Evoked Responses (SER)

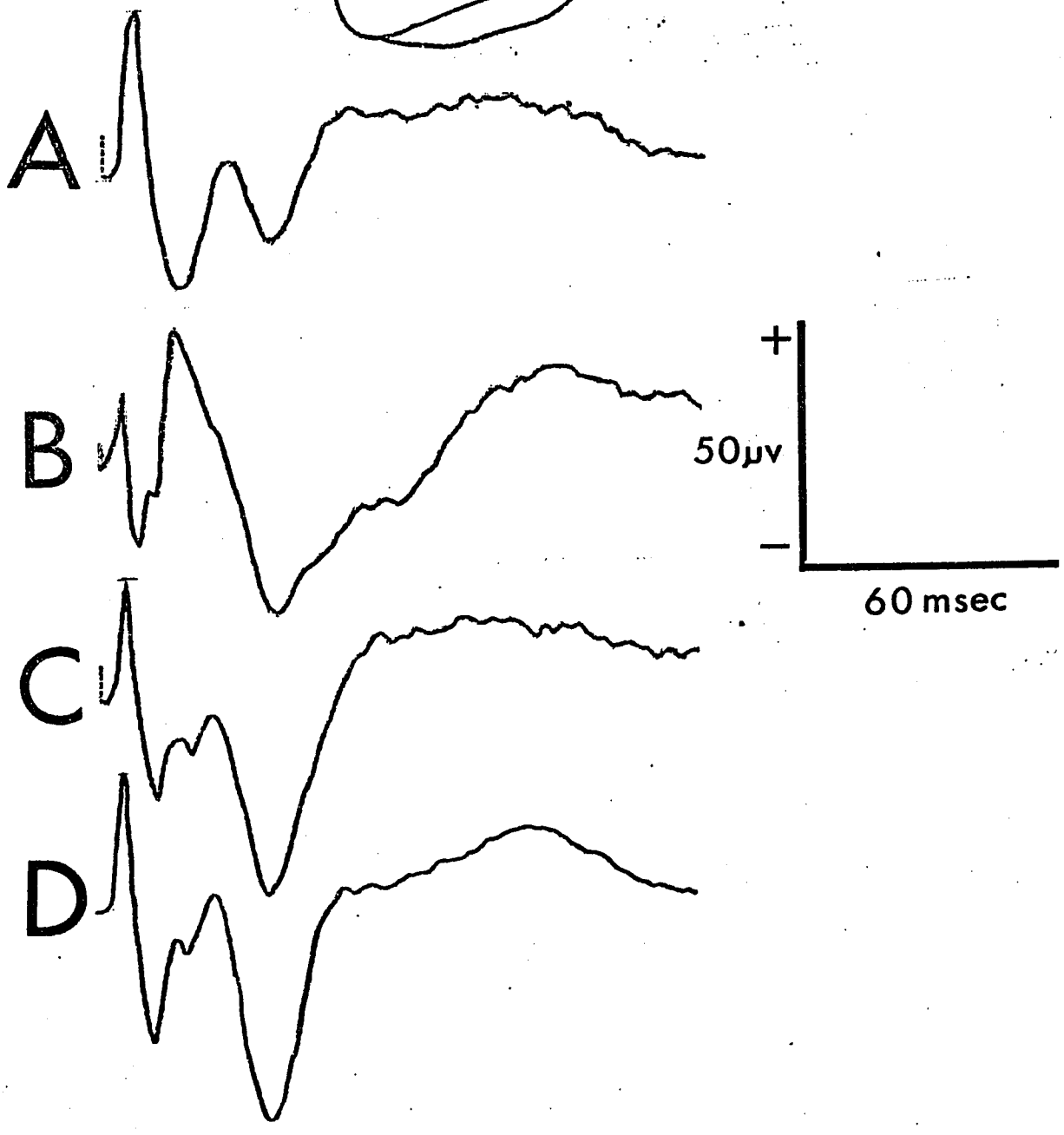
1. Morphology and Epidural Distribution:

The SERs recorded from the dura contralateral to the stimulated extremity differed in waveshape as a function of recording site. Three characteristic SER waveforms were observed. Each was recorded over a different cortical region as depicted in Figure 23. The SER recorded at all electrode sites posterior to the central sulcus (waveform A) consisted of an initial positive component with an absolute latency of 6.0 msec and a peak at 10.0 msec, followed by a "W shaped" wave with peaks at N20, P32 and N42 msec. The response was completed by a broad positivity which peaked at approximately 100 msec.

Figure 23: The three basic waveshapes of the contralateral epidural SER with the locations at which each was recorded. Waveform D is the mathematical addition of waveforms A and B. Monkey G.

G





The SER configuration recorded over the anterior portion of the precentral gyrus and the dorso-lateral frontal cortex (waveform B) began with a small positive deflection which peaked at 7.5 msec, but this activity was soon replaced by a larger negative component which reached a peak at 12.0 msec. The negativity was followed by a positive potential which peaked at 21.0 msec and the SER was completed by a negative component which peaked at 42 msec and by a positivity peaking at approximately 100 msec.

A third SER waveform was recorded primarily in an area overlying the posterior portion of the precentral gyrus, between the regions from which the previously outlined SER were recorded. This configuration (waveform C) comprised a positive component with a peak latency of 8.5 msec followed by a negativity at 16.0 msec. These components were followed by a positive - negative - positive wave with peaks at 20.0, 23.0 and 27.0 msec. The SER in this region was also completed by a negative component at 42 msec and a long-lasting positivity.

Inspection of the SER waveforms recorded from the anterior and posterior extremes of the array suggested that the potentials in the central region might have represented the algebraic summation of two potentials having the form of the postcentral and frontal activity. This was tested by calculating the algebraic summation of waveforms A and B. The resulting potential (waveform D) was

remarkably similar to the empirically recorded SER from the proposed interaction area (waveform C). Thus, the morphology and distribution of the epidural SERs were consistent with the presence of two main cortical sources; one located posterior to the central sulcus which generates the initial positive activity, and a second precentral source with a slightly longer latency.

2. Epidural Reliability:

Epidural SERs displayed consistency both within and across experimental preparations. The upper portion of Figure 24 depicts the SER recorded from comparable electrode sites in two monkeys, while the lower portion of the figure illustrates the response from one electrode at the beginning of the experimental running of monkey G and after a period of four months. The similarity in waveshapes of these potentials reflects the reliability of the data. Standard errors as a function of time were computed for the SERs depicted in the lower portion of Figure 24. As seen in Figure 25, the waveform of the computed standard errors were similar and the maximal excursion which was observed was 8.4 μv.

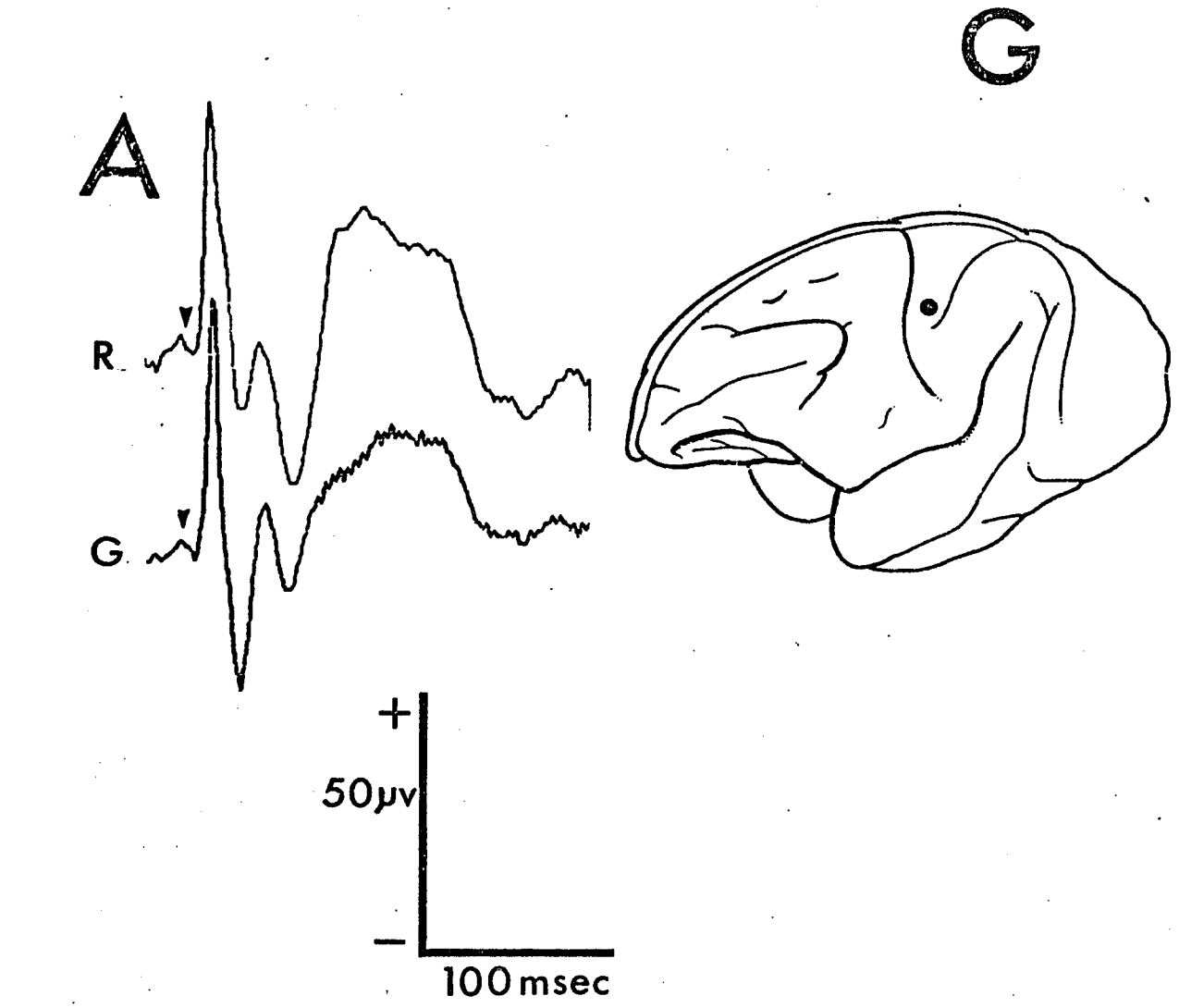
3. Intracortical Fields:

The intracerebral distribution of the contralateral SERs revealed a pattern which was more complex than that observed for the MPs. As inferred from the epidural distributions, two cortical areas were active following electrical stimulation of the forearm. The first generator was in the postcentral gyrus including Brodmann's

Figure 24:

A.) SERs recorded from comparable sites on two subjects. Monkey R and monkey G.

B.) Grand means of ten averaged SERs recorded from the same electrode on the first recording session and after a period of four months. Monkey G.


G
A
R
G
+
50μv
−
100 msec

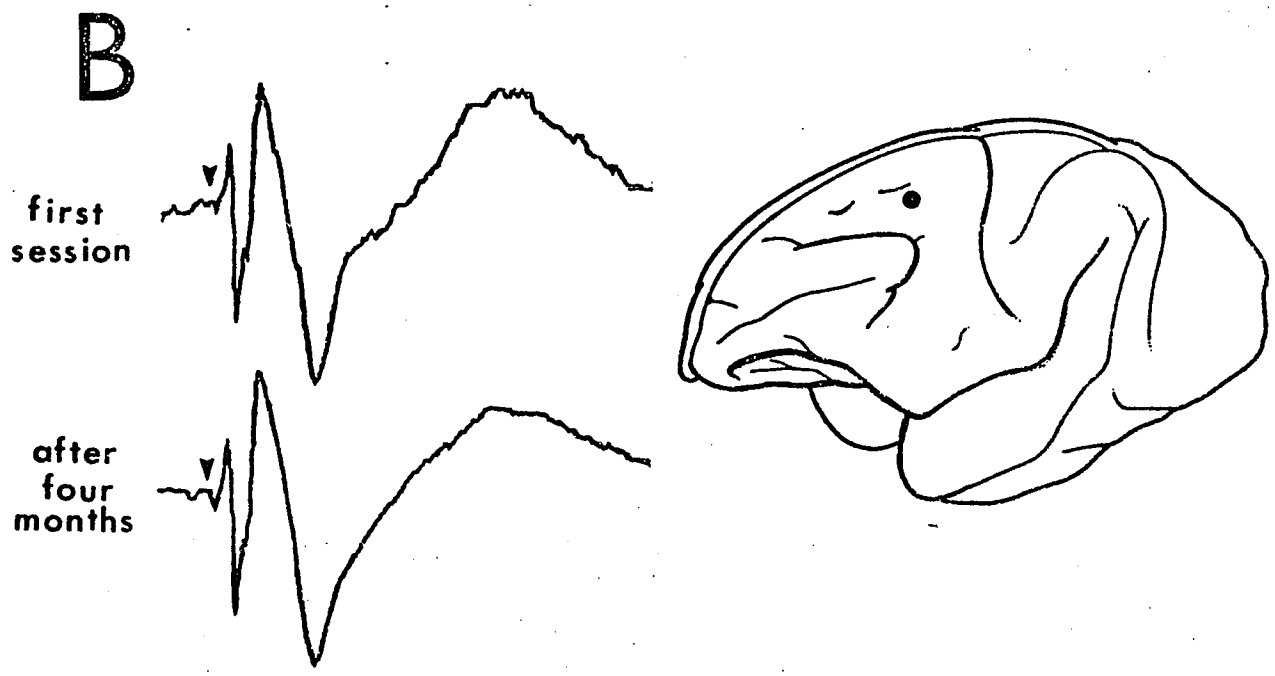
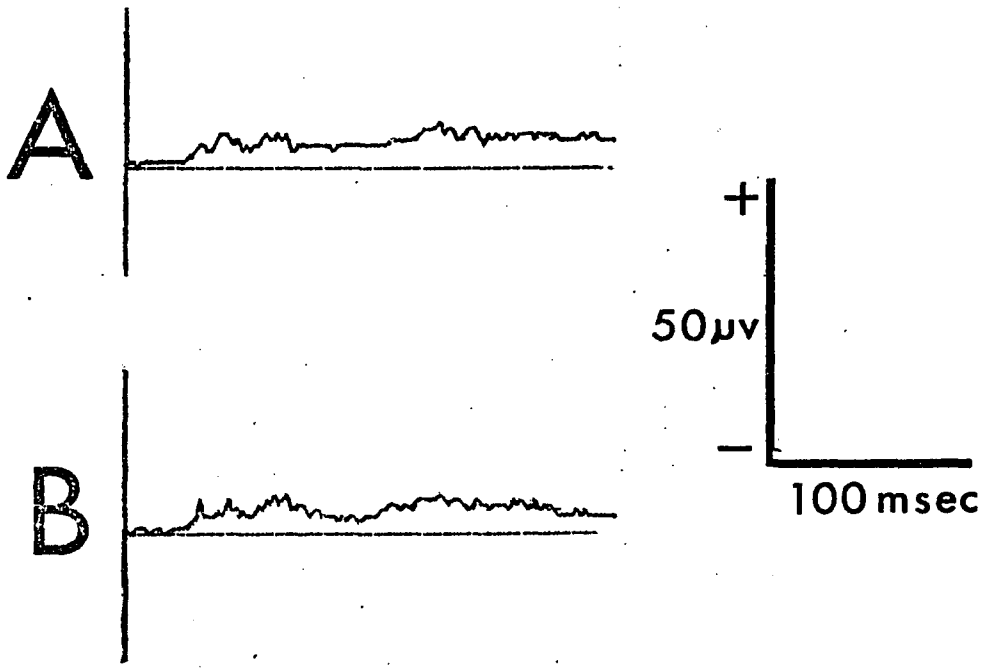

B
first session
after four months

Figure 25: Standard deviations of the grand means depicted in Figure 24. Monkey G.

G



areas 1, 2, 3, 3a and 5; while the second source of activity was located in the anterior bank of the central sulcus and in the posterior portion of the surface cortex of Brodmann's area 4 bordering this sulcus.

Transcortical recordings from Brodmann's area 1 (A in Figure 26) demonstrated a polarity inversion of each component of the SER which was recorded from the overlying dura. Laminar studies from this area (Figure 27) reveal that the 10.0 msec component of the postcentral SER inverted sharply across the fourth cortical layer. This component attained an extremely large amplitude in the depth recordings (approximately 200 μv). The unusual magnitude of the depth activity is consistent with the summation of convergent fields generated in the postcentral gyrus and in the posterior bank of the central sulcus. Transcortical recordings from Brodmann's area 5 (B in Figure 26) also showed an inversion of the 10.0 msec component but the amplitude of this activity was smaller than that detected in the more lateral and anterior areas of the postcentral gyrus. SERs from Brodmann's area 5 showed a predominance of longer latency components, including the surface negativity at 42.0 msec and the surface positive component at 100 msec. This activity inverted across the cortex of Brodmann's area 5 and attained a peak to peak amplitude in the depth recordings of more than 250 μv. The amplitude and distribution of N42 and P100 indicate that Brodmann's area 5 represents

Figure 26: Transcortical SERs recorded from the three indicated contralateral positions on the accompanying brain. Monkey R.

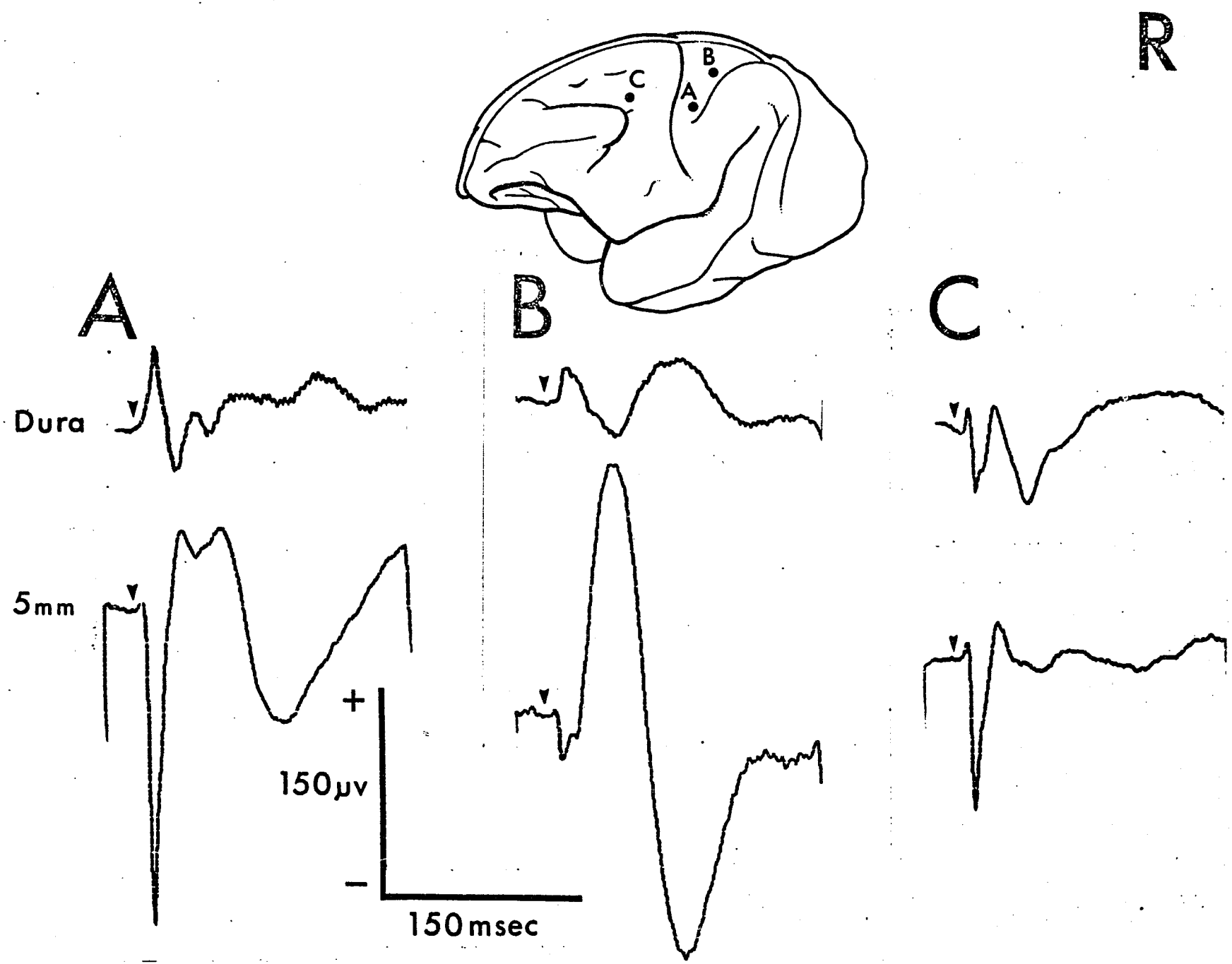
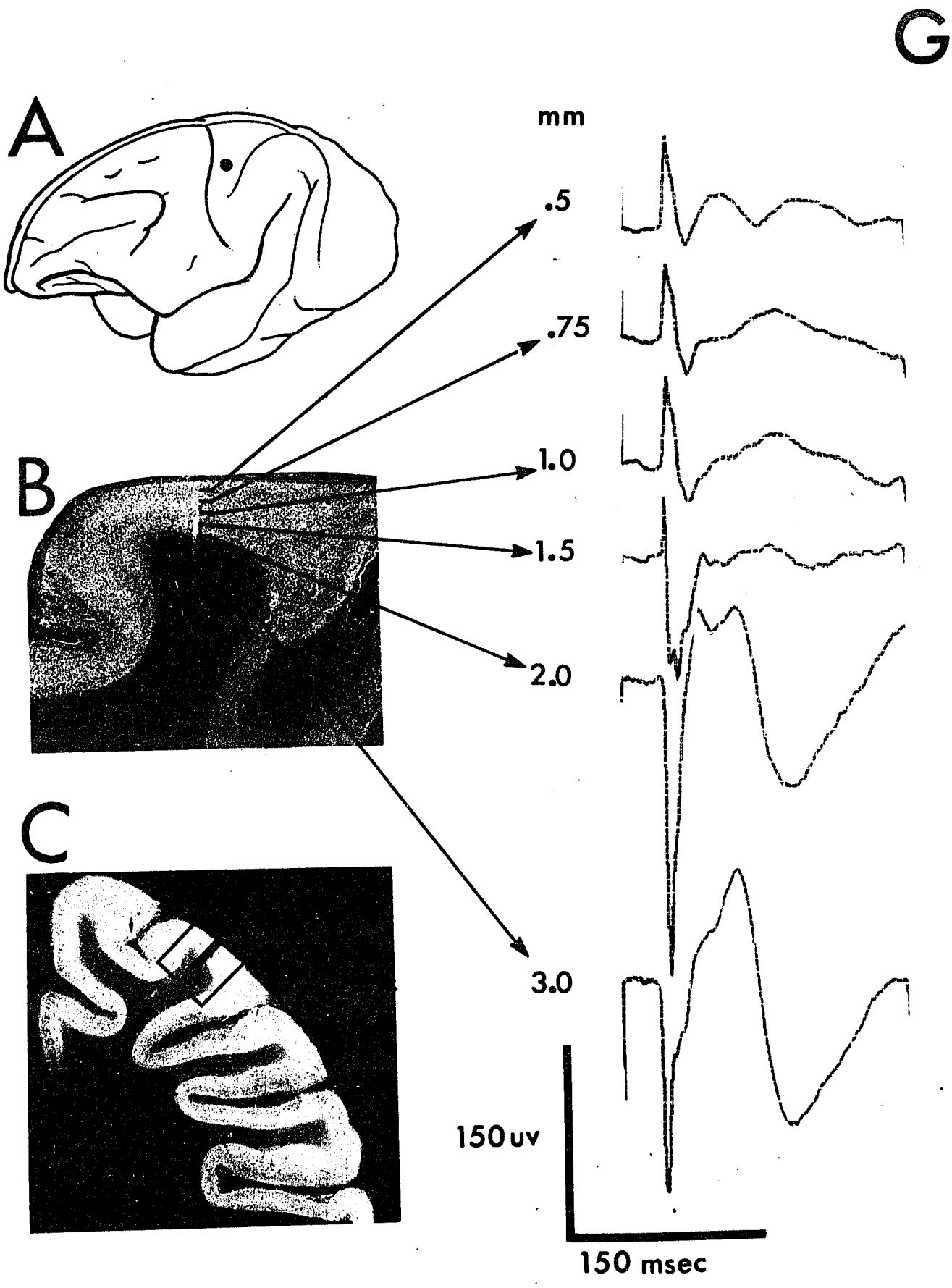

R
A
B
C
A
B
C
Dura
5mm
+
150μv
−
150msec

Figure 27: Intracortical SERs recorded from the postcentral gyrus. Note the inversion of the primary component between 1.0 and 1.5 mm. Monkey G.


G
A
B
C
mm
.5
.75
1.0
1.5
2.0
3.0
150 uv
150 msec

a major generator of these SER components.

None of the components displayed an inversion across the surface cortex of the anterior portion of the precentral gyrus, including most of Brodmann's area 4 and all of Brodmann's area 6. Both surface and depth waveforms at these sites revealed a similar pattern of early activity characterized by a negative potential with a peak latency of 12.0 msec (C in Figure 26). The morphological similarities of the dural and subcortical recordings indicated that this activity was mainly volume conducted. The fact that the components recorded in the depths of the cortex were larger than those of the overlying surface was consistent with the suggestion that this activity was generated by tissue in a sulcus.

Recordings from the cortex forming the anterior bank of the central sulcus and the posterior portion of the precentral gyrus, indicated that this tissue was the active source of the early components of the "frontal" SER. When this area is activated, the superior surface of the cortex generates a positive component at 12.0 msec while the inferior surface projects a negativity at this latency. Because of the orientation of the central sulcus the inferior field is projected anteriorly, medially and dorsally and the summation of this activity with that of the superior field of the postcentral generator accounts for the morphology and distribution of the SERs recorded anterior to the central sulcus.

4. Effects of Barbiturate Anesthesia:

Barbiturate anesthesia is known to suppress the later components of cortical evoked potentials and thus, it permits the identification of the primary activity. Under anesthesia all components of the SER except the positive potential at 10.0 msec and the negativity at 20.0 msec were abolished (Figure 28). The three epidural waveforms which characterized the unanesthetized SER were replaced by a single configuration which was maximal overlying the postcentral gyrus. The amplitude of the SER was rapidly reduced with increasing distance from the postcentral source although the absolute magnitude of the earliest component was only slightly reduced in the anesthetized state (approximately 75 percent). It appears, as expected, that the postcentral cortex represents the primary source of the recorded SERs and that the 10.0 msec activity represents the primary component of this response.

C. Electrical Stimulation of the Cerebral Cortex

Figure 29 presents a summary of the current thresholds and of the movements which were elicited by direct electrical stimulation through each of the recording electrodes fixed at a depth of 5 mm below the dura in monkey G. The pattern of movements obtained under anesthesia agreed with the well documented motor simunculus outlined by Woolsey et al. (1951). A portion of the precentral gyrus which corresponded to the classically defined hand area yielded the lowest response thresholds. Stimulation at these

Figure 28: Epidural SERs recorded under barbiturate anesthesia. Note the simplicity of the waveshapes and the similarity of each of the SERs. The arrows indicate the onset of stimulation. Monkey G.

G

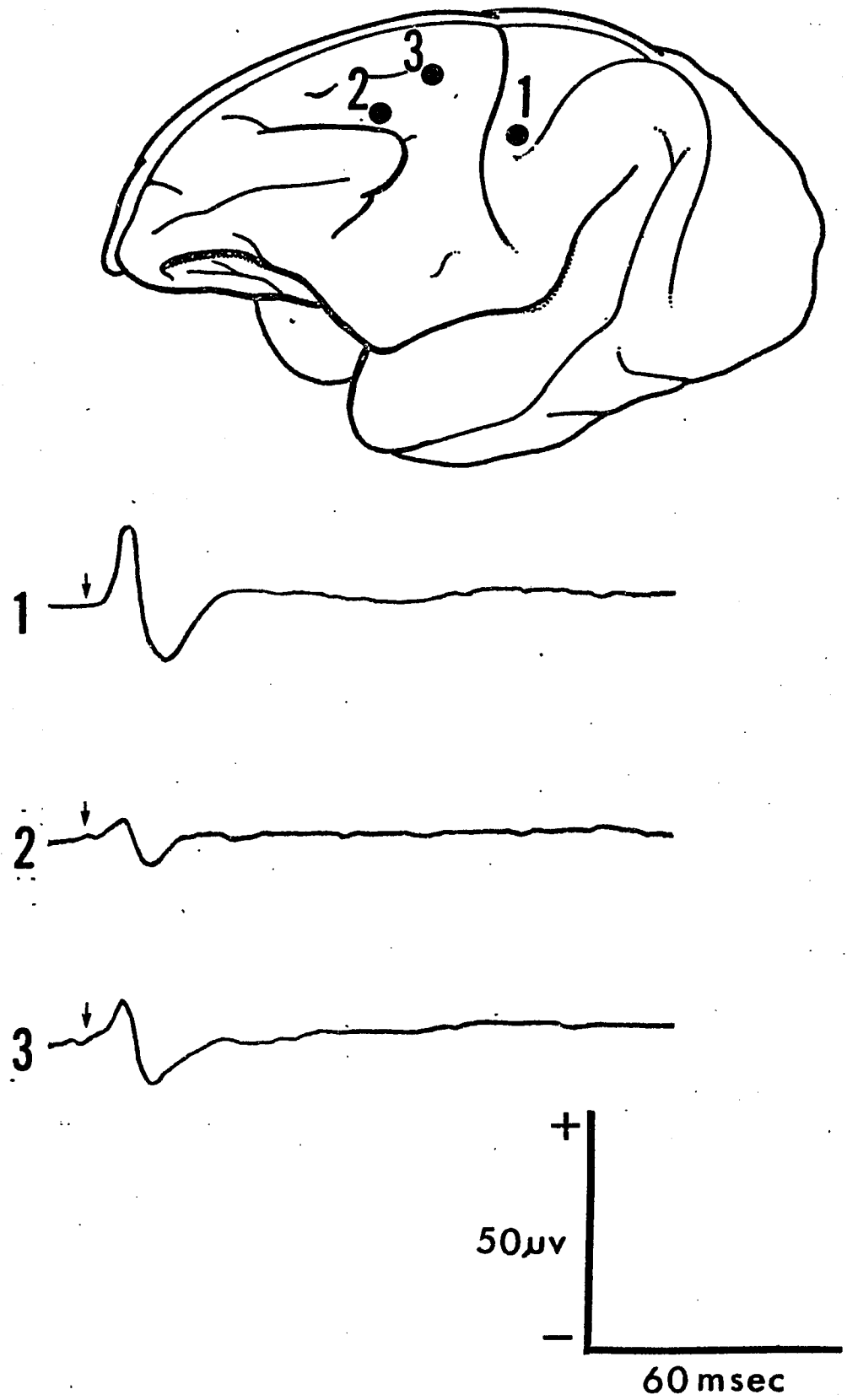
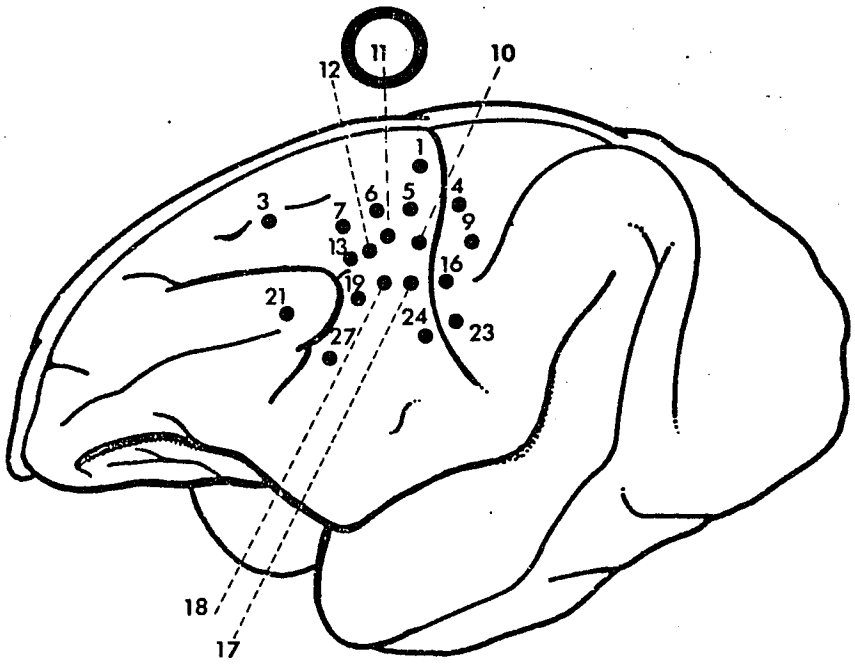


Figure 29: Thresholds and types of movements produced by direct application of electrical stimulation at each electrode site. The site which is circled had the lowest response threshold. Monkey G.



ELECTRODE	MOVEMENT	THRESHOLD CURRENT
1	Foot flexion	4.0 ma
3	None	5.0 ma
4	Trunk (generalized contraction)	4.2 ma
5	Hand and foot flexion	4.8 ma
6	Digit extension - forearm contraction	4.0 ma
7	None	5.0 ma
9	Forearm contraction-hand extension	5.0 ma
10	Forearm contraction-hand extension	2.7 ma
11	Forearm contraction - digit extension	2.1 ma
12	Thumb opposition	5.0 ma
13	None	5.0 ma
16	Thumb opposition	2.3 ma
17	Thumb opposition - forearm contraction	3.2 ma
18	Ear (twitch)	3.0 ma
19	Facial muscle contraction	5.0 ma
21	None	5.0 ma
23	Thumb opposition	3.5 ma
24	Thumb opposition	2.6 ma
27	Eye deviation	4.0 ma

sites resulted in movements of the contralateral hand and thumb, particularly thumb opposition. The specific electrode at which hand movements could be elicited using the lowest level of stimulation was the site at which the largest N2 component of the MP was recorded (Figure 29). Although stimulation to postcentral sites elicited hand and wrist movements the threshold for movement was often more than double that of precentral electrodes. The responsive area of cortex was encircled on all sides by regions which did not yield any overt movement following stimulation up to 5.0 ma. The data in the unanesthetized monkey revealed a similar pattern but the observed movements were more complex often involving several muscle groups and the thresholds for these movements were as little as 350 ua.

Chapter IV

DISCUSSION

The morphology, epidural distribution and sites of polarity inversion for each component of the motor potential (MP) have been examined in monkeys trained to perform self-paced wrist extension movements. The distributions were compared with corresponding data from human MP studies while the points of inversion were utilized to infer the location of the component sources as well as their relative intracortical depth. Figure 30 illustrates the position of the inferred sources of the contralateral MP on a single sagittal section. Due to the distribution of gross electrodes which was utilized in the present study, it was not possible to infer the precise boundaries of the sources and therefore, Figure 30 must be regarded as approximate.

The MP comprised three components which preceded the electromyographically defined onset of hand movements. These were a slow negative wave (N1), a small and inconsistent positivity (P1), and a phasic negative deflection (N2). N1 and N2 were maximal in amplitude over the contralateral precentral gyrus. These components shared a common source within the deep layers of the precentral gyrus and the anterior bank of the central sulcus. The source of N1 and N2 corresponded to the region from which hand movements could be elicited by low intensity

Figure 30: Summary of the locus and depth of the component generators of the contralateral MP illustrated on a para-sagittal section passing through the center of the N2, P2 and P3 epidural distributions.

N1, N2
P2
P3
P4

electrical stimulation of the cortex. P1 was not detected in the intracortical recordings. This component may have been generated in a small area which was not penetrated by the depth electrodes.

Immediately following the onset of muscle contraction the MP records contained a large positive peak designated P2. The epidural distribution of this component straddled the central sulcus and was considerably larger than that of the antecedent potentials. The sources of P2 included the surface cortex of almost the entire pre- and post-central gyrus, as well as cortex within the central sulcus. The intracortical depth of the P2 source corresponded to the approximate level of lamina 3 and 4.

The long latency components of the MP, which were designated P3 and P4 had not been identified previously. P3 was bilaterally distributed over the anterior parasagittal portion of the parietal lobe and was generated in Brodmann's area 5 and in portions of the posterior bank of the central sulcus. P4 was not seen in the epidural recordings but was identified in a small region surrounding the central sulcus. The source of this component is thought to be Brodmann's area 3a.

A. Comparison with Single Unit Studies

The activity of cortical neurons in association with voluntary movements of the monkey have been investigated in several studies

(Evarts, 1966, 1972, 1974; Kubota and Niki, 1971; Schmidt, Jost and Davis, 1974; Thach, 1975; Yumiya, Kubota and Asanuma, 1974). Although each study recorded from restricted areas of cortex, the combined results provide a description of the unit activity in cortical regions surrounding the central sulcus and also in frontal granular cortex.

Evarts (1966) demonstrated that many antidromically identified pyramidal tract neurons (PTN) increased their discharge rate prior to voluntary wrist movements in monkeys trained to perform a reaction time task. The fast conducting PTNs discharged 70 to 100 msec prior to the contraction and were almost exclusively located in the precentral gyrus contralateral to the moving hand. The distribution and timing of the N2 component of the gross MP in man suggests that this activity is related to PTN discharge (Gilden et al., 1966; Vaughan et al., 1968; and Vaughan et al., 1970). The polarity of N2 is also consistent with its proposed origin in pyramidal cells. Slefanis (1963) simultaneously recorded the intracellular potentials from PTNs and the somatosensory evoked potential from the surface cortex of cats and reported that surface negative evoked potentials represent excitatory post-synaptic activity in pyramidal motor units. This finding was supported by a later study (Jasper and Slefanis, 1965) in anesthetized cats in which the spontaneous discharges of pyramidal cells were, in most instances,

associated with a surface negative cortical potential.

The results of the present study are consistent with the suggestion that the N2 component is related to the occurrence of pyramidal cell discharge. Aside from confirming the observation that N2 precedes movement by a margin which is similar to that observed by Evarts for pyramidal units, the present study demonstrates that the source of N2 is located in the hand area of the precentral motor cortex (Brodmann's area 4) when a hand movement is involved. This region has the largest density of pyramidal cells and is also the site of the giant pyramidal cells of Betz (von Bonin and Bailey, 1947). In addition, the source of the N2 component was located in the deep layers of the cortex which contain the cell bodies of the large PTNs.

Evarts (1966) reported that some PTNs, located in the ipsilateral cortex, also increased their firing rate prior to hand movements in conditioned monkeys. This single cell activity presumably reflects the discharge of pyramidal axons which remain uncrossed. Verhaart (1970) reported that as many as 20 percent of PTNs do not decussate at any level of the neuroaxis in higher primates. The gross potential data is consistent with these findings in that a small portion of the ipsilateral precentral tissue was active prior to hand movements and the timing of this activity coincided with that of the

phasic N2 component in the contralateral cortex.

Schmidt et al. (1974) reported that 13 percent of the precentral units which they studied in the monkey displayed a gradual increase in firing which began at least 250 msec prior to EMG monitored wrist flexion or extension. Many of these "anticipatory units" also participated in the phasic pre-movement discharge which characteristically occurred 50 - 100 msec prior to EMG. The timing of the early unit activity suggests that it is related to the N1 component of the MP. The similarity in epidural distribution and points of inversion for N1 and N2 suggests a common cellular origin with the precentral gyrus.

The finding of both pre- and post-central sources for the P2 component is not consonant with the reports of Evarts (1972, 1974) on the single unit activity in these areas. Evarts' studies did not disclose spike activity from cells in the precentral cortex comparable in timing to P2 and, while the post-central unit activity begins at about the same time relative to the movement as does P2, it subsides earlier than the gross potential. Thus, the present study has identified a gross potential generated in both the pre- and post-central region for which there exists no presently demonstrated counterpart in single neuron recordings. This discrepancy points up the advantages of assessing the single cell and gross potential

data concurrently, since each technique provides information concerning a different aspect of neural activity within the region under study. Extracellular single unit recordings detect spike activity from a relatively small number of cells, while the gross potentials correspond to summated post-synaptic potentials generated by a large number of neurons (Creutzfeld, 1974). Since larger cells are more easily isolated for single cell analysis, unit studies are biased toward the sampling of these cells and may therefore fail to represent adequately the responses of smaller units. It is possible that the P2 component of the MP reflects post-synaptic activity of the smaller pre- and post-central neurons.

Single unit studies in the monkey have not identified spike activity which follows a voluntary movement at a latency corresponding to that of the late components of the gross MP (P3 and P4). This is in part due to the fact that investigators have been primarily concerned with the activity of precentral cells and have not examined units in Brodmann's area 5, which is the major source of the P3 component of the gross MP.

Yumiya et al. (1974) have examined units in Brodmann's area 3a, which the present study indicates is the source of P4, in relation to wrist movements in the monkey. The authors reported that some cells in this region respond during the lengthening of the wrist flexors while others were active

during the shortening phase of this muscle. The responsive units were determined to receive Ia afferents from the muscle spindles. Although the location of these cells corresponded to the source of P4, suggesting that they might participate in the generation of that component, the timing of these units with regard to the EMG did not coincide with the latency of P4 but rather with that of P2. It appears, therefore, that afferents from muscle spindles are primarily reflected in the P2 component of the MP which is also generated in Brodmann's area 3a.

B. Afferent - Efferent Cortical Interactions

One immediate consequence of any movement is the stimulation of skin, joint and muscle receptors. The afferent fibers activated by these receptors carry information concerning the position of the moving body part, the force against which it is moving, and the velocity of movement. In view of the fact that animals can adapt their movements to changing peripheral situations, such as differences in load, it is likely that peripheral sensory information is available to the central mechanisms of movement control. When tested by somatic stimulation or passive movement, the precentral gyrus of the monkey has been shown to receive a wide variety of afferents, both directly (Brooks and Stoney, 1971a) and through cortico - cortical connections with the postcentral region (Pandya and Kuypers, 1969). However, the effect of self-initiated movements on these afferents, as well as the role

they play in movement control, remains to be studied in behaving preparations.

Investigators of the MP have attempted to identify the component or components which reflect proprioceptive processing. In man, the P2 component of the MP is similar in appearance and distribution to the evoked potentials elicited by peripheral electrical stimulation (Vaughan et al., 1968) or by brisk passive movements of the extremities (Kornhuber and Deecke, 1965). Therefore it has been assumed that P2 represents kinesthetic feedback which is generated in peripheral receptors.

Vaughan et al. (1970) however, failed to find changes in the waveshape of the MP following deafferentation of monkeys trained to perform self-paced hand movements. This suggested that P2 was not exclusively associated with peripheral afferent feedback. Vaughan and colleagues indicated that peripheral information might be incorporated in the precentral MP during training, but might not be represented during the performance of well-trained repetitive movements. The authors however did not map the distribution of the P2 component and therefore they could not assess the effects of deafferentation on the extent of the P2 generators. Thus, it is possible that the dorsal rhizotomy constricted the cortical sources of this late component and was not detected at the particular precentral recording site utilized by Vaughan et al.

In this study, the possible contribution of somesthetic afferents to the P2 component of the MP was evaluated by comparing the sources of this activity with those of the SER. The primary component of the SER occurred at a peak latency of 10.0 msec and was generated in the central portion of the postcentral gyrus. Sources of later SER components were found in Brodmann's areas 1, 2, 3, 3a, 5 and in the posterior portion of the precentral gyrus. The anterior portion of the precentral gyrus, including Brodmann's area 6 and much of Brodmann's area 4, was not an active source for any SER component. The cortical sources of the MP P2 component extended to the arcuate sulcus and thus included precentral regions more extensive than the area activated by somatic stimulation. This finding was consistent with the suggestion of Vaughan et al. (1970), in that it indicates that P2 represents neural processing which is at least partially independent of reafferent somatosensory feedback reaching cortex. It might be suggested that the parameters of stimulation utilized in the present study were not sufficient to activate all of the cortical areas which receive somatic information. This appears unlikely however since the stimulation elicited a muscle contraction and therefore activated approximately the same skin, joint and muscle afferents which normally accompany a voluntary movement.

A substantial repertoire of movements are possible in deaffer-

ented preparations (Berman and Berman, 1973; Bossom, 1972; Taub and Berman, 1968). This suggests that a central source of information concerning the status of muscle activation during active movements is available to the motor centers of the cortex. Sperry (1950) theorized that an additional motor signal, the corollary discharge, was issued along with the corticospinal outflow, representing a central feedback mechanism. Such central feedback could be mediated by collaterals of pyramidal fibers which terminate in subcortical structures or by many other loops within the motor system (Eccles, 1968) and could reach cortical areas earlier than reafferent information from the periphery. This rapid feedback may be crucial for skilled movements such as piano playing. The P2 component of the MP follows the onset of movement, is resistant to deafferentation, and is at least partially generated in cortex which is not activated following peripheral somesthetic stimulation. These findings raise the possibility that the early portions of P2 in the precentral gyrus reflects the activation of a central feedback loop. This speculation can be experimentally tested by simultaneous recording of MPs from the cortex and from various subcortical nuclei in deafferented monkeys.

The P3 component of the MP is similar in polarity and timing to the P300 component which sometimes occurs in human sensory evoked potentials. P300 has been associated with "cognitive

functioning" such as information processing (Sutton, Braren and Zubin, 1965). It is unlikely that P3 represents the homologue of P300 in that the behavioral paradigm of the present study was not conducive to the elicitation of P300 and the P3 component of the MP remained stable both within and across sessions. The data of the present study rather suggests that P3 represents higher-order somatosensory processing. The source of this component is primarily Brodmann's area 5 which has been shown to have a distinctive somatosensory input in the alert monkey (Sakata, Takaoka, Kawarasaki and Shibutani, 1973). Cells in this area are driven by complex stimuli, involving both joint and skin receptors and they have ipsilateral receptor fields and long response latencies. The long latency of the P3 component in the present study (over 200 msec after the onset of movement) and its bilateral representation, are in conformity with the timing and spatial properties of Brodmann's area 5 responses to somesthetic input. Sakata et al. (1973) speculated that Brodmann's area 5 encodes information concerning body position, and the P3 component of the MP may reflect this processing.

A comparison of the sources of the MP and SER components indicates that most areas of the pre- and post-central gyrus are involved in both motor and sensory events during voluntary hand movements. In a series of studies which employed intra-

cortical single cell recordings and microstimulation, Asanuma and Rosen (1972a, b) examined afferent - efferent interactions within the precentral gyrus of the monkey. They reported that the motor cortex was organized in colonies which were made up of cells oriented in columns approximately 1 mm in diameter. Each column projected to a specific muscle group, particularly to the distal muscles of the hand and fingers, and the afferents reaching each column originated in the skin, joints and spindles which were activated by the same muscles. Asanuma & Rosen (1972a) reported that in a given precentral column the peripheral afferents terminate on the cortical cells in the second and third cortical lamina while the lowest threshold for elicitation of movements were found in layer 5.

It must be emphasized that Asanuma's research did not examine the activity which normally is associated with voluntary movement but rather inferred the organization of motor cortex based on responses to peripheral and cortical stimulation. The results of the present study appear to confirm the vertical processing of information within the cortex of behaving preparations. The sources of the individual components of the gross MP extensively overlap in the horizontal dimension but within a given area the components are generated at different cortical depths. Specifically, the antecedent components were found to invert across the deep cortical lamina, while the components

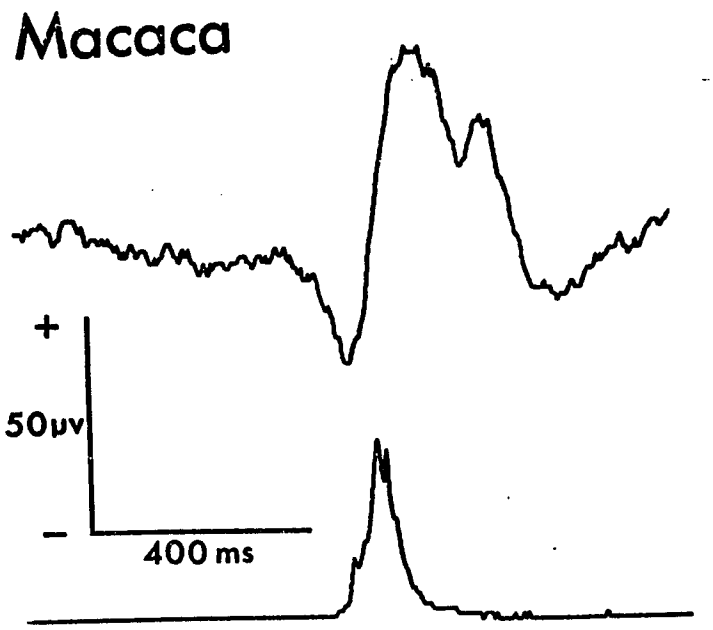
which followed the onset of contraction were generated more superficially. Asanuma and Rosen (1972b) showed that activation of cells in the upper layers of a column results in polysynaptic excitation of neurons located in the deep lamina of that same column and that there is little horizontal spread of activity.

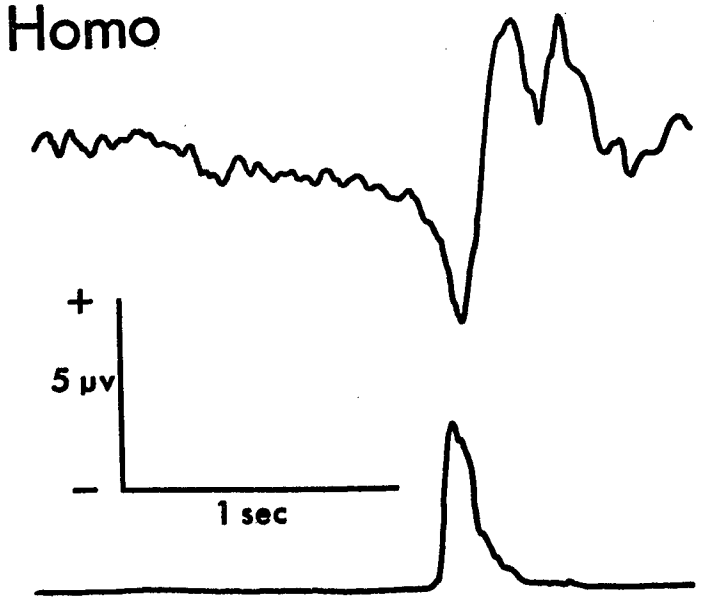
C. Comparison with Human Studies

Studies of the MP in man (Deecke et al., 1969; Deecke, Becker, Gronzinger, Scheid and Kornhuber, 1973; Gerbrandt et al., 1973; Gilden et al., 1966; Kornhuber and Deecke, 1965; Vaughan et al., 1968) have described a similar general waveshape, but have disagreed on the timing and topography of individual components. These discrepancies have been reflected in different designations of the MP components and in controversy as to their functional significance (Gerbrandt, 1974). The study by Gerbrandt et al. (1973) has even challenged the assertion that phasic pre-movement components of the MP can be identified and the authors have stated that they found no components which were primarily related to efferent processes.

MPs recorded from the dura of behaving monkeys are similar in morphology to those described for a self-paced hand movement in man by Gilden et al. (1966) and by Vaughan et al. (1968) as shown in Figure 31. The waveshapes of these potentials are virtually identical, but the duration of the MP as well

Figure 31: MPs associated with self-paced wrist extension movements recorded from the precentral area of the scalp of a human and the dura of a monkey. The rectified and averaged EMG is displayed below each MP. Note differences in time and amplitude scales. The human MP was originally presented in Arezzo and Vaughan, 1975.


Macaca
+
50μv
−
400 ms


Homo
+
5 μv
−
1 sec

as the muscle contraction is shorter in the monkey than in human subjects performing comparable movements. The similarity in the MP waveshapes extends through the long latency components. Although P3 has not been identified in the human studies, a review of the data presented by Vaughan et al. (1968) revealed that a late positive component corresponding to the P3 potential was in fact frequently present in the human MPs.

In the monkey, the onset of the N2 component precedes the onset of muscle contraction and the peak of this negativity occurs prior to the peak of the EMG. Thus, the timing of N2 in the monkey corresponds to that reported in the earlier human studies of Deecke et al. (1969), Gilden et al. (1966), and Vaughan et al. (1968), but conflicts with the findings of Gerbrandt et al. (1973). Gerbrandt and colleagues reported that N2 followed the movement and therefore, suggested that this activity might reflect somatosensory feedback to the postcentral gyrus. Gerbrandt (1974) indicated that the previous MP studies might not have sampled the earliest portion of the EMG activity and that they consequently erroneously concluded that N2 preceded the movement.

In fact, the discrepancies reported in the timing of the N2 component relative to the movement, may have resulted from differences in triggering methods. Gerbrandt et al. (1973) triggered their averages with a signal generated by a finger

movement across a photo cell, while the present study and the human studies by Deecke et al. (1969), Deecke et al. (1973), Gilden et al. (1966) and Vaughan et al. (1968), utilized the onset of EMG for synchronization. Costa, Vaughan and Gilden (1965) compared reaction times assessed by microswitch closure with those defined by the onset of the EMG response. The mechanical switch followed the EMG onset by 42 and 73 msec and there were large intersubject differences in the amount of lag. Similar data have been reported in monkeys trained to move a response lever (Evarts, 1972). Gerbrandt's triggering procedure would have introduced a delay in the identified time of movement onset and possibly a "time jitter" in the averaging process. These technical difficulties may have distorted the time relationships in his data.

The P1 component of the MP in the monkey corresponds to a similar wave which was identified in man by Vaughan et al. (1968). This activity seems to differ from the pre-motion positivity (PMP) identified by Deecke et al. (1969) and Deecke et al. (1973). The issue is confused however by discrepant descriptions of the PMP in the two papers. In their earlier study, Deecke and colleagues (1969) defined the PMP as a small and inconsistent potential which occurred prior to the onset of N2 and which was terminated by that negativity. In 1973, however, Deecke et al. described the PMP as a component which

immediately preceded the EMG and continued as a positivity after the onset of contraction. The authors assigned great importance to this wave, suggesting that it might represent the electrophysiological expression of the "command" to initiate movement. Analysis of the MPs in the monkey suggests that the human PMP, as defined in the more recent paper (Deecke et al. 1973), may reflect the earliest portion of the P2 potential which is revealed in areas where N2 does not mask this activity. This assumption is consistent with the distribution data reported by Deecke et al. (1973) which indicated that the PMP was largest over the parietal lobe. In the monkey, this area was characterized by a relatively small N2 and a large P2 component.

The cortical distributions of MP components could be examined in greater detail in the monkey than in human studies since epidural electrodes could be more closely spaced than scalp placements. The neuroelectric potentials also display a greater spread on the scalp than on the dura due to the impedance of the tissue which intervenes between the cortex and scalp. Taking into account these differences, the spatial distributions of the epidural MP in the monkey corresponds rather closely to the MP topography recorded from the human scalp, as described by Vaughan et al. (1968).

Vaughan et al. (1968) reported that the N1, N2 and P2 components of the MP were largest in amplitude overlying the contralateral hemisphere. The interhemispheric asymmetries for N1 and

N2 were subsequently questioned (Deecke et al., 1969). In the present study each component of the contralateral MP recorded in the monkey, with the exception of P3, was more than twice the amplitude of the corresponding ipsilateral potential. In the monkeys, the spatial extent of the ipsilateral distributions were also reduced.

Vaughan et al. (1968) and Deecke et al. (1969) reported that the N2 component was maximal in amplitude over the contralateral precentral gyrus and on this basis, Vaughan and colleagues proposed that the N2 component was generated in the classically defined motor cortex. Gerbrandt et al. (1973) however indicated that N2 was distributed more anteriorly and was largest over the contralateral pre-motor areas. The findings of the present study are concordant with the conclusion of Vaughan et al.

The distribution of the P2 component has received less detailed attention in the human studies. Deecke et al. (1969) did not map this late activity while Vaughan et al. (1968) measured P2 as the peak to peak amplitude of the N2 - P2 deflection. Vaughan and colleagues reported that P2 displayed a similar, but somewhat more widespread, distribution than the antecedent negativity and suggested that the generators of these potentials were coextensive. The present study shows that, in the monkey, the P2 component has a considerably wider epidural distribution than does N2 and that its source lies

within both the pre- and post-central gyri. Thus, it appears that a column of precentral cells, oriented perpendicular to the surface of the cortex, participates in the initiation of a voluntary movement and, at a different intracortical level, in the processing of the information which results from that movement.

D. Cortical Functional Organization

Studies of the motor system must be designed so as to carefully consider the type of movement examined as well as the circumstances in which it is emitted. Among the more obvious considerations is whether the movement involves primarily the distal or the proximal musculature and whether it is self-initiated or not. The findings of the present study apply to self-paced hand movements and the extrapolation of these results to other types of movement may not be justified.

As previously stated, the N2 component of the MP is believed to be associated with the activation of PTNs. The localized and discrete nature of the generator of this component may appear somewhat surprising in view of the identification of more extensive cortical motor regions, including the supplementary motor area and pre-motor area (Woolsey, 1958). Furthermore, a substantial number of pyramidal fibers originate from regions other than the precentral gyrus (Towe, 1973). The use of hand movements

is an important consideration for understanding this aspect of the present results. Stimulation of both the pre-motor and supplementary motor area of the monkey results in complex movements which are generally confined to the axial musculature (Woolsey et al., 1951). This suggests that these areas of cortex may not be intimately involved in the control of distal movements of the extremities. The results of the present study support this conclusion by demonstrating that motor regions anterior to Brodmann's area 4 are not active prior to hand movements.

As for the pyramidal tract, this corticofugal bundle is composed of approximately 400,000 fibers in the macaque, 90 percent of which are less than 3.0 u in diameter (Towe, 1973). The larger pyramidal cells, which give rise to fibers of 6.0 to 12.0 u are exclusively located in that portion of the precentral gyrus roughly corresponding to the generator of the N2 component of the MP. The larger pyramidal cells have been linked to phasic movements of the distal musculature because of their fast conduction velocities and their mono-synaptic connections with spinal alpha motor neurons (Wiesendanger, 1969). The electrophysiological evidence presented here is consistent with the importance of the "fast pyramidal cells" in the initiation of hand movements.

Interhemispheric asymmetries in the MP components may be

directly related to the use of distal rather than proximal movements in the present study. Brinkman and Kuypers (1972) demonstrated in split-brain monkeys that discrete movements of the extremities were wholly dependent on the integrity of the corticofugal projections from the contralateral hemisphere, while proximal movements could be adequately controlled by the ipsilateral cortex. Thus in the monkey, hand movements appear to be mainly directed by the contralateral cortex. This is reflected in the small amplitude of the ipsilateral MP and by the complete absence of the N1 component over the ipsilateral hemisphere.

In the present study, MPs were not generated in any portion of the frontal granular cortex. However, Kubota and Niki (1971) and Niki, Sakata and Kubota (1972) also using monkeys, found that cortical cells bordering the sulcus principalis discharged prior to a lever pressing response in a delayed alternation task. This discrepancy might reflect the different behavioral paradigms under which movements were performed. Thus, an additional cellular population may be involved in motor programming in the delayed alternation task as opposed to self-paced movements.

The timing of cortical processes is influenced by the circumstances of movement initiation. In a self-paced task cells in the precentral gyrus begin to respond as early as 300 msec prior to a muscle contraction (Schmidt et al., 1974). This is

considerably earlier than reported in the reaction time studies of Evarts (1966; 1972; and 1974) and Thach (1975) in which monkeys responded to an external signal.

These differences in the onset of change in firing rate of precentral neurons in externally signaled as opposed to self-paced movements presumably reflect the differences in motor set which are present in the two experimental conditions. In the case of self-paced movements, the cortex appears to be involved in a "priming" process which precedes the contraction by a substantial period. In contrast, a more stable "motor set", possibly influencing the level of spinal motor neuron excitability, can be established in an RT task.

Correlates of the cortical preparatory process have been reported in human scalp-recorded potentials. Walter, Cooper, Aldridge, McCallum and Winter (1964) reported the occurrence of a slow negative shift, which they called the "contingent negative variation" (CNV), during the foreperiod of an RT task. Similar negative shifts were subsequently found in the monkey by Low, Borda and Kellaway (1966). These workers emphasized the psychological constructs of contingent association such as expectancy, arousal and motivation. However, Kornhuber and Deecke (1965) and Gilden et al. (1966) found that a negative shift, similar in its time course to the CNV, preceded self-paced movements. These observations indicated

that the contingent association (or conditioning) originally emphasized by Walter et al. was not a necessary condition for the appearance of a pre-movement negative shift. In a later topographic study, Vaughan et al. (1968) reported that the N1 component of the MP was maximal in amplitude over the contralateral precentral region. This finding indicated that N1 was specifically associated with motor preparation, and conflicts with suggestions that N1 was related to arousal mechanisms (Gerbrandt et al. 1973) or to motivation (Deecke et al., 1973). The motor specificity of the N1 component of the human MP was supported by the recent study by Kutas and Donchin (1974) which confirmed the contralateral preponderance of N1 and found its amplitude to be affected principally by movement parameters. The present investigation has firmly established that the cortical generators of the slow pre-movement component N1, as well as the phasic component N2, are coextensive in the precentral motor cortex.

Thus, it appears that N1 reflects cortical processes associated with the preparation for executing a specific movement. Furthermore, the timing of its onset indicates that the precentral cortex must be involved in the early phases of processes leading to the initiation of self-paced movements. For this type of movement, the proposal that motor cortex is activated late in a sequence of events which is initiated in the cerebellum

(Holmes, 1939) or in the limbic system (Vanderwolf, 1971) seems untenable.

It seems that the search for a single "center" which initiates voluntary movement is incompatible with what is known of the complex organization of the motor system and with the varied circumstances under which movements are performed. The results of the present study certainly should not be taken to mean that self-paced movements are initiated solely by mechanisms localized within the precentral motor cortex. It is probable that the cortical neuronal activity reflected in the N1 and N2 MP components is merely one aspect of activity within a complex neural system which includes both cortex and a number of subcortical structures. The identity of these structures and the dynamic features of neural activity within them remains largely unstudied in behaving animals.

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