MAGNETIC AND ELECTRIC FIELD MEASUREMENTS OF BRAIN ACTIVITY PRECEDING VOLUNTARY MOVEMENTS: IMPLICATIONS FOR SUPPLEMENTARY MOTOR AREA FUNCTION

by

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ABSTRACT

Recent investigations have indicated that self-paced, "voluntary" movements in humans are preceded by a slow electrical shift over the scalp (known as the Bereitschaftspotential or readiness potential) which is correlated with slow magnetic field changes also recorded at the scalp surface. An accumulation of evidence from a variety of experimental techniques in humans and primates indicates that two important areas of cortex may give rise to such activity; the supplementary motor area (SMA) of the mesial frontal lobe, and the contralateral primary motor cortex (MI).

In order to explore the possibility of discriminating underlying sources of pre-movement brain activity, neuromagnetic (MEG) and EEG activity was monitored during simple and patterned (sequential) movements of the digits in five right-handed subjects. Topographical analysis (spatio-temporal mapping) and current dipole source modelling was performed in order to test the hypothesis that separate cortical generators (MI and SMA) could be identified during the period immediately preceding voluntary movement. An iterative least-squares dipole fitting routine was applied to the source configurations suggested by the topographical maps in order to determine the extent to which such sources could account for the observed data.

Field reversals were observed over both contralateral and ipsilateral Rolandic areas for the period preceding movement initiation as measured by onset of forearm electromyograph (EMG) activity. In some subjects, additional activity in frontocentral areas preceding movement also contributed to the entire pattern of activity over the scalp. Following EMG onset, field reversals could be observed over somatosensory cortex contralateral to the side of movement, corresponding to a proprioceptively-evoked response to finger movement. Laplacian analysis of EEG activity in the same subjects showed current source-sink reversals which were orthogonal to the magnetic field reversals for the above components. Observed patterns suggested that multiple sources configurations may be necessary in order to best account

for the observed patterns and due to the observed bilaterality of pre-movement slow fields premotor sources could not be identified using a two dipole solution. These findings are discussed with regard to previous interpetations of pre-movement brain activity and its relationship to the preparation and initiation of voluntary movement.

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PART A

INTRODUCTION

I. THEORETICAL BACKGROUND

Throughout the history of psychology there has been great interest in the way in which the human brain processes sensory information and the underlying neural mechanisms involved in the the "mind's" apprehension of the outside world. Indeed, much of psychology has its roots in the study of sensation and perception. Accordingly, within the newer field of psychophysiology a great deal of research has focussed on the neurophysiological mechanisms underlying vision, hearing, touch and other aspects of sensory or perceptual processes. Less well understood are the "output" systems of the CNS and their role in various aspects of behaviour such as consciousness, attention and awareness, motivational processes, or even features of affect or personality, i.e., those brain systems involved in the intention or preparation to *act on* the outside world. Although a great deal has been learned about the effectors of the human body, principally the skeletomotor system and its inherent control mechanisms, there are only rudimentary models of the higher control mechanisms governing complex movement, such as the "programming" of motor skills, or other cognitive aspects of complex motor output. The ability to study brain processes associated with volitional aspects of movement provides an interesting avenue for the further understanding of mind/brain relationships and the cognition of motor processes. The following thesis represents an attempt to explore further the application of new methodologies to these aims.

In order to understand the neurophysiological mechanisms underlying the control of movement or movement preparation, it is necessary to consider the many cortical and subcortical motor systems of the brain. These systems are complex in their connectivities, neurochemistry, and patterns of activity. The major components of the motor system of the central nervous system are the primary motor cortices (Brodmann's area 4) which project contralaterally to the effectors of the skeletomotor system -- the so-called *pyramidal system* -- and

the various *extrapyramidal* motor systems which include: cortical areas converging on this system with reciprocal connections (premotor cortex and supplementary motor areas), the basal ganglia, cerebellum, and reticular motor structures (subthalamic nucleus, substantia nigra). These latter structures are thought to receive input from cortex and subsequently exert a "reentrant" influence on cortical motor structures via the motor nuclei of the thalamus.

In recent years, there has been an accumulation of evidence from clinical and experimental studies regarding the role of various brain systems involved in the preparation and initiation of movement. Much of this evidence points to an important role for the region of mesial frontal lobes, known as the supplementary motor area (SMA), in these processes. This brain region appears to be implicated in the preparatory processes for discrete movements of the peripheral musculature, particularly if these movements are spontaneous and "voluntary" in nature. The SMA is also thought to participate in the "programming" aspect of complex, learned movements. Its connections with motivational subsystems of the brain, notably septo-hippocampal pathways of the limbic system, indicates that it may be involved in conveying plans and intentional states to the motor executive apparatus of the cortex. Individuals with lesions to the SMA often show a loss of spontaneity of movement and speech (for left SMA lesions), and in some cases loss of "voluntary" control over the affected limb. The models of SMA function in motor preparation and programming based on these findings, discussed in further detail in the following section, should be of great theoretical interest to both students of motor behaviour and those interested in the biological basis of volitional processes in humans in general. Such theories could advance significantly the understanding of the physiological systems mediating cognitive processes, such as, preparation to act, planning, intention, motivation, and so on, as well as help elucidate the temporal organization of cerebral processes regulating the transformation of sensory input to motor output. In order to clarify the theoretical assumptions underlying the kinds of motor tasks used in the following experimental study and those brain structures that may be expected to play an important role in these

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behaviours, the following section provides a brief review of the present theories regarding the role of motor systems in the brain, and in particular, the existing evidence for the important role played by the supplementary motor area in these systems.

Motor Systems of the Central Nervous System

The Pyramidal System

It is known that, in humans, the precentral gyrus (Brodmann's area 4) is specifically involved in motor control and provides a large proportion (but not all) of the descending input to the spinal motor apparatus via projections to the alpha and gamma motoneurones (referred to as the "segmental" neuronal pool) which have their cell bodies somatotopically arranged in the ventral horns of the spinal cord. These projections are traditionally referred to as the "pyramidal system" (so named because the fibers pass through the medullary pyramids) and is roughly synonymous with the *corticospinal* and *corticobulbar* tracts. Damage to this system is highly correlated with loss of motor function (paralysis) and associated symptoms of a so-called upper motor neuron lesion (spasticity, rigidity, clonus, etc.). This leads to the conclusion that this system comprises the main output to spinal motor structures from central motor systems. However, it is known that there are many groups of descending pathways innervating the segmental motoneurones as well as a great deal of integration within and between segmental neuronal pools via short ascending and descending interneurons. Pathways arising from brainstem structures and descending in the ventromedial portion of the cord (vestibulospinal, tectospinal and reticulospinal tracts) terminate on motoneurones innervating proximal musculature and most likely play a role in balance and postural mechanisms. Pathways arising from the midbrain (rubrospinal tract) and cortex (corticospinal tract) descend in the dorsolateral cord and are more involved in the innervation of distal musculature, innervate smaller numbers of spinal segments, and show a somatotopic organization in the their terminations in the ventral horns. A main distinguishing feature of the human motor system is the well-developed innervation of the corticospinal tracts to the motoneuronal pool, and their role in *fractionated* movements of the distal musculature. Although the paralysis that results from damage to this system may be interpreted as indicating its primacy for motor control, it must be remembered that there are many other motor systems which are also involved in muscular function as is evidenced by the effects of

transections at various levels of the neuraxis. As noted by Hughlings Jackson the rigidities (e.g., decorticate rigidity) which result from these transections as well as other positive or "release" signs which result from damage to the pyramidal system (or are present at birth prior to myelination of the tracts such as the Babinski response), indicate a strong inhibitory influence of these descending pathways on spinal motor structures. It should also be noted that clinical lesions will seldom interrupt only corticospinal pathways, thus, it is difficult to interpret the role of this system from the symptoms which are observed clinically.

Another feature of corticospinal systems in motor control is that there is an increasing development of these systems phylogenetically -- only mammals seem to possess a pyramidal system (see Bizzi & Evarts, 1972) -- and as one ascends the "phylogenetic scale" one notes an increased segregation of distinct somatosensory and motor distributions in pericentral cortex as well as a greater amount of direct innervation of the motoneuronal pool by corticofugal fibers (Ghez, 1985). Thus, as one proceeds from carnivores, to lower primates, to apes, to humans, there is observed a progression from termination of corticospinal neurons in the dorsal regions of the central gray to termination in the ventral horns directly on motoneurones. Concomitantly, there is a trend towards an increased severity of motor loss resulting from damage to the corticospinal tracts with a corresponding decrease in functional recovery following ablation of area 4 in various species (Goldberger, 1974; Carpenter, 1985; Carew, 1985).

In regard to the phylogeny of the role of motor cortex in motor control, Towe (in Bizzi & Evarts, 1972) makes the following statements.

> All vertebrates move, no matter how little cerebral tissue they may possess, and they continue to move after cerebral insult ... only mammals possess a pyramidal tract, but all continue to move after it has been transected ... Further, the motor consequences of cerebral stimulation are altered little ... or not at all [in the domestic cat] following transection of the medullary pyramids ... In the face of these observations alone, one can hardly assign a primary role to the cerebral cortex, and particularly the pyramidal tract, in the initiation and control of movement. Nonetheless, the cerebral cortex clearly *is* involved in the regulation of behavior, and perhaps even movement. (pp. 42-43)

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This perspective on the relative efficacy of the corticospinal motor system has led many to question its exact role in various aspects of both reflexive and voluntary movement. Nevertheless, it is generally agreed that this system is structurally, the closest to the spinal apparatus and, functionally, the lowest in the hierarchy of cortical motor systems. Thus, the pyramidal system arising from cortex in humans is presently seen as a phylogenetically recent development by which cortical structures are able to exert direct control over already somewhat complicated spinal motor structures, particularly for the elaboration of fractionated movements of the hands and digits (cf. Wise & Evarts, 1981). It should also be noted that only about 30% of the corticospinal tract in humans arises from the precentral gyrus; a large proportion arises from post-central cortex, particularly areas 3, 1 and 2 (about 40%) and the rest (about 30%) from the premotor area (Carpenter, 1985). Thus, there is a large degree of input from widespread areas of peri-central cortex converging on this descending system resulting in some (as yet largely unknown) degree of integration in the ventral horns of the spinal cord and brainstem structures.

Many questions regarding the role of motor cortex in movement have, of course, focussed on the representation of the musculature in the motor and premotor cortices and how this relates to specific movements in space. Although it is known that there is a somatotopic organization of the body in the precentral gyrus, it is not clear as to how this localization of function relates to complex movements. Asanuma (1975) found that small circumscribed groupings of cells in the cat's motor cortex could activate single muscle units -- referred to as corticomotoneuronal (CM) "colonies". However, Phillips (1981) has emphasized that these "hot-spots" (Phillips & Porter, 1977) may indicate a columnar-like organization of cells in motor cortex but notes that these may be due to low-threshold regions of highly intermingled groupings of cells which could be accounted for in other ways. Phillips suggests that functional groupings of CM cells may be by necessity composed of overlapping projection areas and intermingling cortical modules stating that, "a mosaic in which each block contained the entire output for a specific movement at a specific joint, might

make for a good puppet but a poor violinist or ballet dancer" (p. 92).

"Primary motor" versus "sensorimotor" cortex

The arguments presented above would seem to indicate that although the motor cortex (area 4) in humans is found to have direct interactions with spinal motor structures, it does not have the "primary" role in motor control as once thought. The additional observations that the descending motor pathways comprising the pyramidal system arise from somatosensory areas of the postcentral gyrus and that there is a great deal of reciprocal innervation of these two regions of cortex, has led to the adoption of the concept of a "sensorimotor" cortex. This concept is related to the general agreement that the elaboration of the pericentral cortex in humans represents a recent evolutionary development of an area of cortex, specialized for the coordination of fine distal limb movements which were of some presumable adaptive significance for the species, such as using tools or language (Wise & Evarts, 1981). Sanides (1970) suggests that this was a necessary development in order to free the forelimbs from their role in tetrapod function, by producing a new sensorimotor representation[1]. In describing the evolutionary development of the primate brain, Sanides outlines three major outgrowths in the expansion of the neocortical mantle from the para-limbic, para-insular and pericentral regions, respectively, giving rise to various cortical representations for motor functions, of which the primary motor cortex represents an expansion of the pericentral regions anteriorly, and is the most recent outgrowth. The regions separating the pre- and postcentral gyri in higher primates appears as more of a transition zone between two areas rather than an abrupt border. The region of transition (area 3a) has been studied extensively in cats and monkeys, however, this has produced somewhat contradictory information regarding its relative role in sensory or motor function. There is input to this area from both muscle afferents and

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[1]As noted by Goldberg (1985) the dolphin, which possesses a highly convoluted cortical mantle, yet has not undergone an evolutionary transition to fine control of distal musculature, shows no development of an architectonic area resembling area 4 (Morgane, Galaburda & Jacobs, 1983).

motor cortex, and it in turn sends projections to area 1, but not directly to precentral gyrus (see Jones & Porter, 1980). Neurons in both the precentral and postcentral gyri receive afferent projections from receptors in the forelimb, as well, there are many projections from sensory cortex (areas 1 and 2) and parietal association areas (area 5) to the precentral gyrus (see Brinkman, 1981 for review).

The conceptualization of "sensorimotor" cortex has also proved to be somewhat problematic, in that this implies that this would constitute a CNS structure for converting sensory input to motor output. Although this is true, to some extent, in the case of transcortical reflex loops, it should be acknowledged that there is a great deal of input from many cortical and subcortical areas converging on the descending motor systems, including the reentrant motor functions of the basal ganglia and cerebellum acting on the motor cortex via thalamus. Accordingly, many object to the use of the terms *sensory* and *motor* in describing the interaction of the pre- and postcentral gyri since both have sensory and motor function (see Evarts, 1972). Nevertheless, it would appear that there is some justification for distinguishing these two brain regions in humans, if only due to the differential effects of lesions in these areas (i.e., paresis or sensory loss).

Extrapyramidal Motor Systems

Any discussion of motor control systems in the brain must address the significant role played by the many subcortical structures involved in movement. These structures act on the descending input to the spinal motor apparatus either by converging on the pyramidal system through motor cortex as described above or directly on motor structures in the brain stem (e.g., red nucleus of midbrain), and are referred to collectively as the *extrapyramidal system*. Structures such the basal ganglia and cerebellum which receive a wide variety of input from cortical and spinal structures, exert what is sometimes referred to as "reentrant" input to the motor cortex via the motor nuclei of the thalamus (ventral anterior (VA) and ventral lateral (VL)), which, in turn, project to the motor and premotor cortices.

Other regions of cortex involved in movement control and preparation (motor "association" cortex) include the premotor and supplementary motor areas (Brodmann's area 6) and regions of the parietal lobe. The basal ganglia (caudate nucleus, putamen, and globus pallidus), cerebellum and their related structures are known to be important in controlling motor ouput as evidenced by their complex connectivities to motor cortex and premotor cortex. The motor dysfunctions resulting from damage to these systems (dyskinesias resulting from basal ganglia disorders such as Parkinsonism and choreiform disorders, and ataxia and tremor resulting from cerebellar damage) point to their important roles in motor control, particularly for "smoothing" and refining complex movements. The findings that there are neural discharges prior to discrete movements in both basal ganglia (DeLong, 1974) and cerebellum (Thach, 1970) indicate that these structures may also be involved in the preparation and programming of movement.

Recent studies have indicated that there are a number of parallel subsystems within the basal ganglia subserving a number of different roles in sensorimotor integration (for review see Alexander, DeLong & Strick, 1986). The caudate nucleus and putamen (neostriatum) receive input from widespread areas of cortex and project to the pallidal segments which, in turn, send projections to thalamic motor nuclei which, in turn, project back to motor cortex. These two pathways are thought to form separate reentrant paths or "loops" related to the preparation for movement -- a "motor" (sensorimotor cortex - putamen - VL - SMA) loop related to motor functions and a "complex" (association cortex - caudate - VA - frontal cortex) loop related to complex behavioural functions -- both of which maintain separate, non-overlapping topographically organized input from cortex which is relayed via separate thalamic relay nuclei to separate regions of motor cortex (DeLong, 1985). Thus, rather than a "funnelling" of cortical input to the basal ganglia and thence to motor cortex there is a "maintained segregation of information relevant to motor and 'complex' functions". Interestingly, output of the motor loop projects more to premotor regions than to area 4. This pathway receives input from sensorimotor cortex and possibly provides information to SMA for the amplitude scaling of presently selected

motor programs. The caudate loop, on the other hand, receives a wide variety of input from cortex and relays this information to prefrontal cortex and may represent a "higher" level of motor organization conveying information related to plans and intent, and functions in parallel to the motor loop (see Brooks, 1986).

The cerebellum, long known to play an important role in motor control, particularly, in the control of posture, balance and in feedback control of learned movements, may also participate in the preparation for movement as evidenced by the activation of dentate neurons prior to movement (Thach, 1970). As in the basal ganglia, the cerebellum is also thought to operate through two separate loops or pathways; one loop consisting of input from the "newer" lateral cerebellum to motor cortex similar to the putamen loop of the basal ganglia, and a second loop involving the older, medial cerebellum which is involved in feeback control of ongoing movements, and sends information to lower levels of the motor output system (MI, red nucleus) or directly to spinal cord. This latter system involves the use of somatosensory and proprioceptive input to feed back information regarding the progression of movements to the motor system, whereas, the lateral cerebellum appears to be involved in feedforward control of movement, for example, in the timing and optimization of limb "trajectories". According to Brooks (1986) it appears that "cerebrocerebellar programming confers motor skill, that is, the maximal ability to use programmed movements with optimal trajectories" (p. 256). Evarts and colleagues (see Evarts, Shinoda & Wise, 1984) have conducted experiments to examine the role of these systems in preparatory set. Specifically, it is suggested that there is a "switching" from an intermediate cerebellum-interpositus-VL-motor cortex pathway to a lateral cerebellum-dentate-VL-motor cortex pathway in terms of cerebellar input to the pyramidal system. It is suggested that this may provide a neurophysiological mechanism accounting for the effects of preparatory-set on reflex action, such as findings of the context-dependent modulation of postural reflexes (Nashner, 1976), or as in the so-called "sherry glass effect" described in a study by Traub, Rothwell and Marsden (1980). In the latter study it was found that there is a late (50-60 msec) EMG response to displacements of a subject's hand when

they held their fingers a few millimeters from a full sherry glass which they were instructed not to knock over and spill. However, if the subjects were instructed to ignore the full glass, the late response was not detected. Thus, both motor cortex and cerebellar circuits may be working together to produce the switching from purely "reflexive" to "set-dependent" modes of motor control.

Although the cerebellum may be active prior to movements its connections are primarily to that of the "middle level" of the motor hierarchy (i.e., sensorimotor cortex and and subcortical motor structures) and does not receive information from higher brain systems such as association cortex as do the basal ganglia. Thus, the cerebellum appears to be involved in the learning, adaptation and optimization of programmed movements which are selected and "enabled" by premotor cortex and basal ganglia systems -- most likely through its ability to make rapid comparisons between selected motor commands and their actual implementation at the level of the lower motor control systems of the midbrain and spinal cord. The basal ganglia, on the other hand, consist of a number of diverse brain systems involved in both the elaboration of goal-directed behaviours into motor acts and amplitude scaling of the selected motor subroutines, possibly through selective inhibition of muscle synergies, and have access to both (higher level) cortico-cortical processing, and sensorimotor and midbrain (middle level) motor systems (for review see Brooks, 1986).

Although it is difficult to produce a simplifying picture of the overall architecture of these various motor systems a model put forth by Allen and Tsukahara (1974) which has been elaborated upon by others, for example, Brooks (1986) (shown in Figure 1), provides a contemporary view of the various interconnections of these structures and the general flow of control. This is probably a great oversimplification of the motor system, as a whole; however, it indicates the presence of both parallel and serial organization in the motor system, as well as the differential flow of feedback and feedforward control signals.

Figure 1

Motor systems of the human central nervous system showing the major pathways and flow of information through various brain structures involved in the preparation and execution of movement (from Brooks, 1986).
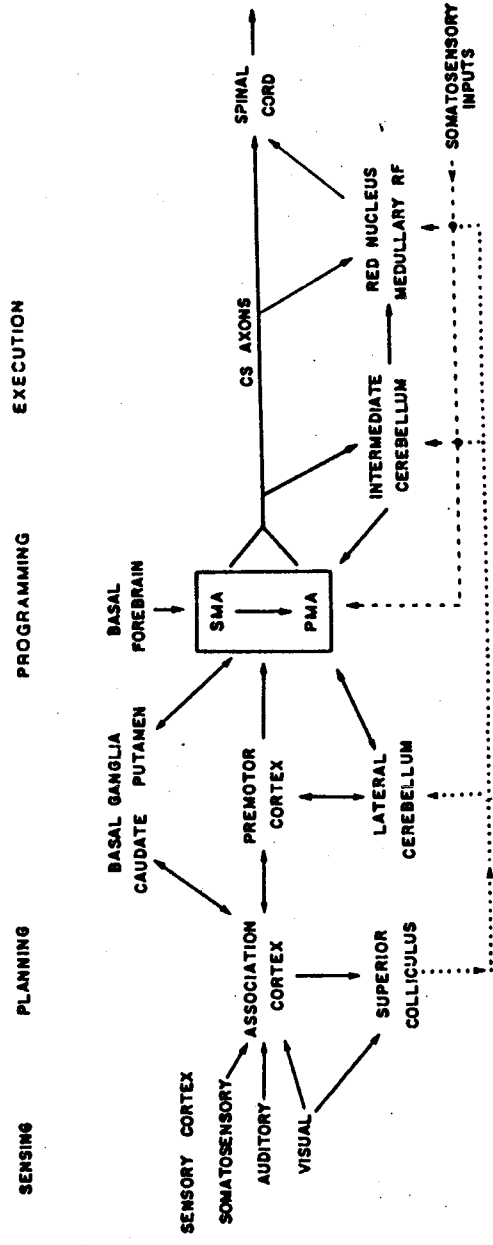
Recently, there has been an increased interest in the supplementary motor area in the direction and control of planned, voluntary movements of the distal musculature. This interest in SMA structure and function has come about as a result of converging evidence from experimental and clinical studies of SMA activity in the preparation and "programming" of intentional movements, some of which is summarized in a 1983 conference on SMA function and motor control (Creutzfeldt, Eccles, Fromm & Wiesendanger, 1985) and in a more recent review by Goldberg (1985). The following is a brief outline of the principal findings of the area of research.

Although the role of the mesial frontal lobe in movement was first suggested in 1919 by Vogt and Vogt, stimulation studies in human epileptic patients by Penfield and Welch (1949) provided the first detailed neuroanatomic evidence for SMA participation in movement. These studies indicated that the mesial posterior frontal cortex is involved in complex, bilateral movements of the limbs, often postural in nature leading to the use of the term *supplementary motor area*. These initial findings were later verified and expanded upon by Erickson and Woolsey (1951) and others (see Goldberg, 1985, for references). Based on similar studies, Woolsey *et al.* (1952) proposed a somatotopic organization of the SMA in monkeys similar to that proposed for the primary motor cortex by Penfield. However, this concept has been criticized more recently on the basis of the complexity of the movements resulting from this type of stimulation (Wiesendanger, Séquin & Künzle, 1973). The connectivities of the SMA in primates have been studied recently in great detail with the aid of horseradish peroxidase tracing techniques and these studies have revealed complex connectivities of the SMA to various motor structures and other brain regions. These findings indicate that the SMA receives highly processed afferent input from a wide range of (non-primary) cortical and subcortical structures and projects to all levels of the descending motor systems of the brain, possibly influencing spinal reflexes as well (Jürgens, 1985; Wiesendanger & Wiesendanger, 1985).

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The participation of the SMA in normal voluntary manipulations of the limbs has been demonstrated in electrophysiological studies of single-unit activity of the premotor areas in monkeys (Brinkman & Porter, 1979; Brinkman, 1985a). Specifically, it is found that neurones in SMA are activated prior to self-paced learned movements in monkeys, but not in response to externally produced manipulations of the limbs or other sensory input. These cells showed similar patterns of activity, regardless of whether the movement was ipsi- or contralateral. Cells[4] in the lateral part of area 6 (arcuate premotor area) responded in a similar manner, but principally to visually-guided movements. Unilateral ablations of SMA in monkeys (Brinkman, 1984) produce interesting effects. Initially, there is a transient loss of coordination in complex manipulations of the hands and fingers. However, the only lasting deficit is a loss of bimanual coordination resulting in mirror movements of the hands in complex tasks. Moreover, sectioning of the corpus callosum eliminates the coordination deficit almost immediately post-operatively and bilateral ablations of the SMA do not produce the deficit. It is thus concluded by Brinkman (1985b) that the SMA may provide information to the opposite hemisphere regarding intended or ongoing movements such that the SMA functions to let "one hand know what the other is doing" (p. A9). Interestingly, a similar transient syndrome of intermanual conflict, sometimes referred to as the "alien hand sign" is seen in commissurotomy patients immediately after surgery (Bogen, 1979) and in some patients with ischemia to the frontomesial cortex (Goldberg, Mayer & Toglia, 1981).

Clinical studies of SMA damage in humans have been unable to provide a clearly defined role of the SMA in movement preparation or programming -- there is no specific apraxia or syndrome that results from damage to this area. Furthermore, discrete bilateral destruction of SMA cortex rarely occurs, given the differential blood supply to either hemisphere. However, studies of small groups of patients with unilateral SMA lesions indicate that damage to this area generally results in deficits in the voluntary production of both speech (for left SMA lesions) and limb movement, reflecting a loss in the will or "drive" for

movement (Damasio & Van Hoesan, 1980). Often there is a loss of spontaneity in speech and movement characteristic of frontal lobe damage (Freund, 1985). The types of movements affected are typically complex, goal-oriented actions in which there is no breakdown in individual "fragments" of the movement sequence (Goldberg, 1985). In a study of 60 epileptic patients with electrodes implanted in or near SMA, stimulation was found to have effects on both speech and movement (Buser, Bancaud & Chauvel, 1985). Stimulation also indicated cortico-cortical connections of SMA as well as reciprocal connections to anterior cingulum and mesial frontal cortex. Stimulation of SMA in in these patients produces arrest of vocalization as well as arm-raising and abduction. In some cases automatic compulsive finger movements are observed. Goldberg, Mayer and Toglia (1981) describe two patients with infarction to the left medial frontal cortex (most likely involving SMA), both of which displayed the "alien hand sign". In these patients the limb contralateral to the affected hemisphere acted in an "extravolitional" fashion in which the limb performed automatized behaviour which the patient appeared unaware of initiating, or was unable to control. Interestingly, neither patient would initiate speech or conversation, but both had good comprehension and ability to respond to questions. These findings correspond to other reported cases of SMA lesions in which mutism, sometimes associated with lack of motor behaviour (akinetic mutism[2]) is observed <u>without</u> loss of "responsive" or non-propositional speech (Jonas, 1981; Kornhuber & Deecke, 1985; Laplane, Talairach, Meininger, Bancaud & Orgogozo, 1977). In this regard, Goldberg also makes reference to the patient described as "Ch" by Luria (1966) who displayed symptoms of both loss of spontaneous speech and ability to carry out sequential movements, as well as the tendency to produce mirror symmetric movements of the hands. This patient also displayed symptoms reflecting the "alien hand sign" and with regard to the lack of spontaneity in his speech the patient apparently responded that "thoughts do not enter my head" (Luria, 1966, p. 226; cited in Goldberg, 1985).

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[2]Also associated with hypothalamic lesions in humans and animals (Segarra, 1970; Teitelbaum et al., 1980).

The non-invasive study of SMA function in normal subjects has involved primarily the use of electroencephalography, and more recently to a limited extent, regional cerebral blood flow. The main body of experimental evidence for localized cerebral activity related to movement in normal subjects has been derived from electroencephalographic studies of pre-movement potentials, most notably the Bereitschaftspotential (BP) (Kornhuber & Deecke, 1965) -- a slow bilaterally symmetrical negative wave beginning approximately 800 msec (in some cases as early as 1.5 seconds) prior to self-paced movements. There are two notable aspects of these slow shifts preceding movement: (1) this slow potential is not present (or is highly attenuated) during identical movements in response to a sensory stimulus (externally paced movements) and (2) the shift is bilateral and precedes, by as much as 1 second EMG onset for the active muscles during the execution of the movement. During unilateral finger movements the precentral BP demonstrates a contralateral preponderance of negativity (CPN) after half its course[3]. Prior to the onset of movement there is a "relaxation" of scalp recorded negativity (premotion positivity or relaxation potential) which tends to have an earlier latency on the side contralateral to the movement and is followed by a negative shift (motor potential) which is maximal over the precentral area during the movement (Deecke, Grözinger & Kornhuber, 1976). These events have been interpreted to reflect the cessation of processing in frontocentral areas that are no longer needed after the movement has been initiated followed by increased processing in areas involved in producing a signal to be sent to the final common pathway (via the pyramidal system) just prior to muscle contraction, contralateral to the side of movement. The differential activation of frontocentral regions (overlying SMA) from contralateral regions (overlying primary motor cortex) is suggested by the scalp distribution of this potential in normal subjects and also by the absence of the primary motor

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[3]Interestingly, an ipsilateral preponderance is found for foot movements, indicating that the electrical generator in precentral cortex may be oriented towards the opposite hemisphere in this case due to the location of the foot area of the motor homunculus on the mesial surface of the frontal lobe (Boschert, Hink & Deecke, 1983).
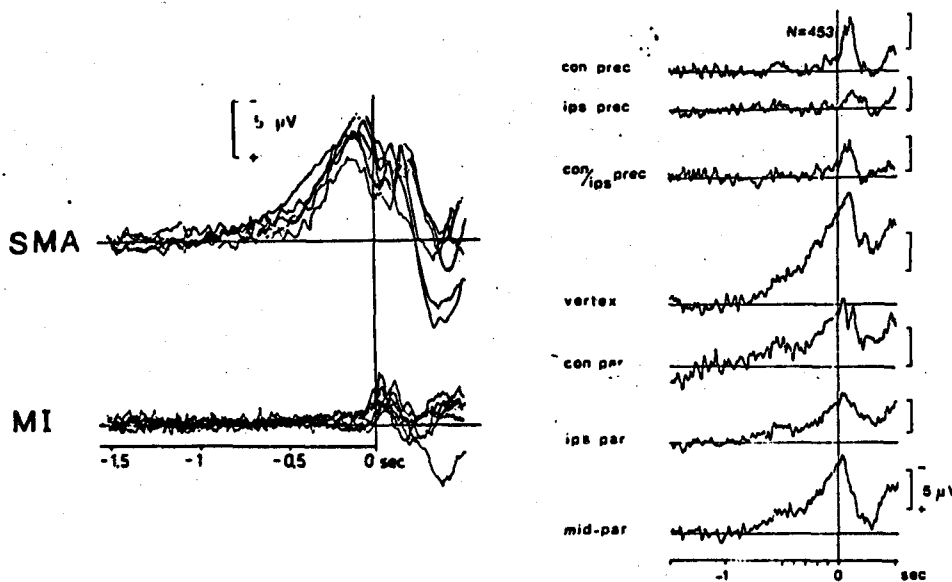
Figure 2. (Left) Pre-movement EEG activity recorded prior to voluntary finger flexions showing a slow negative shift (readiness potential) in a frontocentral lead (SMA) compared to a bipolar derivation over the left and right precentral areas (MI) which only indicates activity immediately prior to the movement (time 0) (from Kornhuber and Deecke, 1985). (Right) Readiness potentials recorded from patients with Parkinsonian akinesia. The absence of negativity over precentral leads with intact slow shifts over vertex suggests that the vertex readiness potential is not due to 'pick up' from the precentral gyrus (from Deecke & Kornhuber, 1978).

cortex "component" in Parkinsonian patients with akinesia (Deecke & Kornhuber, 1978), shown in Figure 2.

More recently, Deecke and colleagues (Deecke, Heise, Kornhuber, Lang & Lang, 1984; Deecke, Kornhuber, Lang, Lang & Schreiber, 1985) have presented evidence that the motivational and attentional components of premovement activity demonstrate a different time course and topography. In a self-initiated tracking paradigm, an earlier relaxation of negativity over fronto-central regions (approx. 100 msec before movement onset) is interpreted as the termination of preparatory processes in SMA, whereas, the fronto-lateral regions relax after movement onset and a late negativity (450 msec after movement onset) over post-Rolandic areas associated with attending to the external stimulus and is termed the directed attention potential (DAP). Thus, there appears to be distinct slow potentials responding to preparation and attention which follow a different time course and have different scalp distributions. Similar patterns were noted

for tactile-tracking conditions. Although these interpretations are highly speculative, the data is quite consistant across subjects and support the view of frontocentral systems as being differentially activated from fronto-lateral and parietal systems in this particular paradigm. Other correlates have been found for BP amplitude and distribution for a variety of factors such as force, reaction time and complexity of movement (for review see Deecke *et al.*, 1984). For example, BP's in musicians were found to be larger and earlier in onset prior to playing melodies as compared to playing a single note (Kristeva, 1984).

The relationship between self-initiated movements and stimulus-evoked movements is somewhat unclear. Although scalp-recorded negativity provides a detailed temporal analysis of the premovement cortical activity, it is difficult to identify the contributing neural generators that may be involved in the processing of different kinds of information. Pre-movement negativity (PMN) for self-paced movement is considered to reflect preparatory processes involving arousal, motivation, and preparation of a motor program or set. PMN preceding stimulus (e.g., visually) triggered movements is thought to involve the ability to anticipate the cueing stimulus as well as preparation for movement. In these tasks PMN amplitude and time course can be manipulated by interstimulus interval (Kutas & Donchin, 1980) controlling the expectancy or spontaneity of the movement. Consequently its amplitude is attenuated with increased reaction time variability. Therefore, PMN for stimulus-evoked movements may be related to the readiness potential in that it reflects increasing preparedness for movement within the experimental situation (Thickbroom, Mastaglia, Carroll & Davies, 1985). However, it is difficult to determine whether the negative shifts are due to structures involved in motor preparation or due to structures involved in expectancy of the cueing stimulus. For the case of a cued motor response preceded at a fixed interval of time by a warning stimulus, referred to as the contingent negative variation or CNV (Walter, Cooper, Aldridge, McCallum & Winter, 1964), there is observed a prolonged negative shift in the baseline of the vertex EEG during this interstimulus interval. A similar controversy has arisen concerning the underlying basis for the "late" component of the CNV although it is generally agreed that

there is an overlapping of expectancy and motor preparation processes occurring betweeen the warning and cueing stimuli (for review see Rockstroh, Elbert, Birbaumer & Lutzenberger, 1982).

Some intriguing findings regarding brain activity accompanying self-paced movements have been recently reported by Libet and colleagues (Libet, Wright & Gleason, 1982; Libet, Gleason, Wright & Pearl, 1983) regarding the timing of "mental" events associated with preparation for movement and conscious awareness of these events. Initially, Libet *et al.* examined the degree of spontaneity in self-paced movements and found evidence for the specification of two types of premovement or readiness potentials. Specifically, an early onset readiness potential (type I RP) was recorded about one second prior to movement which was associated with the subject's being aware of preparing to move prior to a spontaneously initiated movement. These resembled standard Bereitschaftspotentials reported by others. However, when purely "spontaneous" trials were averaged (i.e., the subjects reported no preplanning of the intended movement -- only a sudden "urge" to move) the recorded readiness potential had a later onset (about 550 msec) and was termed a type II RP. Libet thus proposes that two processes may be involved in both preparation for movement and generation of the vertex readiness potential; an early process associated with preparation to act within a few seconds (termed a type I RP) which may overlap with a second process (type II RP) related more specifically to the immediate urge to act. Thus, it appears that upon closer examination a finer-grained analysis of preparatory processes can be applied to the study of such premovement activity. In an extension of this paradigm (Libet, Gleason, Wright & Pearl, 1983) it was found further, that subjects introspectively reported becomming consciously aware of the urge to move approximately 200 msec prior to the EMG onset -- apparently after the onset of RP activity recorded at vertex (the time of awareness was determined by having the subject's estimate the position of a marker on a spatial clock and adjusting for response delay). Libet (1985) concludes that cerebral processes (as indexed by RP onset) related to the initiation of action begin prior to the subjective awareness or intention to

act. I.e., the cerebral initiation of an act begins "unconsciously". Libet therefore suggests that conscious "will" functions in a "permissive" fashion such as to allow, or not allow (veto), a movement; the role of consciousness is not to initiate specific acts but to "select and control volitional outcome". Understandably, Libet's studies and interpretations of the data have provoked severe criticism, both on methodological and philosophical grounds and raise serious questions regarding mental processes and "mind-brain" interactions.

Regional Cerebral Blood Flow Studies

Some of the most interesting evidence for the activation of premotor cortex during voluntary movements has come from new functional brain imaging techniques capable of monitoring, non-invasively, metabolic changes associated with behaviour, such as regional cerebral blood flow (rCBF) using the gamma-emission imaging with ^{133}Xe injection technique (Roland, 1982; Roland, Larsen, Lassen & Skinhoj, 1980) and positron emission tomography (PET), using ^{77}Kr inhalation (Roland, Meyer, Shibasaki, Yamamoto & Thompson, 1982) and more recently using $H_2^{15}O$ (Fox, Fox, Raichle & Burde, 1985). Glucose metabolism has also been monitored using the FDG (^{18}F-labelled deoxyglucose) PET scan method showing increased motor cortex and premotor area function during self-paced finger flexions (Phelps & Mazziotta, 1985). Both techniques have been applied to the study of simple and complex motor activity by Roland and colleagues (see especially Roland, Meyer, Shibasaki, Yamamoto & Thompson, 1982) and have provided some interesting results with regard to the activity of the SMA during movement. The major findings by the Roland group with regard to increases (above resting values) in regional blood flow during movement paradigms can be summarized as follows:

(1) During both sustained contractions and simple repetitive flexions of the fingers, a focal increase is seen in the contralateral sensorimotor (Rolandic) area (with a slight increase in SMA during the repetitive movements).

(2) During a complex motor sequence of finger flexions a 40% to 60% increase is observed in SMA in conjunction with increase in the Rolandic area.

(3) An increase is seen in the SMA while the Rolandic areas remain silent when the subject engages in mentally "imaging" the sequences while not moving the fingers.

(4) An increase in the superior parietal cortex in addition to Rolandic areas and SMA is seen when the subject executes movements in "extrapersonal space".

This last finding corresponds to single-unit studies showing parietal cortex (area 5) in monkeys to be active during movements made in extrapersonal space (as opposed to movements made in relation to the body) by Mountcastle *et al.* (1975). The most intriguing finding from the above results is the fact that the SMA could be shown to be metabolically active during "mentation" (i.e., when the subjects engaged in the thought of initiating movements) while the precentral gyrus showed no activation.

A study by Halsey, Blauenstein, Wilson and Wills (1979) showed increased blood flow in precentral areas to be greater for left hand movements than for right hand movements (in right-handed individuals) indicating possible hemispheric differences for organization of finger movements. A more recent study by Fox, Fox, Raichle and Burde (1985) examined localized changes in rCBF using $H_2^{15}O$ positron imaging with good spatial resolution (12.4 mm FWHM) during both voluntary eye saccades and finger movement tasks. Focal increases were found in SMA during all motor tasks with activation of anterior SMA during voluntary saccades and posterior SMA activation for both simple *and* complex finger flexions. This latter finding conflicts with those of the Roland group who found no SMA increases for simple finger flexions which they attributed to movement complexity (modelled as a Markov chain). However, as noted by Fox *et al.*, the conflicting findings may be attributable to temporal limitations of rCBF techniques which necessitate integration over a finite time interval (45 sec for ^{133}Xe technique, 40 sec for the PET scan using ^{15}O). Therefore, such measures represent the cumulative metabolic activity over repetitions of the task and are dependent on task performance rate as well as concommitant cognitive processes required

by the task (e.g., covert counting or memory retrieval). Fox *et al.* also suggest that the observation of no activation of SMA for simple finger movements by the Roland group may be due to the limited spatial resolution of the rCBF ^{133}Xe technique and the small relative amount of cortex that may be activated by single digit movements. Although the evidence provided by functional imaging techniques using gamma or positron emission indicate SMA to be involved in a variety of motor tasks, it is not yet clear from these studies what aspects of these motor tasks may be exclusively activating SMA or what the temporal relationship of this activation is with respect to other cortical areas (e.g., MI) within the time frame of the movement itself.

Overall, there has been a great deal of converging evidence from various areas of research to indicate that the supplementary motor areas on the mesial surface of the frontal lobes may serve a special purpose in the planning and initiation of specific voluntary movements. Furthermore, the interposition of these areas between limbic system input to cortical motor areas indicates that the SMA may constitute a locus of control for the drive or "will" to execute planned movements, or may serve some mediating function between motivational brain systems and motor output executed through cerebral mechanisms involving both pyramidal and extrapyramidal systems. The indication of a special role of the SMA in motivational or volitional aspects of behaviour has led to a great interest in this brain region as a possible locus for the channeling of information from various brain systems into the "motor-programming" system and subsequently into action. Along with such superordinate motor functions of this putative premotor system, comes the implied significance of such a locus in the mental processes involved in the "decision for action"; i.e., the localization of brain areas for mental constructs such as volition or will. Consequently, a number of theorists have proposed models of the possible implications of SMA function in terms of these sorts of mind-brain interactions.

Kornhuber's model

Kornhuber and colleagues (Deecke, Kornhuber, Lang, Lang & Schreiber, 1985; Kornhuber, 1984a) have described an extensive model in which the SMA is designated as the "motivation" cortex with regard to action; that is frontomesial areas of the cerebral cortex are seen to be critical in the self-initiation of actions by the individual. These hypotheses are based principally on evidence from electroencephalographic studies (Bereitschaftspotentials), as well as the recent corroborating evidence from cerebral blood flow studies. The Bereitschaftspotential is, in effect, an "emitted" potential -- electrical activity in the brain that reflects an internally generated behaviour or "act of will" on the part of the subject, rather than activities related to processing of a sensory

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stimulus. Sensory "evoked" event-related potentials (ERPs), on the other hand, appear to reflect electrical events that are either contingent on parameters of the stimulus and hence modality-specific (exogenous components) or contingent upon mechanisms of cognitive processing of sensory input, such as outcome expectancies, memory updating, response contingencies and modality independent (endogenous components). Thus, ERP components involve attentional mechanisms in which there is a relationship between response and attentional states, whereas, the BP is seen as reflecting internally motivated behaviour or as stated by Kornhuber, "a way in which drive and will are channeled into action" (1984a, p. 421). Kornhuber therefore forms a distinction between the *motivational* brain and the *attentional* brain, the latter referring to sensory association areas for different modalities and the traditional posterior association cortex and the former referring to prefrontal and frontomesial (SMA) cortex. Kornhuber also stresses distribution of motor function in the cortex, arguing that movement is produced by a *distributed system* (Kornhuber, 1984b). This view has gained increasing acceptance in recent years (cf. Wise & Evarts, 1981) and is supported by both cerebral blood flow studies (Roland, Meyer, Shibasaki, Yamamoto & Thompson, 1982) and present knowledge of the anatomical pathways involved in motor control (Rolls, 1983). Kornhuber thus proposes that brain systems controlling the motivational aspects guiding motor behaviour can be classified in the following manner:

(1) The drive towards a certain behaviour is guided by fronto-orbital cortex via hypothalamic and limbic connections.

(2) An adaption to the external situation is achieved through the integration of sensory input guided by fronto-lateral cortex via connections to sensory assocation cortices. The role of the fronto-lateral cortex in integrating polymodal sensory stimulation is supported by recent cerebral blood flow studies (Lassen & Roland, 1983; Roland, 1982).

(3) The supplementary motor cortex is then involved in initiating the appropriate motor routines controlled by the feedback-control and programming functions of extrapyramidal motor systems.
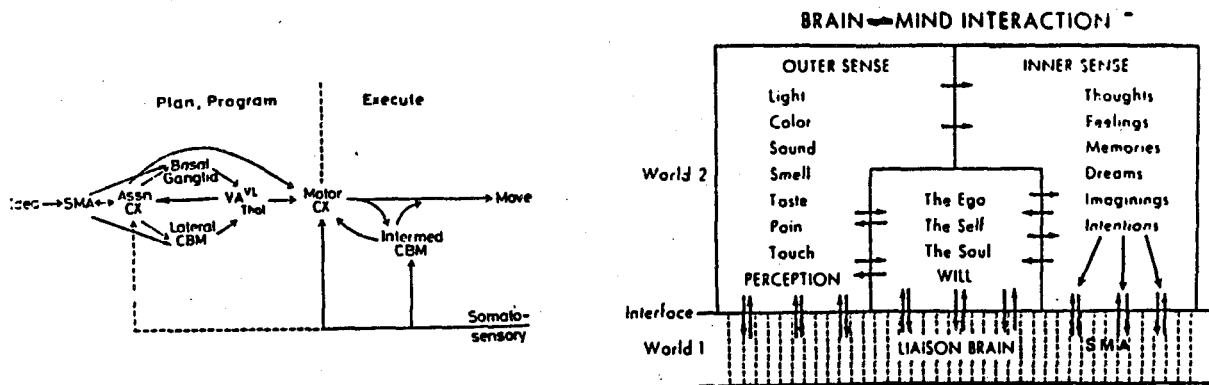
Figure 3. (Left) Eccles' model of central motor system architecture derived from the model of Allen and Tsukahara (see Fig. 1). Note the addition of SMA interposed between "decision to move" and reentrant cortical and subcortical motor systems (from Eccles, 1982). (Right) The SMA is seen here as acting as the "liaison" brain interacting between the "self" (World 2) and the "brain" (World 1) (from Eccles, 1985).

Thus, these three phases of neural activity can be seen as constituting the neural mechanisms which sequentially give rise to, as Kornhuber puts it, the organism's *what to do*, *how to do it*, and, *when to start doing it*, respectively. Such systems are thus seen to be working together to organize the "temporal coherence of behaviour".

A similar model of the motivational control of behaviour has been proposed by Eccles (1982) who suggests that the SMA may be capable of acting as a "reference" library of learned motor subroutines which may be stored elsewhere, most likely the basal ganglia, cerebellum and association cortices. The SMA which has access to these subroutines would provide the appropriate motor responses to *intentions* and is thus interposed between idea and action as indicated in Figure 3. In a philosophical sense, the SMA is seen by Eccles as acting as a liaison between "self" and "brain" in terms of mind-brain interactions (see also Figure 3). Although these models of motivational processes, consciousness, and free will raise serious philosophical issues, they indicate that

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the SMA may provide a localization of activity to a relatively discrete brain region in which a variety of highly distributed processes become focussed in order to provide an coherent temporal organization of output from the system. In this respect, the role of the SMA may be likened to a "steering" function over behaviour which has been, in the past, ascribed to a variety of cortical and subcortical brain structures with ambiguous function (e.g., frontal association cortex).

Goldberg's model

The role of the SMA in motor function should, of course, be interpreted in relation to the variety of modes of control which may exist for complex motor behaviour in higher organisms. Although the SMA may play an important role in intentional movements of the limbs, this "goal-oriented" system must function in conjunction with a number of other motor systems which handle automated or reflexive movement patterns and into which motivational systems of the brain do not enter. Goldberg (1985) has provided an instructive overview of SMA structure and function in which he speculates on the evolutionary development of premotor cortical areas, proposing that two separate systems, a *lateral* and a *medial* system, can be distinguished on the basis of their relative roles in motor control. The medial system is seen as being phylogenetically "older" cortex and involved in "model-based" execution of motor program sequences. This system revolves primarily around SMA function. The lateral system is seen as being more "interactive" in nature and involves polymodal sensorimotor integration. This latter system involves traditional *premotor* cortices (lateral area 6) which are known to be important in the preparation for movement, particularly sensory guided movements, such as reaching for visual targets (Weinrich & Wise, 1982; Wise, 1985).

Figure 4 outlines the respective connectivities of these two postulated motor systems. Although subserving different aspects of motor behaviour and having different phylogenetic origins, these two systems are seen as two different routes through which information regarding preparation for output can be

a

MI   MI
APA   SMA ← → SMA   APA
              cc

b

MI   MI
APA   SMA ← → SMA   APA

c

MI   MI
APA   SMA ← → SMA   APA
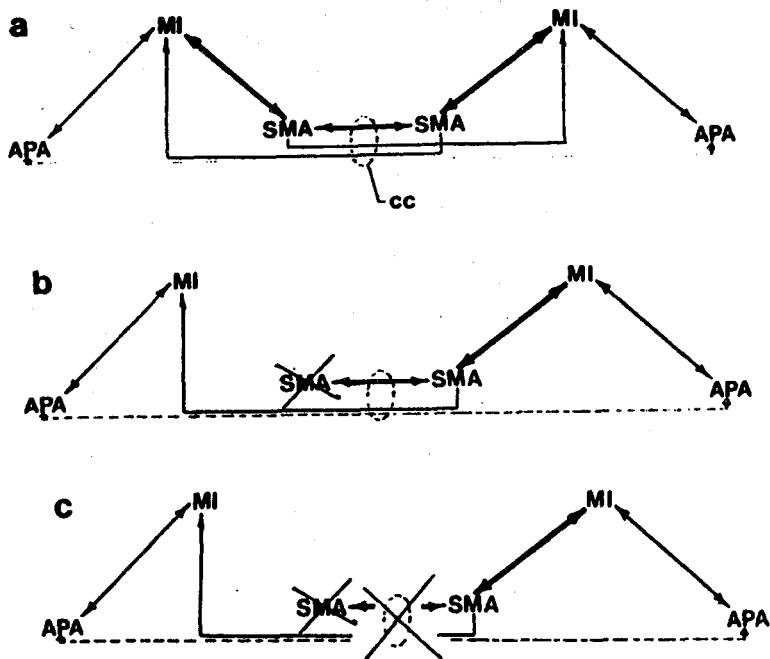
Figure 4. A comparison the putative medial and lateral motor-programming systems showing their bihemispheric connectivities to the primary motor cortices (MI). Intermanual conflict produced by unilateral frontal lobe damage is suggested to be due to the (normally) bilateral organization of movement by areas such as the supplementary motor area (SMA). (a) Normal patterns of connection showing bilateral influence of SMA. (b) Unilateral damage to SMA producing an imbalanced input from right SMA to contralateral hemisphere, possibly producing deficits of intermanual dexterity and mirror symmetric hand movements. Subsequent destruction of corpus callosum connections (c) can improve bimanual coordination to some degree, most likely by removing the influence of the contralateral SMA on MI but may result in greater independence of the two systems producing syndromes such as the alien hand syndrome in commisurotomy patients (from Goldberg, 1985).

channeled through, what Goldberg refers to as, "protomotor" regions which subsequently project to the primary motor cortex and pyramidal system for execution. Others have used the term "supramotor" areas (Orgogozo & Larsen, 1979) also referring to the fact that the SMA and premotor cortices may act as brain systems involved in converting "motive into action" and having a direct influence on area 4 (Goldberg, 1985, p. 586). Goldberg formulates much of his hypotheses around the evolutionary aspects of neocortical function proposed by Sanides (1964, 1970) in which there is postulated three major systematic trends in architectonic differentiation of the mammalian cortex which he terms "protogradations". The medial protomotor system, including the SMA, is seen as

evolving from an "outgrowth" of paralimbic structures and is closely interconnected with the septo-hippocampal system through the underlying cingulate cortex. The lateral motor-programming system, including the arcuate premotor area (APA) in primates (premotor cortex in humans) is seen as developing from an outgrowth of parainsular cortex and being more closely connected to cortical areas relaying polysensory and (foveal) visual input. The primary motor cortex (area 4), by contrast, is seen as evolving from a third, more recent protogradation arising from the Rolandic area and proceding poleward which is most highly evolved in humans for the purpose of fractionated movements of distal musculature. The APA and SMA are also seen as having different connectivities to reentrant subcortical systems; the APA receiving primarily cerebellar input and the SMA receiving primarily pallidal (basal ganglia) input. It is further proposed that these two systems may interact with subcortical motor structures by way of two hypothesized cortico – thalamo – cortical loops involved in motor preparation. One loop involves the bilateral activation of basal ganglia input to SMA in which strategies for action are prepared or selected. A second loop is subsequently activated involving a unilateral involvement of cerebellar input to MI for execution of motor subroutines selected by the first loop; the latter loop performing "context-dependent adjustments" of the parameters of the selected subroutines.

Goldberg's model is derived from a wide variety of clinical and experimental evidence, as well as the speculations on the evolutionary development of the premotor cortex put forth by Sanides (1964, 1970). Goldberg's conclusions regarding the role of the SMA in motor behaviour are summarized in the following quotation.

> There appears to be some convergence of evidence regarding the role of the SMA in the cortical organization of action. Anatomic data suggest that the SMA stands on an interface between limbic outflow and the motor executive apparatus. Physiological and clinical evidence indicates that one aspect of SMA operation may be efferent integration, that is, the association of limbic inputs conveying internal decisions about action plans with contextual cues from the environment in order to select and monitor the execution of appropriate subcortically resident motor subroutines. Although the SMA representation has been historically "secondary" by virtue of its being detected long after the classical "primary" representation, the SMA can be viewed as a paralimbic medial "protomotor" (Sanides, 1964) cortex,

which functions in a "supramotor" (Orgogozo & Larsen, 1979) fashion, participating earlier than MI in the translation of motive to intention to action, and exerting control over MI. It can be distinguished in a number of different anatomic and implied functional ways from a lateral "protomotor" APA which also directly projects to areas of MI. Its relationship with cingulate cortex and its presumed evolution over phylogeny out of a hippocampal primordium, suggest a meshing of these concepts with a new theory of septo-hippocampal system (SHS) function, proposed by Gray [1982], in which the SHS is hypothesized to detect a mismatch between actual and expected stimuli ... The role of the SMA as an interface between the cingulate cortex and other cortical and subcortical motor areas would imply that the SMA is involved in the transformation of "intent", as conveyed to it by the SHS via the cingulate cortex, into the specification of action. The SMA thus may play a key transitional role in volitional processes." (1985, pp. 586-587)

Thus, the model proposed by Goldberg regarding the medial motor system not only accounts for the putative role of structures such as the SMA in motor preparation, but also suggests a possible route of limbic outflow regarding intentional processes. Models of limbic function, such as that proposed by Gray (1982) involving the septo-hippocampal system, have been criticized in terms of their difficulty in explaining how limbic generated patterns of neural activity are converted into overt behaviours (cf., Woodruff, 1982). However, the hypotheses presented by Goldberg may be of particular interest in the application of such ideas to higher primates where such limbic outflow accesses complex motor-programming systems related to movements of the distal motor apparatus, the control of which is highly dependent upon cortical motor areas such as the precentral gyrus. Much of the experimental evidence provided in theories such as Gray's has focussed on the behavioural effects of stimulation or lesions of septo-hippocampal and hypothalamic structures. However, it should be kept in mind that the cortical motor systems in animals used in these studies (primarily rodents and cats) are less developed than in higher primates, particularly with regard to the role of the motor cortex in movement. Therefore, in an attempt to apply animal models of motivational brain systems to humans it should be noted that the output systems appear to be somewhat more complex in humans and may involve specialized cortical regions such as the koniocortex of the precentral gyrus and its connections to premotor areas such as the SMA.

It should also be noted here that the concept of motor programming is used in these studies in its broadest sense. Although the term "motor program" generally implies the feed-forward control of complex motor activity wherein feedback correction is either unavailable (as in the case of ballistic movements) or unnecessary (due to learning), many of the tasks described in the above studies may involve a variety of feedback and feed-forward movement paradigms. The case of independence from sensory feedback for skilled movements was initially used by Lashley (1951) as an argument against reflex-chaining models of serial behaviour and is often held as evidence for the existance of "pre-compiled" motor subroutines for skilled movements (Rosenbaum, 1985). The term motor program has been typically used to refer to a set or sequence of stored instructions for movements which can be carried out independently of, or uninfluenced by feedback (cf. Keele, 1968; Schmidt, 1975). Evidence for the ability to perform skilled movement in the absence of peripheral feedback has been provided by experimental studies in primates (Taub & Berman, 1968) and in a limited number of clinical cases in humans (Lashley, 1917; Marsden, Rothwell & Day, 1984). However, there still remains a great deal of controversy over exactly what parameters of movement are coded for and stored in the case of motor programming. For example, at the level of the more abstract cognitive motor program or *schema*, timing patterns or "schedules" may be more important than the spatial attributes or specifications of "commands" to the musculature as evidenced by timing invariances in sequential movement tasks (see Rosenbaum, 1985) and other examples of motor *equivalencies*[4]. Motor programs have not been held exclusively to the concept of independence from sensory feedback. For example, in their model of motor programs for finger movements in skilled typists, Rumelhart and Norman (1982) propose that,

> motor programs are flexible, interactive control structures capable of calling upon sub-programs, passing parameters to be bound to program

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[4] One example of such equivalencies is that of the tendency to write one's signature with a consistant pattern or style which is independent of the muscle groups used to do so (e.g., writing with pen on paper or chalk on a blackboard (see Stelmach & Diggles, 1982).

variables, and making local decisions as a result of current conditions (which might include information from feedback channels, from perception, or other sources of knowledge). A motor program is not a fixed action pattern of movements. It is a set of specifications or control statements that govern the actions that are to be performed (pp. 7-8).

Moreover, a distinction should be drawn between the concepts of "programming" and "planning" of movements, as pointed out by Rosenbaum (1985; see also Shaffer, 1981) in which "plans" generally span longer periods of time and may have a greater "conscious" component than that of "programs". The preceding review of SMA function in primates indicates that this brain motor system may pertain to both the planning (i.e., intentionality) of movements as well as the execution and timing of motor programs and that cortical – basal ganglia – cortex loops controlling both these aspects of behaviour may feed into premotor areas *in parallel*. Thus, it may be premature to delineate task specificity to SMA activation on the basis of seriality or feed-forward aspects of the task, although the concepts of *timing* (of execution) and *intending* are not exclusive to either case. Thus, the temporal relationships of activation of cortical motor areas needs to be further addressed (e.g., SMA versus MI) and methods which are capable of exploring the relative timing and contributions of these areas for specific motor behaviours may be useful in resolving these questions.

II. PRESENT STUDY

Methodology

As indicated in the previous section, the primary experimental technique for the observation of cortical activity in the intact human subject involves the recording of electrical potentials from the scalp. The slow potentials observed prior to self-paced movements (readiness potentials or Bereitschaftspotentials) indicate, to some extent, different electrical sources for various phases of the pre-movement period as derived from the relative scalp distribution of this activity under various experimental conditions. Additional evidence from cerebral blood flow studies conducted in human volunteers supports claims for the role of the SMA in the programming of complex movements but requires the use of ionizing radiation and extensive time periods per sample. Due to this limited temporal resolution, this activation cannot be pinpointed in time for a given movement. EEG measures, on the other hand, have a suitable temporal resolution for the discrimination of specific components of pre-movement activity and provide a non-invasive method of exploring the temporal relationships between brain activity and complex behaviour. However, in the case of these electrically recorded potentials there is some question as to the degree to which these measures are capable of localizing neural sources producing the electrical changes recorded at the scalp.

Electroencephalographic Measures

One problematic aspect of the use of scalp recorded potentials is the distortion of the electric fields produced by the brain generators[1] or sources and

----
[1]Some authors have taken exception to the use of the term "generator" to describe the hypothetical origin of observed fields since there is no *a priori* assumption of the kind of electric field producing entity involved. Hence, the term *source* will be used herein to describe the localization of an estimated circumscribed region of current flux in the brain producing an electric or magnetic field.

the dependence of the observed potential field on the location of the reference electrode since, in electroencephalography, one does not measure the electric field directly, rather one estimates the field from a distribution of potential through the measurement of a current circuit which passes through the electrode-scalp interface (see Appendix D). The main drawback of this approach is that the patterns of isopotential lines thus observed are difficult to interpret because of the arbitrariness of the placement and use of the two electrodes forming the aforementioned circuit. However, reference-invariant analysis techniques have recently been introduced which produce more readily interpretable field patterns by calculating spatial gradients and derivitives of the referential potentials. Some preliminary investigations have applied these techniques such as the *Laplacian*[2] derivation, (see Appendix D) to the study of movement-related potentials in order to better estimate discrete sources of the diffuse referentially recorded readiness potentials. An on-line Laplacian analysis has been applied to movement-related potentials by MacKay (1984) in which it was found that the Laplacian derivations were relatively less sensitive to muscle artifacts and eye movements and readiness potentials appeared clearly lateralized to the contralateral Rolandic and parietal areas. However, this study used only 13 widely spaced electrodes arranged in triangular configurations for use with a limited number of amplifiers, and extensive spatiotemporal mapping of the scalp activity was not provided. Furthermore, the experiment did not utilize a standard BP paradigm (movements were in response to a visual-tracking task) and was conducted in only one subject.

A more extensive analysis of movement-related potentials using the Laplacian technique has been carried out by Gevins and colleagues (Gevins et al., 1984; Gevins et al., 1987). These studies indicate that the use of Laplacian

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[2]Although the term "Laplacian derivation" will be used throughout when referring to the transformations described in Appendix D, it should be noted that these techniques are *approximations* of the Laplacian (the spatial derivative of the potential gradient) achieved by simple numerical estimation of partial derivatives. However, the term "source derivation" used by some authors to describe these approximations is not used since this term is somewhat misleading (Laplacian estimates are not current dipole source estimates but source-sink estimates) and should not be confused with *source localization* methods also described herein.

spatial pattern enhancement produced much more spatially discrete information than that of the corresponding amplitude distributions over the scalp surface. These studies indicate distinct phase (source–sink) reversals between anterior scalp locations near premotor/SMA cortex and primary motor cortex locations for left and right hand movements as well as significant covariance between these sites and parietal regions in a visuo–motor task (button presses to visually–cued force of applied finger pressure). Interestingly, activity at the antero–central site was greater for accurate performance by the non–dominant hand than for the dominant hand. Additionally, diffusely organized but strongly covariant patterns distributed over the scalp during inaccurate non–dominant hand performance seemed to suggest that such inaccurate performance may result from disorganized or possibly conflicting motor sets as evidenced by distributed cortical activation (Gevins et al., 1987).

Magnetoencephalographic Measures

Although the use of Laplacian–based spatial enhancement techniques has produced somewhat better information regarding hypothetical brain sources active during visuo–motor and pre–movement potential activity, due to the remaining "smearing" of the currents passing through the tissues of the head from brain, there is still only crude localization of such sources. As a result, source localization techniques (see Appendix F) applied to electrical data thus far are hampered by the need to model the head as a spherical conductor, where in actuality, the observation points are voltage differences between electrodes of arbitrary distance from each other on a non–spherical, non–uniformly conducting head. This makes the relationship between modelled sources and anatomical structures difficult to estimate and dependent upon approximations of the head radius and estimated correction factors for the differing conductivities of the head in order to estimate "depth" of such sources. More preferable would be a method of measuring the electric field emanating from discrete brain generators which is undistorted by these tissues. The development of neuromagnetic measurement techniques (termed *magnetoencephalography* when applied to surface recordings of the brain's magnetic fields) offers some promise in this regard.

These techniques came about as a result of the development of sensors capable of discriminating the very small fields produced by biological tissue with suitable signal-to-noise ratios. This now provides a means of monitoring current flux within the brain by measuring the magnetic (rather than electric) field at the surface of the scalp. Furthermore, such detected magnetic flux is not distorted by the varying conductivity of biological tissue since it is believed that the primary fields observed outside of the head are due to intracellular current flow (as a result of cellular depolarization) and not due to volume-conducted currents over large regions of brain tissue, which most likely produce the patterns of electrical potential measured by the EEG. Thus, the MEG is thought to reflect somewhat more functionally meaningful electrical activity than that of the EEG. Therefore, the combined use of EEG and MEG methods can contribute quite different information regarding electrical current sources in the brain, and furthermore, are selectively sensitive to dipolar sources of different kind and orientation when the head is taken to approximate a more or less spherical volume-conductor (see Appendix E for details).

Previous Studies

Magnetic field shifts preceding movement were reported by Weinberg and colleagues (Deecke, Weinberg & Brickett, 1982; Weinberg, Brickett, Deecke & Boschert, 1983) in which slow shifts of magnetic flux were recorded over frontocentral areas prior to voluntary finger flexions which followed a similar time course to the Bereitschaftspotential and were termed Bereitschaftsmagnetfelds or "readiness fields". Similar shifts can be observed prior to both finger and toe movements (Deecke, Boschert, Weinberg & Brickett, 1983; Hari et al., 1983). Figure 5 illustrates the averaged magnetic flux recorded from the head surface preceding 80 self-paced right finger flexions in one subject, in which it can be seen that slow magnetic shifts accompany the electrical shift observed in the EEG signal recorded at vertex. However, these magnetic shifts demonstrate a reversal over the central contralateral scalp

37
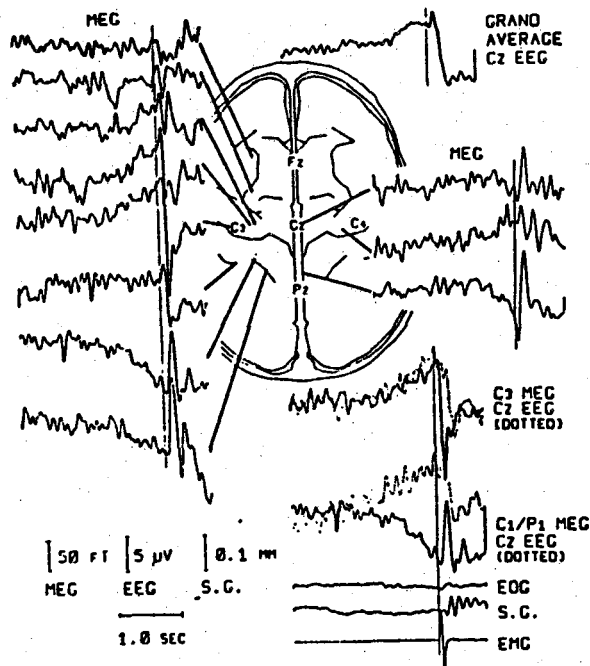
Figure 5. Averaged MEG recordings over different scalp locations as indicated by lines for 80 self-paced right finger flexions in one subject. EEG grand average from Cz is shown at upper right. EMG onset was used as trigger (shown on lower trace at bottom right). EOG and head movement (S. G.) were also monitered for artifact rejection of trials. (from Deecke, Weinberg & Brickett, 1982).

indicating that a single postulated source for these shifts would lie somewhere between the field maxima in the region of the Rolandic fissure (note: this assumption is based on the theoretical model of a magnetic field encircling a current dipole source which would lie tangential to the scalp and midway between field maxima (peaks) of opposite direction in and out of the head). Deecke, Boschert, Brickett & Weinberg (1985) conducted a further experiment in order to test for supplementary motor area (SMA) participation in movement preparation by employing a complex finger touching task and measuring magnetic field changes prior to the initiation of each touching sequence. Although only a selected distribution of 11 MEG recording positions were obtained from one subject, the preliminary findings showed field direction reversals which suggest at least two separate sources for these slow shifts -- one in the region of the SMA and another in contralateral motor cortex, though, the orientation indicated for the SMA source is not what would be expected for a laterally oriented

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dipole layer on the mesial surface of the frontal lobe and the entire pattern of slow shifts over the area of the head sampled shows some variability. These data do suggest, however, the capability of MEG to discriminate cortical sources associated with pre-movement brain activity. More extensive mapping of the surface fields is needed in order to specify the exact number and location of generators and their relative temporal relationships. Thus, MEG measures may be capable of providing additional information regarding source localization for components of these pre-movement shifts and most importantly, provide an indication of whether SMA or MI sources can be distinguished for volitional movements.

Dipole Modelling of Electrical Sources

The spatial resolution afforded by the MEG method has also encouraged the application of *source localization* techniques, modelling sources of brain electrical activity as *current dipoles*[3]. Basically, this approach to the specification of discrete sources of electrical activity in the brain assumes the "equivalent current dipole" conceptualization of a source, wherein, the source is assumed to be produced by current flux at some instant in time, such as those produced by the localized depolarization of neuronal processes lying in differing cortical laminae which is best modelled as a current dipole. Such theoretical sources are sometimes referred to as "equivalent" in that it may represent the vector sum of some more diffuse or distributed activity (see Appendix F for details). Although there may be some theoretical drawbacks in applying this concept to the neural basis of *complex* cognitive processes (cf. Weinberg, Brickett, Baff & Cheyne, 1985) this approach has yielded interesting results regarding verification of suspected sources for various components of averaged evoked brain activity in humans. For example, dipole sources have been localized in temporal lobes near primary auditory cortex for components of transient auditory evoked responses (Romani, Williamson, Kaufman & Brenner, 1982; Arthur, Sullivan, Flynn &

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[3]Specifically, a positive and negative charge separated in space with current flowing from positive to negative, producing a dipole moment measured in units of current x length (ampere-meters).

Williamson, 1986) and for responses to steady-state auditory stimuli (Makäkelä & Hari, 1987; Weinberg et al., 1987). Sources have been localized to primary (SI) and secondary (SII) somatosensory cortex for electrical stimulation of peripheral nerves by Hari and colleagues (for review see Hari & Kaukoranta, 1985). A recent study conducted by the author and colleagues using a steady-state vibrotactile stimulus applied to the right index finger indicated a discrete source in the contralateral post-central gyrus, near the region of primary somatosensory cortex expected to be active for this stimulus (Weinberg, Cheyne, Brickett, Gordon & Harrop, 1987).

Experimental Study

Initial studies demonstrated that the use of MEG recordings show a great deal of promise in localizing equivalent "sources" associated with pre-movement brain activity. This would provide a means of studying directly, patterns of SMA activity in human subjects during various aspects of motor behaviour, and a means of validating present theories of the role of the SMA in movement preparation. The purpose of the study herein, is to explore the possibility of using the combination of MEG source localization techniques and reference-invariant (Laplacian) EEG measures to determine the relative contribution of cortical areas in preparation and initiation of simple and patterned movements. Such measurements could provide experimental evidence for the differential participation of brain systems involved in the preparation and execution of movement and the ways in which these systems may interact during the organization of voluntary motor output. As indicated in the introduction, present theory holds that there is significant bilateral organization of movement in premotor and subcortical motor structures, which becomes contralaterally organized prior to motor execution. One hypothesis that may be tested using non-invasive source localization methods is whether supplementary motor cortex becomes active prior to primary or other motor areas, or demonstrates a differential time course and level of activity for *complexity* of movement (e.g., sequential movements versus simple joint flexion).

The combined use of MEG and EEG studies has only been recently applied to the study of event-related brain activity (e.g., Stok, 1986) and shows a great deal of promise in discriminating localized sources in cortex associated with sensory evoked responses. As Nunez (1986b) has recently pointed out, EEG and MEG measures may be used in a complementary fashion since both may contain unique information regarding tangentially oriented and radially oriented generators, but only if reference-invariant analysis of EEG (or large numbers of electrode *pairs*) are used. The following thesis was undertaken to both develop the combined use of these two techniques to study the localization of discrete

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sources of brain activity associated with components of averaged movement-related potentials and to assess the usefulness of this approach to monitor brain systems which are active during movement preparation. It was of particular interest to test the ability of this experimental approach to measure SMA activation prior to movement since this would be useful for confirming that pre-movement negativities observed in the EEG are, in fact, arising from these brain areas and to test the hypothesis that SMA activation would precede motor potentials arsing from primary motor cortex (MI) activity related to firing of corticospinal pathways.

In the interest of studying complex, pre-programmed, movements which may engage brain systems such as the SMA, it would be of benefit to apply techniques for the accurate localization of brain activity during complex movement tasks, particularly those which involve patterned or complex movements which can be measured with accuracy in terms of their initiation and which can also be compared to simpler movements of the same musculature. Previous attempts at using complex movement tasks for the purpose of invoking the "programming" of movements have used sequential finger patterns such as repetitive finger apposition tasks (Deecke, Boschert, Brickett & Weinberg, 1985; Orgogozo & Larsen, 1979; Roland, Larsen, Lassen & Skinhoj, 1980) or keyboard-like movements (Kristeva, 1984; Taylor, 1978). Cerebral blood flow studies indicate that these tasks may elicit greater overall processing for movement, as demonstrated by cerebral blood flow increases observed in the above studies, although, as noted in the previous section, this concept has been brought into question by the findings of Fox, Fox, Raichle & Burde (1985). Consequently, there remains some debate as to whether SMA activation is specific to complex pre-programmed motor tasks or whether the SMA is involved in all preparatory states as the electrical readiness potential seem to indicate (cf., Deecke, Kornhuber, Lang, Lang & Schreiber, 1985). Thus, further examination of SMA activity during specific motor tasks is needed.

The following experiment involves the use of magnetoencephalographic measures obtained from a single-sensor 3rd order spatial biogradiometer and

electroencephalographic measurements obtained from a distributed electrode montage taken during self-paced movements in human volunteers. Due to the limitations of a single sensor MEG device and the requirements of signal averaging large numbers of responses, it was desirable to limit the number of tasks used in this study, yet include tasks which may address some of the above issues. Thus, experiments were conducted in right-handed subjects using two simple motor task conditions, performed with the right hand only. Additional recordings were also conducted in two subjects comparing left and right hands for the simple motor task only. Motor tasks involved voluntary (self-paced) movements of the fingers. The simple condition involves self-paced flexions of the index finger (i.e., a standard readiness potential paradigm). The "pattern" condition involves a sequential pattern of finger flexions which required the subject to prepare the motor sequence or "program" prior to each movement. Although other studies have employed variable finger patterns based on a numerical sequence, a single pattern was used in this study in which there may be less tendency for subjects to engage in internal verbalization (counting, etc.) during the movements (since SMA appears to be involved in language processing) and in an attempt to minimize learning effects over the duration of the MEG recording sessions.

PART B

METHOD

Extensive measurements were conducted in five right-handed subjects (4 male and 1 female) from the Brain Behaviour Laboratory and Simon Fraser University student population (25 to 53 years in age).

Electrical Measurements

EEG was recorded from an extended International 10-20 system (Jasper, 1958) electrode placement montage, modified from Thickbroom *et al.* (1984) with additional electrodes interposed between the standard 10-20 positions in order to provide a denser distribution of equally spaced electrodes (Fig. 6A). Electrodes were small (10 mm) Beckmann Ag-AgCl electrodes held in place with Grass EC2 paste and all referenced to a single electrode (nose or left mastoid) in order to provide a single reference for computation of the Laplacian derivation and a monopolar referential derivation which could be used to observe standard readiness potential waveforms. Electrode impedences were approximately 2 Kohms or less for all recordings. In all recording conditions a Cz (vertex) electrode was included in the montage for comparision of response magnitude across trials. Thirteen EEG signals could be recorded simultaneously, using a Nihon-Kohden 16 channel EEG polygraph (Model 4217) with a low-pass filter setting of 15 Hz and time constant of 5 sec. The total number of analog channels was limited to 15 by the A/D capabilities of the data acquisition computer, leaving two channels for EOG and rectified EMG. EEG distributions were recorded as two separate recordings of two interlaced montages (labelled 1 and 2 in Fig. 6A).

Magnetic Measurements

Magnetoencephalographic recordings were obtained using a 3rd order biogradiometer system (Vrba *et al.*, 1982) with a sensing coil diameter of 38 mm and an intercoil separation of 55 mm. The MEG signal consisted of an attenuated wideband signal provided by the digital SQUID electronics (DSQ-400, CTF Systems, Inc.) with a gradiometer gain of 270 picoTesla/phi_0 which was passed through an analog 60 Hz comb filter before being amplified using an

Elema–Schonander amplifier with a low–pass filter setting of 15 Hz and time constant of 5 seconds. The gradiometer was positioned with the sensing coil oriented normal to the scalp at the pre–selected sites using a computer–guided mechanical gantry system (Vrba *et al.*, 1985). This system utilizes digitized models of each subject's head to move and position the tip of the recording instrument and to record the exact orientation and position of the gradiometer coils with respect to an origin near the center of the head. This origin is taken as a point on a horizontal plane defined by the anatomical landmarks nasion and preauricular points where the line which passing through nasion and inion projected onto this plane intersects the line passing through pre–auricular points (see Figure 7). Comparisons and measurements taken from anatomical, stereotaxic and skull and brain specimens by myself and co–workers using this head–modelling system for anatomical localization (F. Coolsma, pers. comm.) have ascertained this origin to lie roughly in the vicinity of the brainstem at the midline of the ventral surface of the upper pons although position along the antero–posterior axis may show the maximum variability due to the variations in the relative lengths of individual's skulls and also along the lateral axis due to observed asymmetries in the estimation of the occipital protuberance (inion).

Recording Methods

Both EEG and MEG signals were digitized at a rate of 128 points/sec and stored continuously on magnetic tape using a Nova 4/D mini–computer. Bipolar surface EMG was recorded from large Beckmann Ag–AgCl electrodes affixed with Grass EC2 paste and adhesive collars on the long flexors of the subject's dominant forearm which control flexion of the digits (*flexor digitorum profundus and flexor digitorum superficialus*) so as to elicit the maximal response for a variety of finger flexions. Previous studies using indwelling EMG electrodes indicate that the surface EMG signals from the long flexors provide a good indication of the onset of muscle units involved in initiating the movement (Deecke, Grözinger & Kornhuber, 1976). EMG was rectified on–line and recorded onto tape using a hard–wired rectifier/Schmidtt trigger unit which produced a TTL (+5V) trigger pulse which was detected by a Zenith microcomputer. The

FIGURE 6. Distribution of EEG and MEG recording positions

A

1

Fpz

F3 Fz F4

T3 C3 Cz C4 T4

P3 Pz P4

Oz

2

F7   F8

FC3 FC1   FC2 FC4

Cz

CP3 CP1   CP2 CP4

T5   T6

90°

B

65°
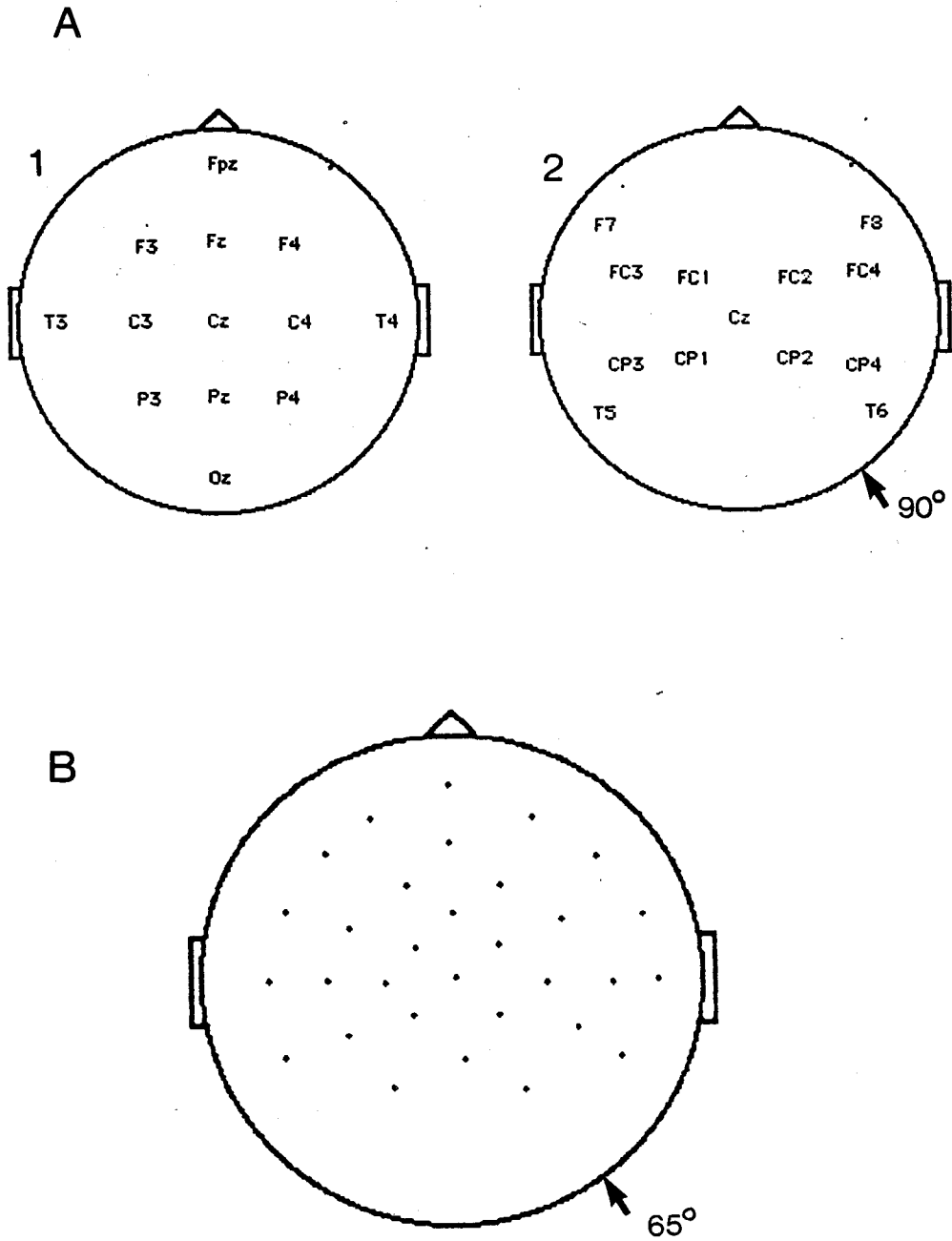
microcomputer placed a digital marker on the data tape which could later be used to identify movement-onset for off-line averaging of responses. The experimenter could reject on-line trials which were contaminated by subject artifact (e.g., eye movements) or slow magnetic noise (traffic on nearby roads) by button presses relayed to the microcomputer which placed additional markers on the tape. Off-line averaging was achieved by a tape-scanning program which could scan the digital channel for the appropriate trigger pulses.

Experimental Conditions

Three right-handed subjects were recorded from during performance of the two above conditions (simple and pattern) with their dominant hand. In addition, two right-handed subjects were included in which left and right hands were compared for the simple task only (in order to investigate bilateral activity observed in the initial recordings for unilateral movements). For the EEG distribution, data were collected in two separate recordings using the two montages described above – a standard 10-20 montage distributed over the head and an additional montage of interpolated electrode sites similar to those used by Thickbroom et al. (1984) in order to provide an equally spaced montage for the estimation of the Laplacian derivation. Cz (vertex) was always included, producing a total of 25 positions (including Cz once). MEG recordings were conducted separately and consisted of 31 or more successive recording positions producing a widespread distribution over the upper portion of the head (Fig. 6B). Subjects were seated upright in a specially designed non-magnetic chair or lay on a bed fitted with a wooden head-holding device. Digitized models of the subject's head allowed the gantry to move the sensing coil over pre-selected sites stored in the computer in a selective manner. This consisted of moving the biogradiometer sequentially from position to position a random manner (positions were typically chosen on the basis of accessability due to the limited tilt of the instrument). The subjects then performed each of the tasks while the instrument was in position. During all conditions subjects were instructed to fixate on a target in the center of their visual field and to avoid eye movements and

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Figure 7.

Head model coordinate system used for positioning of MEG
sensor and dipole localization program showing relationship
of head coordinates to equidistant projections shown in
Figure 6. (see text for details).

map border
= 90 deg.

Z

Y

inion

nasion
X

pre-auricular

50
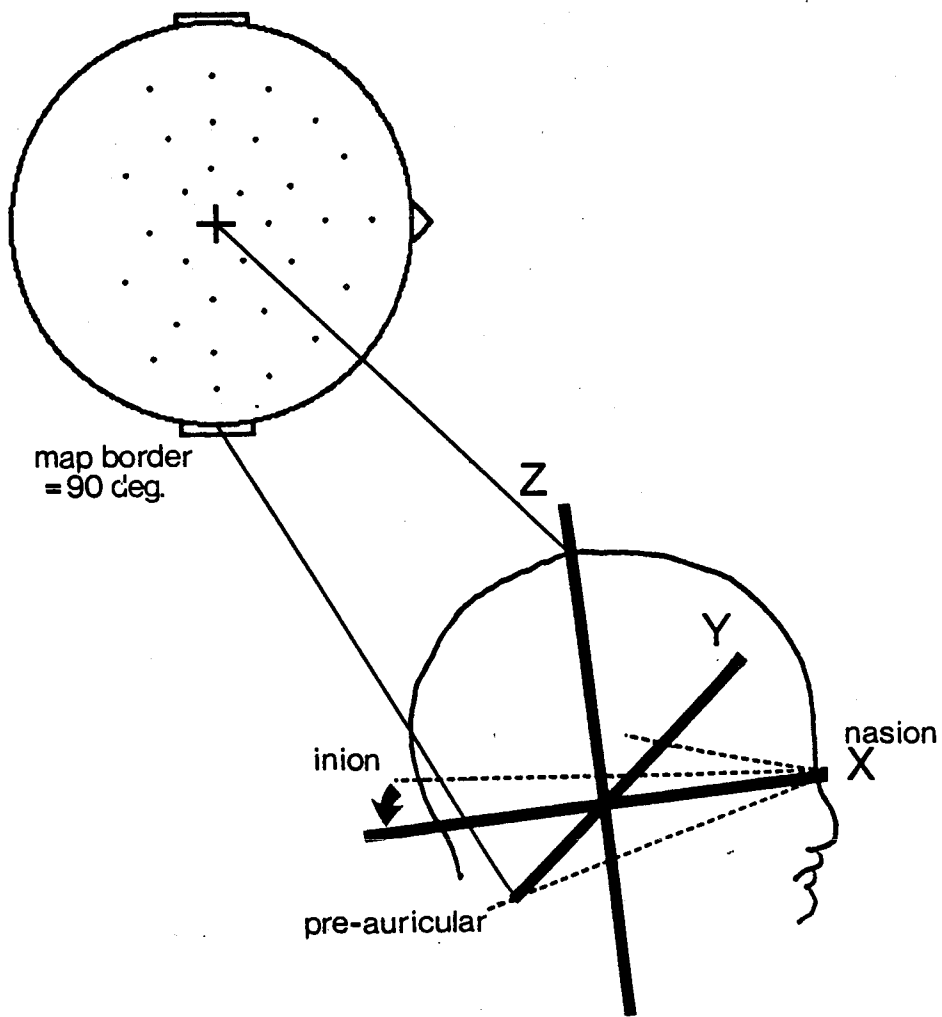
blinking, and to arrest breathing prior to and during their voluntary movements. Head movement was kept to a minimum by placing the subject's head in a wooden headrest and pillow arrangement which was necessary for positioning of the gantry. Since the MEG is extremely sensitive to movement, possible time-locked movements of the head preceding finger flexions were monitored in the first two subjects using a strain gauge, attached to the subject's forehead with string (head movements were minimal and the strain gauge was eliminated from the subsequent recordings). Recordings were taken from subjects for the following conditions after a few practice runs during which they achieved consistancy in their movements. Sessions were kept to a maximum of four or five hours due to fatigue in most subjects, an entire MEG distribution could be obtained in about five or six sessions over a period of about one week.

Condition 1: "Simple" - Unilateral finger flexions.

This condition involved instructing the subject to make rapid, biphasic flexions of the right index finger at their own volition until 40 artifact free movements were recorded (60 trials for EEG recordings). Subjects were instructed to initiate movements no faster then once every five or six seconds and were informed when their movements proceeded too quickly or became too regular in order to maintain a variable inter-trial interval. Since practice effects are problematic for sequential recordings of MEG activity, subjects were told that their performance should remain consistant over time and to try to maintain the same speed and force of flexion.

Condition 2: "Pattern" - Unilateral patterned flexions

This condition consisted of instructing the subject to make a pattern of flexions of the digits consisting of rapid flexion of the index finger followed by the third, fifth and fourth digits (i.e., a 2-3-5-4 pattern), again at their own volition. This pattern was not found to be overly difficult for most subjects to achieve with a fair degree of consistancy after a few practice trials (as indicated by EMG tracings and the average time for a set of trials) but required more concentration prior to movement.

PART C

RESULTS

Electrical Recordings

Averages of electrical activity preceding and during voluntary movement were produced by averaging off-line 2 second (256 point) epochs beginning 1.5 seconds prior to onset of EMG activity indicated by the tape trigger pulse, using the first 250 milliseconds as baseline. Figures 8.1.(1-3) show the averaged EEG waveforms for both recording montages combined for simple right finger flexions. Recordings using both left mastoid (subject T.R.) and nose as reference show presence of a readiness potential as a slow, centrally widespread wave of negativity, showing contralateral (left hemisphere) preponderance prior to onset of activity in forearm flexor muscles as indicated by the rectified EMG signal (REMG). This pattern is similar for both simple and pattern finger flexion conditions. In subjects D.C. and H.W. amplitude at Cz is greater for left finger movements than for right finger movements and there is a corresponding preponderance of negativity over the right hemisphere for left finger movements (Figure 8.3.4 and Figure 8.3.5). Similar patterns can be seen for patterned finger movements in Figures 8.3.(1-3). EEG data in one subject contained unidentifiable artifact apparently not related to eye-movement which contaminated the responses (but was included for the Laplacian analysis to determine the degree to which noise could be successfully eliminated). EEG activity during pattern movements shows a sustained negativity after movement onset related to continued activity in the EMG in which EMG bursts for the first two finger flexions can be seen. Subject T.R. (Figure 8.3.1.) shows pre-movement shifts greater in amplitude and later in onset for the pattern condition than for the simple condition, however, no differences in topographical distributions are evident for the two conditions. Some difference in the topography of the readiness potential can be seen between recordings with mastoid versus nose reference — the nose reference producing greater negativity in the posterior sites and somewhat greater degree of lateralization of the premovement shifts, although use of the left mastoid should produce conservative estimates of lateralization for right finger movements, if closer to active left hemisphere sources.

In order to examine the topography of electrical changes at the scalp associated with pre-movement activity, "Laplacian" transformations were performed on all referentially recorded EEG waveforms, using all points in the montage, weighted by their distances (refer to Appendix D), using the "source derivation" technique for approximation of the Laplacian of potential taken from Thickbroom et al. (1984, see also Doyle and Gevins, 1986). Since the EEG data were collected in separate averages with different contributions of noise due to artifact (e.g., eye movement) this transformation was applied separately to the two montages and the resulting waveforms were then combined for topographical analysis. Initial analysis of transformation on the combined montages produced similar results, although transformation of each montage separately tended to be more effective in removing some sources of noise. This indicates that the use of separate montages is a viable approach for systems with limited numbers of EEG channels although simultaneously recorded data would most likely provide better approximations of the potential gradients. Laplacian waveforms are shown for each subject in Figures 8.2.(1-5) and 8.4.(1-5), indicating a similar pattern current "sink" (negativities) and "source" (positivities) across subjects which show a differential distribution over the central regions of the scalp which change over the pre- and post-movement period. Most notably, these patterns are similar in subject R.G. although the referential activity was highly variable between the two montages (note in particular in Figure 8.2.2. the removal of the pre-movement shift seen in the corresponding referential recordings shown in Figure 8.1.2, particularly for the central positions, such as Cz, where the gradients are best estimated.

Spatio-temporal mapping of EEG fields

In order to examine the topography of the pre-movement shifts observed in the referential and Laplacian waveforms, interpolated isocontour maps were produced from intervals averaged over 5 point epochs at 39 millisecond (5 point) intervals for the period preceding and immediately following finger movement. These maps represent an equidistant projection of the top of the head modelled as a sphere, with vertex (Cz) at the center and the outer border of the map

indicating a line about the circumference of the head expressed as a angle of declination from vertex (a line passing through nasion-inion and preauricular points was taken as 90 degrees). The mapping technique used employs an inverse distance weighting algorithm (Weinberg, Brickett, Coolsma & Baff, 1986) which interpolates a high resolution 50 X 50 rectangular array onto which the recording locations are projected. The isocontour line maps were produced using an algorithm modified from Bourke (1987, see Appendix G). Each contour represents 1.2 microvolts for the referential data with the map border of 90 degrees and 3.8 microvolts for the Laplacian waveforms with a map border of 65 degrees (lying above the line passing through 1020 positions, Fpz, T3, Oz and T4). Isocontour maps of EEG referential EEG activity over the period leading up to and following EMG onset are shown in Appendix A. Maps are computed for contiguous 5 point (39 msec) intervals for both simple and pattern conditions (Figures 14.1.(1-3) and 14.2.(1-3)) and right and left finger flexions (Figures 14.1.(4-5) and 14.2.(4-5)). (Due to excessive artifact referential maps are not shown for subject R.G.) The Cz EEG waveform is shown below each map with a solid vertical line indicating EMG onset and a dotted vertical line indicating the time of the map, also given in milliseconds preceding EMG onset above. Referential maps show a gradual increase in negativity over the central regions of the scalp becoming, slightly lateralized to the contralateral hemisphere between 150 and 100 milliseconds prior to EMG onset (onset of lateralization varied slightly between subjects) and becoming more concentrated over contralateral Rolandic areas after movement onset. These findings are consistant with previous reports of contralateral preponderance of negativity for unilateral finger movements.

For spatio-temporal mapping of Laplacian transformed EEG, peripheral electrode positions (Fpz, F7, F8, T3, T4, T5, T6, and Oz) were removed from the data since the boundary conditions affecting these positions are not corrected for, and are therefore not directly interpretable (Nunez, 1981). However, these data points are included in the calculation of the gradient change for the inner positions, since they will be sensitive to spread of artifact currents from the

lower portion of the head and provide a better estimation of the Laplacian of the electrical field at the top of head. Thus, the Laplacian EEG maps shown here are considered to provide a conservative estimation of the pattern of current sinks (solid lines) and sources (dotted lines) over the upper surface of the head. Figures 15.1.(1-5) and Figures 15.2.(1-5) (see Appendix B) show isocontour maps of the Laplacian transformed data shown in Appendix A. These maps demonstrate a consistant pattern of source and sink reversal over the Rolandic areas can be seen in all subjects. For the pre-movement period this pattern is characterized by a fronto-central source and a large centro-parietal area of current sink overlying the hemisphere contralateral to movement which becomes more concentrated immediately prior to and during EMG onset, but is fairly widespread. This pattern is followed by a more concentrated pattern of current sink parietally and current source centrally thus, overlying the Rolandic areas in the hemisphere contralateral to movement and shifted more posterior and maximal at about 100 milliseconds after EMG onset. These latter source-sink patterns correspond to peak negativities in the vertex EEG. In some subjects with a subsequent positive phase in the vertex EEG, another source-sink reversal can be seen overlying the same region (see Figure 15.1.2.) but of opposite orientation (anterior sink - posterior source). These latter reversals can also been seen in the Laplacian waveforms (Figures 8.2, 8.4) as distinct peaks overlying C3, and C4 for right and left finger movements, respectively.

FIGURE 8.1.1. EEG activity (referential) preceding unilateral finger flexion - Simple condition (subject T.R.)
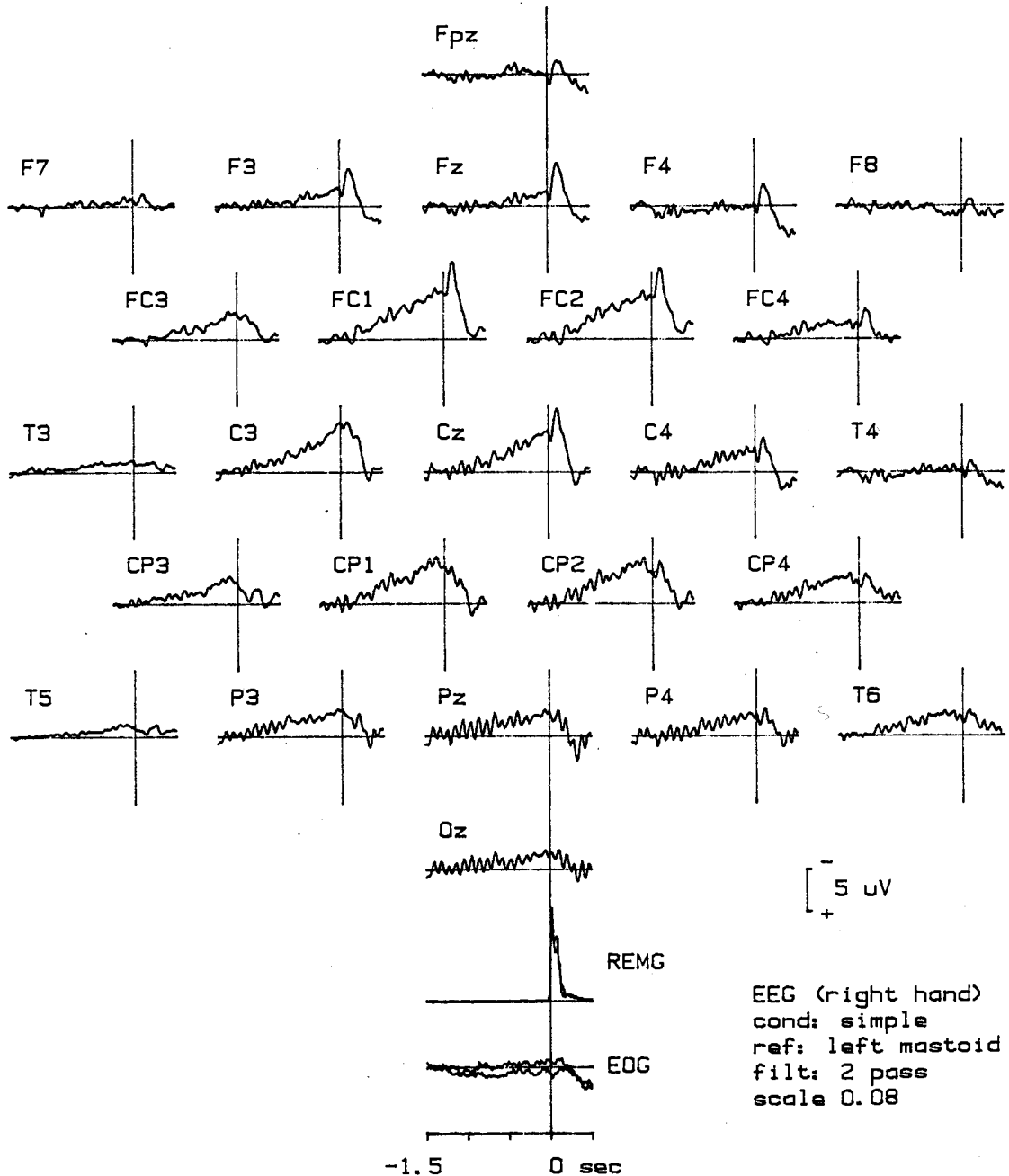
FIGURE 8.1.2. EEG activity (referential) preceding unilateral finger flexion – Simple condition (subject R.G.)

Fpz

F7   F3   Fz   F4   F8

FC3   FC1   FC2   FC4

T3   C3   Cz   C4   T4

CP3   CP1   CP2   CP4

T5   P3   Pz   P4   T6

Oz

$\begin{bmatrix} - \\ 5 \text{ }\mu V \\ + \end{bmatrix}$

REMG

EOG

EEG (right hand)
cond: simple
ref: nose
n=60
filt: 2 pass
scale: 0.08

-1.5   0 sec
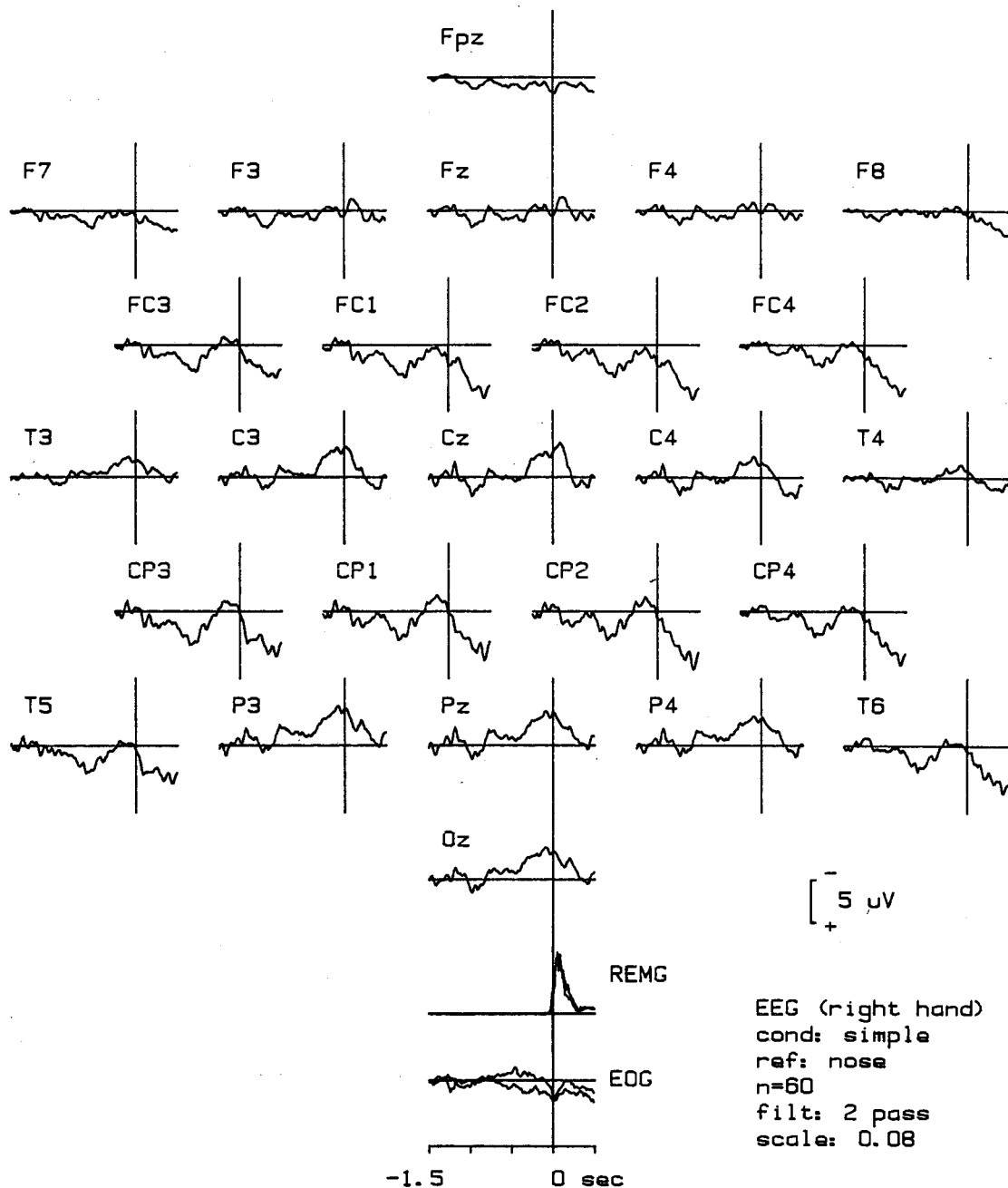
FIGURE 8.1.3. EEG activity (referential) preceding unilateral finger flexion - Simple condition (subject B.J.)

EEG (right hand)
cond: simple
ref: nose
n=60
filt: 2 pass
scale 0.08
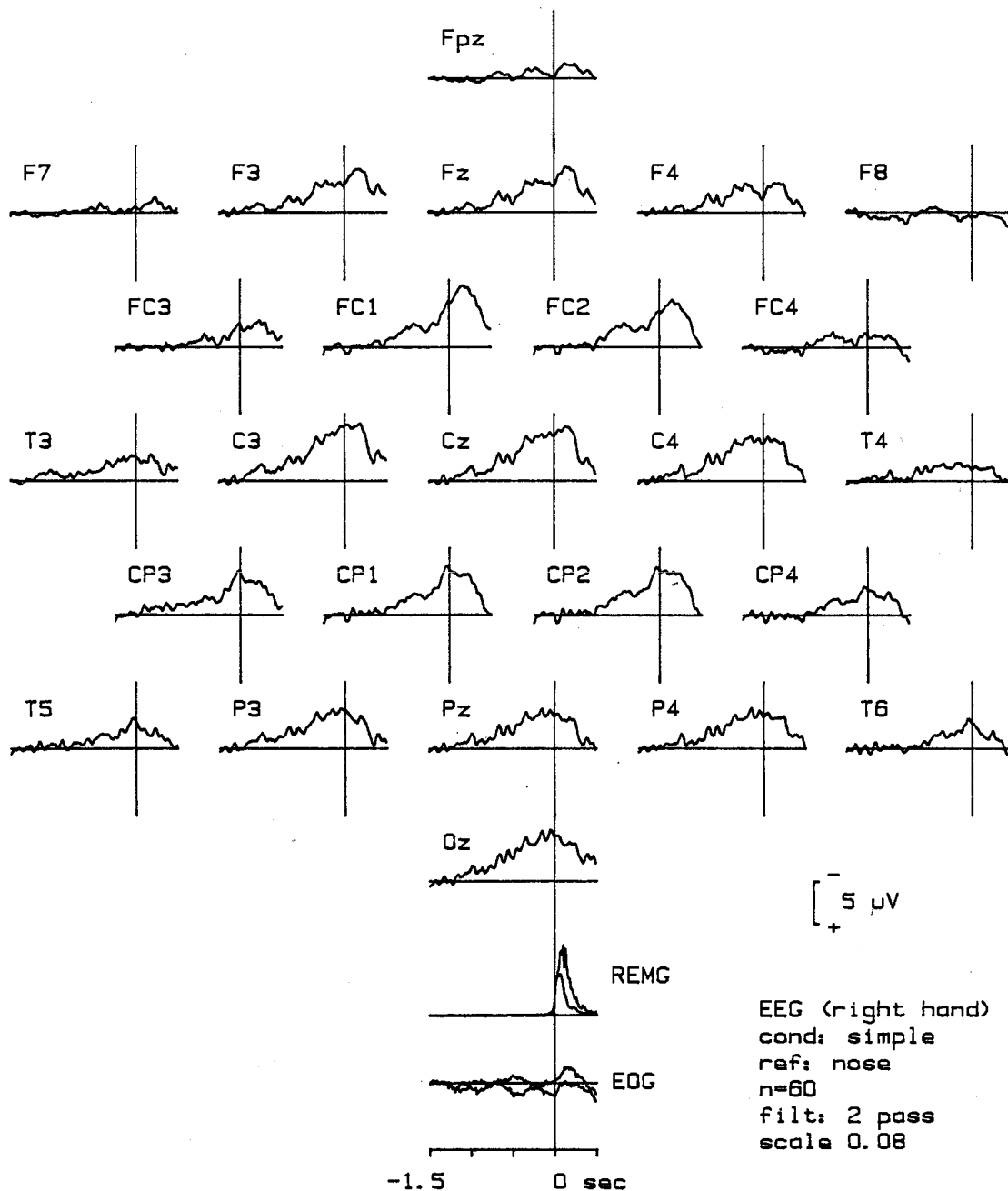
FIGURE 8.1.4. EEG activity (referential) preceding unilateral finger flexion – Right hand (subject D.C.)

5 uV

EEG (right hand)
cond: simple
ref: nose
n=60
filt: 2 pass
scale: 0.08

-1.5   0 sec
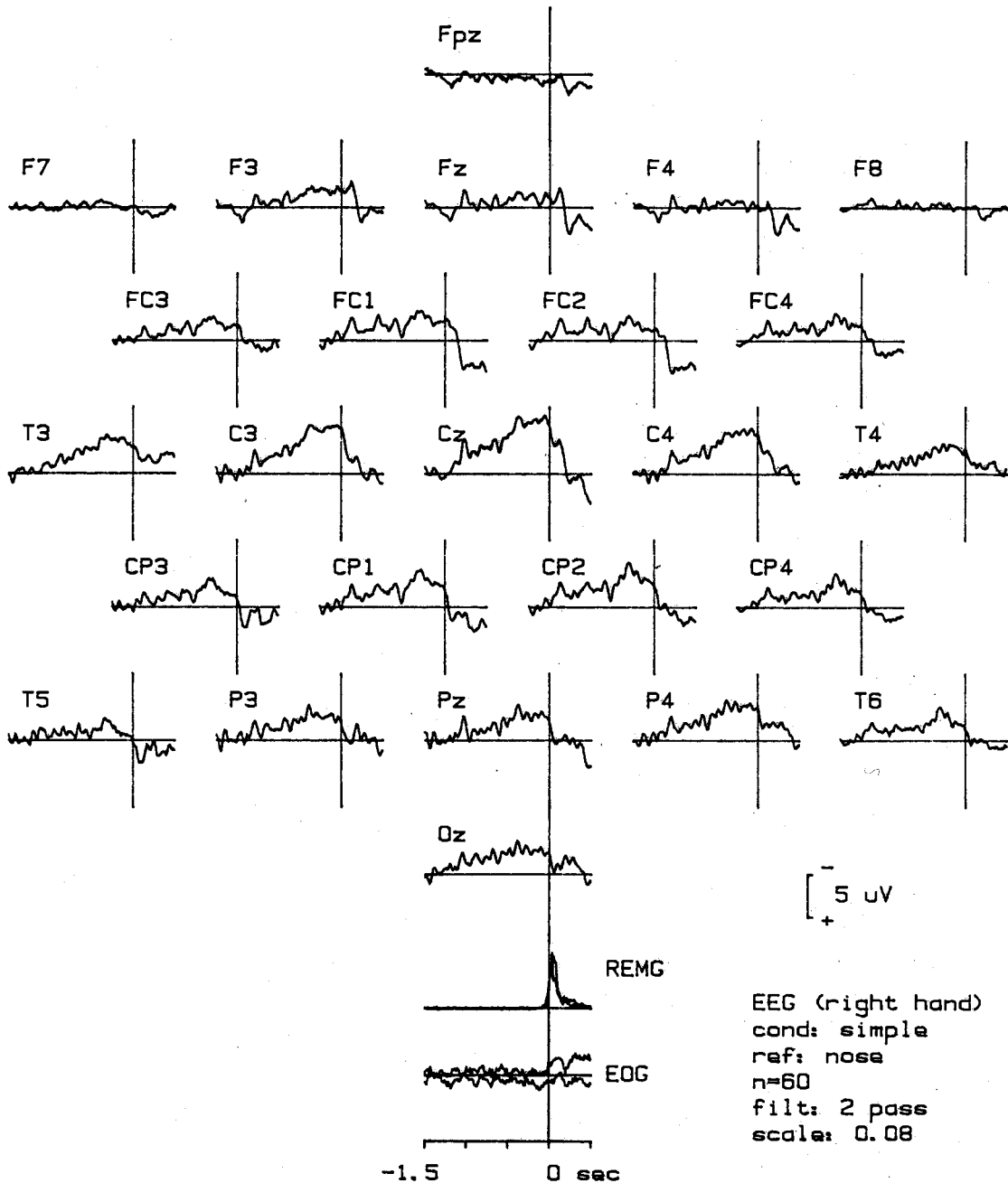
FIGURE 8.1.5. EEG activity (referential) preceding unilateral finger flexion – Right hand (subject H.W.)

Fpz

F7   F3   Fz   F4   F8

FC3   FC1   FC2   FC4

T3   C3   Cz   C4   T4

CP3   CP1   CP2   CP4

T5   P3   Pz   P4   T6

Oz

$\begin{bmatrix} \bar{} & 5 \ \mu V \\ + \end{bmatrix}$

REMG

EOG

EEG (right hand)
cond: simple
ref: nose
n=60
filt: 2 pass
scale 0.08

-1.5   0 sec

61
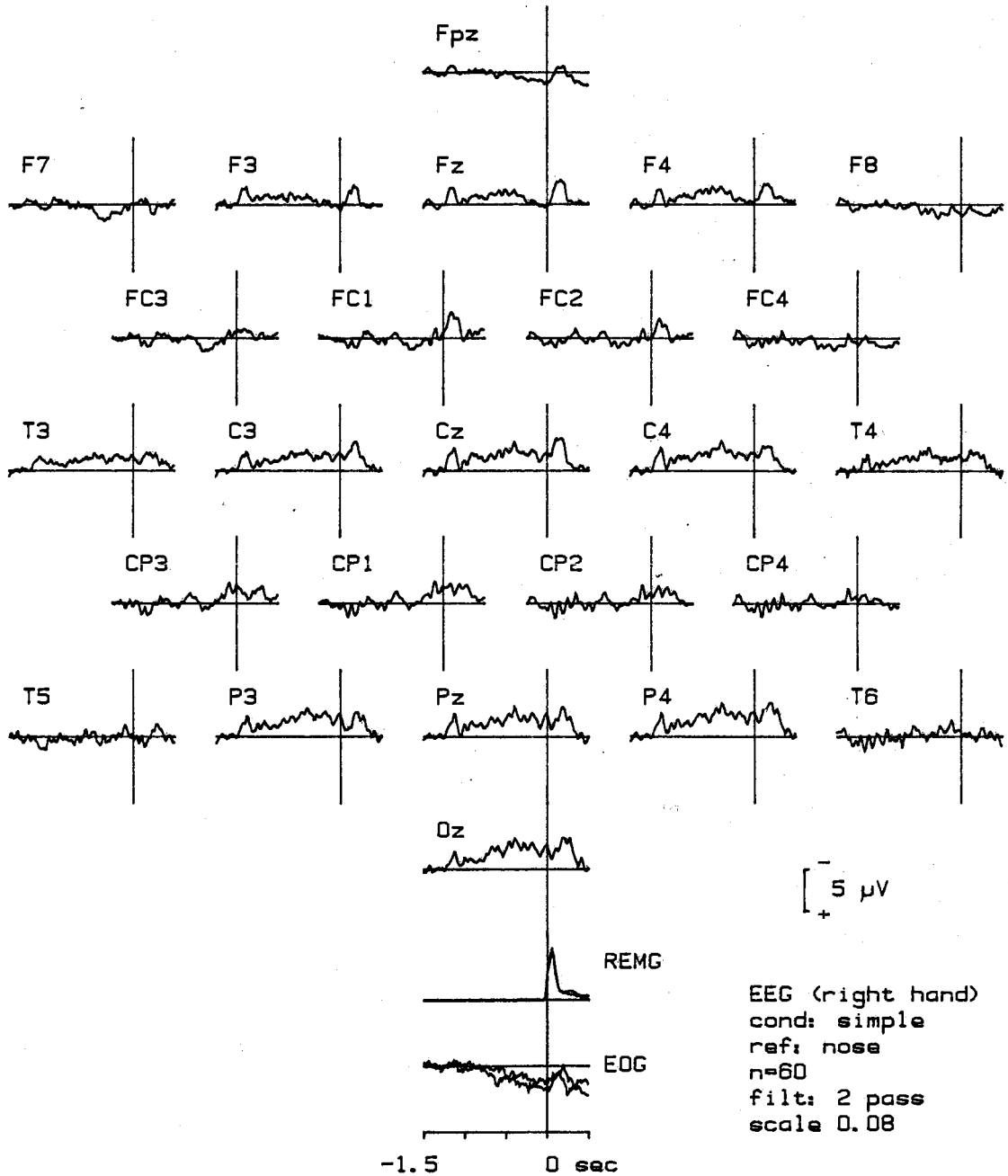
FIGURE 8.2.1. EEG activity (Laplacian) preceding unilateral finger flexion – Simple condition (subject T.R.)
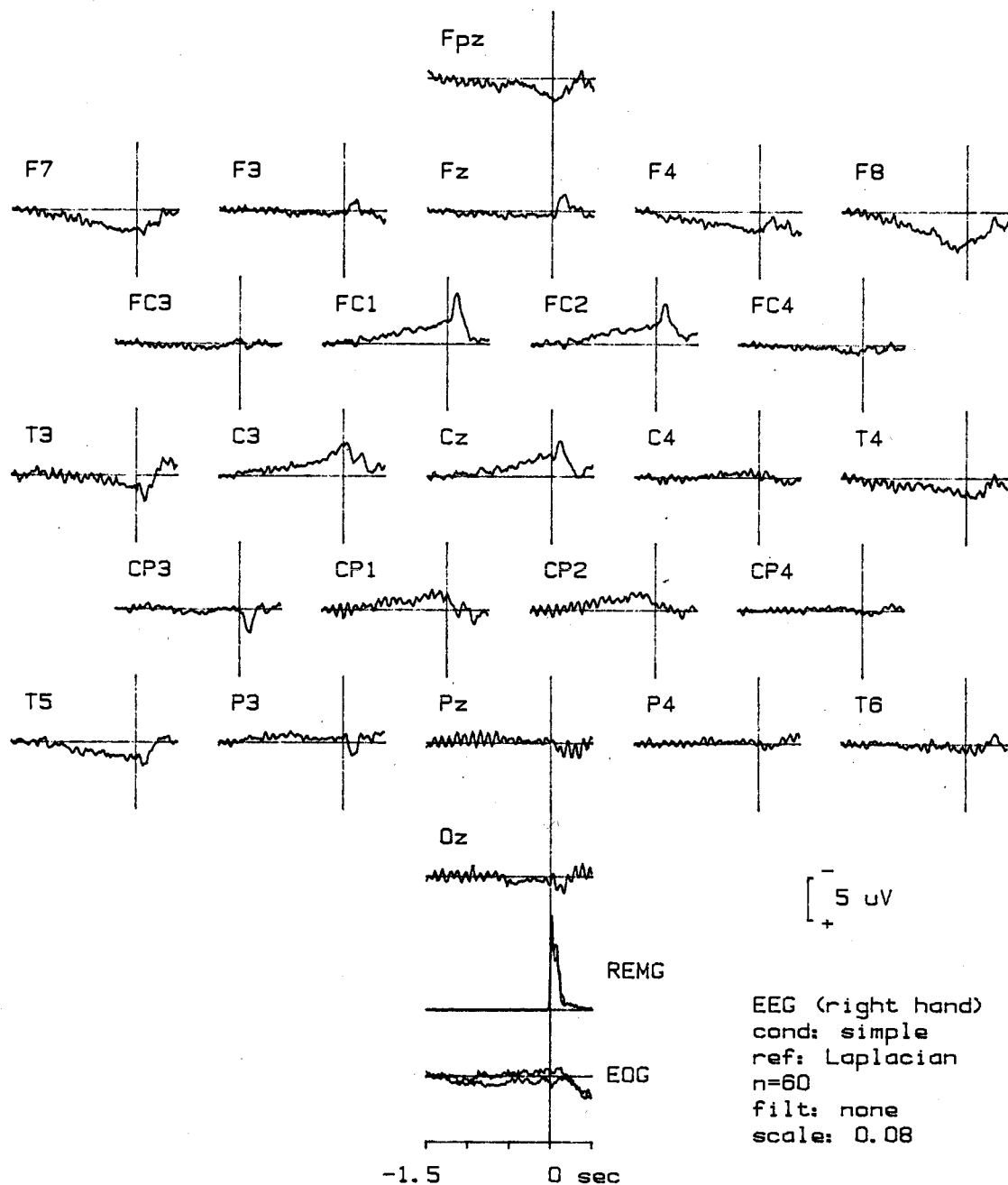
FIGURE 8.2.2. EEG activity (Laplacian) preceding unilateral finger flexion – Simple condition (subject R.G.)

Fpz

F7   F3   Fz   F4   F8

FC3   FC1   FC2   FC4

T3   C3   Cz   C4   T4

CP3   CP1   CP2   CP4

T5   P3   Pz   P4   T6

Oz

REMG

EOG

5 uV

EEG (right hand)
cond: simple
ref: Laplacian
n=60
filt: none
scale: 0.08

-1.5   0 sec
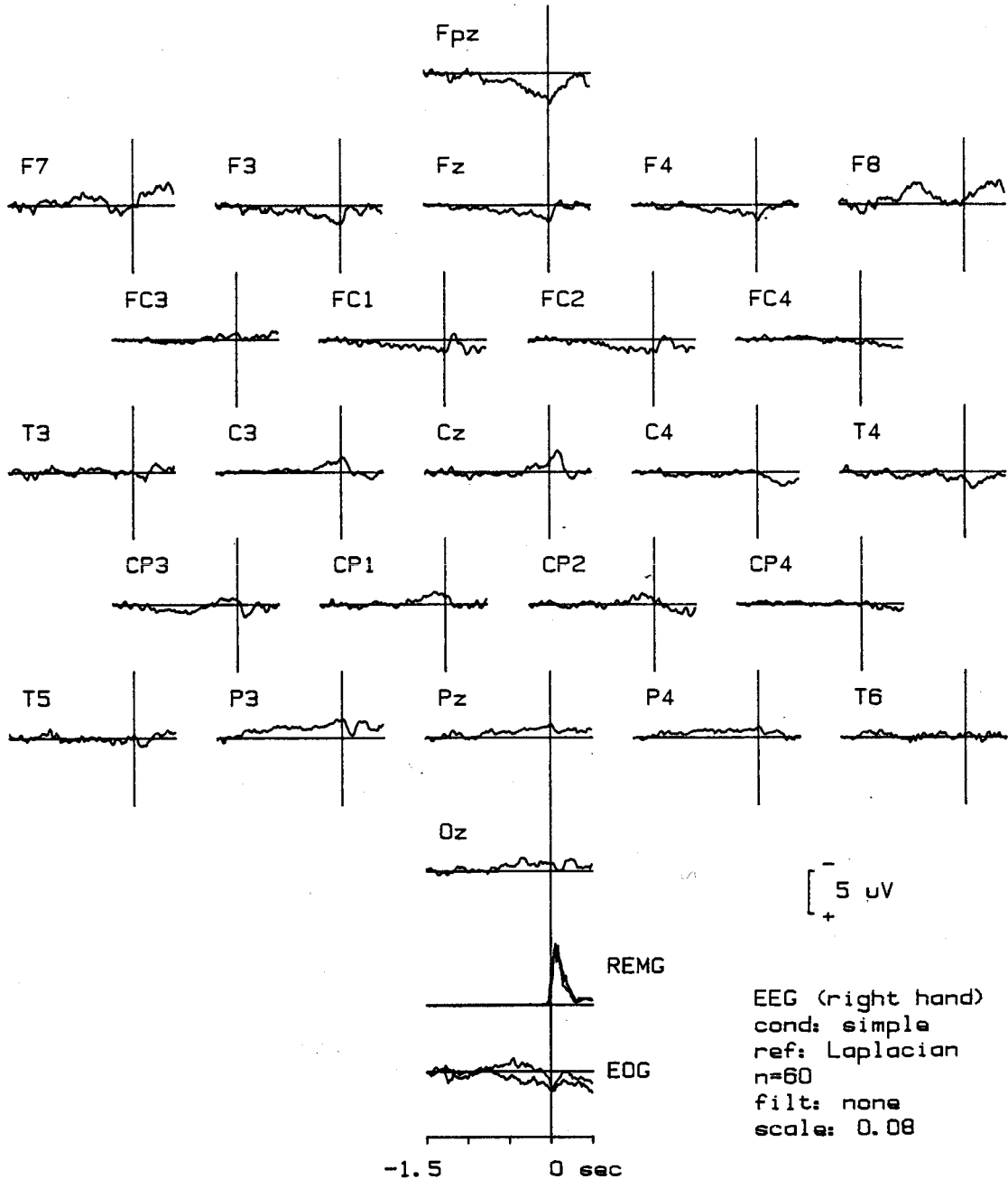
FIGURE 8.2.3. EEG activity (Laplacian) preceding unilateral finger flexion - Simple condition (subject B.J.)

Fpz

F7   F3   Fz   F4   F8

FC3   FC1   FC2   FC4

T3   C3   Cz   C4   T4

CP3   CP1   CP2   CP4

T5   P3   Pz   P4   T6

Oz

5 µV

REMG

EOG

EEG (right hand)
cond: simple
ref: Laplacian
n=60
filt: none
scale 0.08

-1.5   0 sec
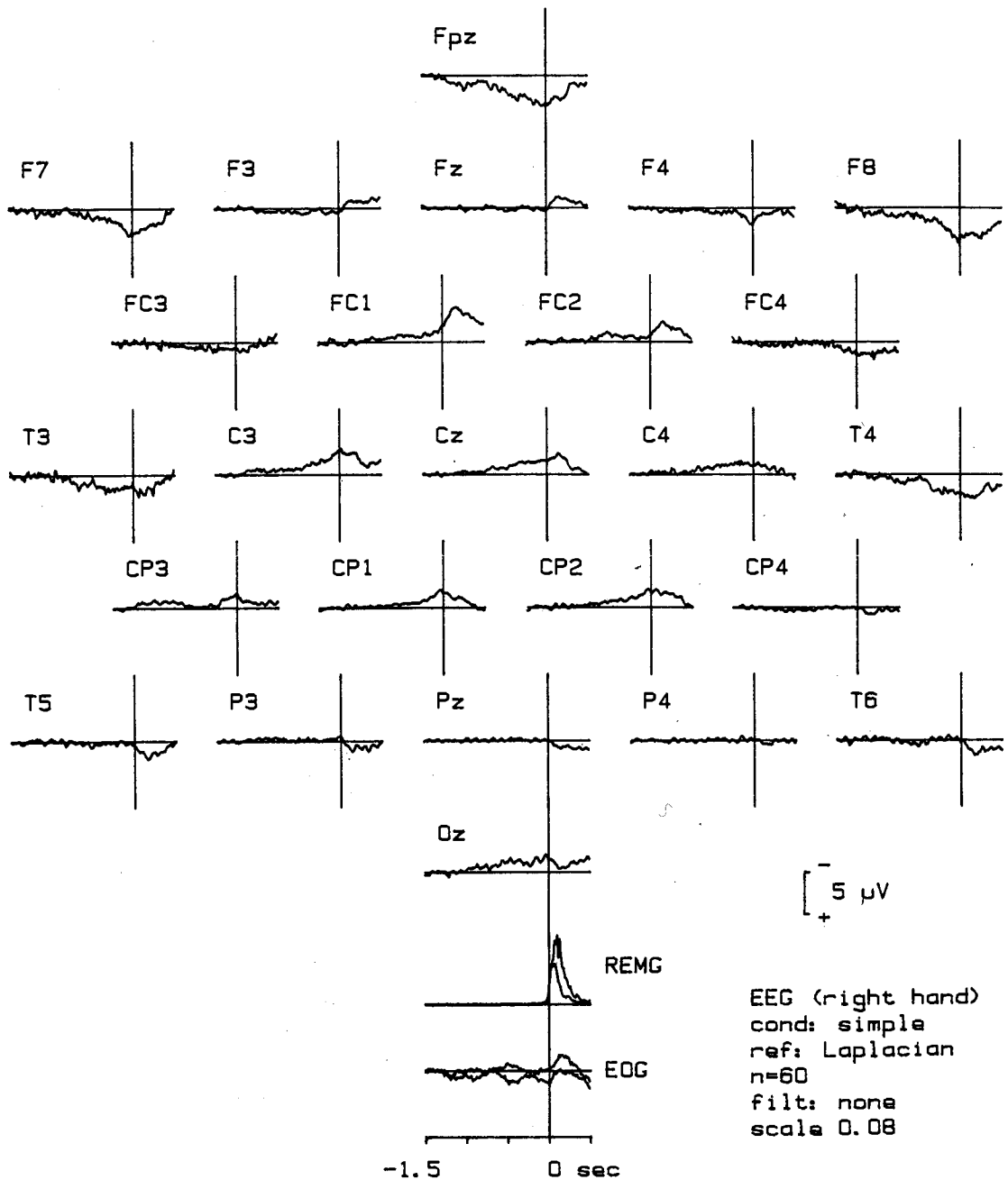
FIGURE 8.2.4. EEG activity (Laplacian) preceding unilateral finger flexion - Right hand (subject D.C.)

EEG (right hand)
cond: simple
ref: Laplacian
n=60
filt: none
scale: 0.08

-1.5   0 sec
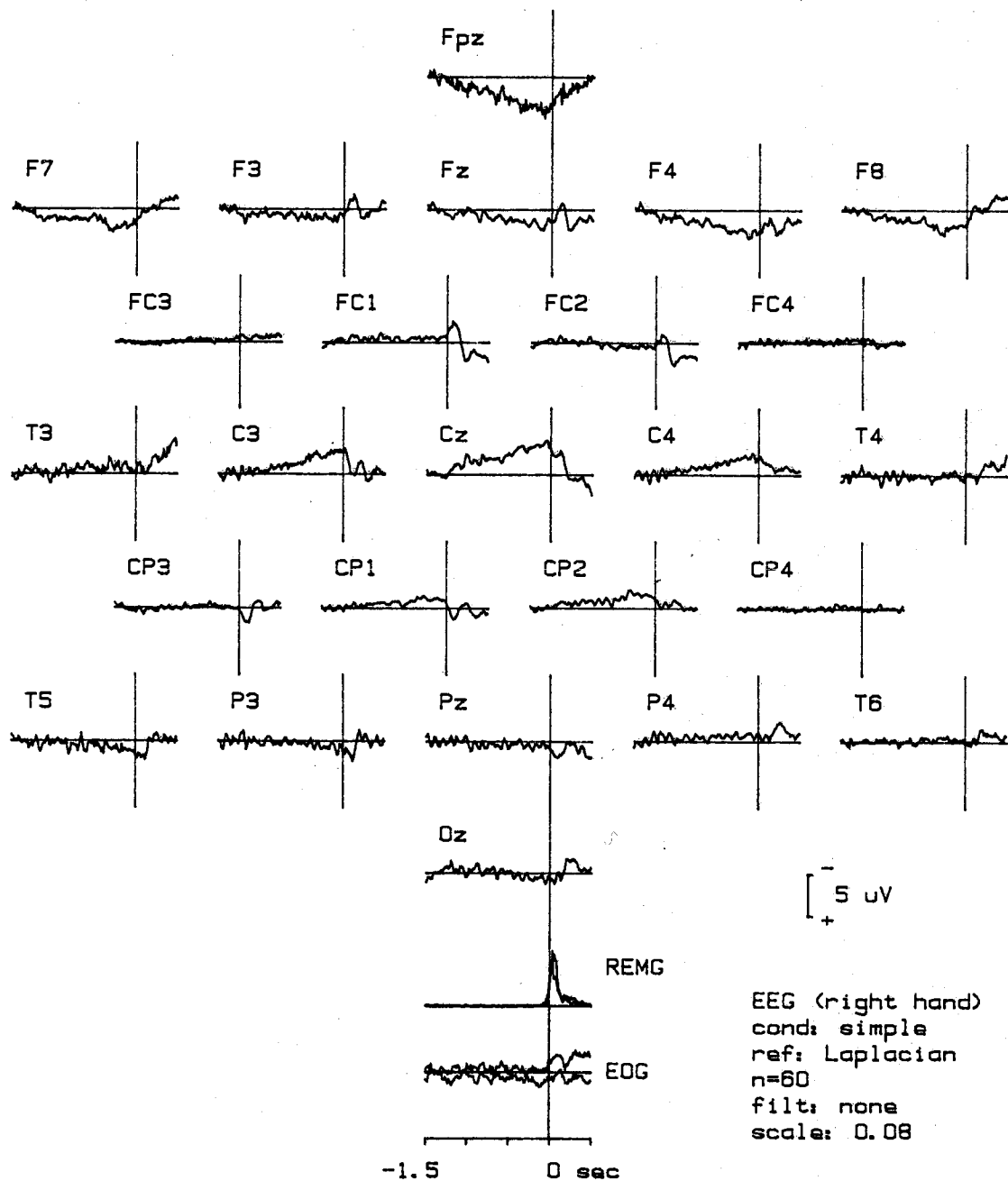
FIGURE 8.2.5. EEG activity (Laplacian) preceding unilateral finger flexion – Right hand (subject H.W.)

Fpz

F7   F3   Fz   F4   F8

FC3   FC1   FC2   FC4

T3   C3   Cz   C4   T4

CP3   CP1   CP2   CP4

T5   P3   Pz   P4   T6

Oz

2.5 μV

REMG

EOG

EEG (right hand)
cond: simple
ref: Laplacian
n=60
filt: none
scale 0.16

-1.5   0 sec
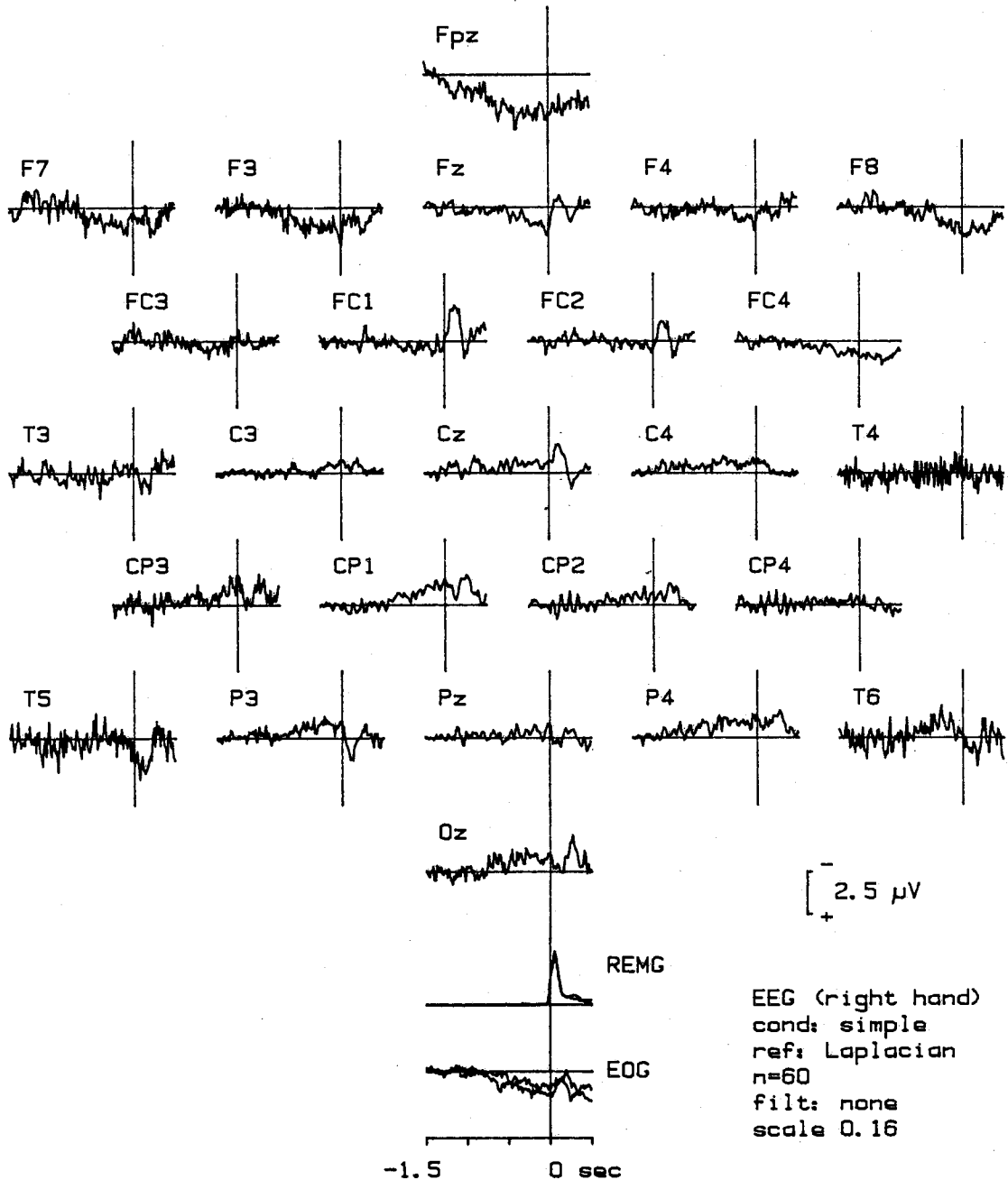
FIGURE 8.3.1. EEG activity (referential) preceding unilateral finger flexion - Pattern condition (subject T.R.)
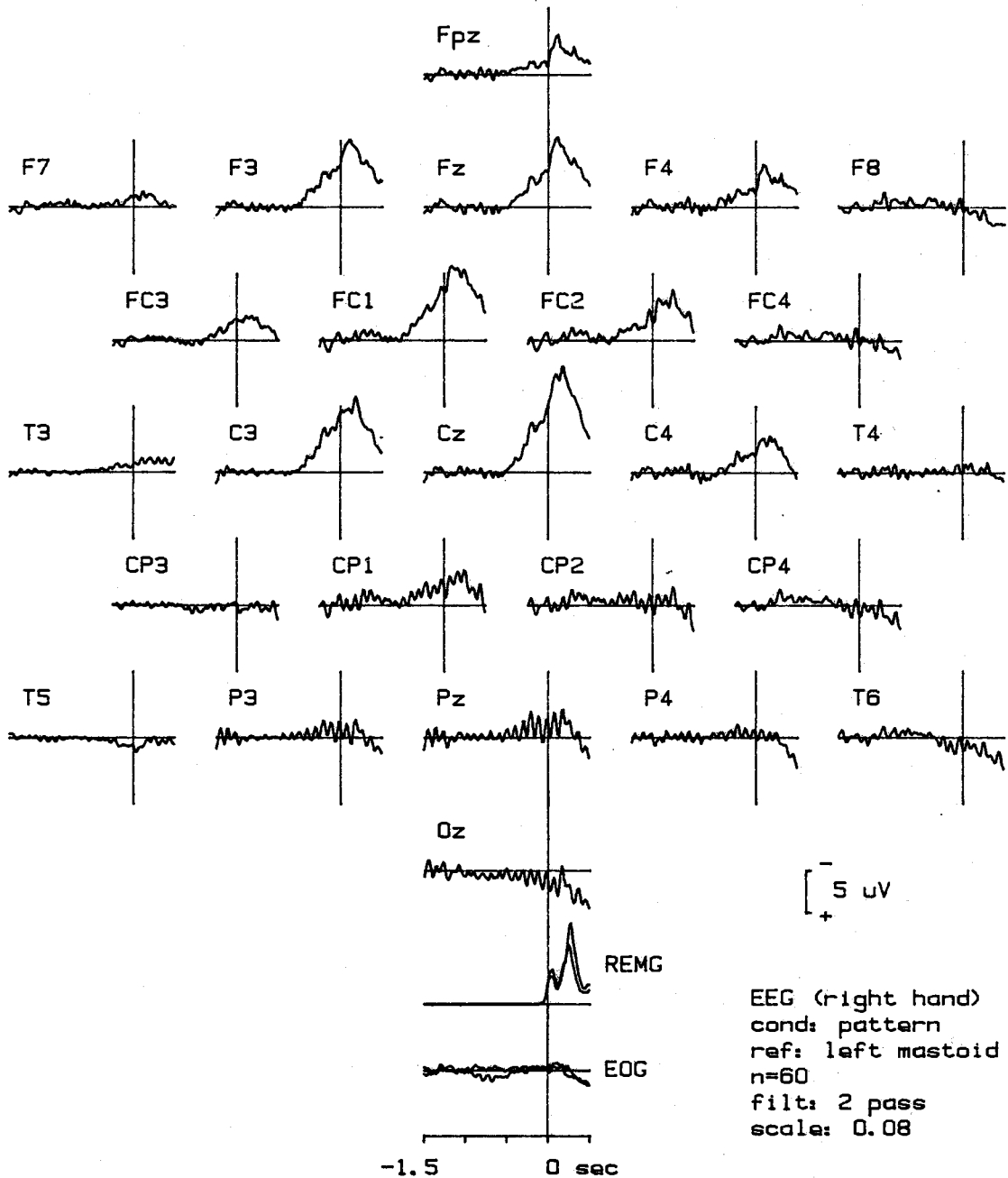
FIGURE 8.3.2. EEG activity (referential) preceding unilateral finger flexion – Pattern condition (subject R. G.)

EEG (right hand)
cond: pattern
ref: nose
n= 60
filt: 2 pass
scale: 0.08
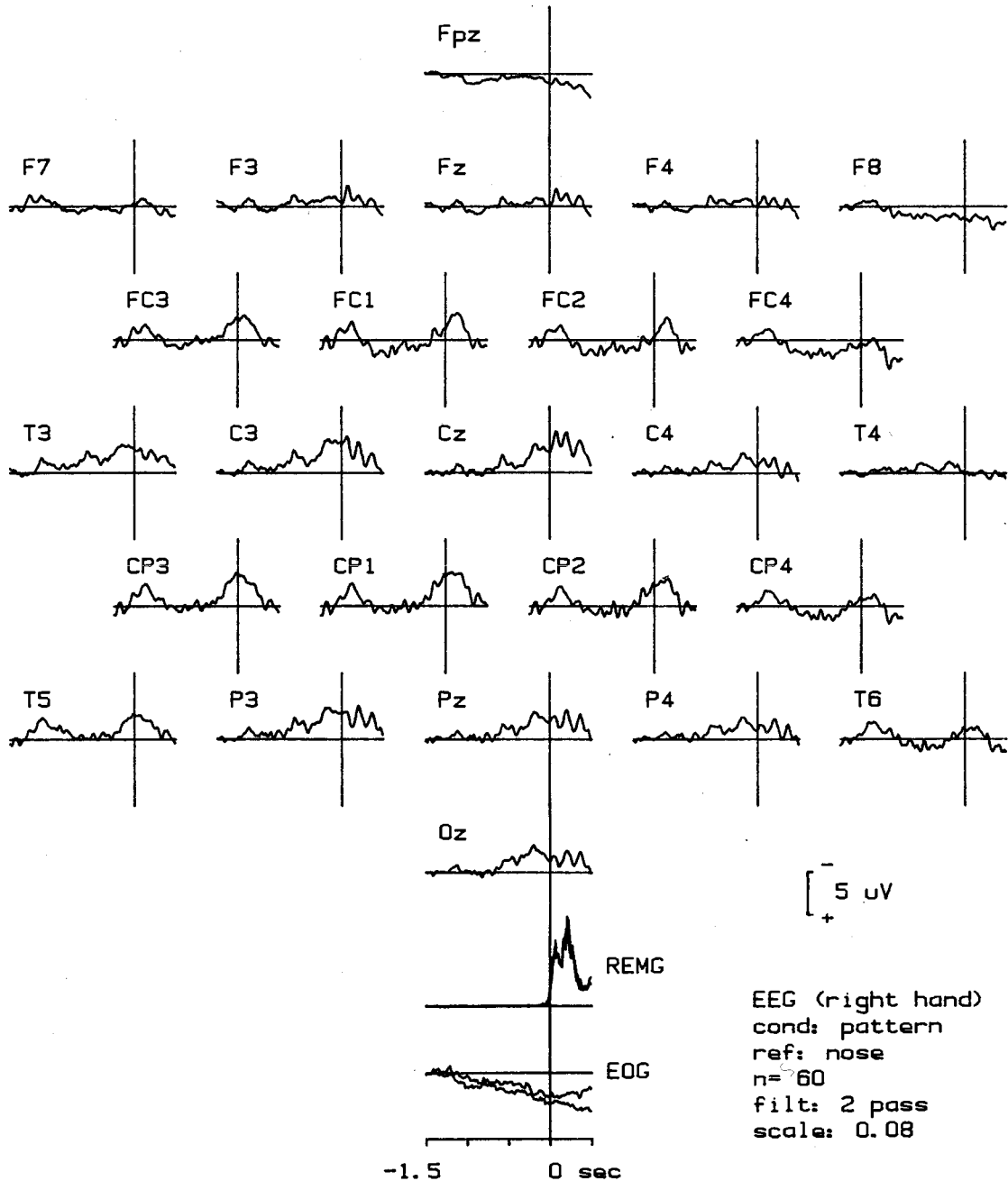
FIGURE 8.3.3. EEG activity (referential) preceding unilateral finger flexion - Pattern condition (subject B. J.)

-1.5   0 sec

5 µV

EEG (right hand)
cond: pattern
ref: nose
n=60
filt: 2 pass
scale: 0.08
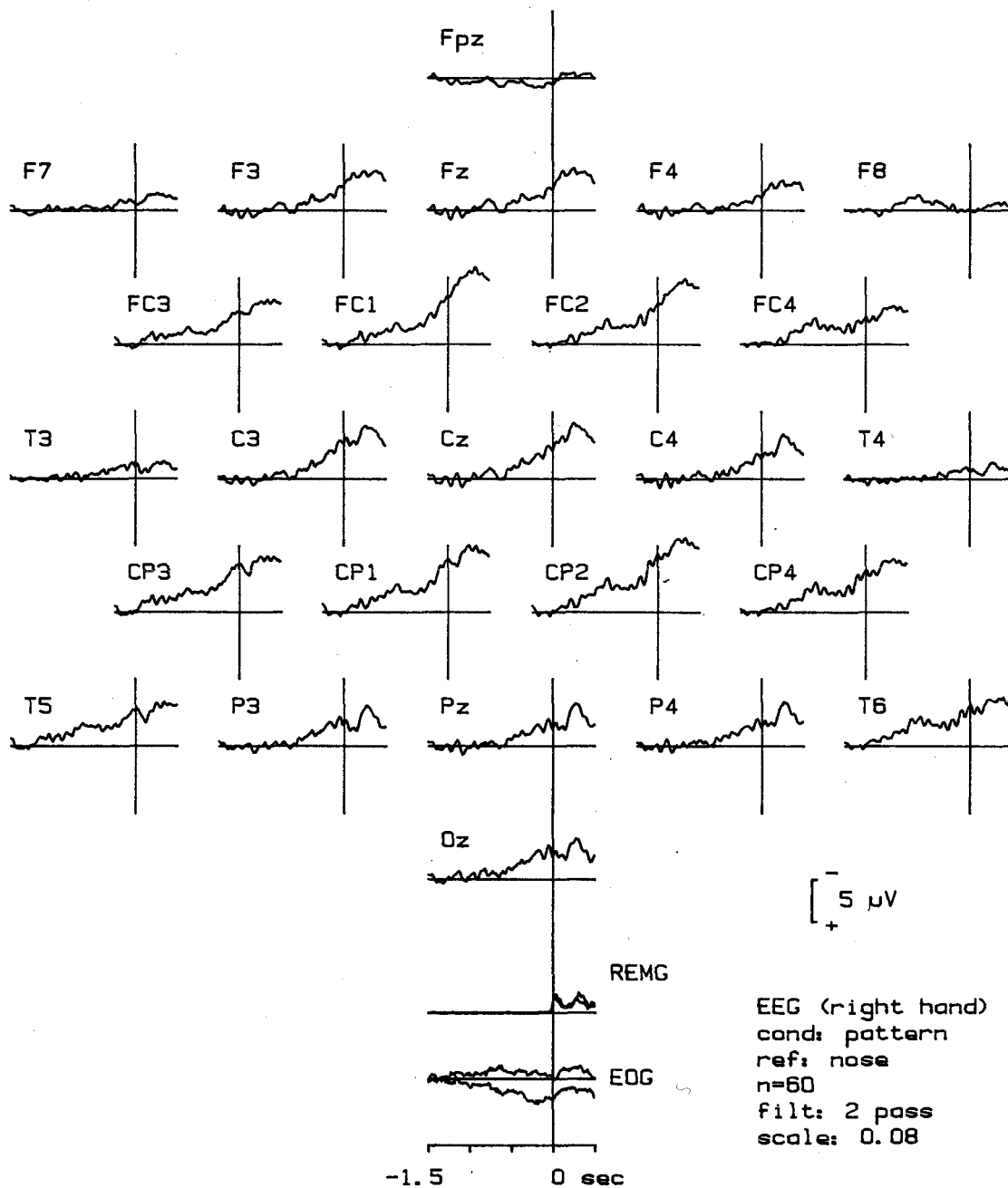
FIGURE 8.3.4. EEG activity (referential) preceding unilateral finger flexion - Left hand (subject D.C.)
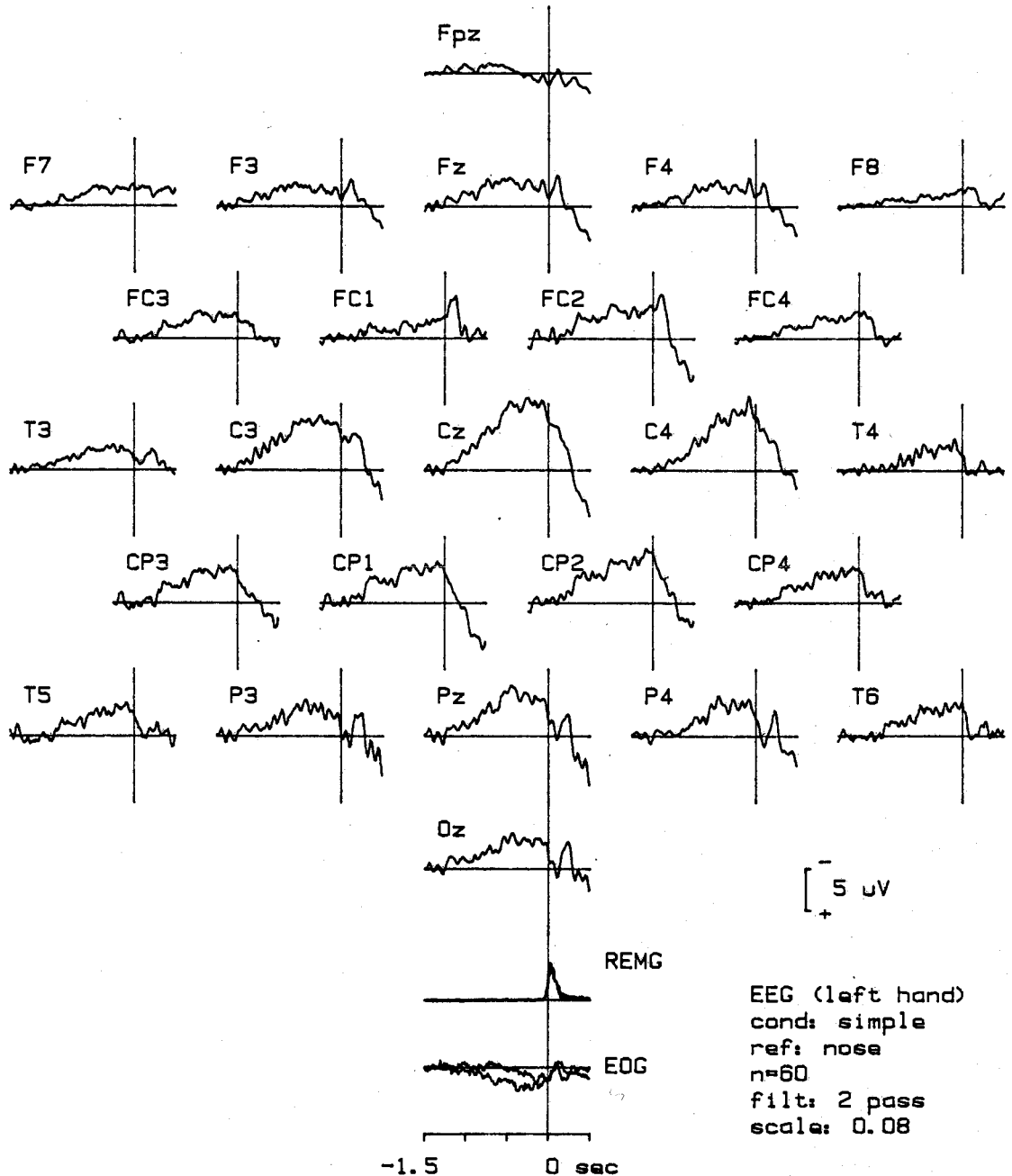
FIGURE 8.3.5. EEG activity (referential) preceding unilateral finger flexion – Left hand (subject H.W.)

EEG (left hand)
cond: simple
ref: nose
n=60
filt: 2 pass
scale: 0.08
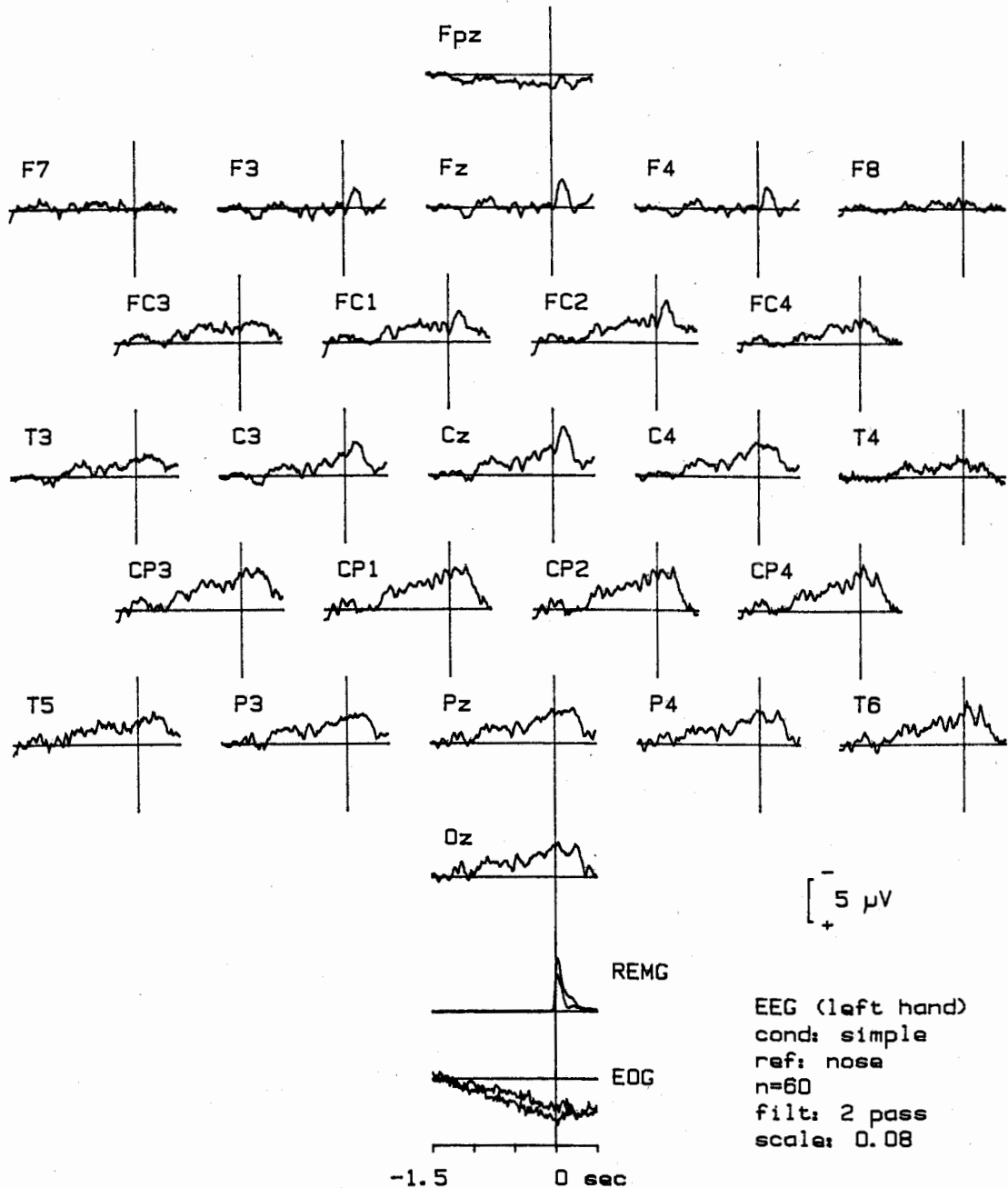
FIGURE 8.4.1. EEG activity (Laplacian) preceding unilateral finger flexion - Pattern condition (subject T.R.)

EEG (right hand)
cond: pattern
ref: Laplacian
n=60
filt: none
scale: 0.08
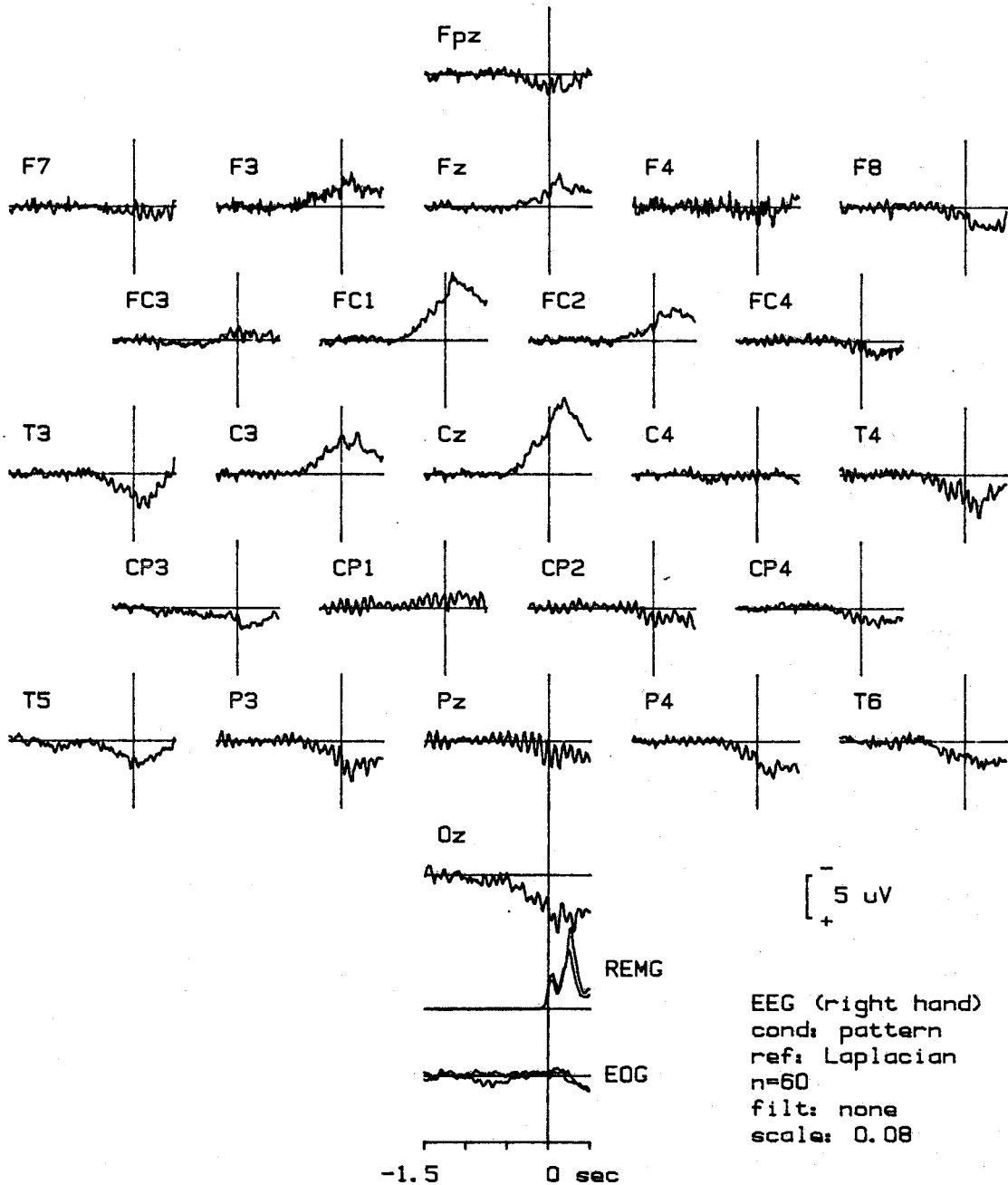
FIGURE 8.4.2. EEG activity (Laplacian) preceding unilateral finger flexion - Pattern condition (subject R.G.)

Fpz

F7   F3   Fz   F4   F8

FC3   FC1   FC2   FC4

T3   C3   Cz   C4   T4

CP3   CP1   CP2   CP4

T5   P3   Pz   P4   T6

Oz

$\left[\begin{array}{c} - \\ 5 \text{ }\mu V \\ + \end{array}\right.$

REMG

EOG

EEG (right hand)
cond: pattern
ref: Laplacian
filt: none
scale: 0.08

-1.5   0 sec
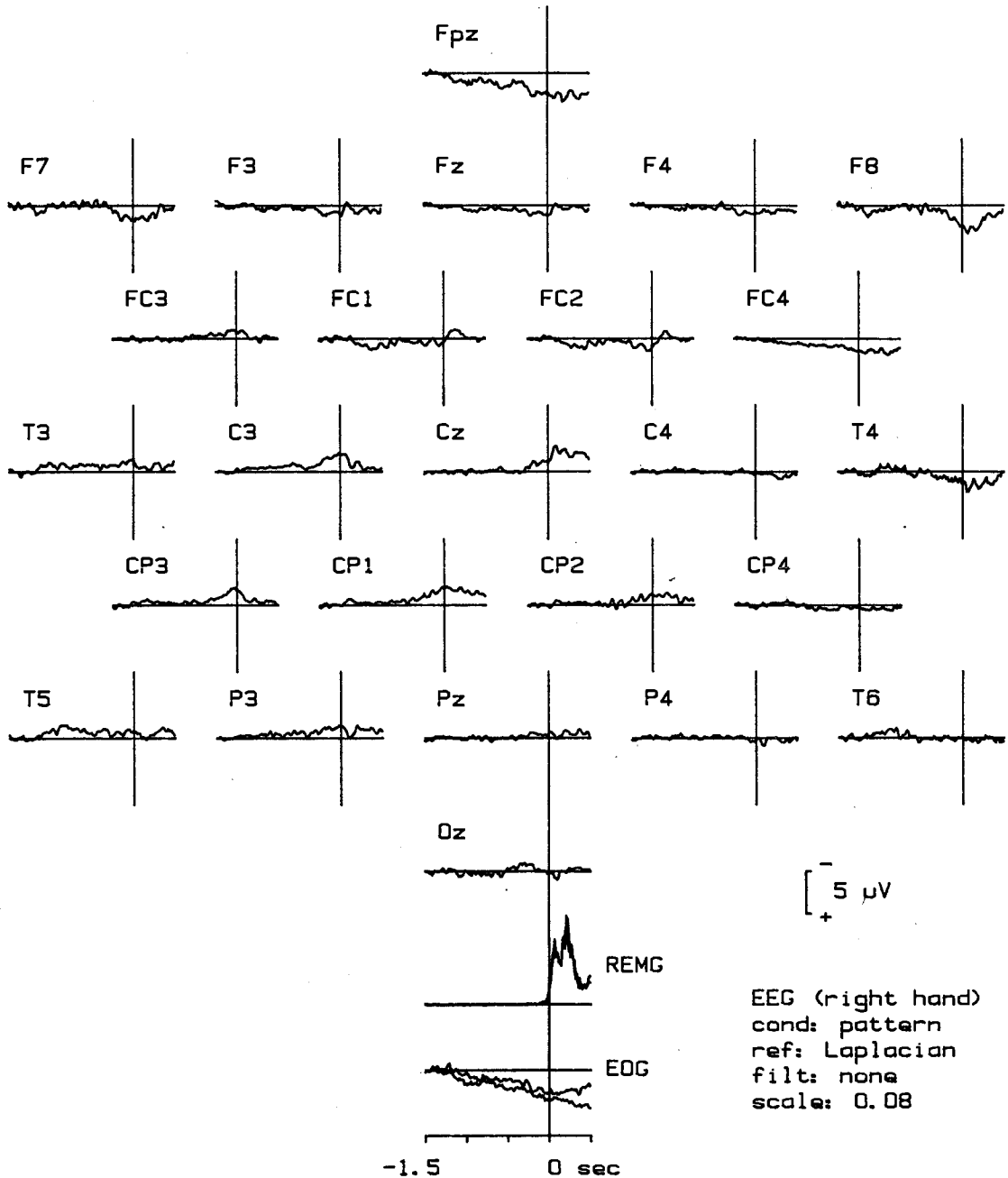
FIGURE 8.4.3.   EEG activity (Laplacian) preceding unilateral finger flexion - Pattern condition (subject B.J.)

Fpz

F7   F3   Fz   F4   F8

FC3   FC1   FC2   FC4

T3   C3   Cz   C4   T4

CP3   CP1   CP2   CP4

T5   P3   Pz   P4   T6

Oz

$\begin{bmatrix} ^- \\ 5 \ \mu V \\ _+ \end{bmatrix}$

REMG

EEG (right hand)
cond: pattern
ref: Laplacian
n=60
filt: none
scale 0.08

EOG

-1.5   0 sec
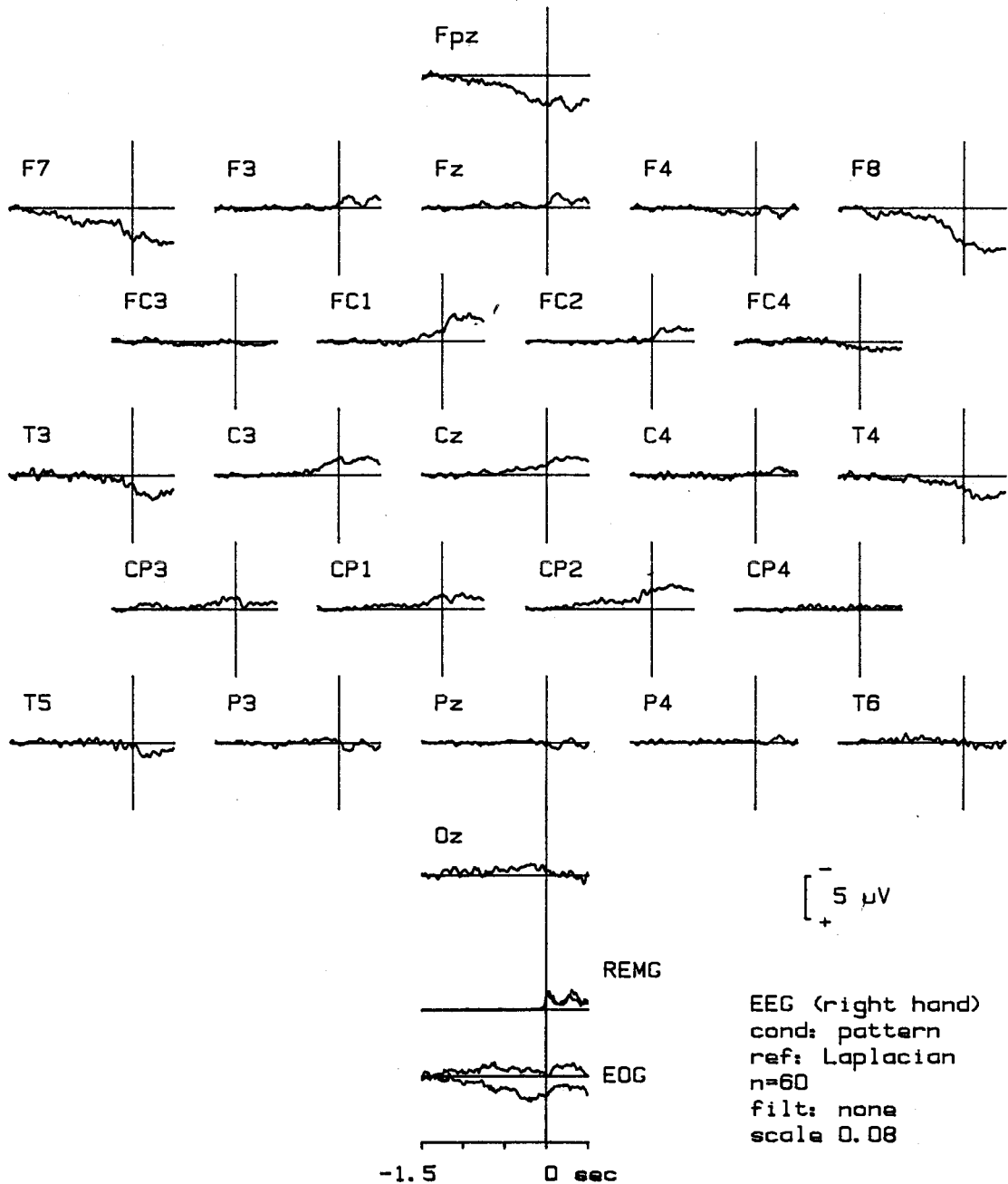
FIGURE 8.4.4. EEG activity (Laplacian) preceding unilateral finger flexion - Left hand (subject D.C.)

EEG (left hand)
cond: simple
ref: Laplacian
n=60
filt: none
scale: 0.08

−1.5   0 sec

75
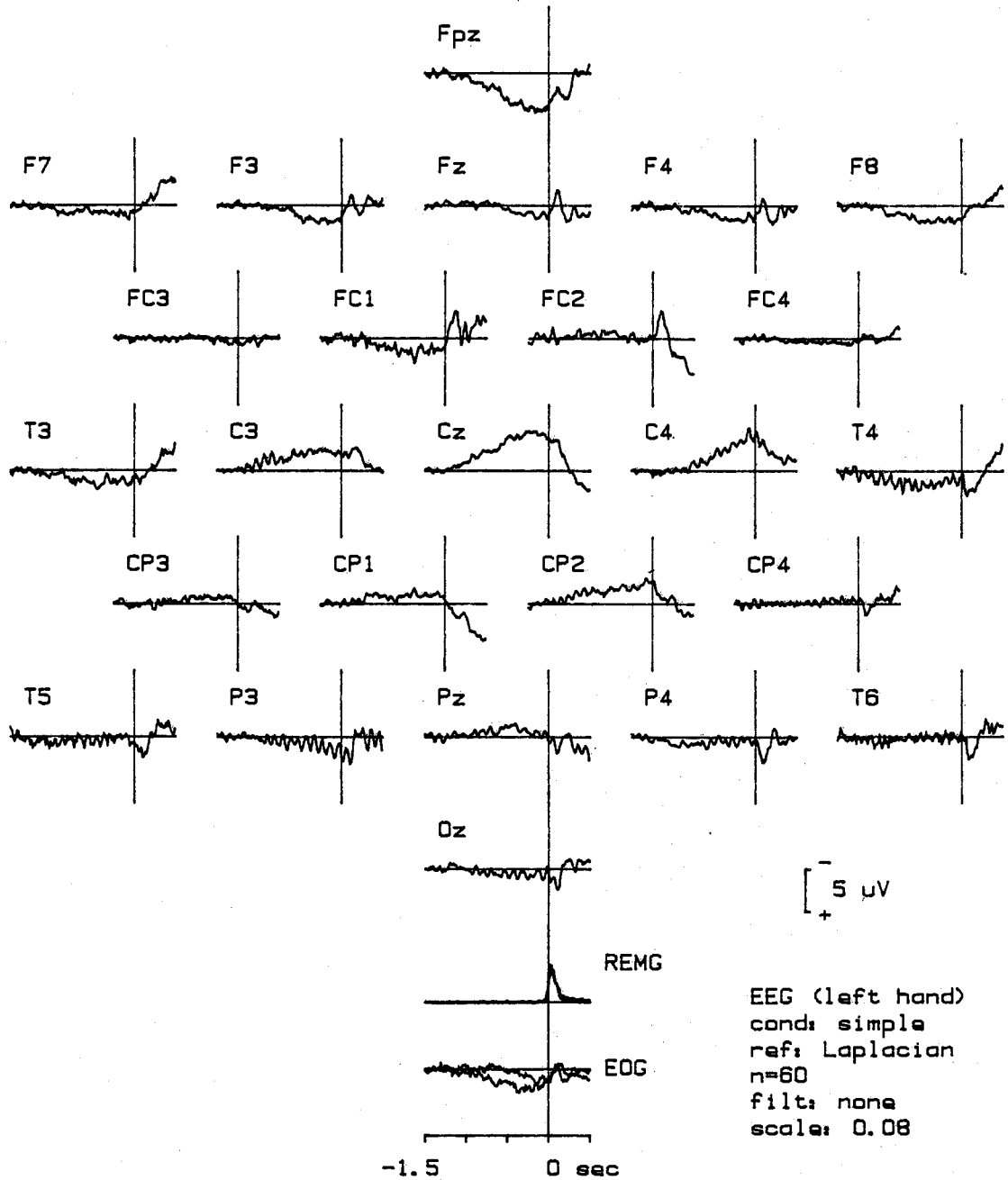
FIGURE 8.4.5. EEG activity (Laplacian) preceding unilateral finger flexion – Left hand (subject H.W.)

Fpz

F7   F3   Fz   F4   F8

FC3   FC1   FC2   FC4

T3   C3   Cz   C4   T4

CP3   CP1   CP2   CP4

T5   P3   Pz   P4   T6

Oz

5 µV

REMG

EOG

EEG (left hand)
cond: simple
ref: Laplacian
n=60
filt: none
scale: 0.08

-1.5   0 sec
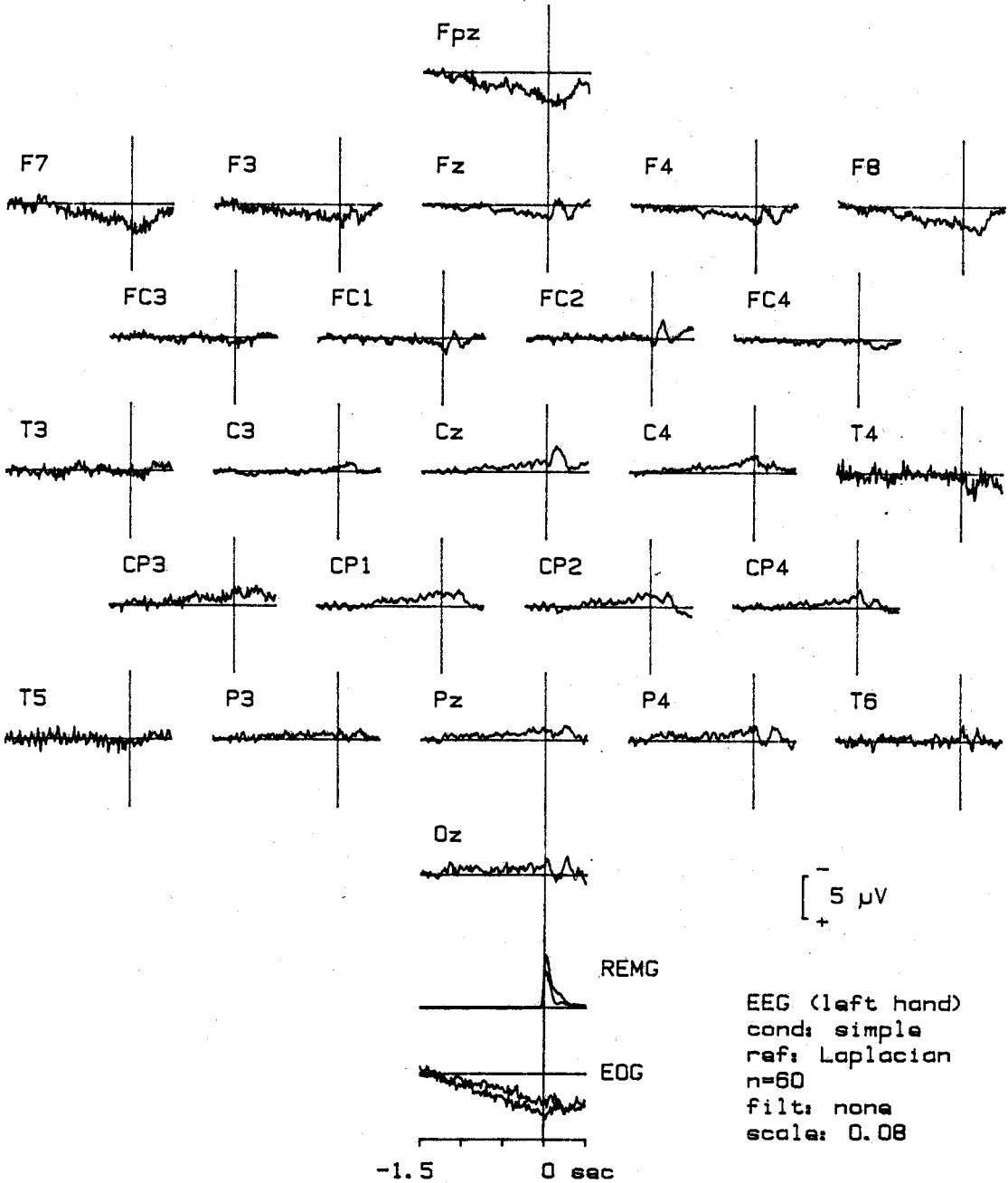
Magnetic Recordings

Averaged MEG waveforms were produced for the same time epochs as the EEG recordings, using averages of 40 trials for each recording location, 2 seconds in duration beginning 1.5 seconds prior to EMG onset, the first 250 milliseconds of which were used for the baseline. Consistant patterns of magnetic field changes preceding finger movement were observed in all subjects, with some variation in the topographical distribution between subjects. These changes consisted of slow shifts of magnetic flux in and out of the head which followed the same time course as the readiness potentials observed in the EEG prior to EMG onset. These shifts are approximately 100 to 150 femtoTesla (fT) in amplitude and reverse in direction over the Rolandic areaa contralateral to the side of movement. In addition, a similar shift of opposite orientation is seen over ipsilateral Rolandic areas. These pre-movement shifts are followed by a sharp reversal of field direction immediately following EMG onset producing a large biphasic shift which is restricted to the centro-parietal regions of the hemisphere contralateral to movement, reaching amplitudes of as much as 400 fT in some subjects.

Figure 9 illustrates the similarity in the MEG waveforms observed at a position anterior to the Rolandic area (position 14, approximately 1.5 cm anterior to C3) across subjects. Note that these shifts are also present, but smaller in amplitude for left (ipsilateral) finger movements. Although the MEG recordings were made sequentially over separate sessions on separate days, there did not appear to be any systematic changes in the magnetic field shifts over the duration of the recordings, although with a single channel sensor it was not feasable to replicate recordings from all positions. In three subjects (T.R., R.G. and B.J.) position 14 was recorded twice, once in the first recording session and again at the end of the subsequent sessions and are superimposed in Figure 9. These waveforms show no attenuation of the slow shift preceding movement, although there is some indication of decreased amplitude in the post-movement peak for the last session in both subjects indicating that some changes may

have occured over the duration of the recordings.

In order to test for movement artifact in these shifts strain gauge recordings were conducted in two subjects, shown in Figure 10.2.2 and Figure 10.2.3 along with superimposed averages of the first and last 20 trials, indicating good replication for each set of trials. Strain gauge measures indicated some degree of slow time-locked movement preceding the movement (most likely respiration related). These were followed by larger movements following EMG onset due to physical movement of the subject during muscular contraction in the limb. However, many of the MEG waveforms show flat baseline activity, suggesting that movement artifact was minimal prior to movement, but more substantial during the movement itself, making interpretation of MEG shifts occuring at this time more difficult. Strain gauge monitoring did not show sufficient variability from trial to trial to warrant individual trial rejection (once the subject's head was positioned for gantry positioning it remained relatively stationary) and was not used in further subjects. Additionally, the strain gauge attached to the subject's forehead did not always detect other sources of movement artifact (e.g., subject moving their feet or arms). However, these movements could be detected as large deflections in the MEG signal and were rejected on-line by the experimenter.

Figures 10.1.(1-3) shows comparisons of MEG fields for the simple and pattern conditions. These waveforms indicate some differences across subjects for the two tasks, as indicated by additional shifts at recording locations primarily over central regions of the scalp, although these differences do not show any systematic pattern and overall, the distribution of activity is similar for the two conditions. MEG activity for right versus left simple finger flexions is shown in Figures 10.2.(4-5) and Figures 10.3.(4-5), respectively and superimposed in Figures 10.1.(4-5). These fields show quite similar patterns except for the large amplitude post-movement shift which is over left hemisphere for right finger movements and over right hemisphere for left finger movements.

FIGURE 9. MEG WAVEFORMS FOR SIMPLE AND PATTERN MOVEMENTS (all subjects)
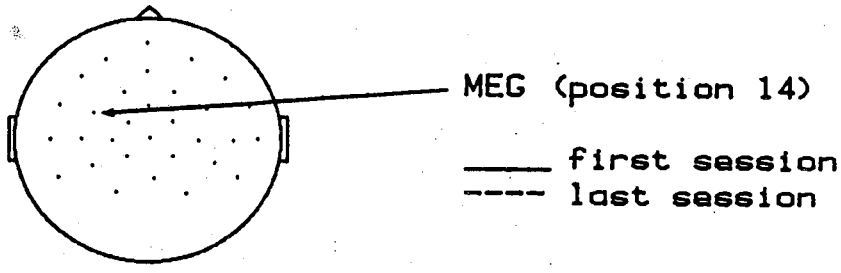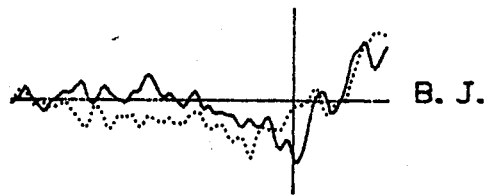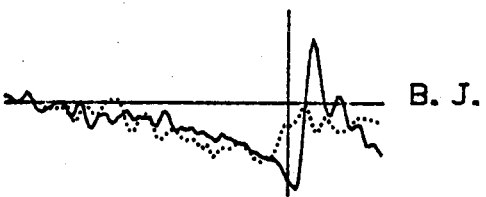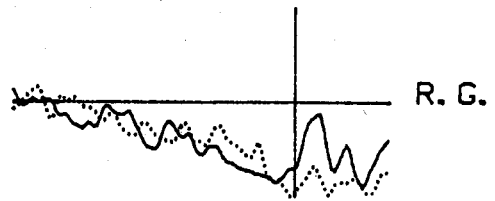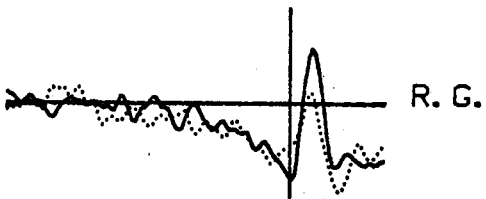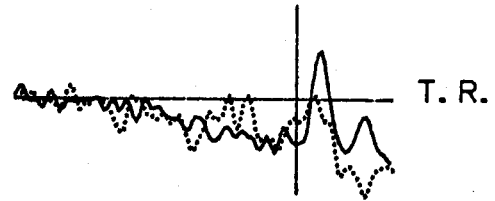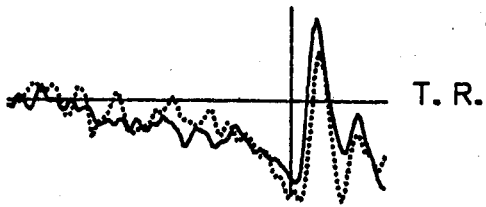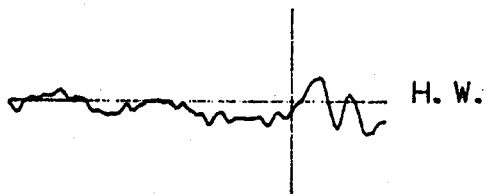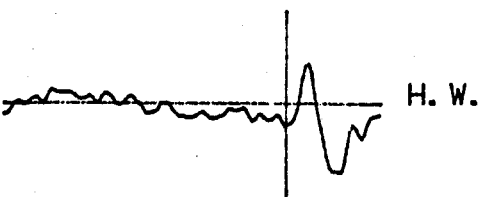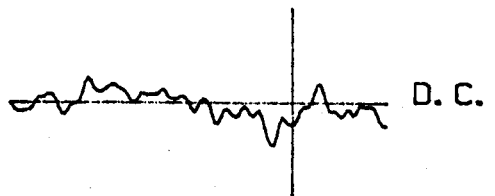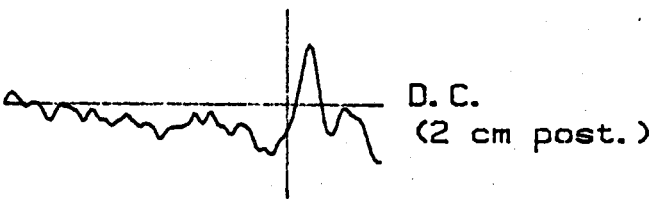
FIGURE 10.1.1. MEG activity preceding unilateral finger flexions—both conditions (subject T.R.)

EEG (Cz) $-\begin{bmatrix} 5 \ \mu V \\ + \end{bmatrix}$

EOG

REMG

out $\begin{bmatrix} 100 \ fT \\ in \end{bmatrix}$

MEG (right hand)
simple
---- pattern
(n=40)

-1.5   0 sec
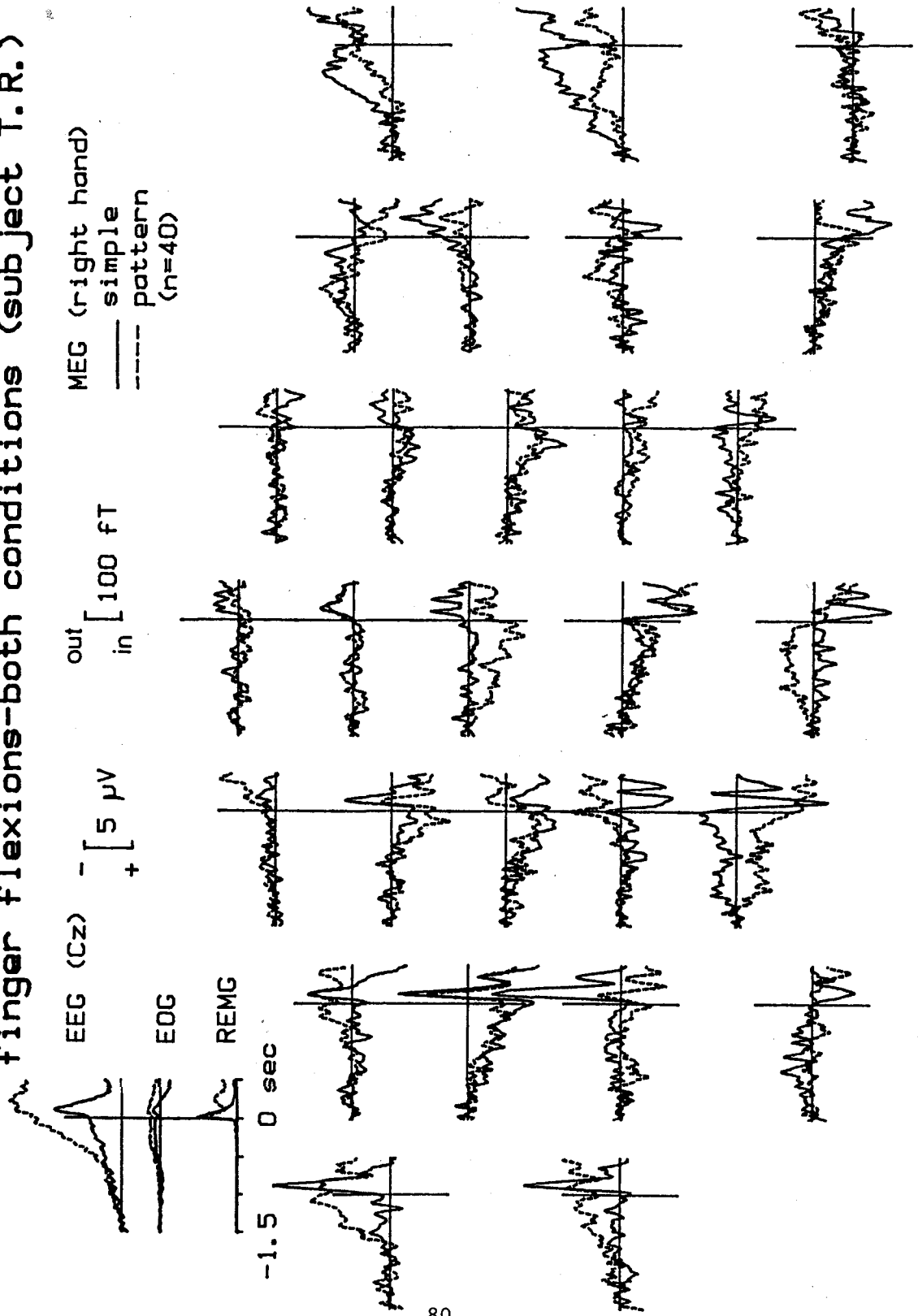
FIGURE 10.1.2. MEG activity preceding unilateral
finger flexions - both conditions (subject R.G.)

EEG (Cz)   − ⎡ 5 μV
            + ⎣

EOG

REMG

out ⎡ 100 fT
in ⎣

MEG (right hand)
——— simple
‑ ‑ ‑ pattern
        (n=40)

−1.5   0 sec

81
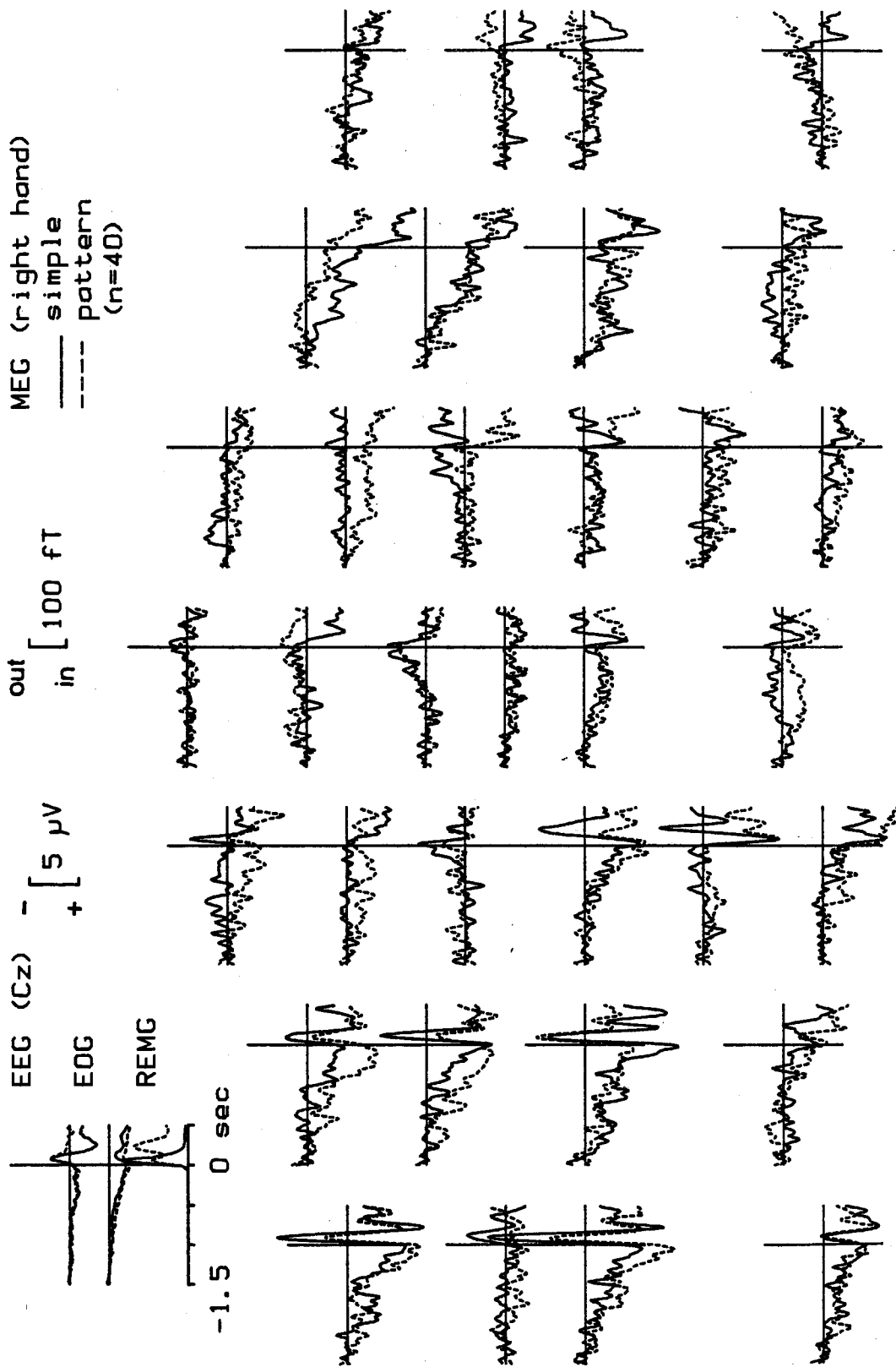
FIGURE 10.1.3. MEG activity preceding unilateral finger flexions - both conditions (subject B.J.)

82
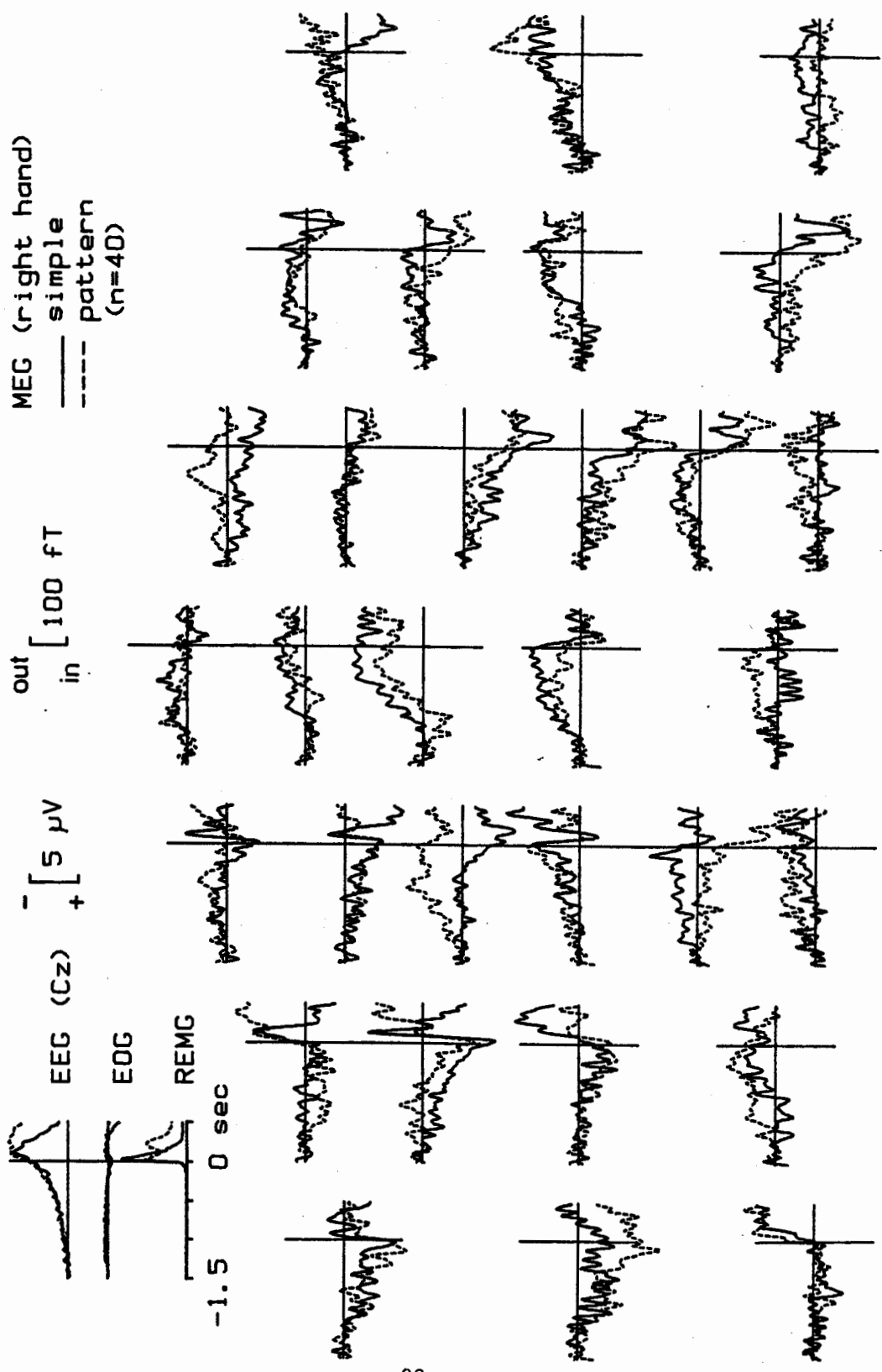
FIGURE 10.1.4. MEG activity preceding unilateral
finger flexions – left vs. right (subject D.C.)

EEG (Cz)

EOG

REMG

-1.5   0 sec

$-\begin{bmatrix} 5 \ \mu V \\ + \end{bmatrix}$

out $\begin{bmatrix} 100 \ fT \\ in \end{bmatrix}$

MEG
——— right hand
- - - left hand
(n=40)
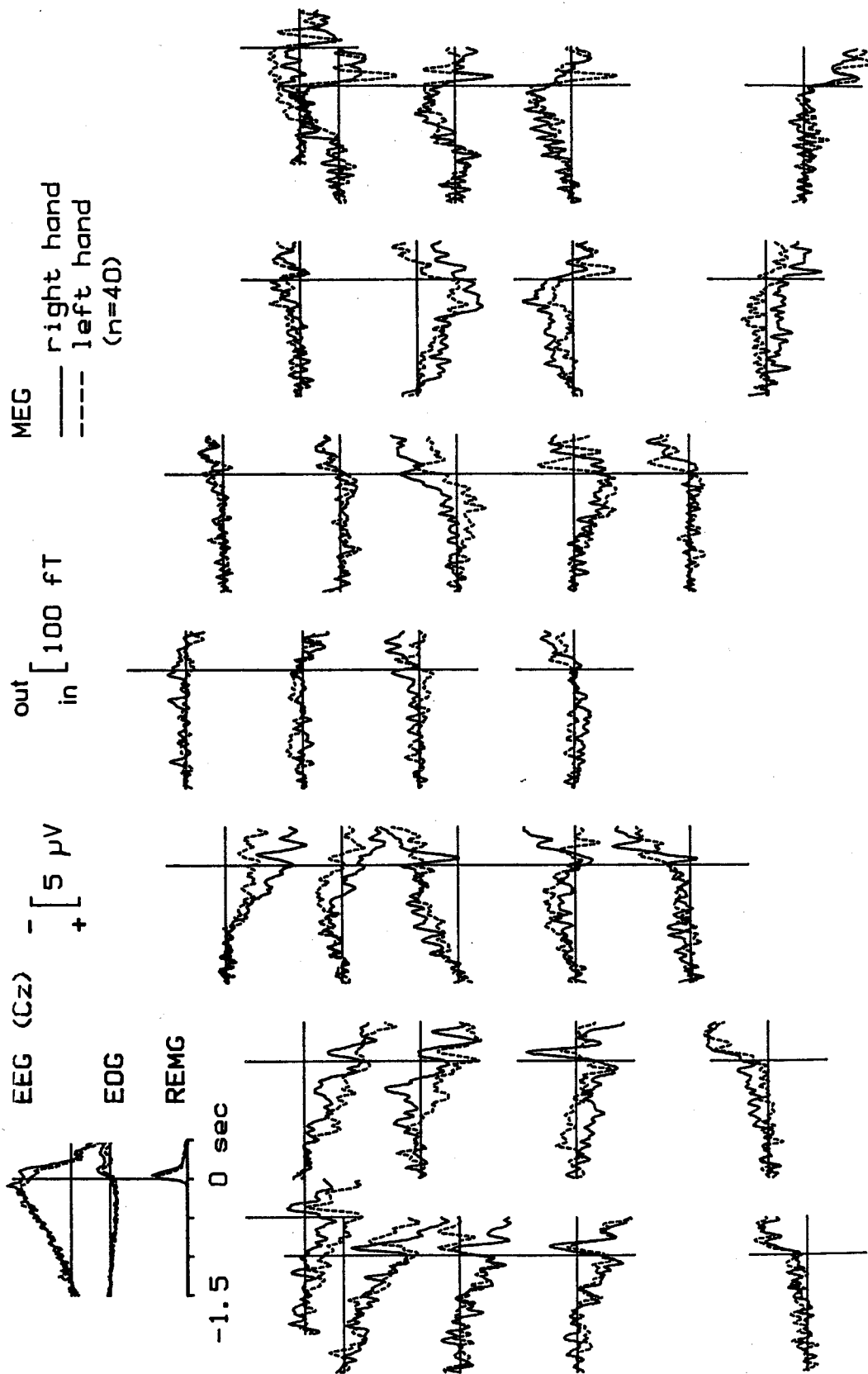
FIGURE 10.1.5. MEG activity preceding unilateral finger flexions – left vs. right (subject H.W.)

EEG (Cz)

EOG

REMG

MEG
—— right hand
---- left hand
(n=40)

-1.5   0 sec

out
in [100 fT

- [5 μV
+

FIGURE 10.2.1. MEG activity preceding unilateral finger flexions—simple condition (subject T.R.)

EEG (Cz)

EOG

REMG

MEG (right hand) (n=40)

out
in [100 fT

− [5 μV
+

0 sec

−1.5
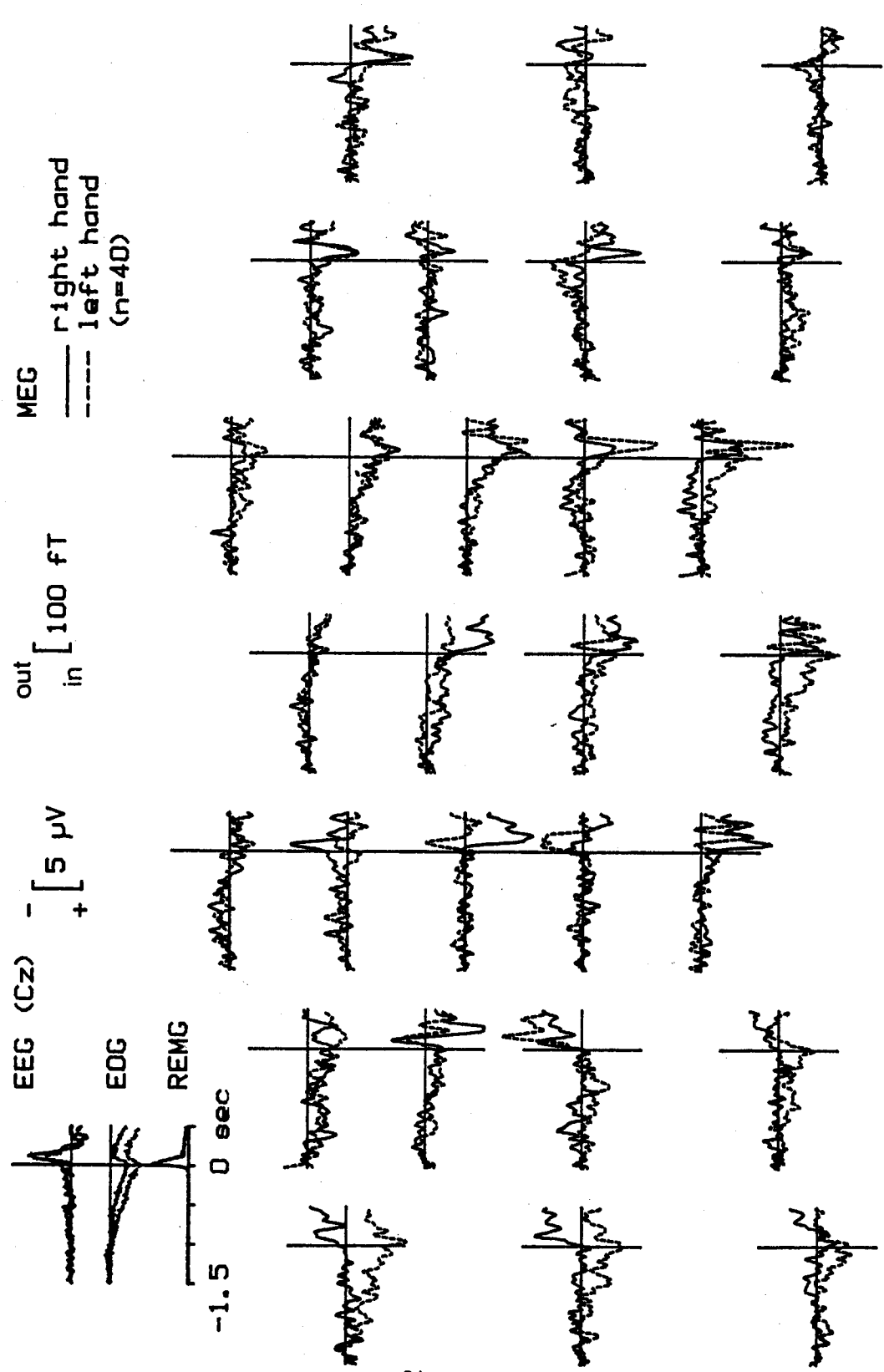
FIGURE 10.2.2. MEG activity preceding unilateral
finger flexions - simple condition (subject R.G.)

MEG (right hand)
(n=20)

out
in [100 FT

strain
gauge

-1.5   0 sec

86
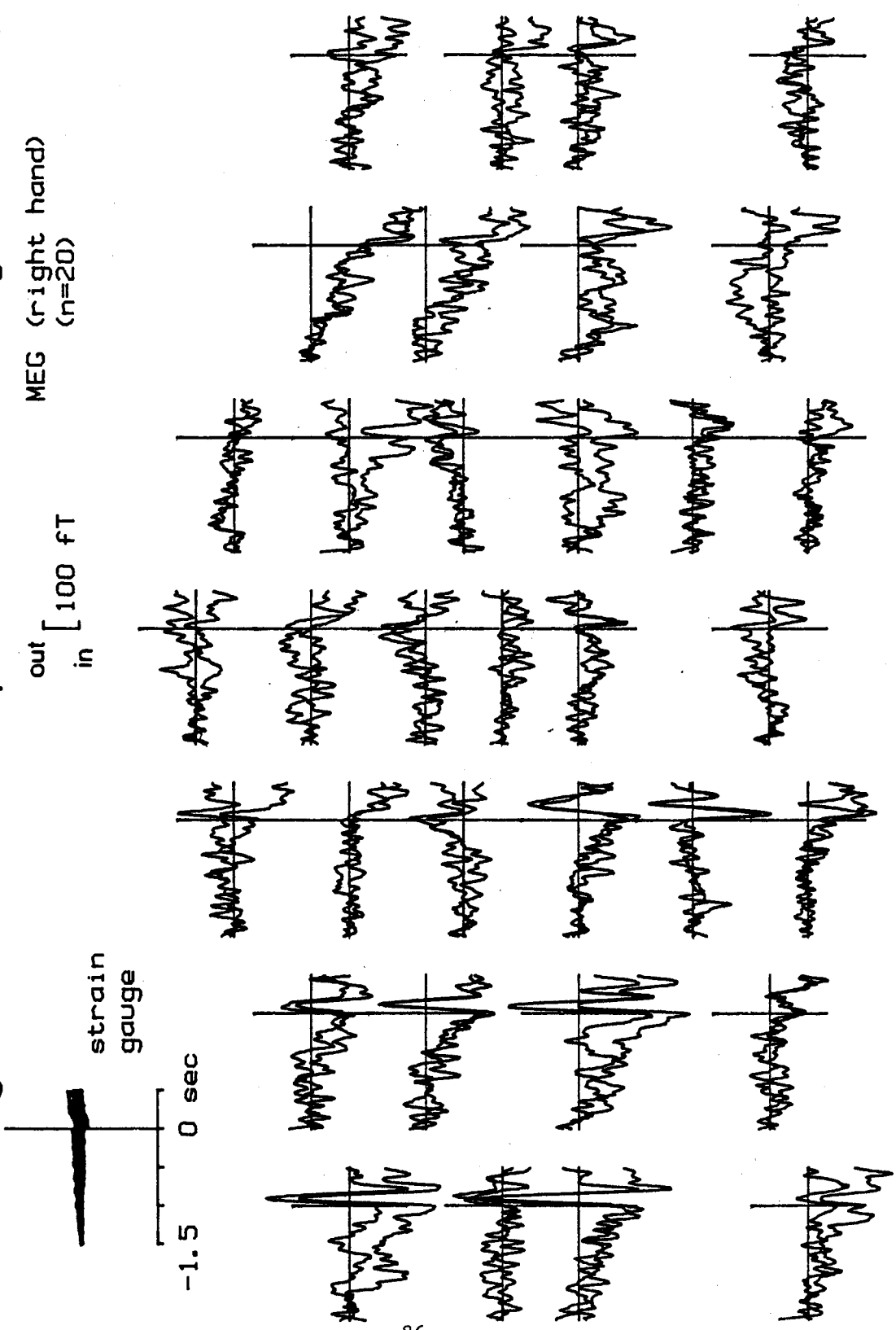
FIGURE 10.2.3. MEG activity preceding unilateral
finger flexions - simple condition (subject B.J.)

MEG (right hand)
(n=20)

out
in $\left[\right.$ 100 FT

strain
gauge

-1.5   0 sec

87
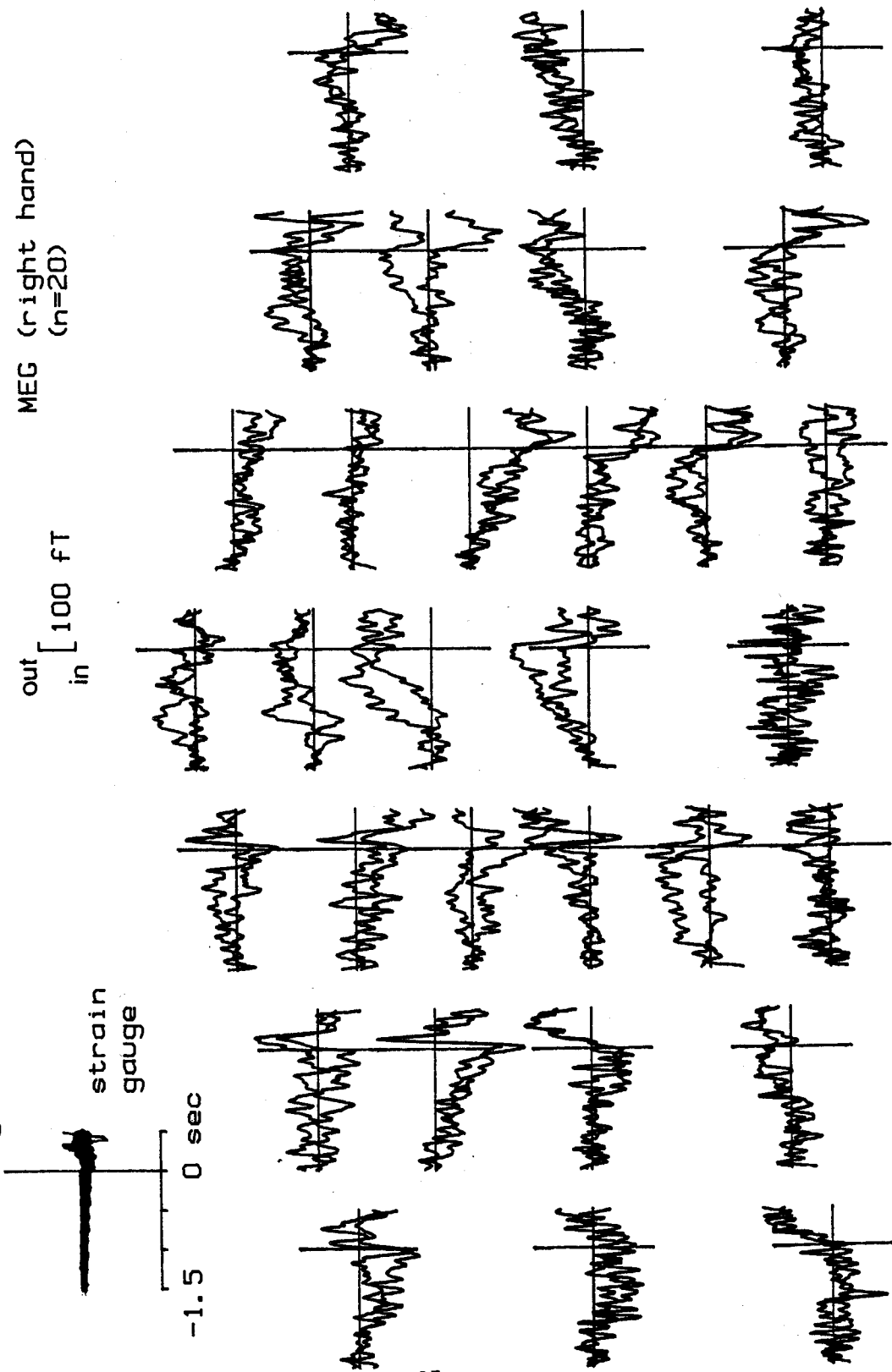
FIGURE 10.2.4. MEG activity preceding unilateral
finger flexions - right hand (subject D.C.)

EEG (Cz) $-\begin{bmatrix} 5 \ \mu V \\ + \end{bmatrix}$

EOG

REMG

-1.5   0 sec

out $\begin{bmatrix} 100 \ fT \\ in \end{bmatrix}$
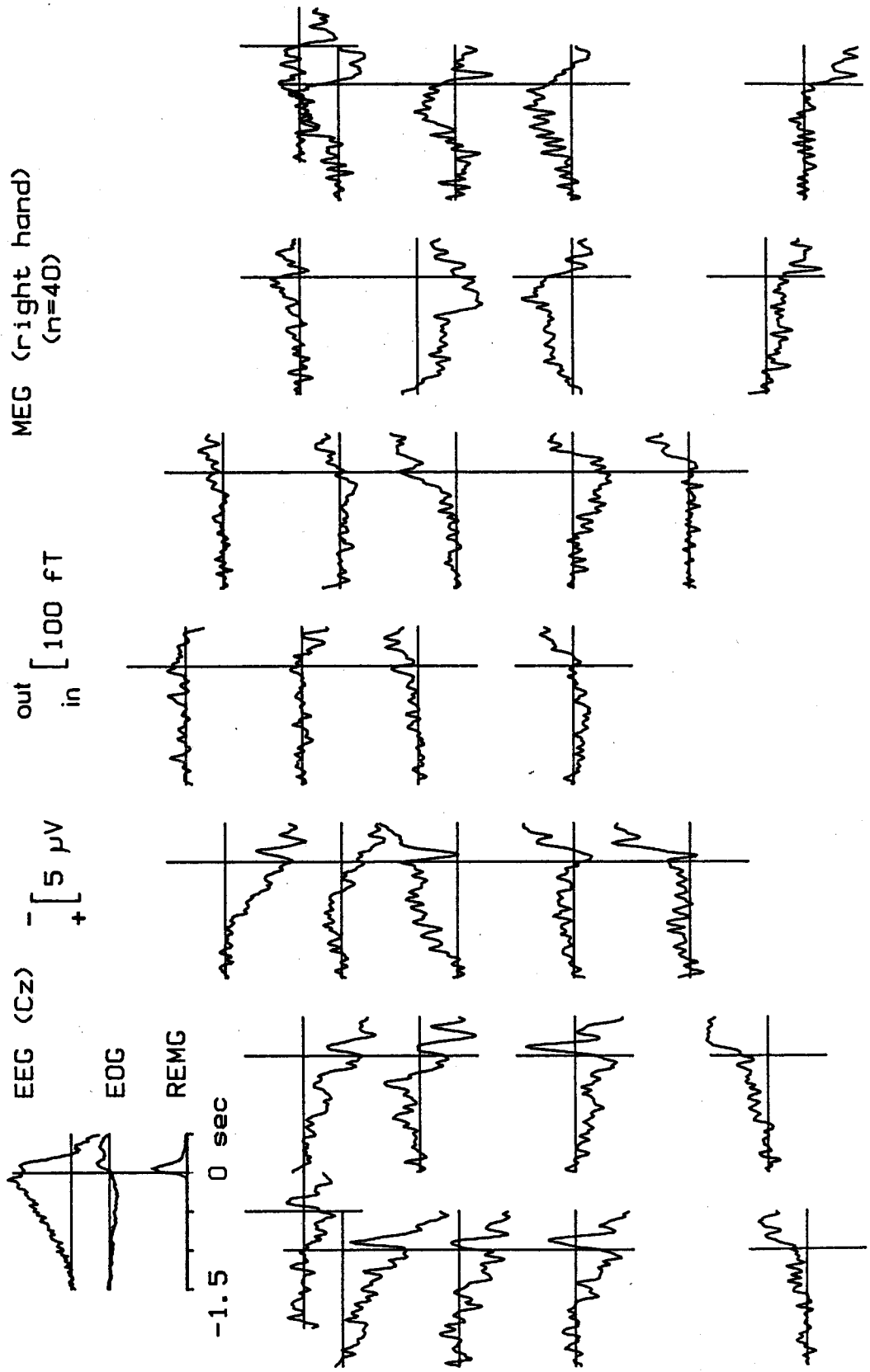
MEG (right hand)
(n=40)

FIGURE 10.2.5. MEG activity preceding unilateral
finger flexions – right hand (subject H.W.)

EEG (Cz)

EOG

REMG

$-\begin{bmatrix} 5 \ \mu V \\ + \end{bmatrix}$

out $\begin{bmatrix} 100 \ fT \\ in \end{bmatrix}$

MEG (right hand)
(n=40)

-1.5   0 sec

89
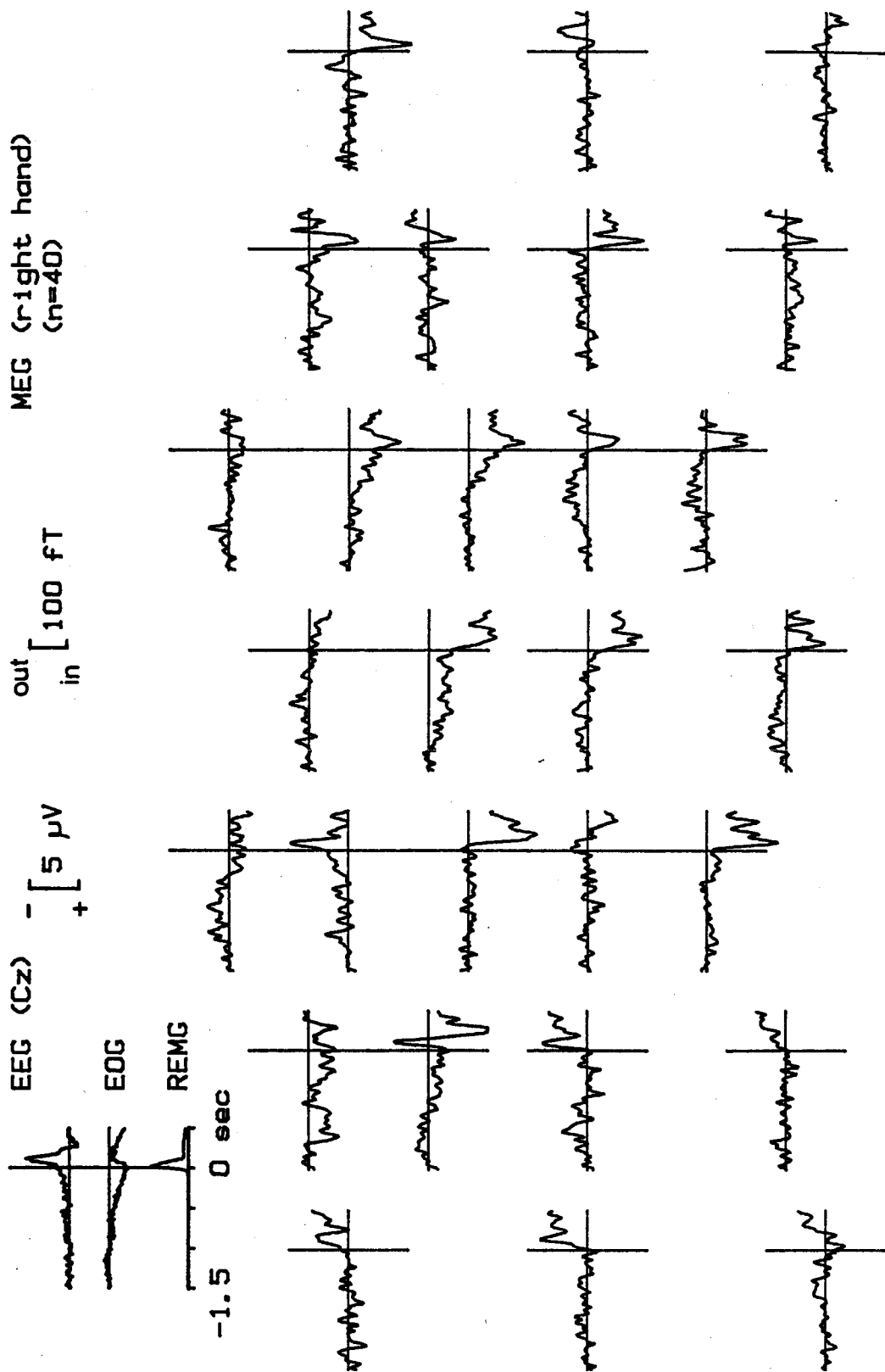
FIGURE 10.3.1. MEG activity preceding unilateral finger flexions-pattern condition (subject T.R.)

EEG (Cz) $-\begin{bmatrix} \\ \\ + \end{bmatrix}$ 5 μV

EOG

REMG

0 sec

-1.5

out $\begin{bmatrix} \\ \\ \text{in} \end{bmatrix}$ 100 fT

MEG (right hand) (n=40)

90
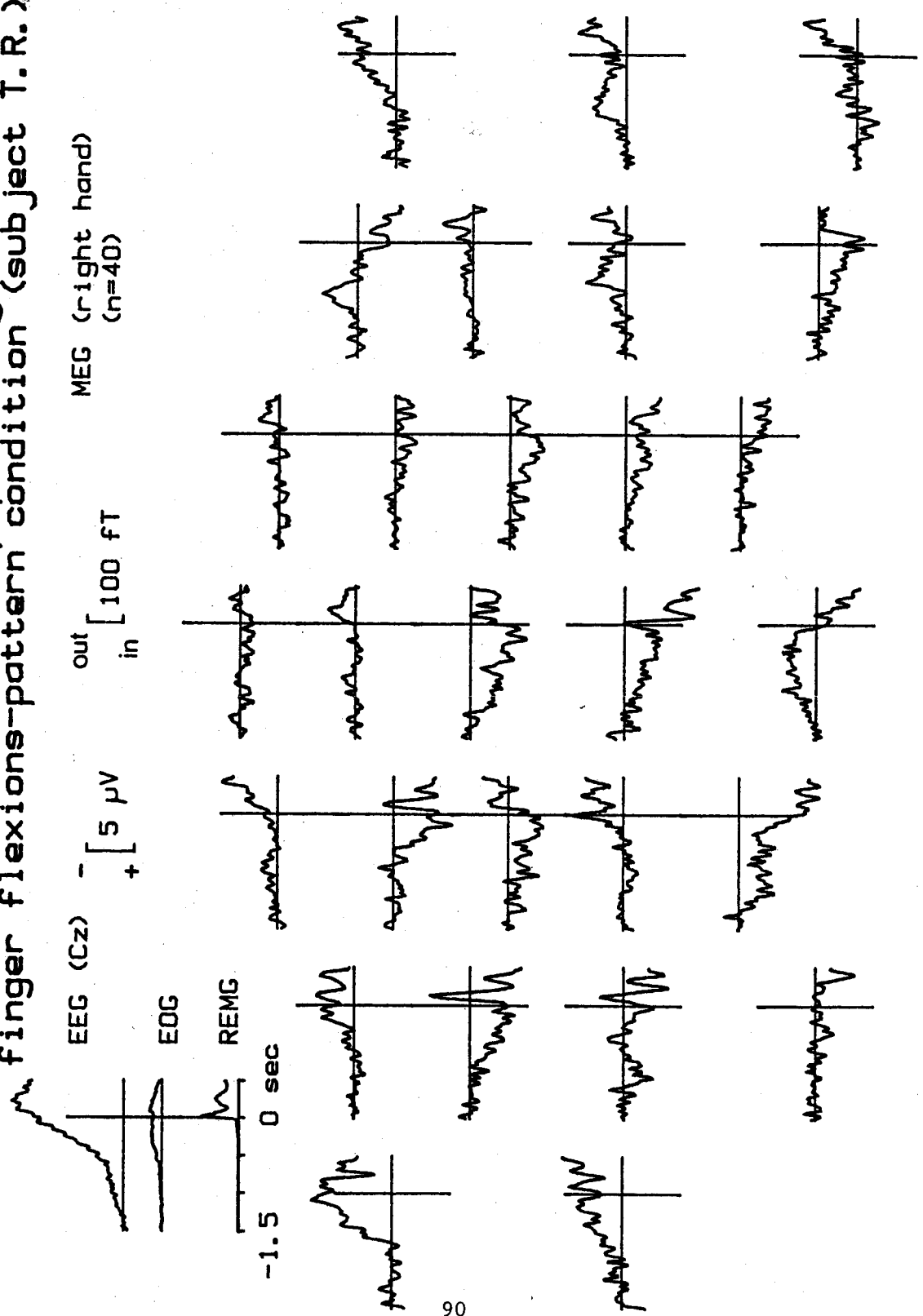
FIGURE 10.3.2. MEG activity preceding unilateral finger flexions - pattern condition (subject R.G.)

MEG (right hand)
(n=20)

out
in [100 fT

strain gauge

-1.5   0 sec

91
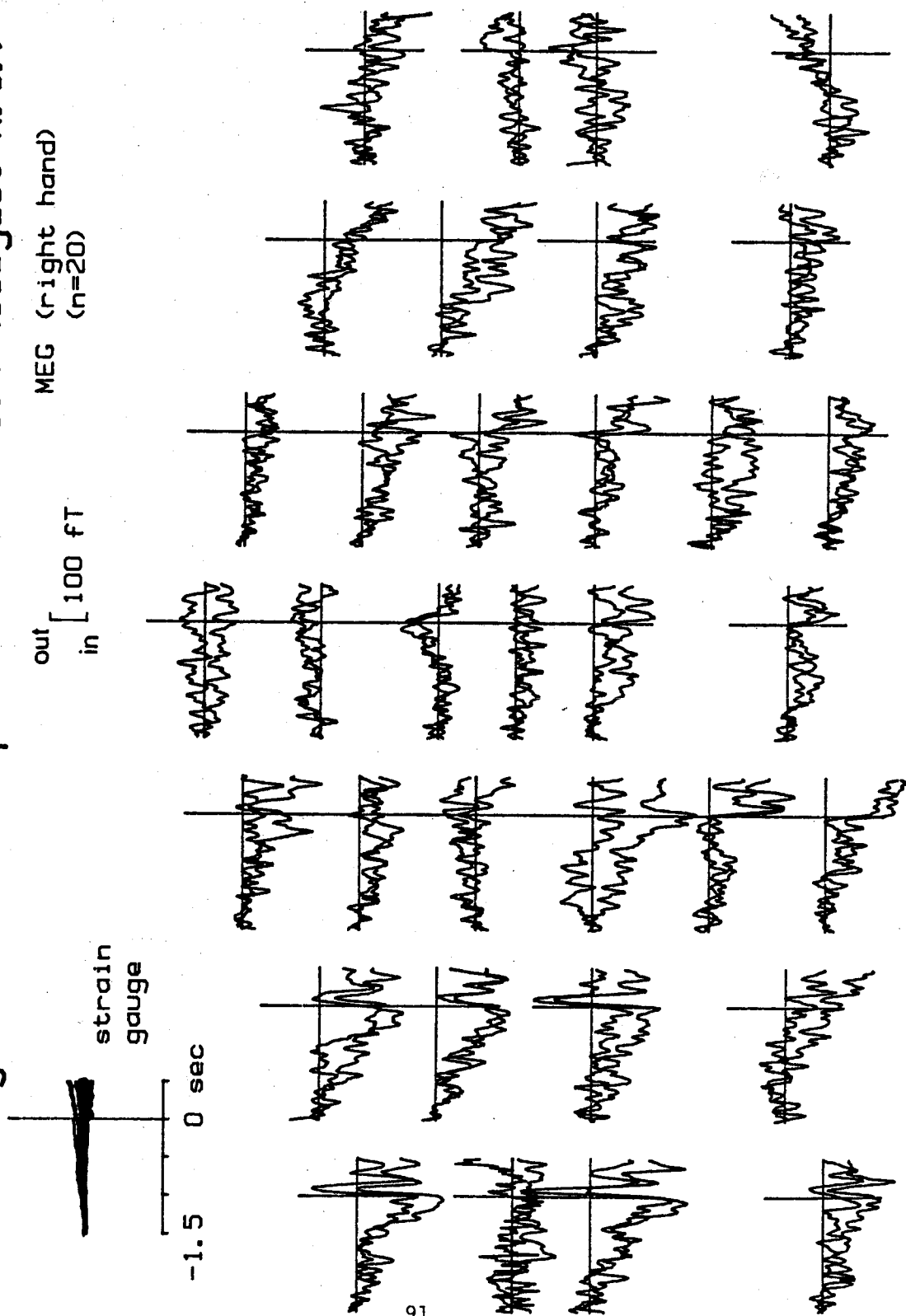
FIGURE 10.3.3. MEG activity preceding unilateral finger flexions - pattern condition (subject B.J.)

MEG (right hand)
(n=20)

out ⌈ 100 fT
in ⌊

strain gauge

-1.5   0 sec

92
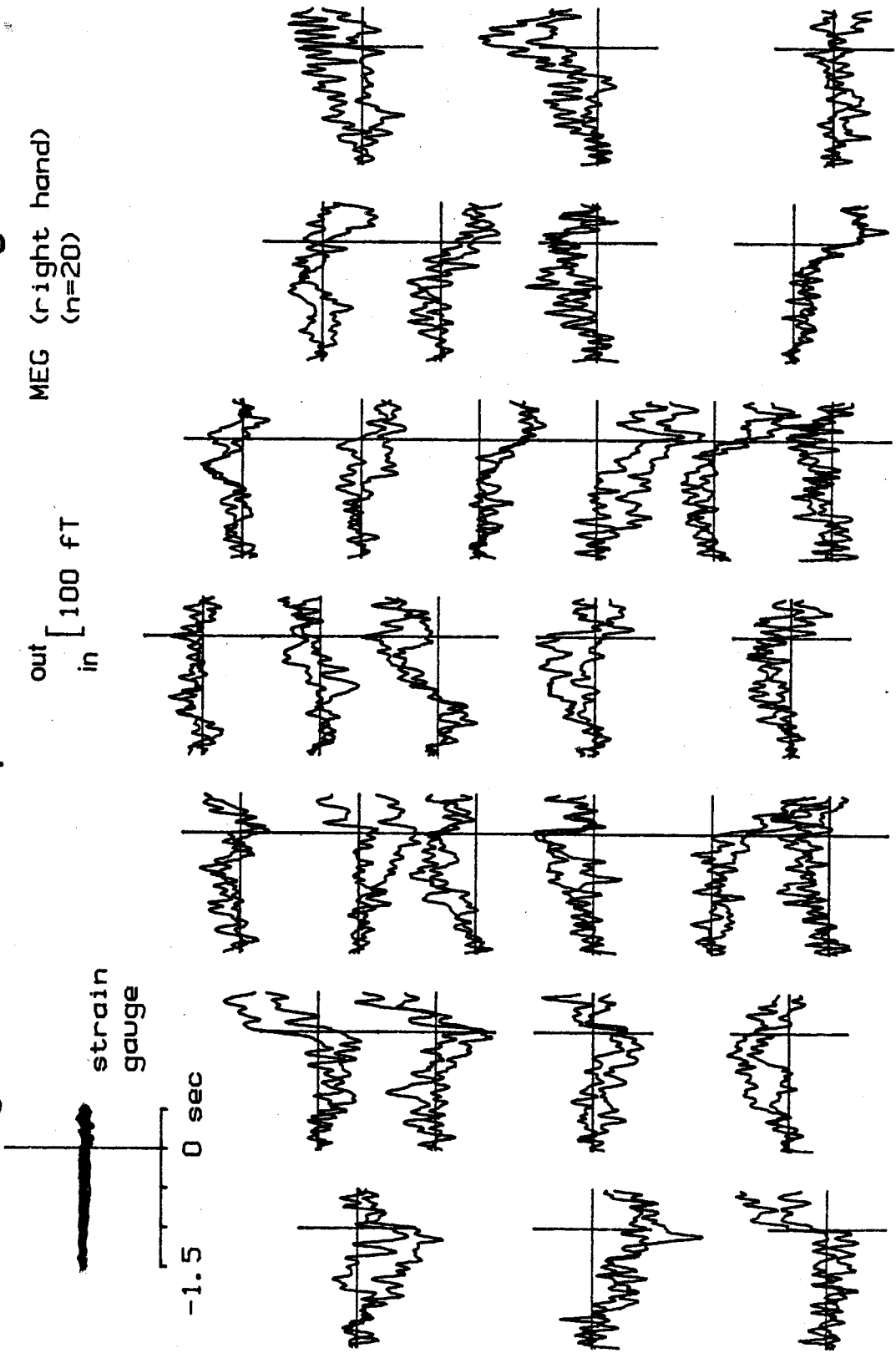
FIGURE 10.3.4. MEG activity preceding unilateral
finger flexions - left hand (subject D.C.)

EEG (Cz)

EOG

REMG

EEG (left hand)
(n=40)

out
in [100 fT

- [5 µV
+

0 sec

-1.5

93
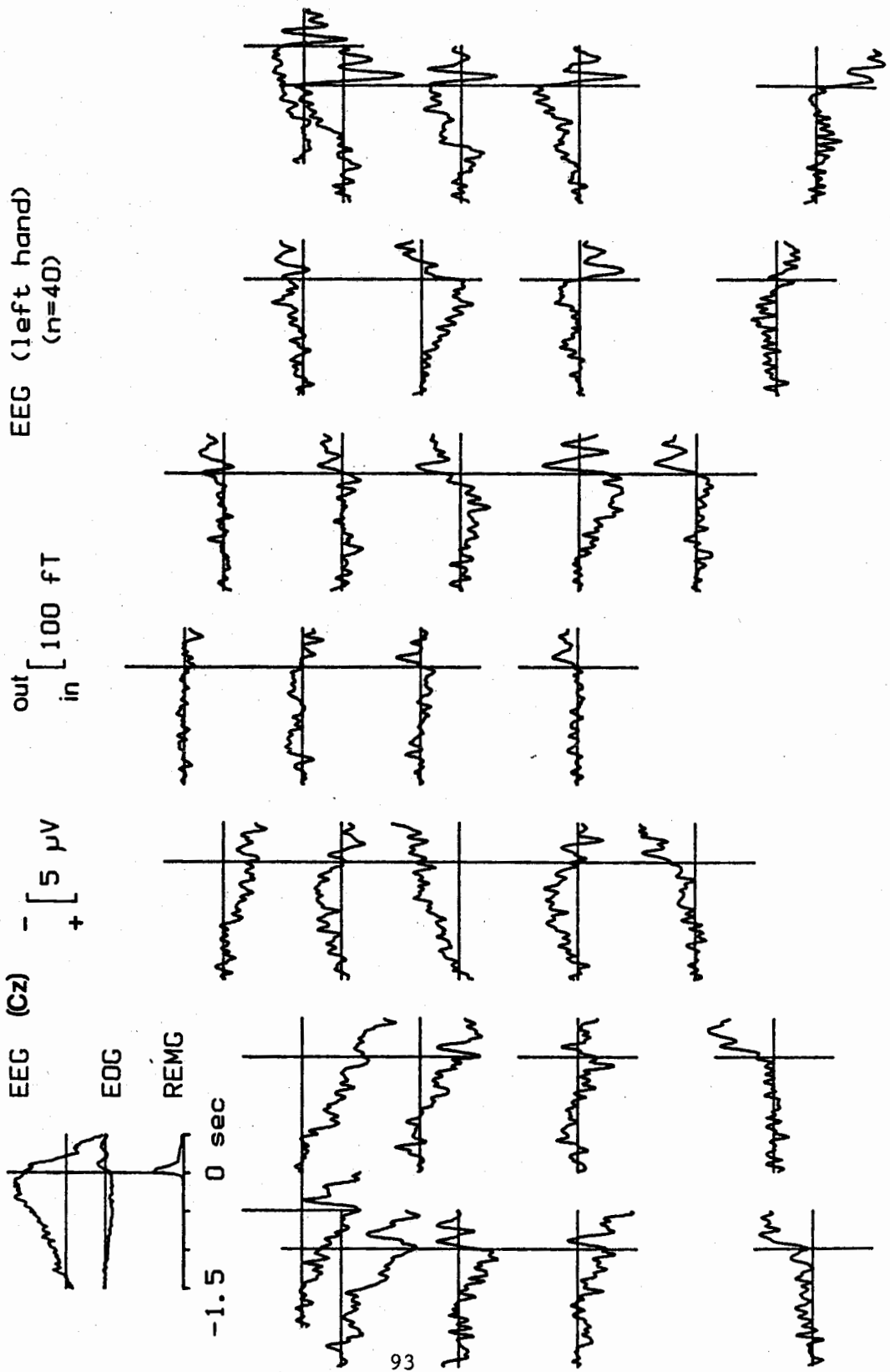
FIGURE 10.3.5.   MEG activity preceding unilateral
finger flexions - left hand (subject H.W.)

MEG (left hand)
(n=40)

EEG (Cz)

EOG

REMG

out $\lceil$ 100 fT
in $\lfloor$

$-\lceil$ 5 μV
$+\lfloor$

0 sec

-1.5
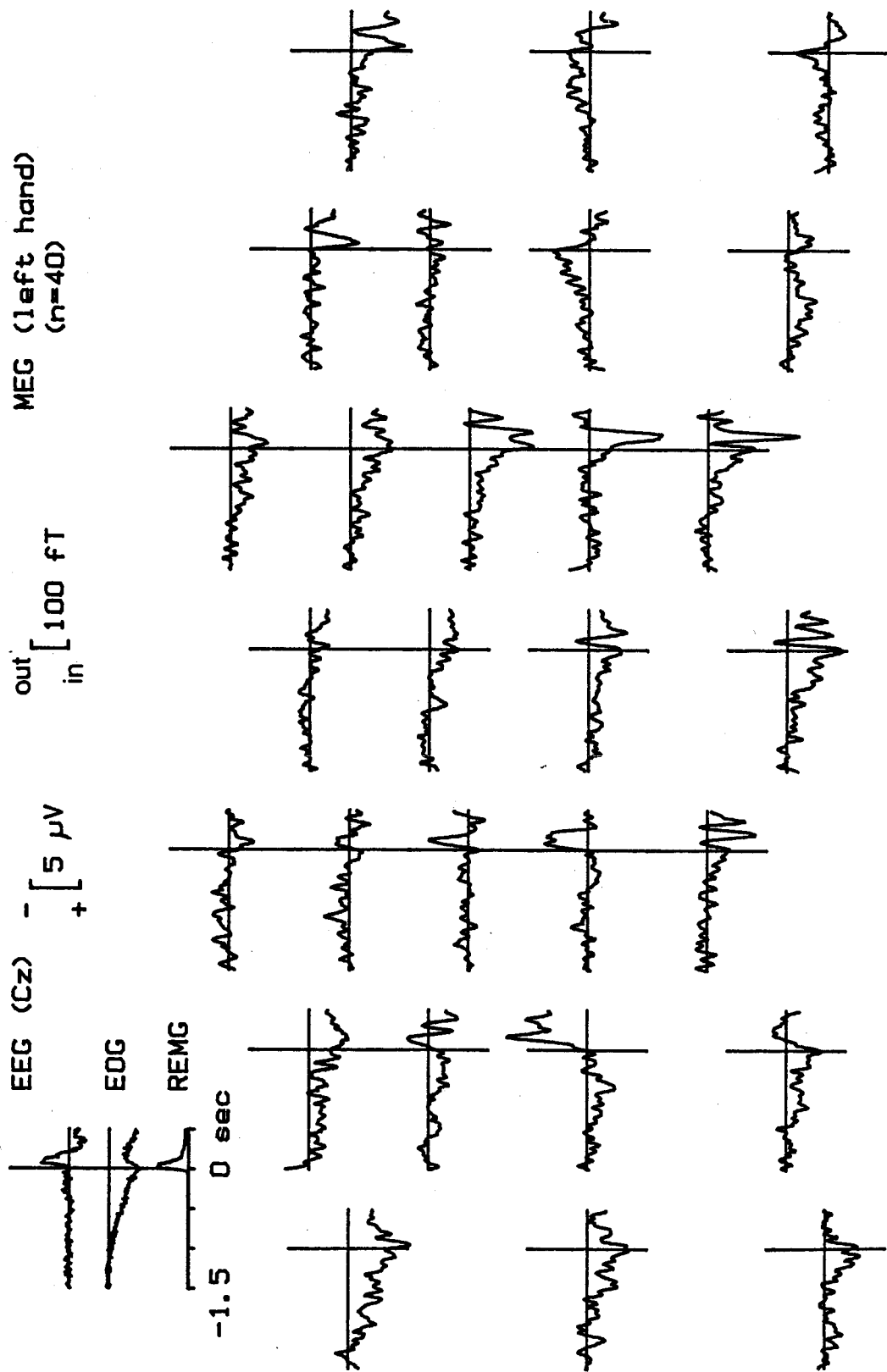
Isocontour maps were produced for averages of 5 points each at intervals of 39 milliseconds similar to the maps constructed for EEG activity and are provided in Appendix C. Figures 16.1.(1-3) and Figures 16.2.(1-3) show MEG activity preceding and during simple and pattern finger flexions, respectively for three subjects. Figures 16.3.(1-2) and Figures 16.4.(1-2) show activity for right and left simple finger flexions, in two subjects. In these maps each contour represents 18 fT, solid lines indicating fields directed out of the head and dotted lines indicating fields directed into the head. The map border on these maps lies slightly above T3 - T4, Fpz - Oz, approximately the same lateral extent as for the Laplacian maps of EEG activity.

For each map the grand average EEG for Cz (recorded over all MEG recording sessions) is shown below with a dotted cursor at the indicated time point for each map. Although there is a considerable degree of variability in the field strength and distribution within each individual[4], examination of the spatio-temporal maps for all five subjects for the simple and pattern finger flexions indicates similar topography and time course for the magnetic field shifts preceding and during voluntary movement. In all subjects for both right and left unilateral finger movements, field reversals are observed over both hemispheres in a similar orientation -- ingoing fields over anterior left hemisphere laterally and outgoing fields over anterior left hemisphere medially. The same topography is observed over right hemisphere but reversed, ingoing fields medially and outgoing fields laterally. These patterns represent slow steady shifts, indicated by a gradual emergence of bilateral reversals in the maps approaching EMG onset which persist for a period after EMG onset but are most

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[4]Note on MEG spatial maps. It should be noted with regard to the examination of the interpolated maps for recorded MEG activity, that radius values are not presently incorporated into the mapping algorithms. This can result in the distributions being somewhat distorted, since larger fields will be recorded if the sensing coil is closer (or more tangential) to underlying sources. Since the head tends to be narrower, and the skull thinner at the temporal regions this could result in fields appearing stronger towards the outer boundary of the maps. Also, these maps are equidistant projections, therefore, the further from the center of the map the more distorted distances will be in the azimuthal direction.

pronounced over the contralateral Rolandic area immediately prior to EMG onset. This pattern persists for a short period following EMG onset (about 50 milliseconds) after which, a clear reversal of opposite orientation emerges overlying the Rolandic area contralateral to the side of movement, and slightly posterior to the earlier shift while the reversal over ipsilateral cortex continues throughout the movement period. Each subject shows some variation on this pattern. In subject T.R. the contralateral reversal is rotated slightly in the antero-posterior direction. Subject R.G. shows a slightly rotated ipsilateral reversal. In subject B.J. there appears to be additional central activity producing a more complex pattern. In subject D.C. these reversals are very bilaterally symmetric and in subject H.W. a similar pattern is present but the amplitudes are much smaller and displaced in the anterior direction.

Field patterns for the pattern motor task vary from those for the simple task primarily in their complexity. These differences are greatest in subject T.R. for whom there is an additional outgoing shift in the left hemisphere (possibly related to greater respiration artifact observed in this subject for lateral positions which were recorded from subjects in a lying down position). Subjects R.G. and B.J. also show additional ipsilateral and posterior activity during the pre-movement period.

Subjects D.C. and H.W. show a great deal of similarity of magnetic field shifts over the head for both left and right unilateral finger flexions, with stronger fields over the contralateral hemisphere and localization of the post-movement reversal to the contralateral side. In order to test for possible sympathetic movements of the ipsilateral limb, rectified EMG was recorded from both arms during unilateral movement in subject H.W.. Plots of individual averages of EMG activity for single recording positions indicated traces of EMG activity in left forearm for right finger movements for *some* but not all positions, and no EMG activity was noted in right forearm for left finger movements. (Thus, grand averages of ipsilateral rectified EMG produced only baseline activity and were not included in Figure 10).

From the above data three major components of voluntary movement-related magnetic fields may be identified as follows.

(1) Readiness fields. These fields consist of slow magnetic field shifts over both hemispheres beginning as early as 1 second prior to EMG onset in some subjects, centered over the Rolandic fissure region and consistant in orientation; entering the head to the left and exiting the head to the right, thus encircling dipolar sources directed posteriorly in either hemisphere. These shifts increase in amplitude gradually over the movement foreperiod, producing bilateral maxima of 50 to 100 fT in amplitude. Figures 11.1(a-b) show the early component of these shifts for each subject. Good correspondence can be seen across individuals, except for subject H.W. in which these fields are small in amplitude. These shifts for both right and left finger movements in subject D.C. are quite similar. These patterns are somewhat more widespread and complex for the pattern condition, particularly for subject T.R. (who also demonstrates the largest difference in vertex EEG), and are greater in amplitude.

(2) "Motor" field. This component consists of a sharp increase in magnetic flux over the Rolandic fissure, contralateral to the side of finger movement beginning 100 to 200 milliseconds prior to EMG onset and reaching amplitudes of up to 150 fT in some subjects. This shift is continuous with the slow readiness field over the same area and represents this dipolar field becoming more concentrated over this area (while the ipsilateral shift continues a more steady increase in amplitude). In some subjects, this shift is quite gradual and may not be significantly distinguishable from the readiness field described above, and simply denotes the contralateral readiness field reaching its apex. This component appears to be arising from primary motor areas contralateral to the side of finger movement. Figures 11.2(a-b) show the time interval 47 milliseconds prior to EMG onset in which this component appears in a consistant form for most subjects.

(3) Proprioceptive evoked field (PEF). This component consists of a sharp field direction reversal in the motor field approximately 50 milliseconds following

EMG onset, localized over the Rolandic area but slightly posterior, producing a highly localized field reversal opposite in orientation to the motor field. This component is the largest event associated with voluntary finger flexions reaching amplitudes between 200 to 400 fT in the five subjects tested. This field appears to arise from somatosensory areas contralateral to the side of movement and is most likely associated with proprioceptive responses to the physical movement of the finger. During this period the ipsilateral slow shift (continuous with the shift observed leading up to EMG onset) continues its increase in amplitude in some lateral locations but may also show changes in direction at medial locations. The medial shifts appear in some subjects to be spread of the proprioceptive evoked field from contralateral hemisphere. It is not known to what extent these post-movement shifts may be distorted by movement artifact produced by the finger movement itself, however, the contralateral evoked field is quite robust across subjects as shown in Figures 11.3(a-b). There are some differences in these shifts between simple and pattern conditions which may be attributed to the fact that the subject is producing more movement in the pattern condition.

Comparisons of EEG and MEG Fields

There is notable similarity in the patterns of MEG and EEG activity over the surface of the head throughout the time period leading up to and immediately following movement, particularly when comparing the Laplacian transformed EEG distributions, which demonstrate source-sink configurations which are orthogonal in orientation to the MEG fields for the same time point. Figure 12 shows the orthogonal distribution of electric and magnetic fields in one subject (T.R.) for two of the above time points, in which reversals of source and sink appear rotated 90 degrees to that of the ingoing and outgoing MEG field maxima. These reversals in the MEG are highly suggestive of dipolar current sources located between the two maxima at a depth that is relative to their separation, particularly for the PEF. The suggested current dipole source configurations based simply on the location of the field maxima are indicated by heavy arrows. The projection of these hypothetical sources onto the EEG maps

illustrates the possible underlying sources that may account for the orthoganality of the observed fields in which positive and negative poles of the equivalent dipole source (current source and sink, respectively) would account for the Laplacian field distributions quite well, particularly for the post-movement (109 ms latency) component. However, as noted above the estimation of sources based on interpolated spatial maps is problematic when radius information (distance of the sensing coil from brain tissue) is not included.

FIGURE 11.1a. Isocontour maps of MEG activity preceding unilateral finger flexion: Early component (Simple).

−515ms

search rad = 20%
clip. level = 180
maximum = 144.0 fT
contours = 18.0 fT
map border = 64°

field out
field in

B.J.

RG.

T.R.

H.W.
(l. hand)

H.W.
(r. hand)

D.C.
(l. hand)

D.C.
(r. hand)
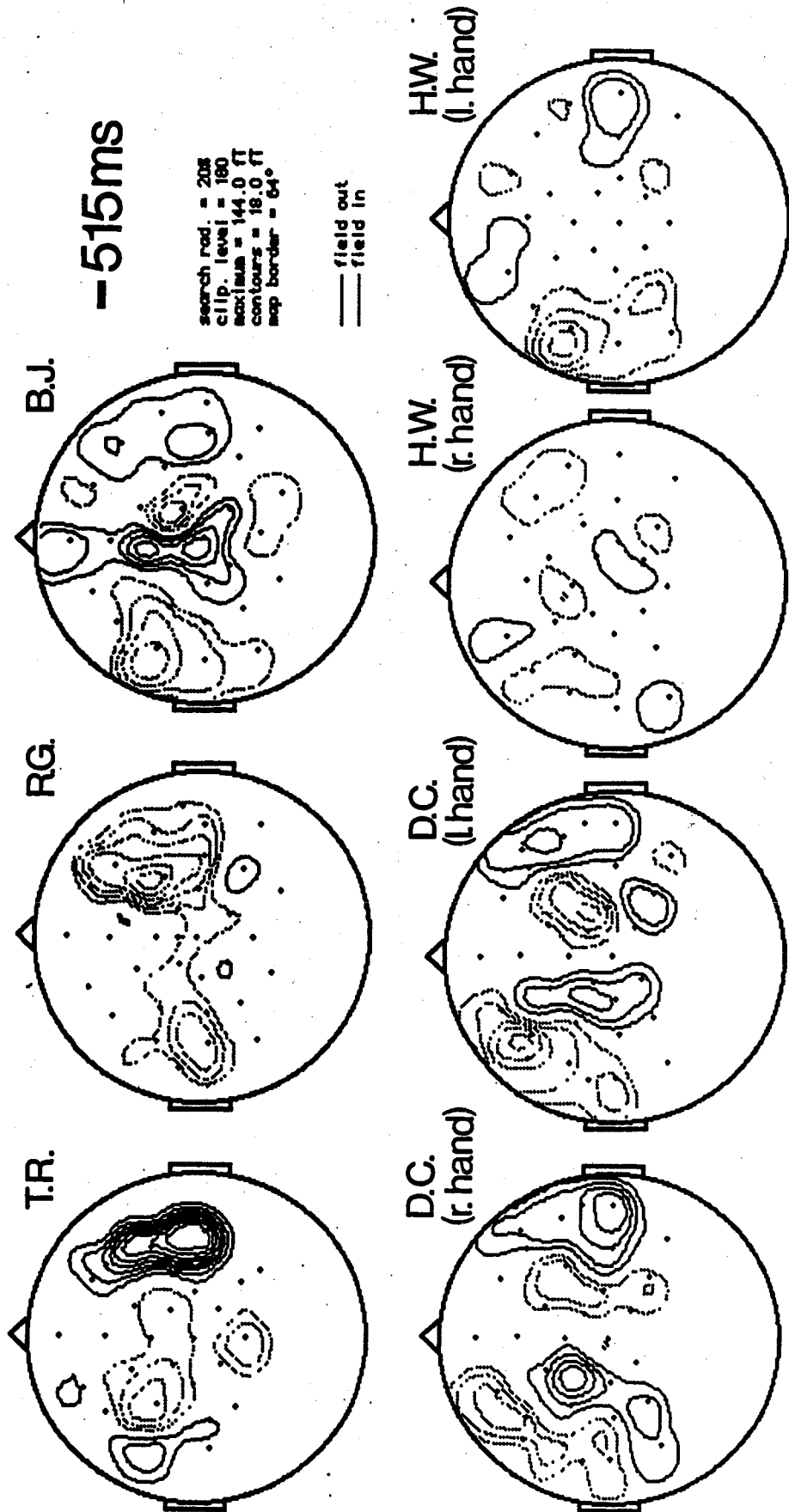
FIGURE 11.1b. Isocontour maps of MEG activity preceding
unilateral finger flexion: Early component (Pattern).

−515ms

search rad. = 208
clip. level = 180
maximum = 144.0 fT
contours = 18.0 fT
map border = 64°

―――― field out
―――― field in

T.R.

R.G.

B.J.
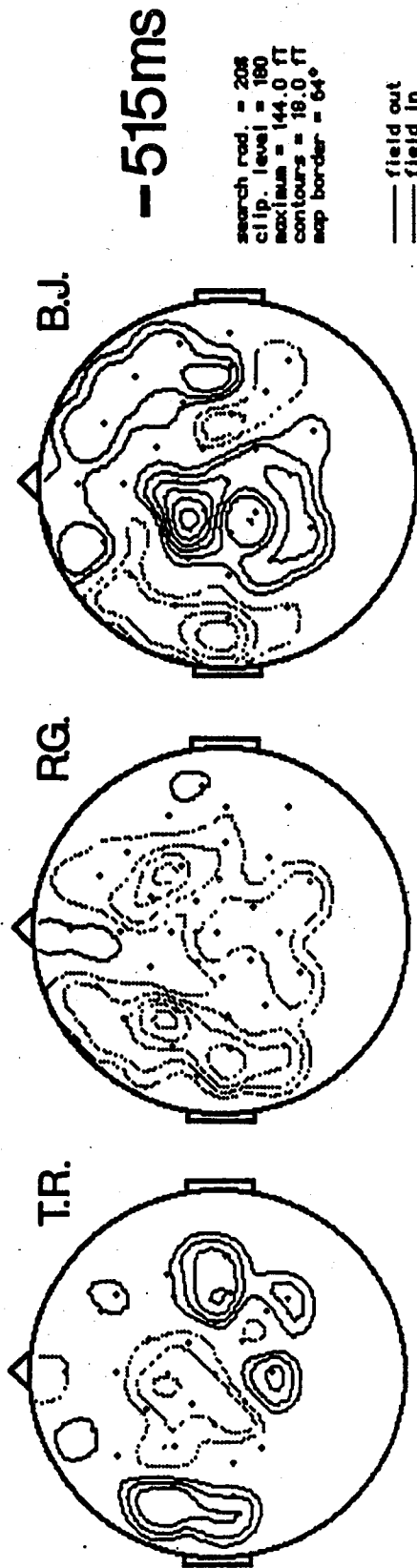
FIGURE 11.2a. Isocontour maps of MEG activity preceding unilateral finger flexion: "Motor" component (Simple).

−47 ms

search rad. = 208
clip. level = 180
maximum = 144.0 fT
contours = 18.0 fT
map border = 64°

——— field out
——— field in

B.J.

RG.

T.R.

H.W.
(l. hand)

H.W.
(r. hand)

D.C.
(l. hand)

D.C.
(r. hand)

102
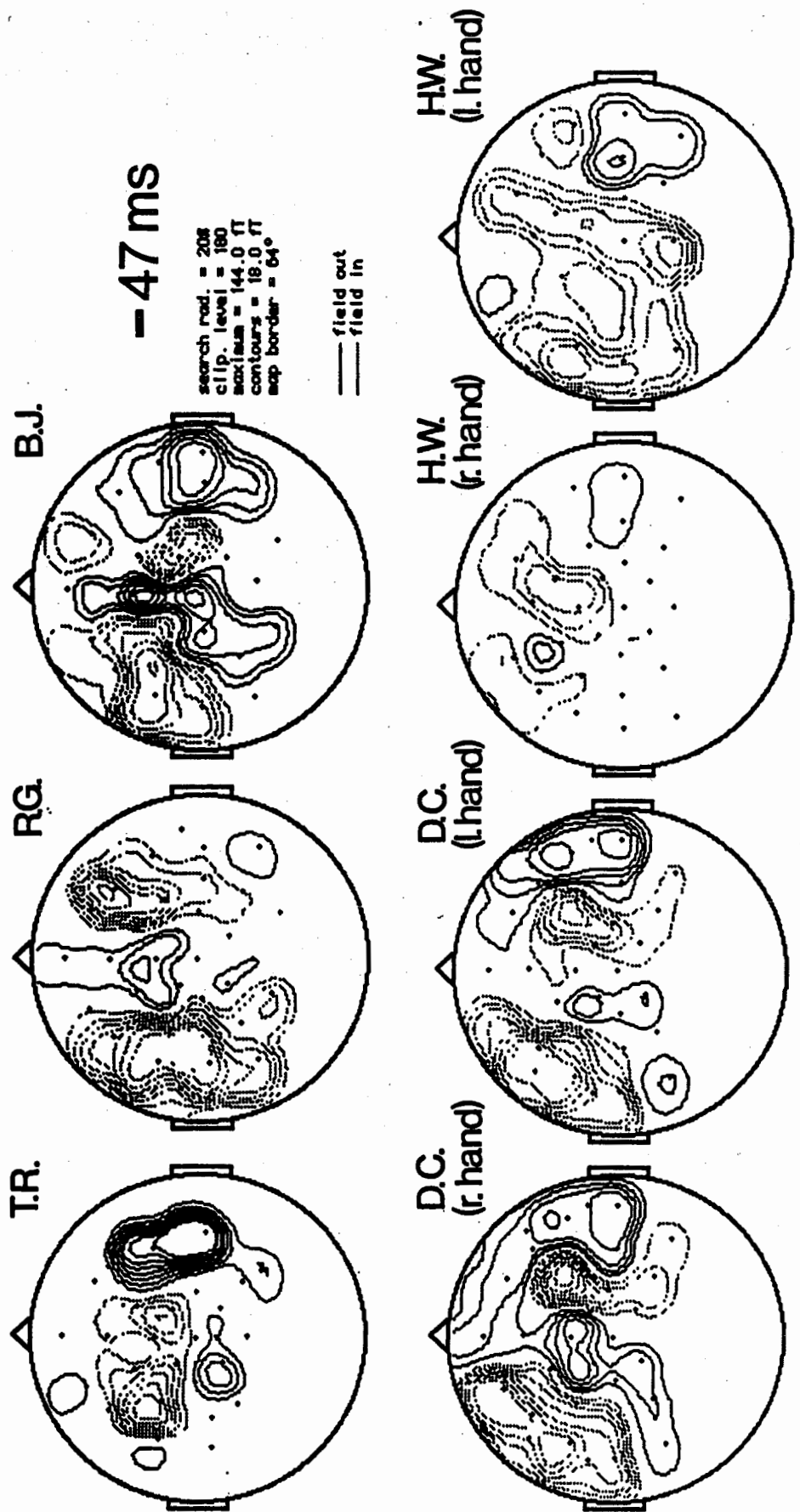
FIGURE 11.2b.   Isocontour maps of MEG activity preceding
              unilateral finger flexion: "Motor" component (Pattern).

−47mS

search rad. = 208
clip. level = 180
maximum = 144.0 fT
contours = 18.0 fT
map border = 64°

———— field out
———— field in

T.R.

R.G.

B.J.
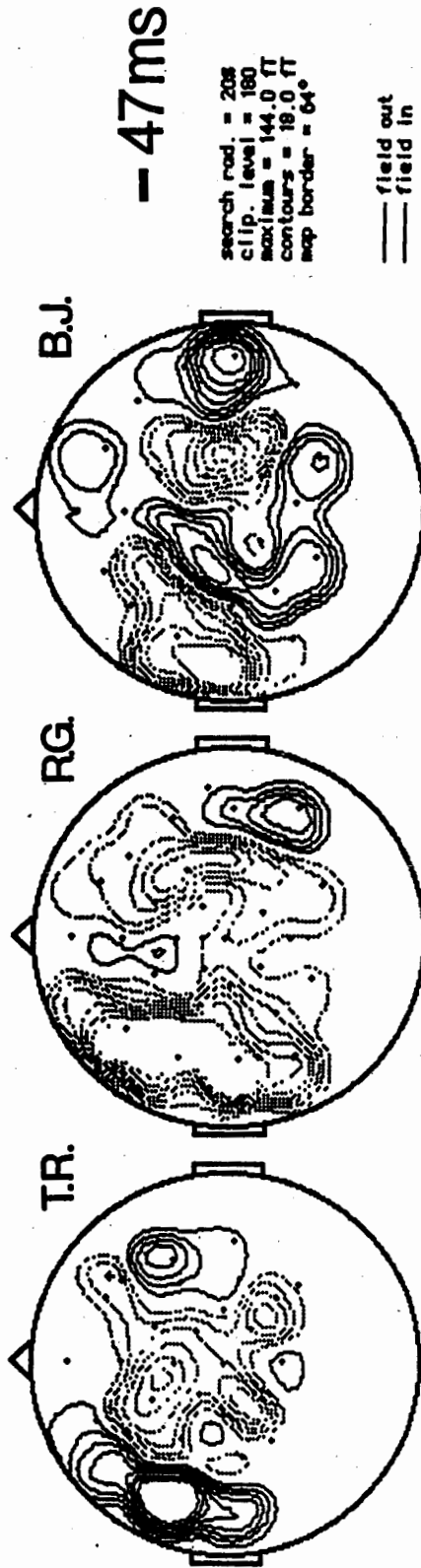
FIGURE 11.3a. Isocontour maps of MEG activity during unilateral finger flexion: Proprioceptive E.F. (Simple).

109ms

search rad. = 208
clip level = 180
maximum = 144.0 fT
contours = 18.0 fT
sep border = 64°

——— field out
------- field in

B.J.

RG.

T.R.

H.W.
(l.hand)

H.W.
(r.hand)

D.C.
(l.hand)

D.C.
(r.hand)
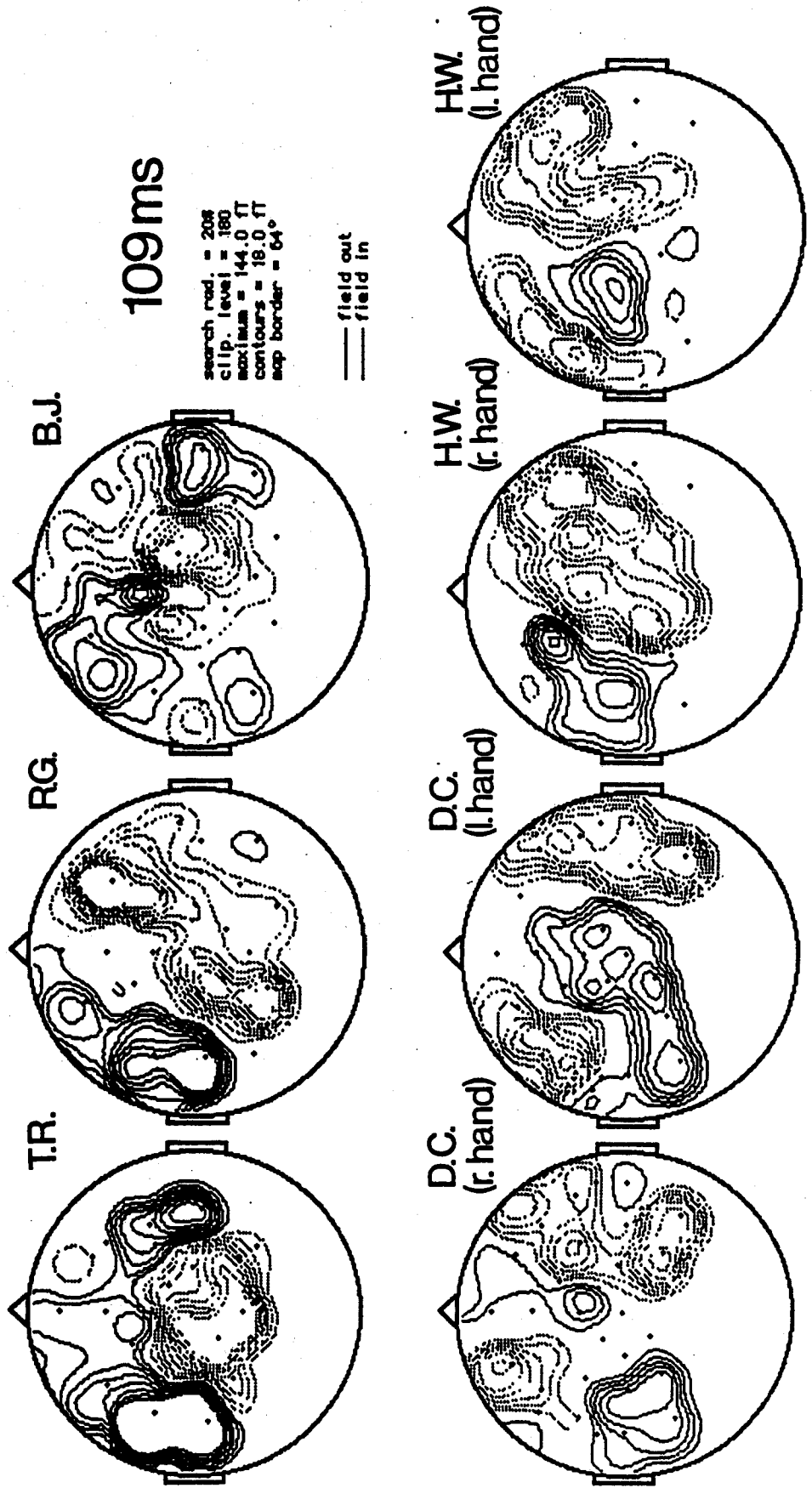
FIGURE 11.3b. Isocontour maps of MEG activity during unilateral finger flexion; Proprioceptive E.F. (Pattern).

109 ms

search rad. = 208
clip. level = 180
maximum = 144.0 fT
contours = 18.0 fT
map border = 64°

——— field out
——— field in

B.J.

R.G.

T.R.
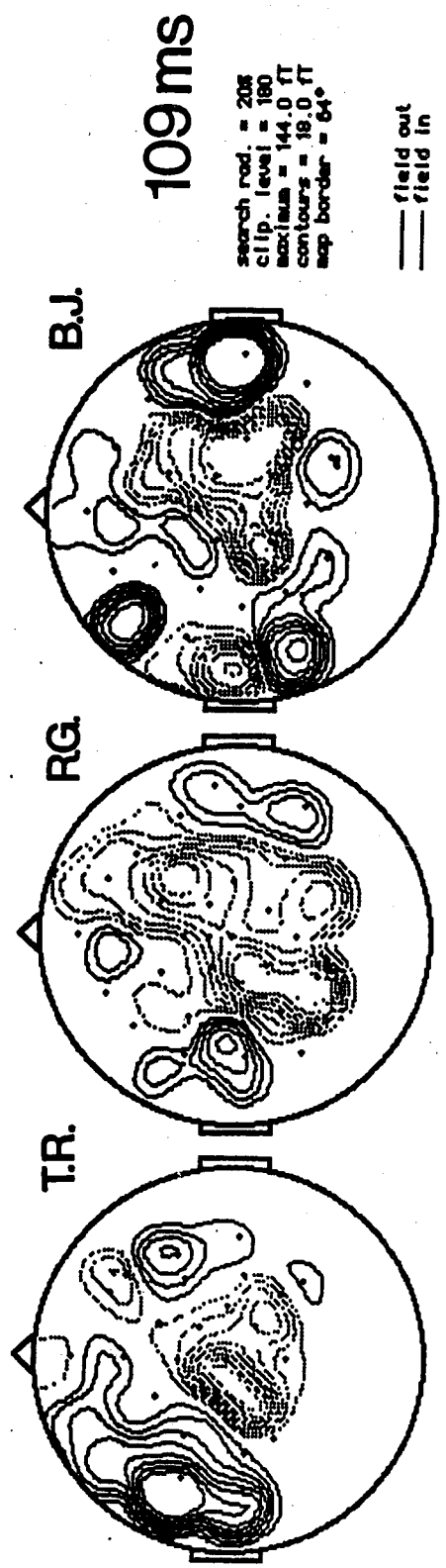
FIGURE 12. Comparison of MEG and EEG (Laplacian) distributions preceding and during unilateral finger flexion

-47 ms   subject T. R.

MEG   EEG

————— field out   ————— neg.
·············· field in   ·············· pos.

– ◄——— +
current
dipole

109 ms   subject T. R.

MEG   EEG
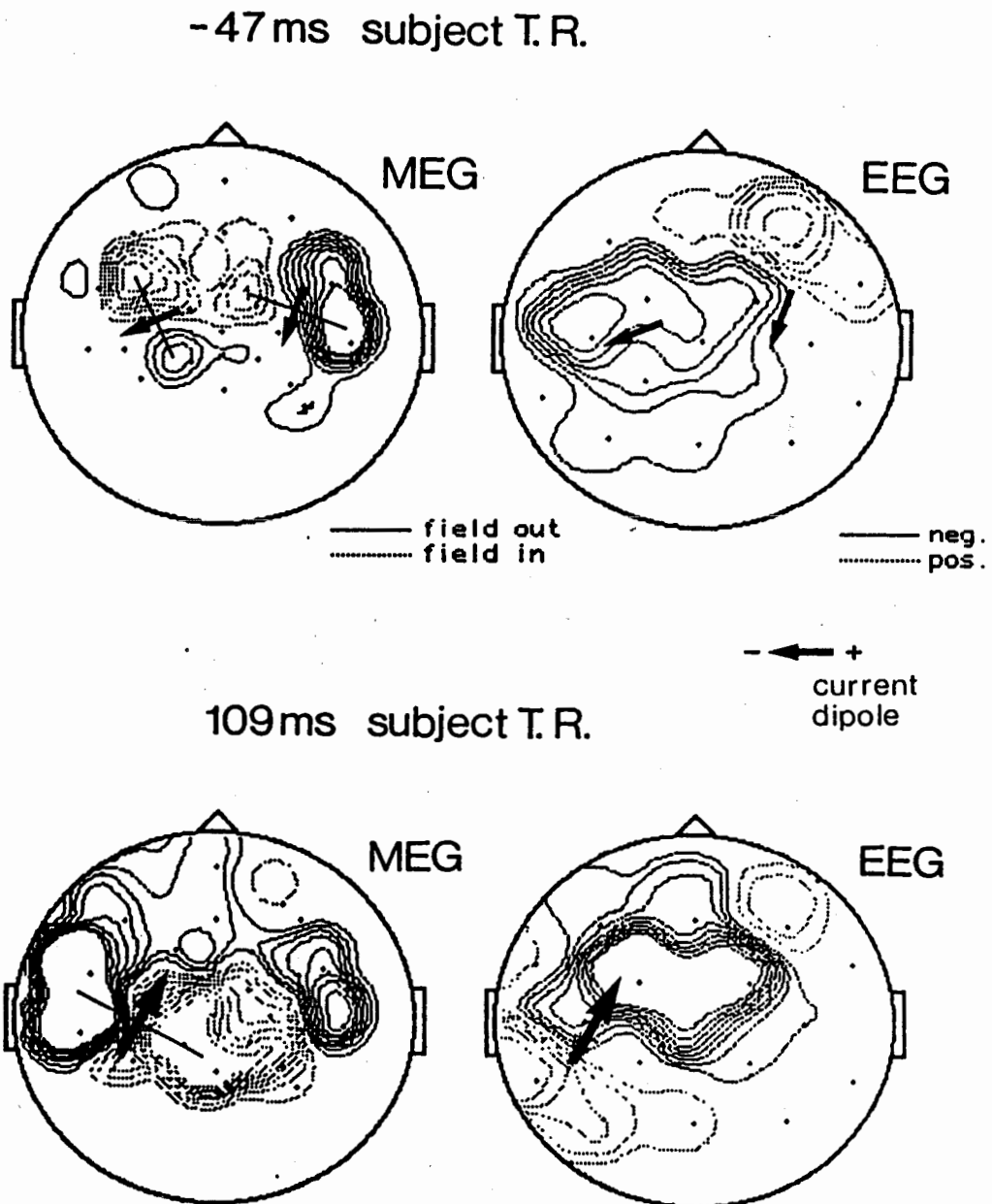
Current Dipole Source Estimation

The presence of localized field reversals over the scalp in the above data suggests that the patterns of magnetic field activity observed over the movement foreperiod and onset can be attributed to circumscribed areas of current flow in specific brain structures, and modelled as "equivalent" current dipole sources. Such sources would account for dipolar field patterns over the head of the amplitude and orientation observed and can be modelled in various configurations to produce the complex patterns in which more than one reversal is observed, although it is, computationally, much simpler to model small numbers of such sources which may be simultaneously active. An important advantage of applying such modelled sources is the ability to test to what extent the assumed source configurations can account for the observed data. The nature of the possible sources of the field reversals described above rely on *a priori* assumptions about the brain areas that are active during these events, i.e., which maxima may be assumed to be associated together as arising from the same source. Accordingly, one may assume an equivalent dipole source model in which case a source may be defined which is the assumed sum of activity producing a single reversal. The ability to test goodness of fit for modelled dipole sources using least-squares fitting algorithms (in which case a number of sources are provided to the algorithm which fits them to the locations which best account for the observed data) can be used to validate to some extent these assumptions (see Appendix F).

The dipole localization program used in this study was developed by Harrop and colleagues (Harrop *et al.*, 1986) from an earlier version (Weinberg, Brickett, Coolsma & Baff, 1986) which employed an iterative least-squares fitting algorithm based on the Simplex method (Caceci & Cacheris, 1984) to fit six or more parameters to the derivation of the Biot-Savart law for the measured radial magnetic flux (Appendix E, Eq. 4). The modified program takes into account the calculated field strength at each of the recording coils of the 3rd order gradiometer and their respective positions and orientations with respect to the

head origin defined by the automated gantry system. This allows for the "non-normality" of the recording sensing coil with respect to the vector pointing from the head origin to the observation point as well as accurate information regarding the distance of the sensing coil to the head and its origin. This also allows for the fitting of non-orthogonal dipoles, allowing for the consideration of so-called secondary sources (see Appendix E) requiring the fitting of at least 6 parameters for each dipole. Non-orthogonal solutions were employed in this study since successful source estimation of dipolar sources for sensory evoked fields has been achieved in previous studies using this algorithm (Weinberg et al., 1987). However, comparisons of orthogonal and non-orthogonal fits for the same data sets provide similar results, but usually with lower goodness of fit for orthogonal solutions. The dipole fitting algorithm also provides for the fitting of two current dipole sources simultaneously active, which has proven successsful in cases where more than one active source is suspected, for example, the localization of bilateral temporal lobe dipole sources for binaurally evoked magnetic fields (Weinberg, Cheyne, Brickett, Gordon & Harrop, 1986; Weinberg et al., 1987).

Due to the restriction to modelling a maximum of two simultaneously active dipole sources, dipole models used in the following source estimates had to be restricted to simple configurations athough it should be noted for some conditions, and in some subjects, the specified fields (in which there are large numbers of reversals or maxima are widespread and overlapping) may be better described by more complex configurations of sources. In such cases, dipole fits typically account for less of the total variance in the observed data or anatomical locations are difficult to interpret in the context of the components described above. Three time intervals were chose for initial dipole modelling for the aforementioned movement-related magnetic field components and correspond to the fields shown in Figures 11.1(a-b) to 11.3(a-b). Two dipole fits were used for the pre-movement time intervals and a single dipole fit for the PEF component. Goodness of fit for the dipole estimates is defined as the percentage of variance in the observed field accounted for by the field

calculated for the dipole sources (Weinberg, Brickett, Coolsma & Baff, 1986; Harrop et al., 1986). Only fits accounting for more than 50 percent of the variance are included, except in cases where dipole positions were consistant with other data, particularly in the case of single dipole fits for the PEF in which additional activity in the other hemisphere decreased the overall variance accounted for. The fitted dipole coordinates given are with respect to the gantry axis system (shown in Figure 7) thus dipoles with positive y values are in the left hemisphere, dipoles with negative y values in right hemisphere. The dipole strength is given as a current density (expressed in nanoAmpere – meters). The times given for source estimates is the center time for the interval used in mapping and represents the integration of activity over a 5 point (39 millisecond) interval, since source estimates were utilized for the localization of slow rather than fast changes in the MEG signal and in order to eliminate the effects of high frequency content in the selected intervals (e.g., alpha activity which is of high amplitude in posterior locations.

Table 1A and Table 1B show two dipole fits for the interval of –515 milliseconds (time 0 is defined as EMG onset) during the early onset of the bilateral readiness fields for simple and pattern movements respectively. Table 2A and Table 2B show two dipole source estimates for the time period –47 milliseconds for simple and pattern movements, respectively, where the contralateral readiness field (motor field) is approaching its maximum. Good fits were achieved for most subjects at this time period, particularly for simple finger flexions. These fits accounted for significant amounts of the total variance in the observed data (89% in subject T.R. and 86% in subject R.G.). Although the field maps indicate bilaterally symmetric fields, the source estimates tended to produce asymmetrical dipole fits, with ipsilateral dipoles deeper (non–cortical), or in some cases outside of the head. These source estimates are interpreted as the inability of one dipole to account adequately for the ipsilateral activity or possibly low signal–to–noise ratio for the data accounting for poor estimates of the flux at the surface of the head.

Tables 3A and 3B show one dipole solutions for the time period 109 milliseconds, where the proprioceptive evoked field reaches its maximum over the contralateral hemisphere. The percentage of total variance accounted for by these fits is, overall, lower than for the above estimates, most likely due to the additional activity in ipsilateral hemisphere, however, the fitted dipoles for most subjects, attain stable positions in the region of postcentral gyrus of the contralateral hemisphere. For example, in subjects D.C. and R.G. these dipole locations are in similar locations, but slightly posterior to dipole estimates for the pre-movement period.

Table 1A: Two dipole source estimates for time interval -515 ms (Simple condition)

Subject	N	Dip	Q (nA·m)	Position (cm)			*Orientation (cm)			Variance accounted for
				x	y	z	x	y	z	
T.R. (r. hand)	28	C	0.2	-0.14	6.06	5.44	0.74	0.57	-0.34	71%
		I	1.2	0.57	-4.59	7.06	0.95	0.04	0.30	
R.G. (r. hand)	34	C	4.7	-1.28	1.95	9.26	0.53	0.22	0.82	81%
		I	13.6	3.77	-1.58	4.87	0.86	0.25	0.45	
B.J. (r. hand)	31	C	16.9	-0.48	3.11	10.39	0.40	0.39	0.82	58%
		I	2.5	1.39	-6.88	12.11	0.95	-0.16	-0.28	
D.C. (r. hand)	32	C	2.2	3.43	5.44	10.6	0.56	-0.82	-0.09	69%
		I	2.1	0.61	-6.70	9.25	0.93	-0.28	0.22	
D.C. (l. hand)	32	I	2.1	3.21	4.68	10.3	0.89	-0.34	0.29	74%
		C	6.7	3.68	-5.58	9.12	-0.09	0.88	-0.45	
H.W. (l. hand)	28	I	2.8	-1.27	4.78	10.3	0.30	0.66	0.68	62%
		C	22.9	1.95	-0.07	4.48	-0.04	0.61	-0.79	

N = number of recording positions. dip = dipole position with respect to side of movement (C - contralateral, I - ipsilateral). *Note: orientation of dipoles are in opposite sense (ie., vector is directed towards positive pole).

Table 1B: Two dipole source estimates for time interval -515 ms (Pattern condition)

Subject	N	Dip	Q (nA·m)	Position (cm) x	y	z	*Orientation (cm) x	y	z	Variance accounted for
T.R. (r. hand)	28	C	0.8	0.90	6.83	3.65	0.94	0.35	-0.01	62%
		I	4.4	1.20	-3.15	10.0	0.79	-0.11	0.61	
R.G. (r. hand)	34	C	12.8	-2.21	2.37	8.4	0.02	0.75	0.67	64%
		I	33.6	-2.54	-2.33	5.20	0.19	-0.97	0.15	

N = number of recording positions. dip = dipole position with respect to side of movement (C - contralateral, I - ipsilateral). *Note: orientation of dipoles are in opposite sense (ie., vector is directed towards positive pole).

Table 2A: Two dipole source estimates for time interval -47 ms (Simple condition)

Subject	N	Dip	Q (nA·m)	Position (cm)			*Orientation (cm)			Variance accounted for
				x	y	z	x	y	z	
T.R. (r. hand)	28	C	6.9	0.53	3.69	11.4	0.20	0.35	0.92	86%
		I	1.6	-0.10	-3.40	6.22	0.99	-0.13	-0.02	
R.G. (r. hand)	34	C	9.4	3.11	2.27	8.75	0.33	-0.38	-0.87	89%
		I	13.5	3.57	-2.57	4.82	0.32	0.95	-0.03	
B.J. (r. hand)	31	C	21.4	-0.56	3.49	10.06	0.40	0.27	0.87	64%
		I	4.1	1.29	-7.13	11.91	0.99	-0.01	-0.12	
D.C. (r. hand)	32	C	10.9	2.80	1.47	9.19	0.96	-0.27	-0.05	72%
		I	13.3	0.65	-7.35	10.6	0.45	-0.76	0.47	
D.C. (l. hand)	32	I	7.6	1.82	4.16	9.66	0.69	0.40	0.59	76%
		C	8.6	3.81	-5.65	9.09	-0.04	0.85	-0.53	

N = number of recording positions. dip = dipole position with respect to side of movement (C - contralateral, I - ipsilateral). *Note: orientation of dipoles are in opposite sense (ie., vector is directed towards positive pole).

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Table 2B: Two dipole source estimates for time interval -47 ms (Pattern condition)

Subject	N	Dip	Q (nA·m)	Position (cm)			*Orientation (cm)			Variance accounted for
				x	y	z	x	y	z	
T.R. (r. hand)	28	C	2.7	2.82	5.89	3.36	0.87	0.36	0.35	56%
		I	7.8	-1.70	-4.78	9.62	0.60	-0.59	-0.54	
R.G. (r. hand)	34	C	7.0	3.82	2.51	9.30	0.31	-0.38	-0.87	82%
		I	49.0	-2.1	-1.31	5.55	0.39	-0.92	0.02	
B.J. (r. hand)	31	C	11.2	-1.51	5.29	9.06	0.60	0.08	0.80	70%
		I	6.6	0.74	-8.49	11.09	0.73	-0.31	0.62	

N = number of recording positions. dip = dipole position with respect to side of movement (C - contralateral, I - ipsilateral). *Note: orientation of dipoles are in opposite sense (ie., vector is directed towards positive pole).

Table 3A: One dipole source estimates for time interval 109 ms (Simple condition)

Subject	N	Dip	Q (nA·m)	Position (cm) x	y	z	*Orientation (cm) x	y	z	Variance accounted for
T.R. (r. hand)	28	C	34.1	0.82	2.37	8.54	0.08	0.74	0.67	78%
R.G. (r. hand)	34	C	24.8	-0.42	1.34	8.35	-0.49	-0.03	-0.87	67%
D.C. (l. hand)	32	C	22.4	2.65	-3.25	8.70	0.01	-0.76	0.65	51%
H.W. (r. hand)	28	C	11.2	-0.18	2.62	9.99	-0.85	-0.04	-0.52	60%
H.W. (l. hand)	28	C	5.7	2.11	0.28	9.98	-0.29	-0.19	0.94	40%

N = number of recording positions. dip = dipole position with respect to side of movement (C - contralateral, I - ipsilateral). *Note: orientation of dipoles are in opposite sense (ie., vector is directed towards positive pole).

Table 3B: One dipole source estimates for time interval 109 ms (Pattern condition)

Subject	N	Dip	Q (nA·m)	Position (cm)			*Orientation (cm)			Variance accounted for
				x	y	z	x	y	z	
T.R. (r. hand)	28	C	6.6	0.82	1.63	9.87	-0.61	0.79	0.06	54%
R.G. (r. hand)	34	C	24.1	-3.79	1.72	7.09	-0.05	-0.86	-0.51	48%

N = number of recording positions, dip = dipole position with respect to side of movement (C - contralateral, I - ipsilateral). *Note: orientation of dipoles are in opposite sense (ie., vector is directed towards positive pole).

FIGURE 13.1a. Projections of estimated dipole sources for readiness fields: Early component (Simple condition)

1 T.R.
(r. hand)

2 R.G.
(r. hand)
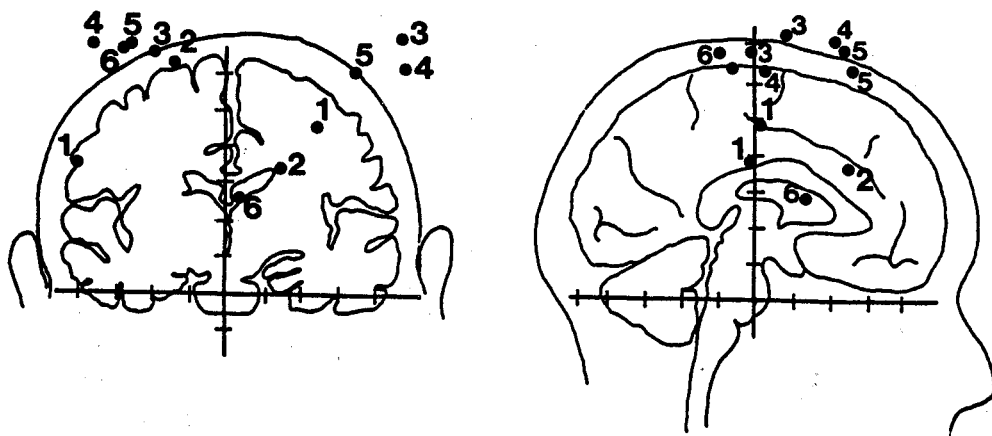
3 B.J.
(r. hand)

4 D.C.
(r. hand)

5 D.C.
(l. hand)

6 H.W.
(l. hand)

scale 3:1

FIGURE 13. 1b. Projections of estimated dipole sources for readiness fields: Early component (Pattern condition)
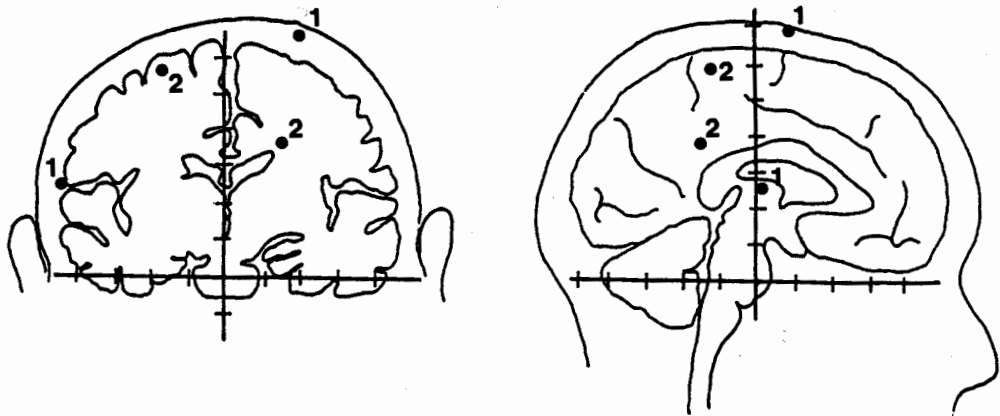
1 T.R.
   (r. hand)

2 R.G.
   (r. hand)

scale 3:1

FIGURE 13.2a. Projections of estimated dipole sources for readiness fields: "Motor" component (Simple condition)

1	T.R. (r. hand)	scale 3:1
2	R.G. (r. hand)	
3	B.J. (r. hand)	
4	D.C. (r. hand)	
5	D.C. (1. hand)	

FIGURE 13. 2b.   Projections of estimated
dipole sources for readiness fields:
"Motor" component (Pattern condition)

1 T.R.
  (r. hand)
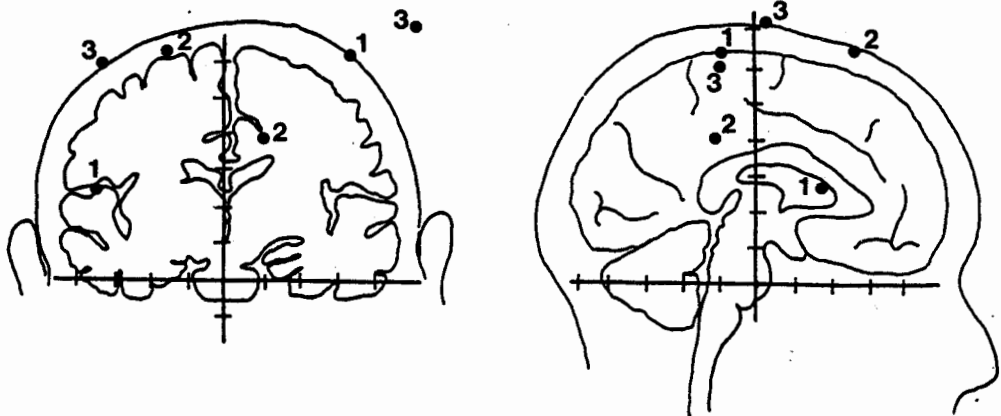
2 R.G.
  (r. hand)

3 B.J.
  (r. hand)

scale 3:1

FIGURE 13.3a.   Projections of estimated
  dipole sources for Proprioceptive
  evoked field (Simple condition)
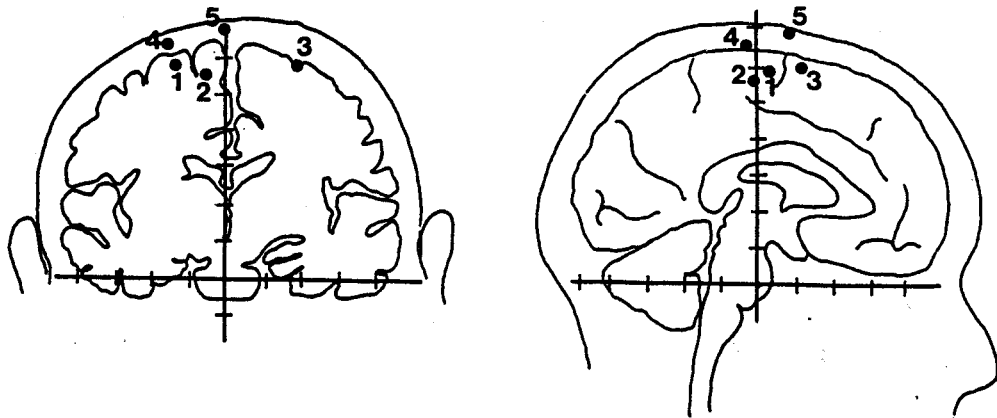
scale 3:1

1 T.R.
  (r. hand)

2 R.G.
  (r. hand)

3 D.C.
  (l. hand)

4 H.W.
  (r. hand)

5 H.W.
  (l. hand)

FIGURE 13.3b. Projections of estimated dipole sources for Proprioceptive evoked field (Pattern condition)
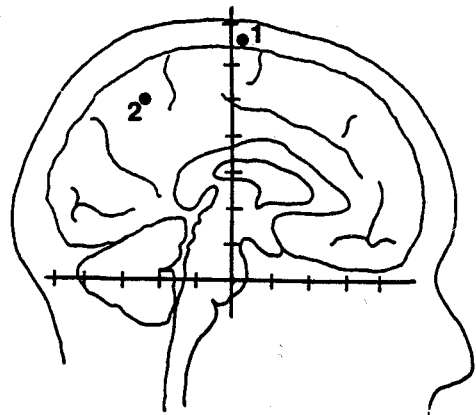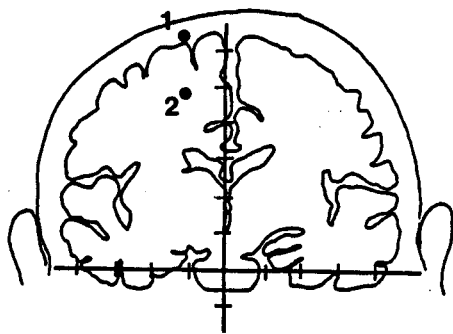
scale 3:1

1 T.R.
(r. hand)

2 R.G.
(r. hand)

PART D

<u>DISCUSSION</u>

The slow magnetic field shifts observed prior to voluntary unilateral flexions of the index finger, in all subjects tested, resemble the previously reported slow fields preceding movement over contralateral motor areas of the brain (Deecke, Weinberg, & Brickett, 1982, Hari et al., 1985), also termed *Bereitschaftsmagnetfelds* by Deecke and colleagues in recognition of their similarity to the electrically recorded readiness potentials. This shift is best observed at sites anterior to C3 and displays a similar waveform morphology across all subjects for the period preceding EMG onset, beginning about one second prior to EMG onset in the active muscle groups and immediately following the initiation of movement. Previous studies have not, however, reported the slow shifts over ipsilateral hemisphere, accompanying these shifts, which were observed in all subjects tested for both simple and sequential finger flexions (although there is some indication of such bilateral shifts in the data reported by Deecke, Weinberg, and Brickett (1982) which was not fully examined).

Dipole source estimates for periods prior to and during movement initiation indicate field reversals observed over contralateral Rolandic areas are associated with an equivalent current dipole source directed posteriorly. This pattern can be hypothesized to arise from localized current flow within the central sulcus in primary motor area (MI) possibly due to current sinks in superficial layers of area 4. Least-squares fitting routines achieved stable and consistant estimates of dipole locations to this region in contralateral hemisphere for the time interval immediately preceding movement, particularly for the simple finger flexion task. Location and orientation vary across individuals to some extent, although this is not unexpected due to the extensive folding of the central sulcus which is known to have a quite variable morphology across individuals. The orientation of these MI sources vary accordingly, as indicated by the rotation of field maxima in two subjects in this study (T.R. and H.W.)

Ipsilateral slow fields

The additional finding in this study of ipsilateral magnetic field shifts which show steady amplitude increase throughout the movement foreperiod and during the movement itself represents an interesting phenomenon related to voluntary movement production and warrants further investigation. The fact that this shift has not been reported in previous studies of movement–related MEG activity may be due to the number of observation points used (previous studies have used single sensor systems with manual positioning systems allowing for only limited distributions). Recordings of ipsilateral EMG activity indicate that these shifts cannot be entirely explained by movements of the contralateral limb in association with directed side of movement. However, there were some indications that this sympathetic movement may occur to some extent, occasionally in individual trials, without the subject's awareness. The role of this type of unintentional bilateral movement in many readiness potential paridigms should be further investigated as a possibly confounding variable, where subjects are instructed to make unilateral voluntary movements.

The origin of ipsilateral slow fields is not clear. In two subjects, dipole source estimates indicate a deeply located equivalent source that may be attributed to subcortical structures (e.g., basal ganglia) which are known to be bilaterally active during movement preparation. However, such sources have not been previously reported. Furthermore, there is some question as to the sensitivity of the MEG to activity at these depths (when gradiometer baseline effects are taken into consideration), or whether the cellular morphology of subcortical structures such as basal ganglia would support dipole layer models of current sources. Also, since dipole estimates were restricted to two dipole models, it is not known to what extent these solutions represent the best fit for a single dipole where additional generators may be expected. In other subjects, ipsilateral dipole estimates achieved best fits outside the head, suggesting an inadequacy of one dipole to account for ipsilateral fields. Thus, extreme variations in radii for these fitted dipoles may indicate that the two solutions (i.e., a strong deep source or weak source outside the head) may be best approximations of single dipole fits for complex field configurations. Additional

activity in fronto-central areas, particularly for sequential movements indicate that a three dipole configuration may better account for the observed fields. However, until such methods are developed it is difficult to determine to what extent fronto-central sources, possibly arising from premotor structures such as the supplementary motor area may be combining with ipsilateral motor cortex soures to produce the observed surface fields. As a result of the complexity of the pattern of pre-movement MEG and EEG shifts, it is difficult to determine the extent to which premotor sources, such as supplementary motor area, are active for different type of voluntary movement in all subjects.

The orientation of the bilateral field was quite similar across subjects. This is suggestive of bilaterally active dipole layers in precentral gyrus, even though source estimates were interpretable only for the contralateral sources. These contralateral source estimates are quite consistant with a dipolar source in primary motor area corresponding to the known somatotopic organization of MI (Penfield and Jasper, 1954). It is also interesting to speculate on the possible role of bilateral sources in movement preparation. For example, the models provided by Goldberg (1985) described in the introduction are consistent with the data, in that they suggest bilateral activity in motor systems during preparation and initiation of voluntary movements, attributable in part to bilateral input from supplementary motor areas to MI in both hemispheres.

The sources of activity preceding movement as estimated with MEG may also account for the electric field or field potentials at the scalp measured with the EEG (readiness potentials), in which there is bilateral activity leading to contralateral preponderance of negativity over the centro-parietal areas and posititivy over anterior sites. The relationship between EEG and MEG measures is demonstrated more effectively in the Laplacian transformed EEG maps which demonstrate current source anteriorly, and current sink localized over the contralateral Rolandic area. A configuration of bilateral, posteriorly directed dipoles would account for this pattern, and in some subjects source-sink reversals for the premovement period are quite orthogonal to the MEG field reversals, as shown in Figure 12, indicating a good correspondance between the

two separate measures. The source-sink reversals in EEG are somewhat widespread which would be consistant with the effect of two bilateral dipoles summating with slightly stronger dipole moments in the contralateral hemisphere (as indicated by greater Q values for dipole estimates for these fields).

MEG fields during unilateral finger movement

Although MEG activity during and following motor activity is difficult to interpret due to the extensive sensitivity of the MEG to movement of the head with respect to the sensing coil and the conduction of movements through the limbs during finger flexion tasks, there appears to be good localization of MEG activity related to proprioceptive feedback following movement of the fingers and is referred to here as a proprioceptive evoked field (PEF). This component also corresponds to the proprioceptive evoked potential identified in the EEG by Deecke and colleagues (Deecke, Grozinger & Kornhuber, 1976; Kornhuber & Deecke, 1965) at a similar latency (100 ms after EMG onset). The PEF consists of a reversal over contralateral somatosensory cortex, which is biphasic in form and possibly related to Ia afferent activity due to stretch in antagonist muscles (since subjects did not perform finger touching tasks somatosensory feedback may be considered to have been restricted to proprioception-related input from joint rotation and stretching of skin around the finger). The first phase of the PEF occured approximately 100 milliseconds after EMG onset and corresponds to the point of maximum negativity in the vertex EEG. This initial phase may be attributed to an anteriorly directed current dipole source in somatosensory cortex in the central sulcus (e.g., area 3b). The second phase of the PEF occurs about 120 milliseconds after the first phase and shows a clear reversal of direction, indicating a dipole source in the same location, but directed posteriorly.

Dipole source estimates for the initial phase of the PEF showed a high degree of similarity in position and orientation across subjects. In addition, consistant source-sink configurations were observed in the Laplacian EEG at the same latencies, and showed similar polarity reversals. These source-sink reversals appear orthogonal to the MEG maxima, as shown in Figure 12, demonstrating the

same relationship between the EEG and MEG as that found for pre-movement activity. The identified components of the PEF and the modelled sources also correspond quite well to biphasic MEG responses resulting from ulnar and median nerve stimulation recently reported by Huttenan, Hari and Leinonen (1987). They observed similar shifts at post-stimulus latencies of about 50 and 150 milliseconds and achieved similar estimates of source locations using a least-squares approximation.

Conclusions

The observed magnetic field changes during voluntary movement have estimated the location of sources in brain active prior to and following unilateral movement of the digits. These estimates are consistent with previous observations of slow magnetic fields over motor areas of the brain preceding voluntary movement. In this study the spatial distribution of these fields show some variability across individuals, but overall, they indicate a consistant pattern and time course for both simple and patterned sequential movements of the fingers. An important observation in this study was the presence of slow magnetic fields overlying the hemisphere *ipsilateral* to the side of finger movement. These ipsilateral shift is of unknown origin, but the data suggest a possible ipsilateral motor cortex source.

This findings also indicate that it is possible to discern post-movement events that appear to be of cerebral origin. In particular, a strong event-related magnetic field during finger flexion can be observed over contralateral somatosensory areas.

During movement preparation there appears to be some additional activity in fronto-central areas during sequential motor tasks. The patterns of magnetic flux over these areas is complex and, due to the presence of strong ipsilateral fields, it is not possible to verify sources in premotor areas without being able to fit multiple sources. Although the present knowledge of the neurophysiology of motor organization supports assumptions that SMA sources are active during motor preparation, the data observed here do not demonstrate specific dipole sources in SMA. However, there is some indication that such sources may be present in some of the complex patterns observed in individual subjects. It may also be speculated that if SMA is bilaterally active during movement preparation, and bilateral sources were symmetrically oriented in mesial frontal lobes, then the fields of these sources would tend to cancel, thus producing highly attenuated or no observable activity at the surface of the scalp.

With regard to these findings, the following conclusions can be stated with regard to the movement-related magnetic activity of the brain.

(1) Preceding voluntary movements there is bilateral activity overlying cortical motor areas, even for unilateral movements. The presence of ipsilateral slow fields preceding voluntary movement presents an interesting phenomenon which must be further examined and which is consistent with claims regarding the bilateral organization of volitional movement. Further studies which could determine the extent to which such fields are related to inhibition of ipsilateral motor cortex would provide important information regarding the means through which lateralization of motor output in the central nervous system occurs as well as the way in which organization of bimanual motor tasks is achieved.

(2) Magnetic field changes arising from sources in somatosensory cortex can be observed during voluntary finger movement. These changes correspond to event-related magnetic fields associated with peripheral somatosensory stimulation in the polarity and relative latencies of early and late components. These findings also lend support to earlier claims that identified EEG components following voluntary and passive finger movements arise from somatosensory areas of the brain associated with proprioceptive feedback related to movement.

(3) The combined use of MEG and EEG measures indicates good correspondence in the electric and magnetic field configurations over the surface of the scalp for movement-related brain activity, particularly if reference-free spatial transformations such as the Laplacian approximation are applied to referentially recorded EEG. The use of widespread EEG montages and these spatial enhancement techniques provides a useful alternative as well as supplementary measure for the localization of circumscribed sources of activity provided by MEG techniques. The orthogonality of the observed electric and magnetic fields lends further support to the application of current dipole models of localized brain activity (although such models can be most convincingly applied for simple field patterns and may not be suitable for more complex configurations of brain activity). The further development of measurement and

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source localization techniques, however, may help to elucidate some of the complex events involved in the preparation and initiation of movement and other preparatory brain states.

Appendices

APPENDIX A: SPATIO-TEMPORAL ISOCONTOUR MAPS OF EEG ACTIVITY DURING UNILATERAL FINGER FLEXIONS.

FIGURE 14.1.1. Isocontour maps of EEG
(referential) — Simple condition (T.R.)

search rad. = 28%
clip. level = 400
maximum = 10.0 μV
contours = 1.2 μV
map border = 90°

-359 msec   -320 msec   -281 msec   -242 msec

-203 msec   -164 msec   -125 msec   -86 msec

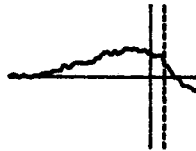-47 msec   -8 msec   31 msec   70 msec
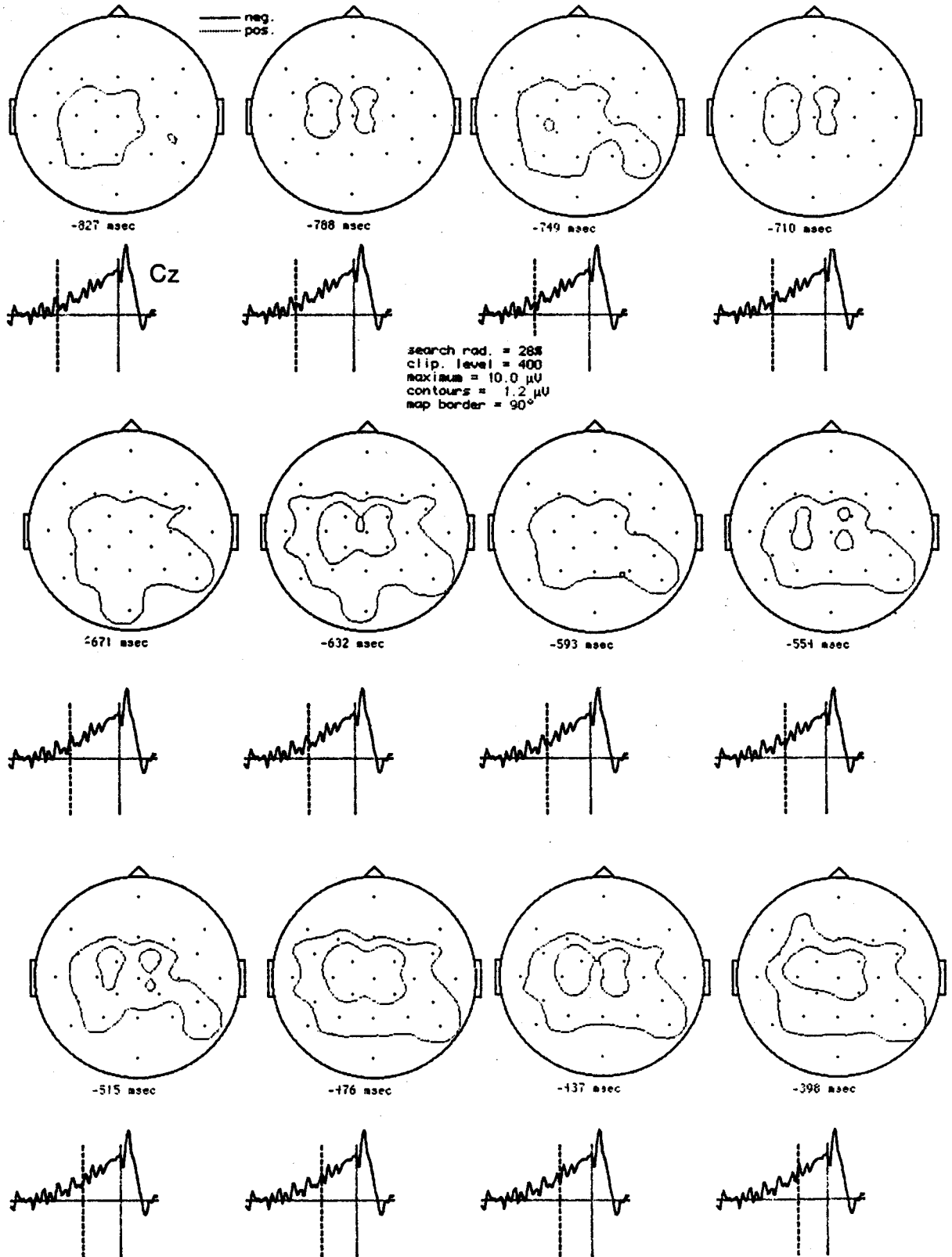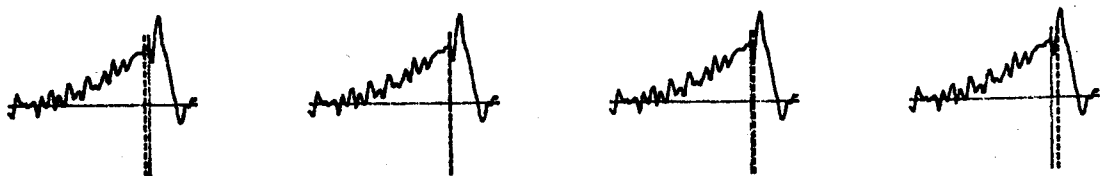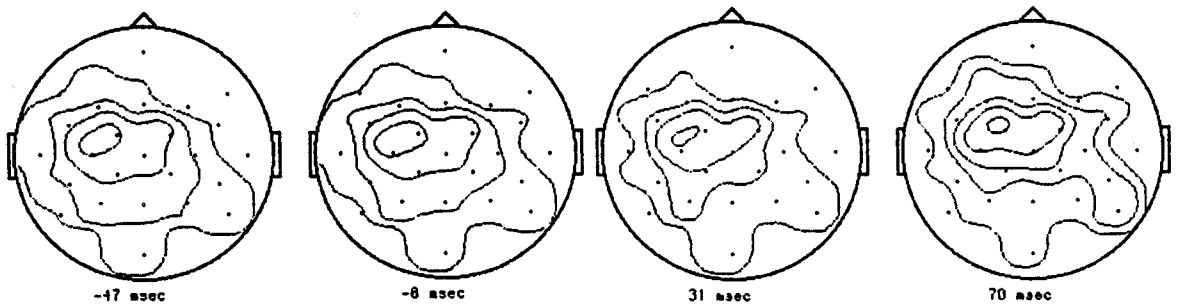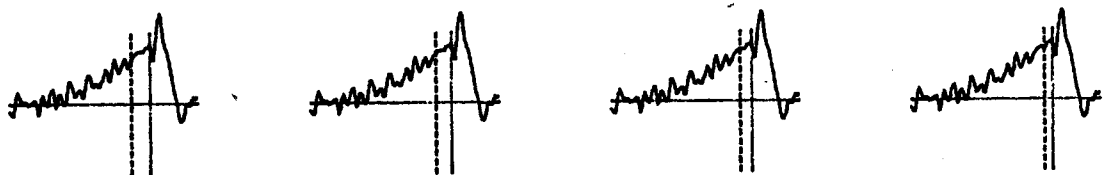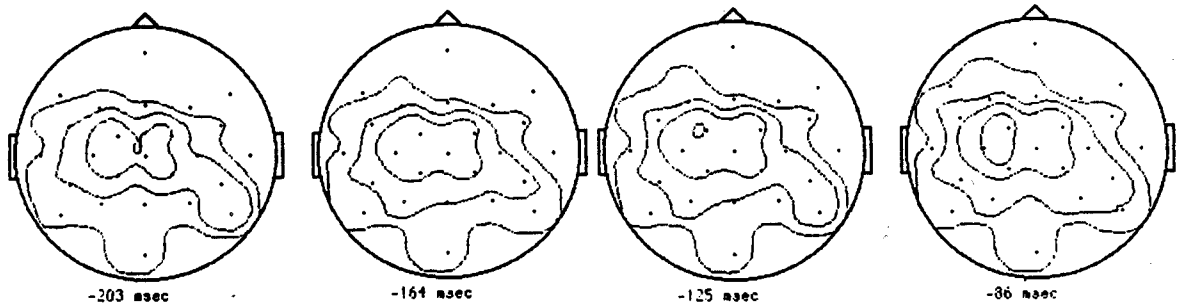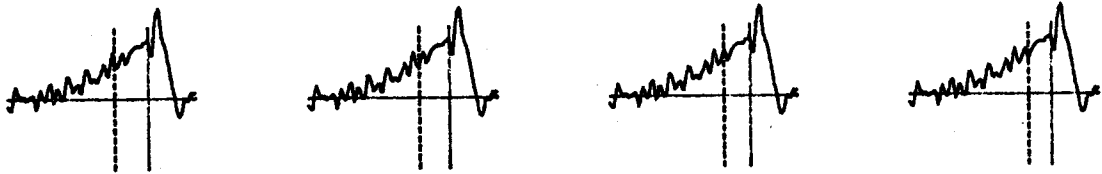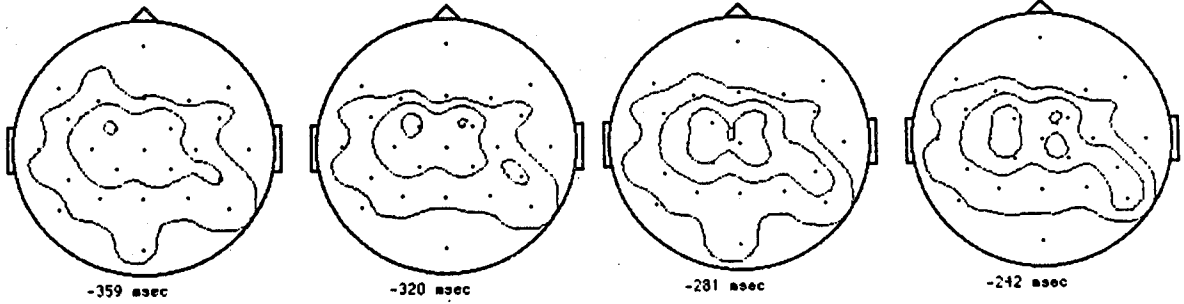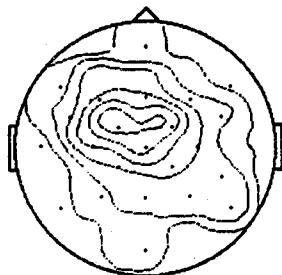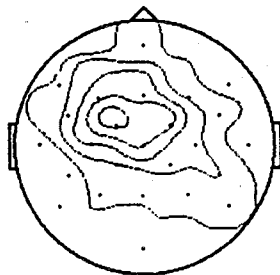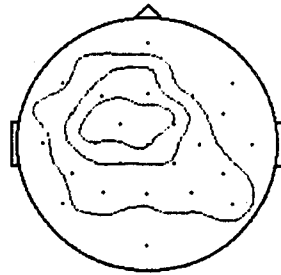
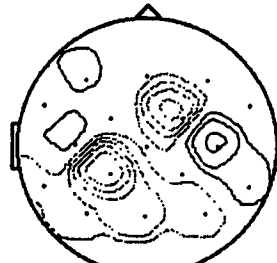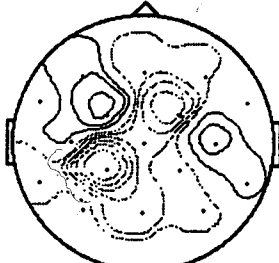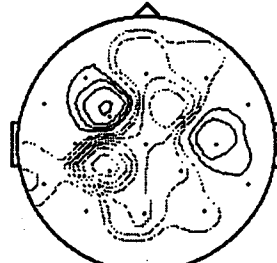109 msec   148 msec   187 msec   226 msec
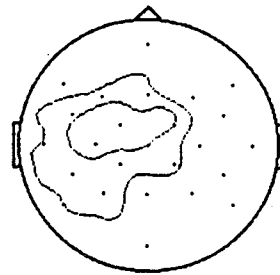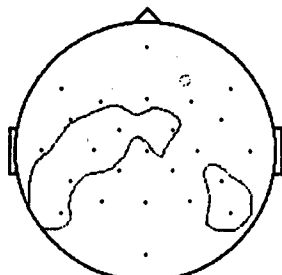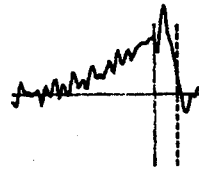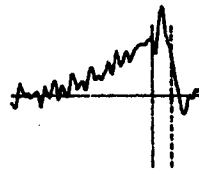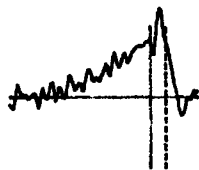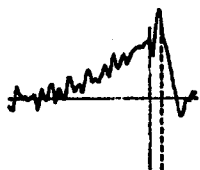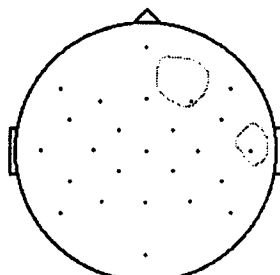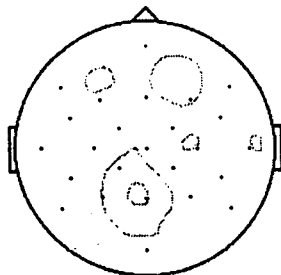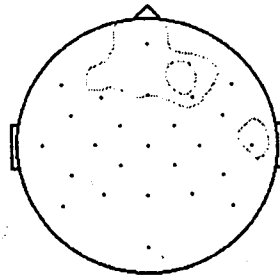
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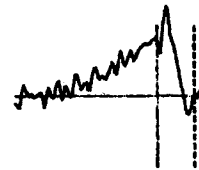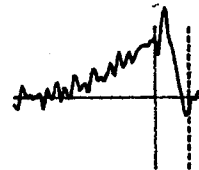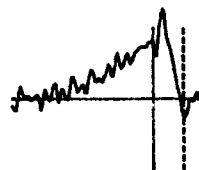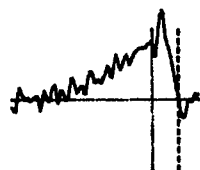
FIGURE 14.1.3. Isocontour maps of EEG
(referential) - Simple condition (B.J.)
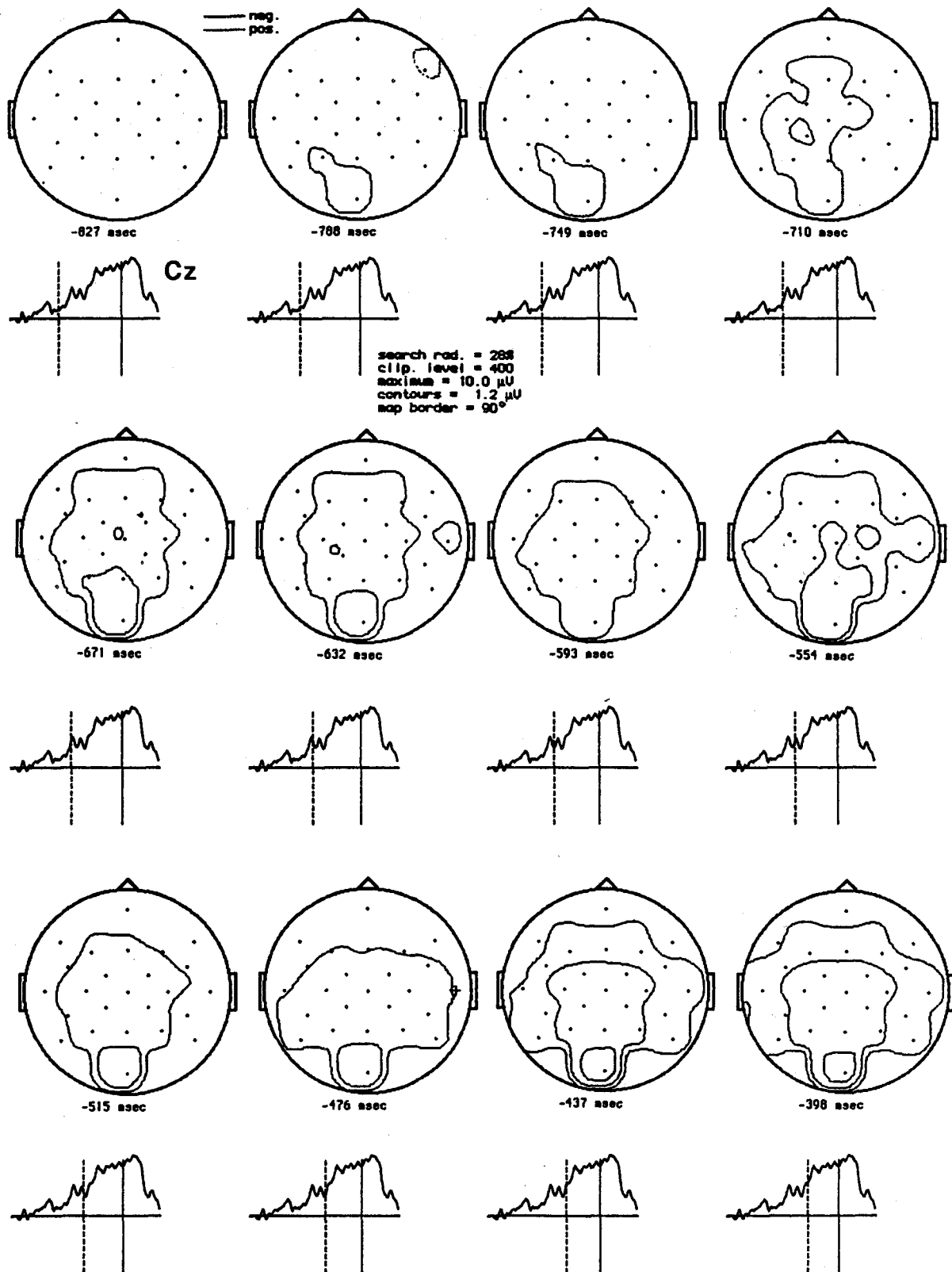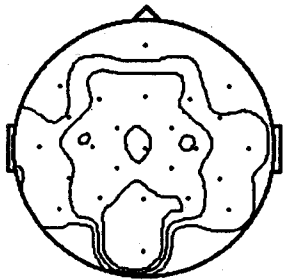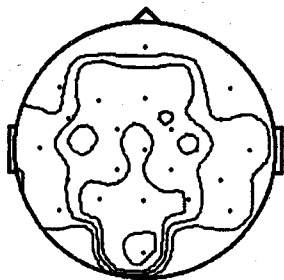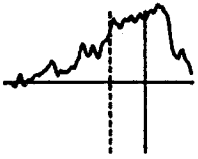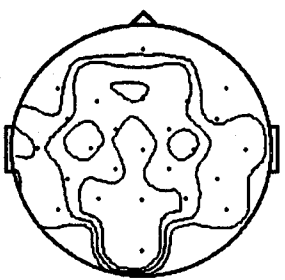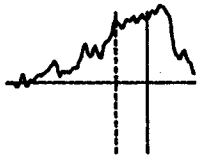
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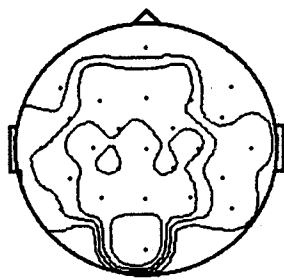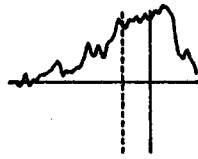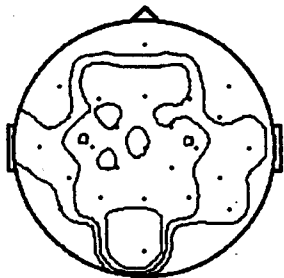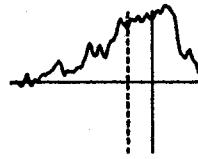
-281 msec -242 msec -125 msec -86 msec

-47 msec -8 msec 31 msec 70 msec

138
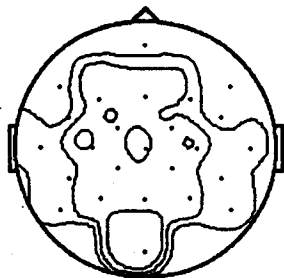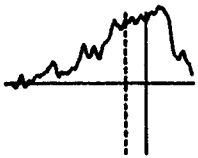
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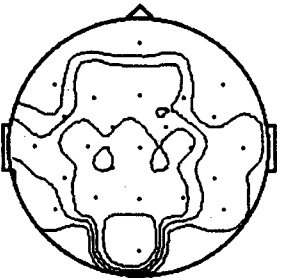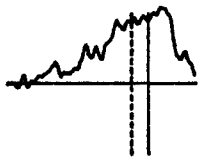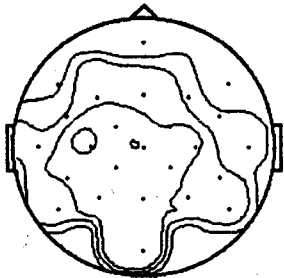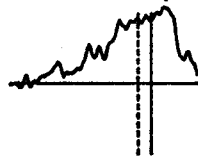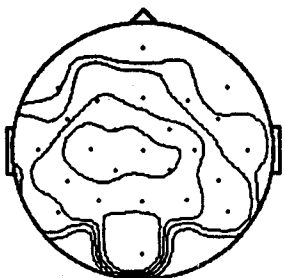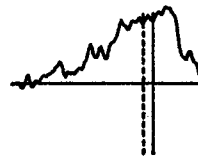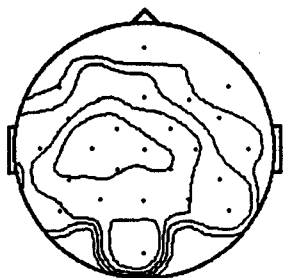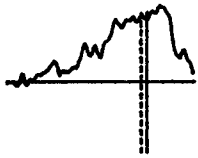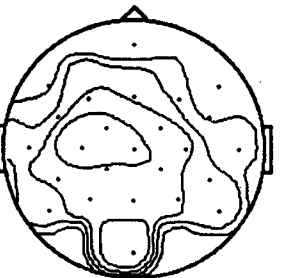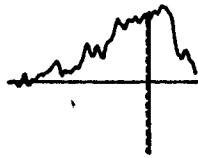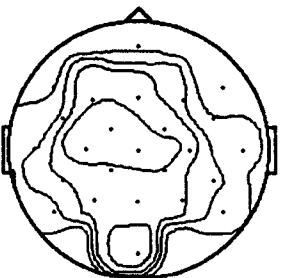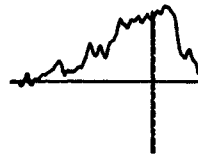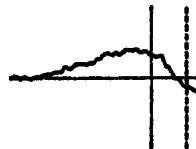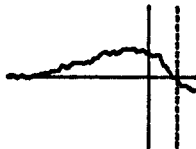
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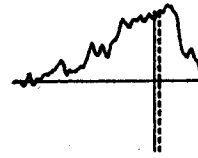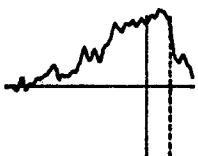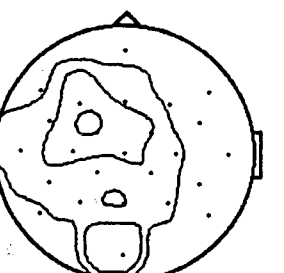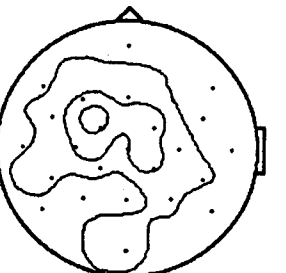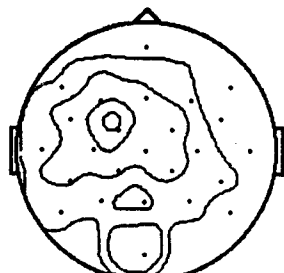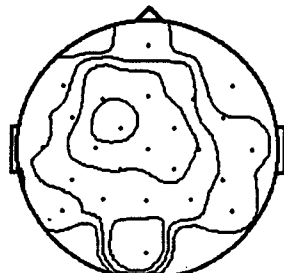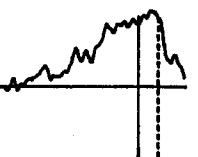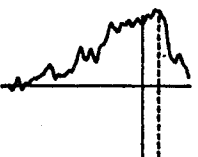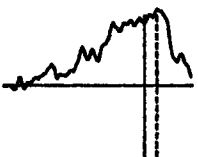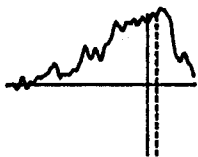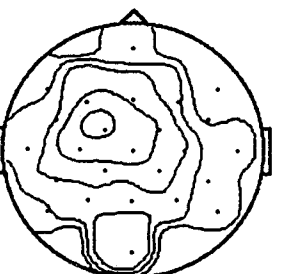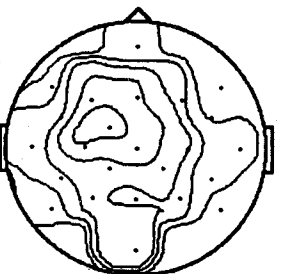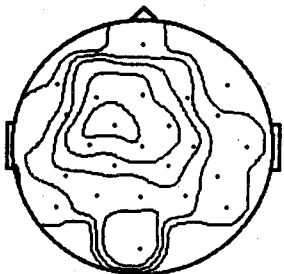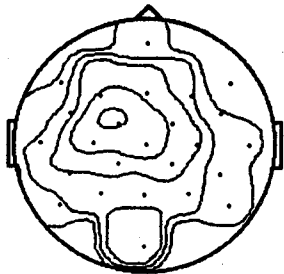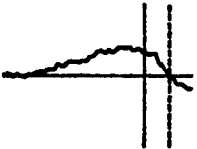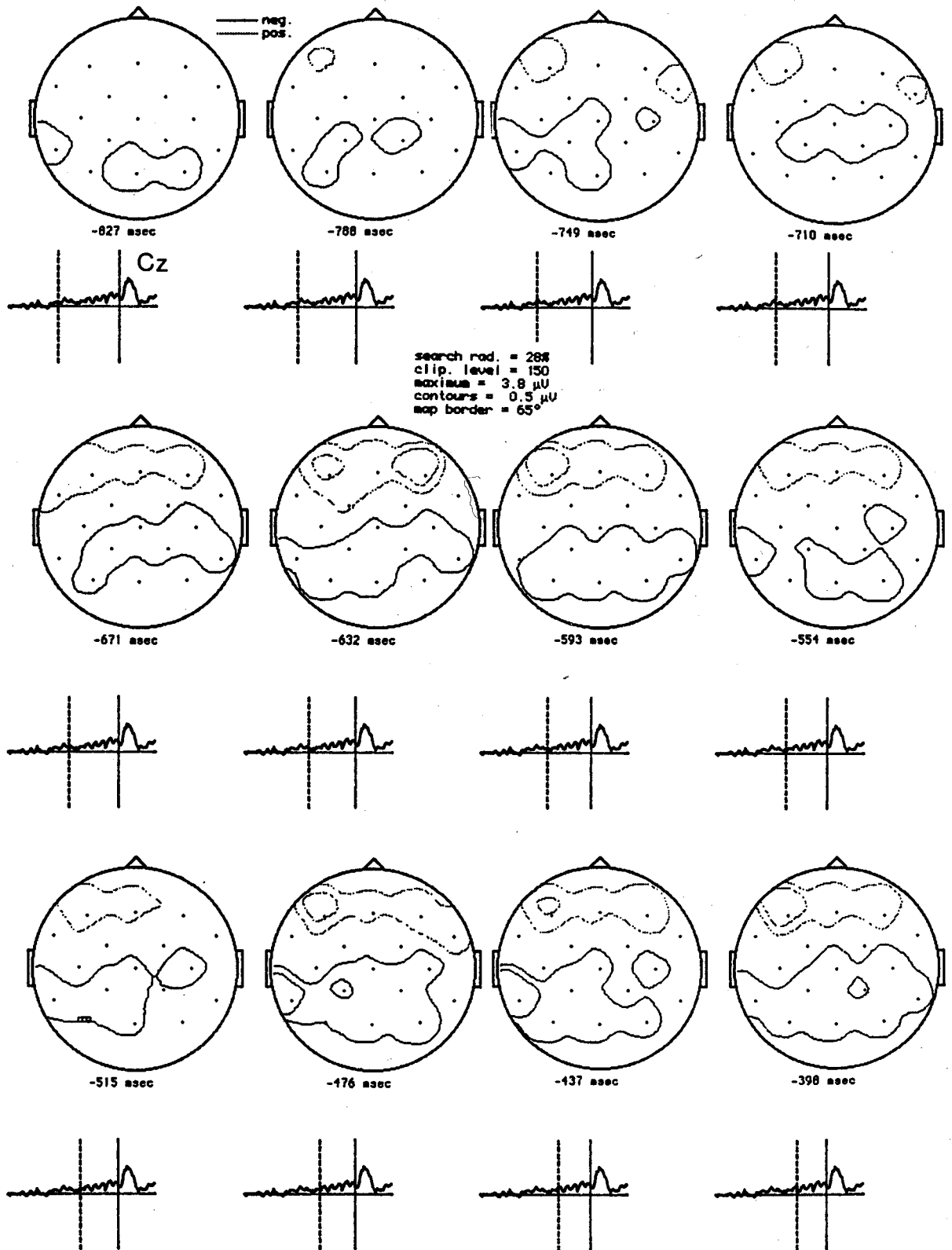
FIGURE 14.1.4. Isocontour maps of EEG (referential) - Right hand (D.C.)
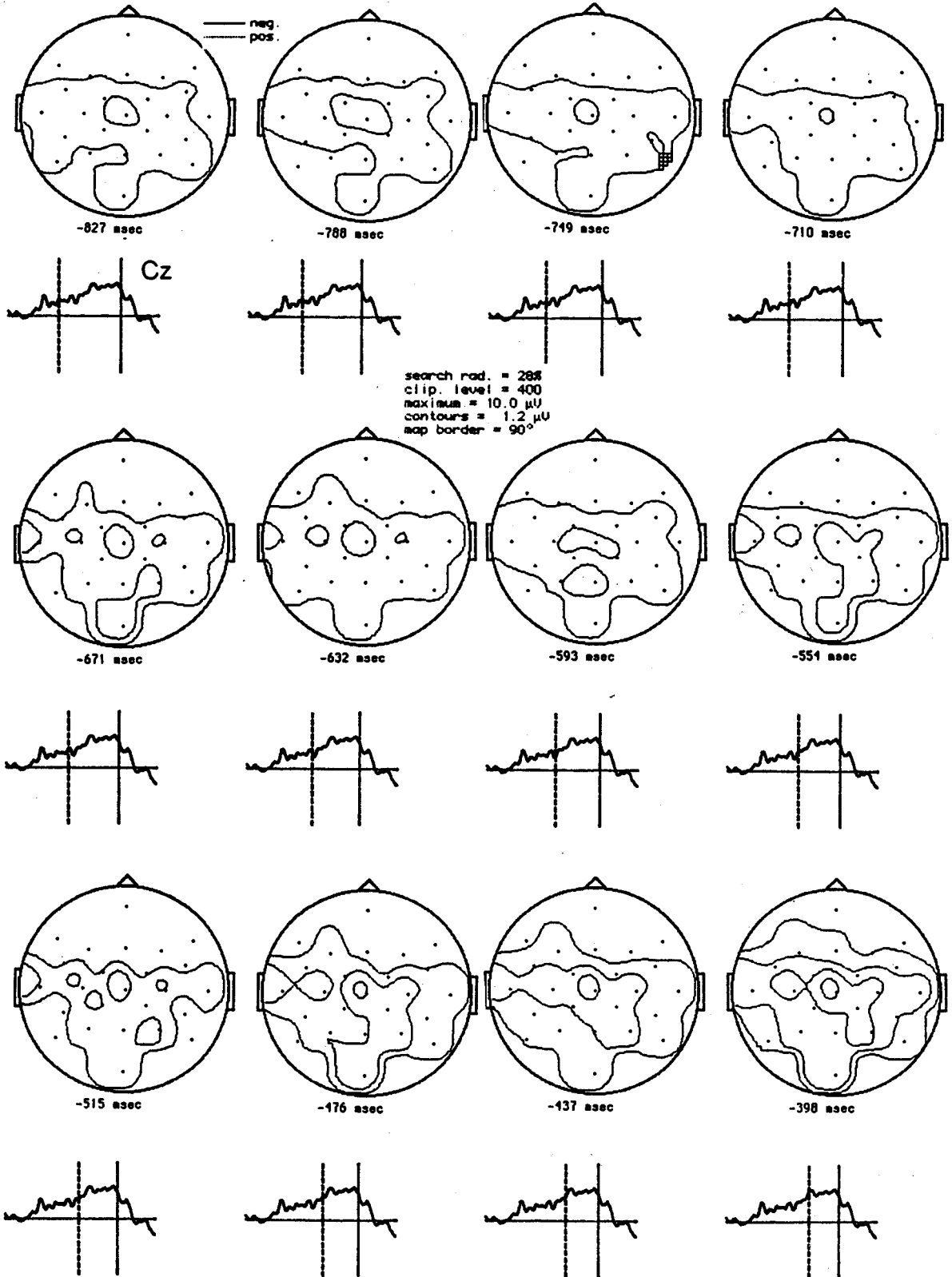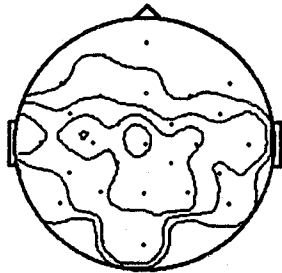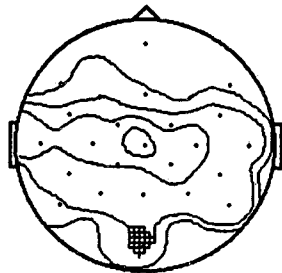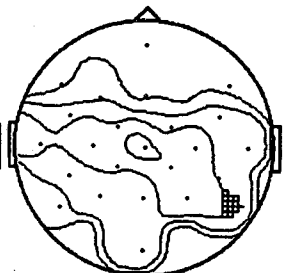
neg.
pos.

-827 msec   -788 msec   -719 msec   -710 msec

Cz

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maximum = 10.0 µV
contours = 1.2 µV
map border = 90°

-671 msec   -632 msec   -593 msec   -551 msec

-515 msec   -176 msec   -137 msec   -398 msec

140

-359 msec -320 msec -281 msec -242 msec

-203 msec -164 msec -125 msec -86 msec

-47 msec -8 msec 31 msec 70 msec

141

109 msec   148 msec   187 msec   226 msec
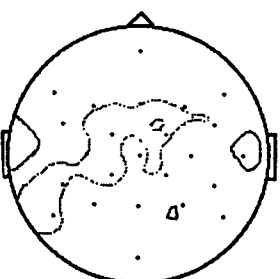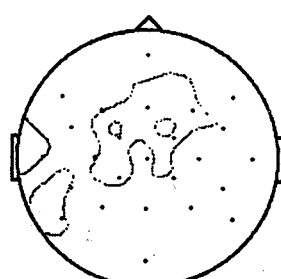
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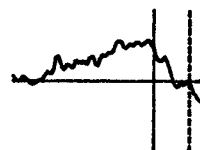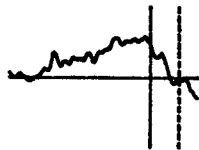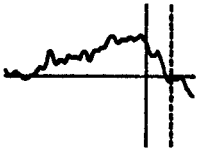
FIGURE 14.1.5.   Isocontour maps of EEG (referential) - Right hand (H.W.)
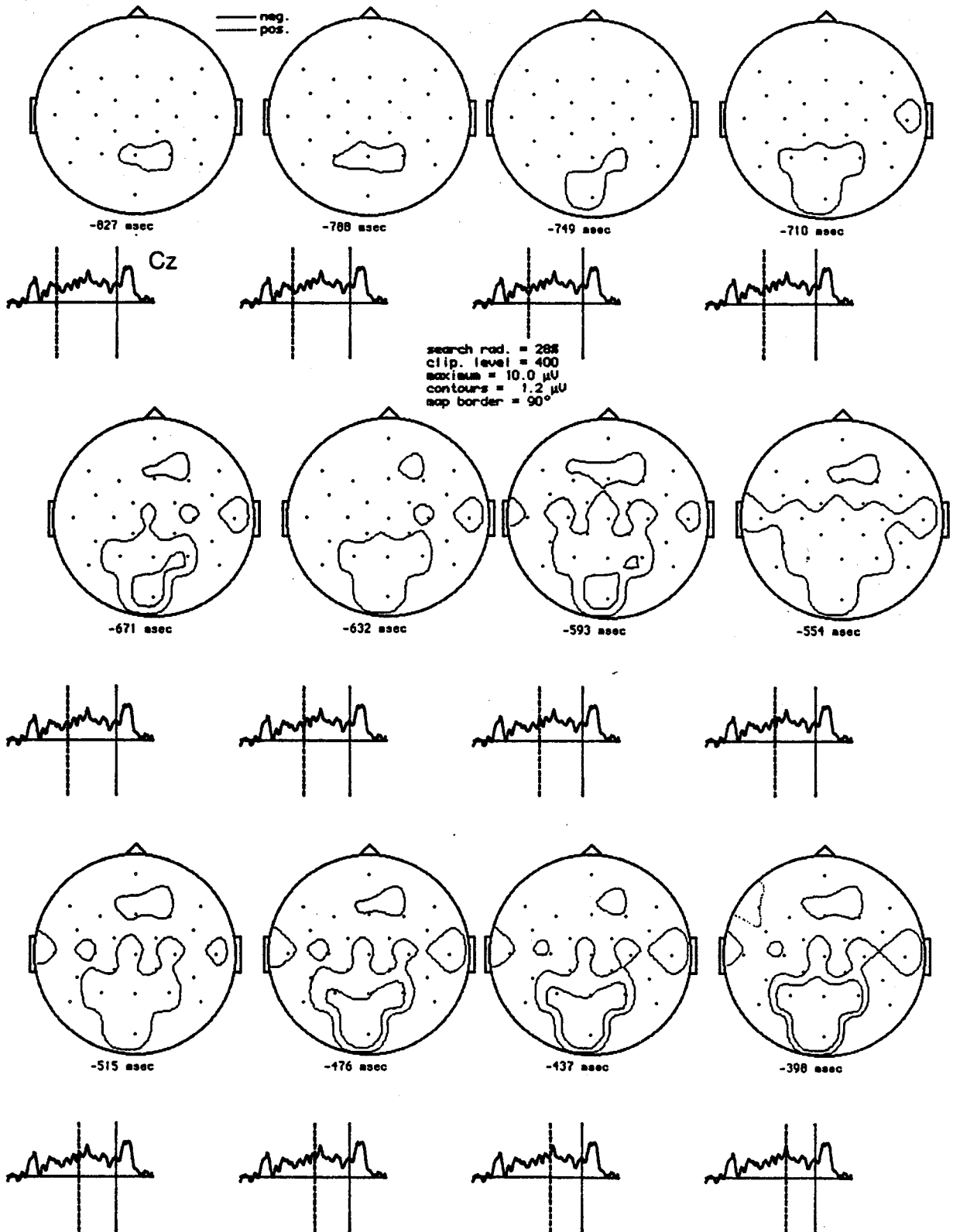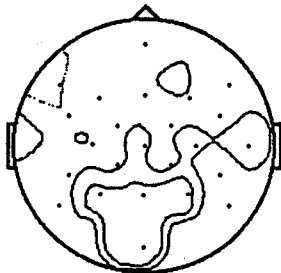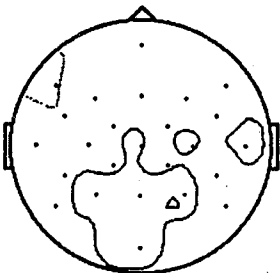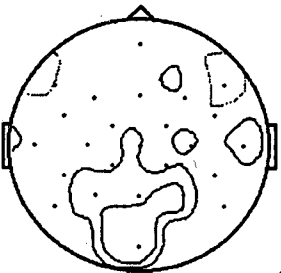
search rad. = 28%
clip. level = 400
maximum = 10.0 μV
contours = 1.2 μV
map border = 90°

-827 msec   -788 msec   -749 msec   -710 msec

-671 msec   -632 msec   -593 msec   -554 msec

-515 msec   -476 msec   -437 msec   -398 msec
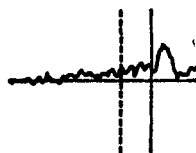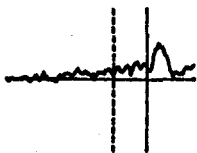
143

-359 msec   -320 msec   -281 msec   -242 msec

-203 msec   -164 msec   -125 msec   -86 msec

-17 msec   -6 msec   31 msec   70 msec

144

109 msec   148 msec   187 msec   226 msec

265 msec   304 msec   343 msec   382 msec

145
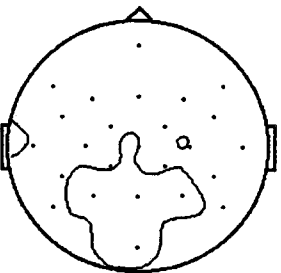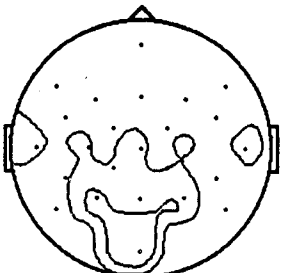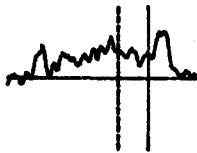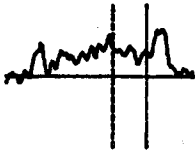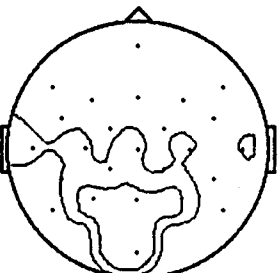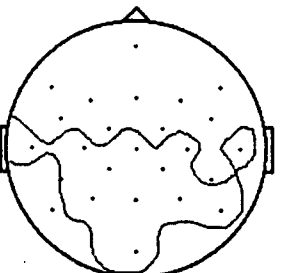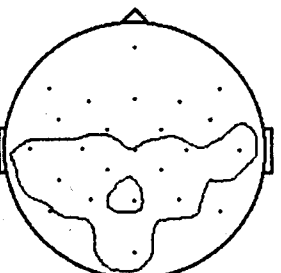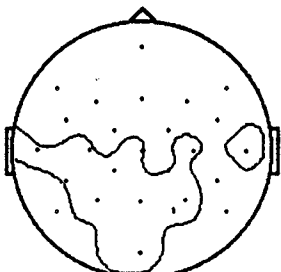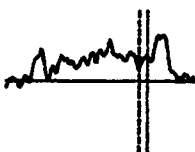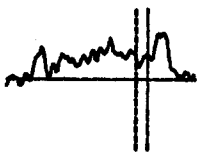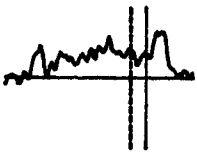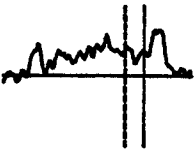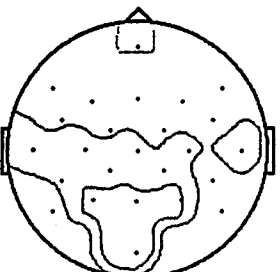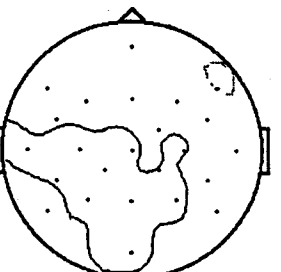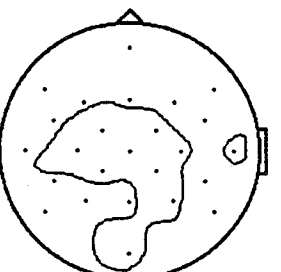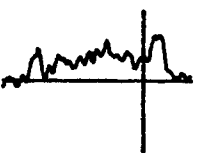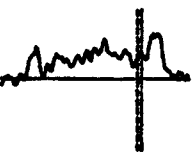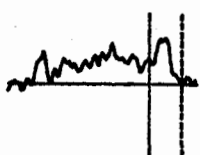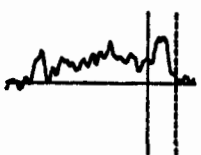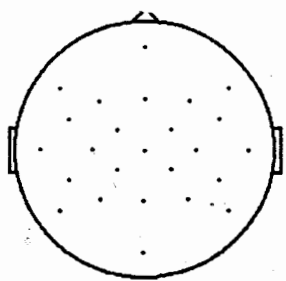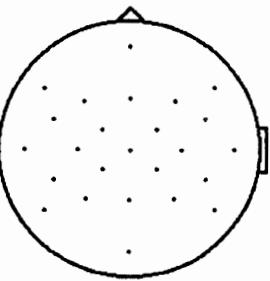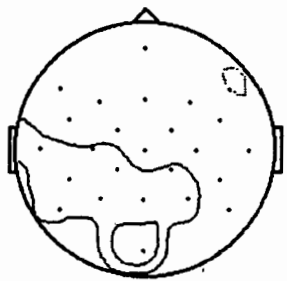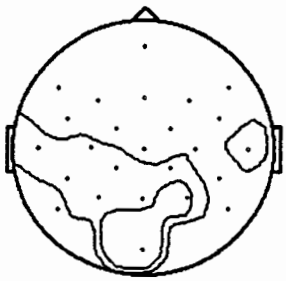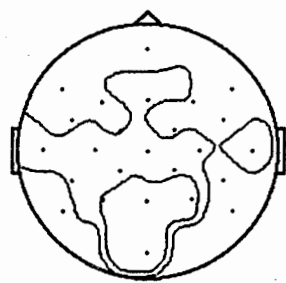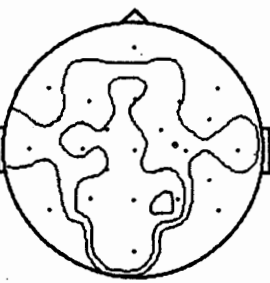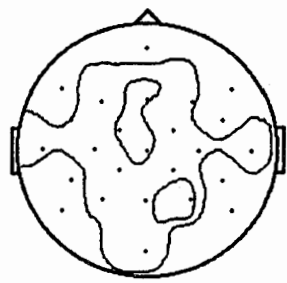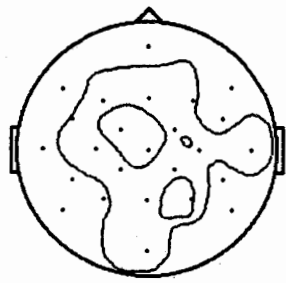
FIGURE 14.2.1. Isocontour maps of EEG (referential) - Pattern condition (T.R.)
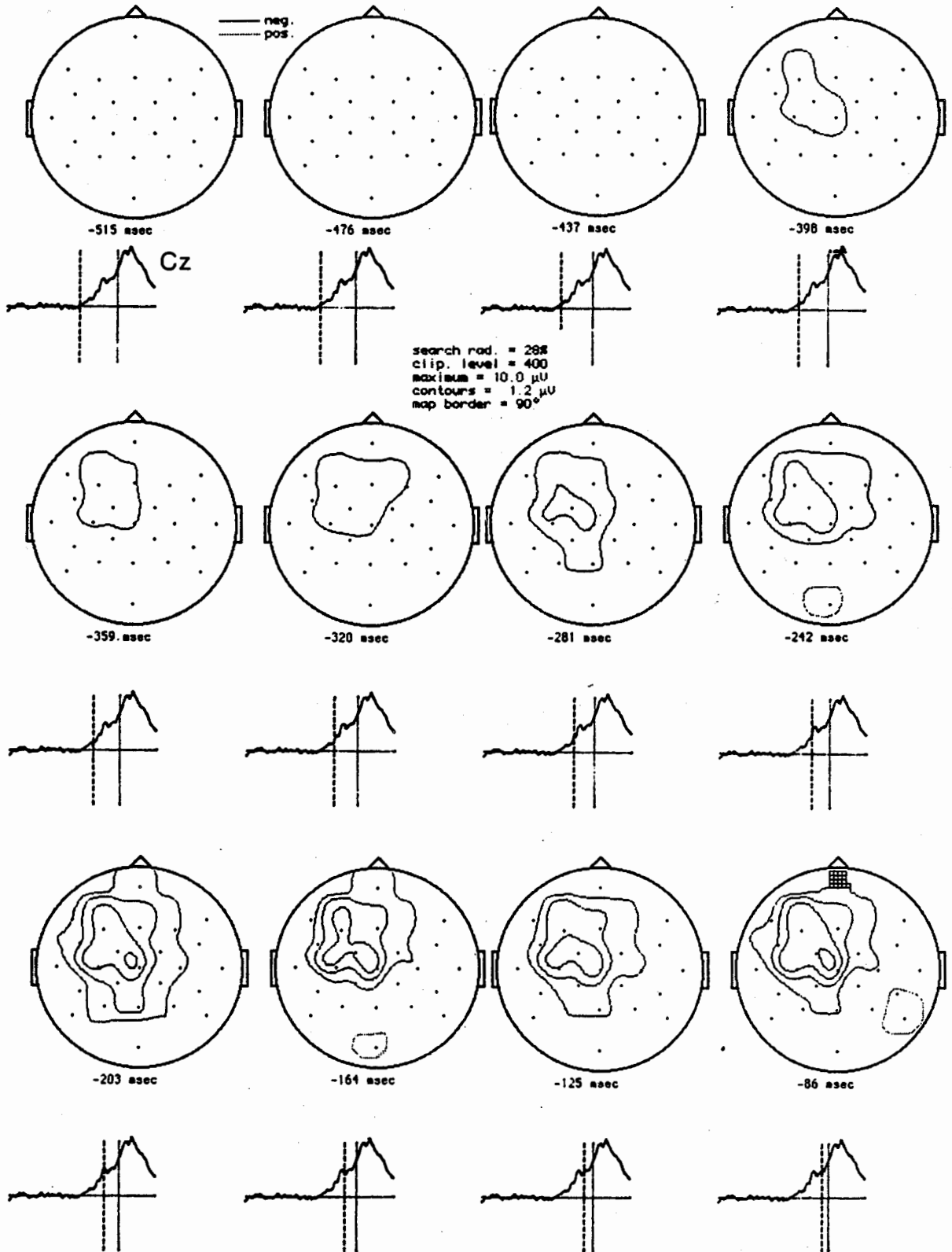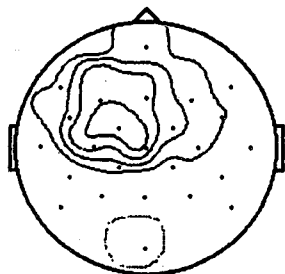
-17 msec   -8 msec   31 msec   70 msec
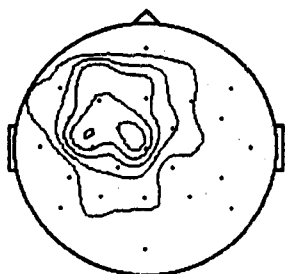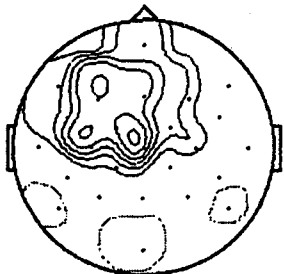
109 msec   148 msec   187 msec   226 msec

265 msec   304 msec   343 msec   382 msec

147

FIGURE 14.2.3. Isocontour maps of EEG (referential) - Pattern condition (B.J.)

search rad. = 28%
clip. level = 400
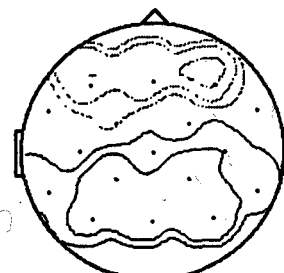maximum = 10.0 μU
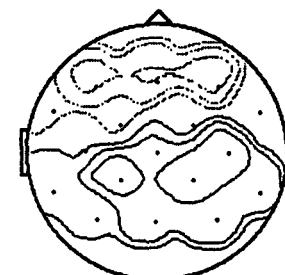contours = 1.2 μU
map border = 90°

-359 msec   -320 msec   -281 msec   -242 msec

-203 msec   -164 msec   -125 msec   -86 msec

-47 msec   -8 msec   31 msec   70 msec

149
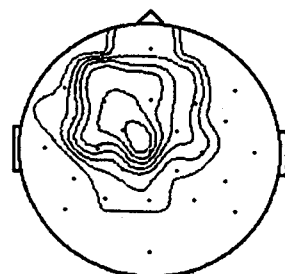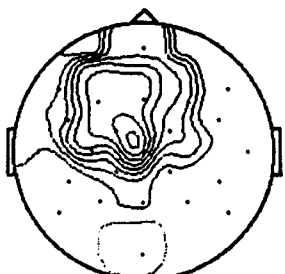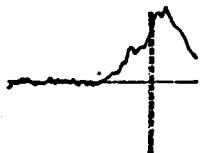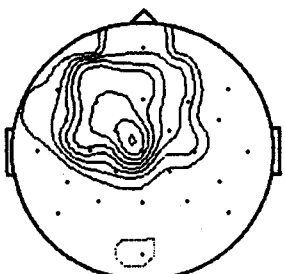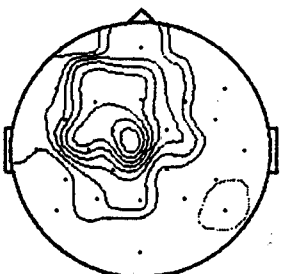
109 msec   148 msec   187 msec   226 msec
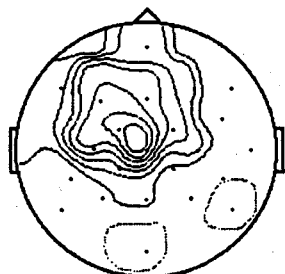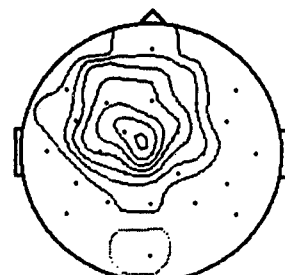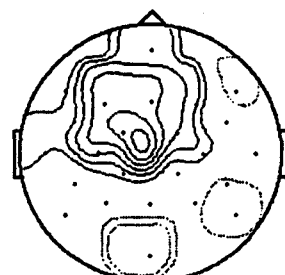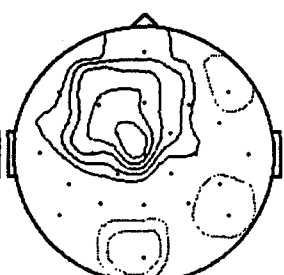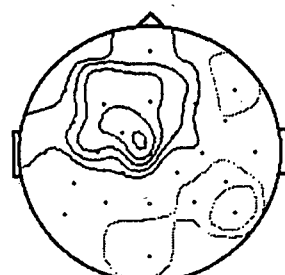
265 msec   304 msec   343 msec   382 msec
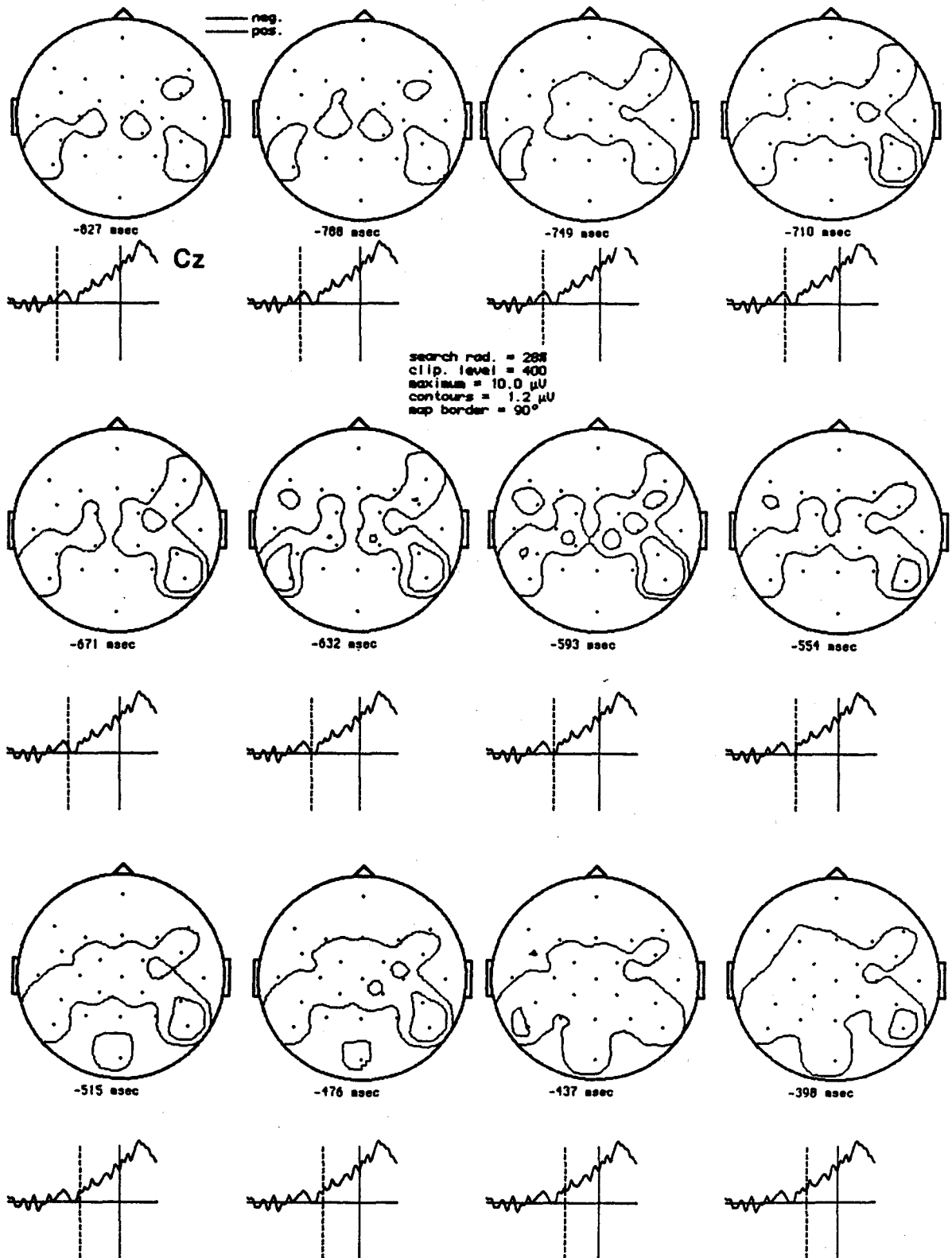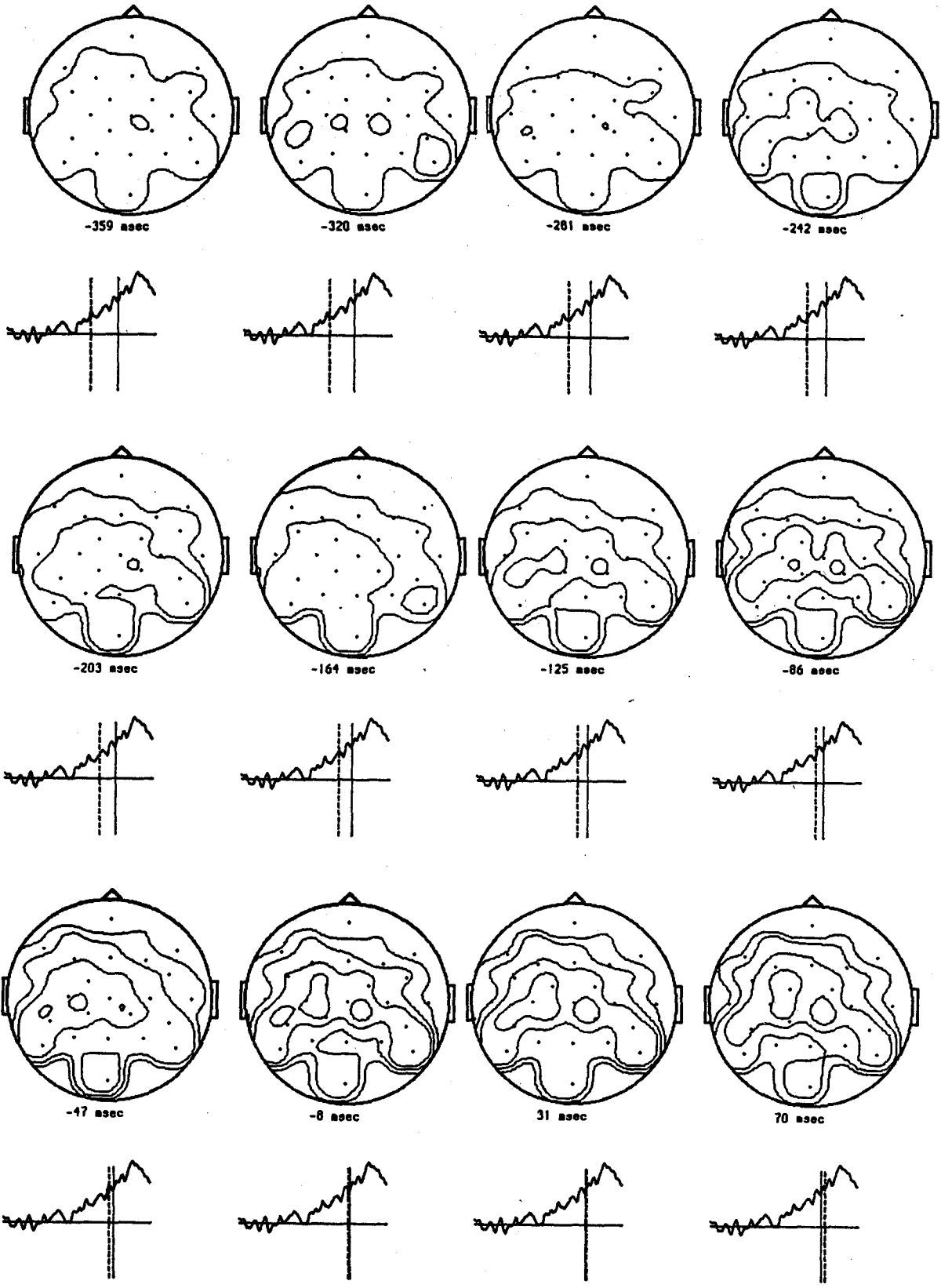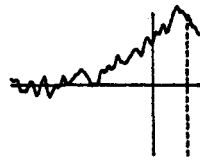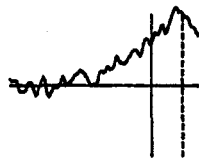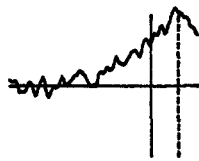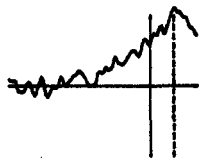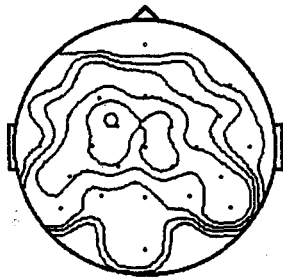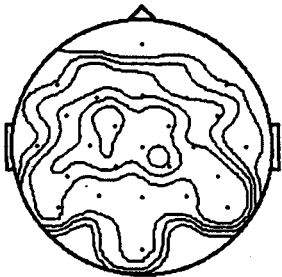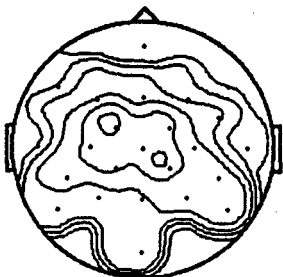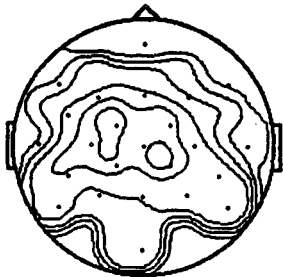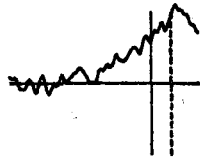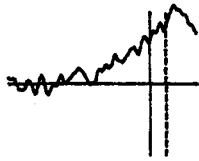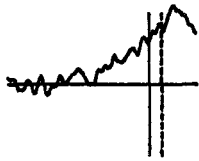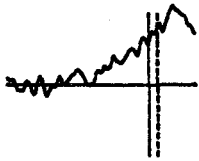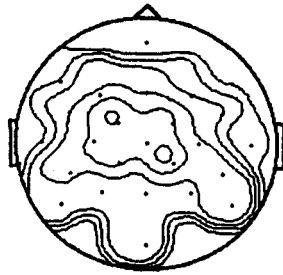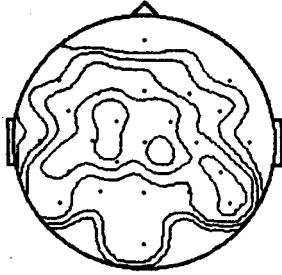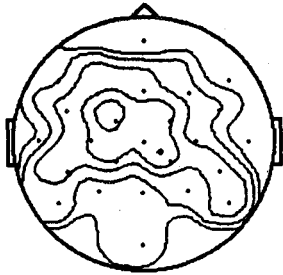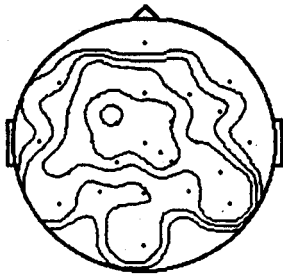
FIGURE 14. 2. 4.   Isocontour maps of EEG
(referential) – Left hand (D. C.)
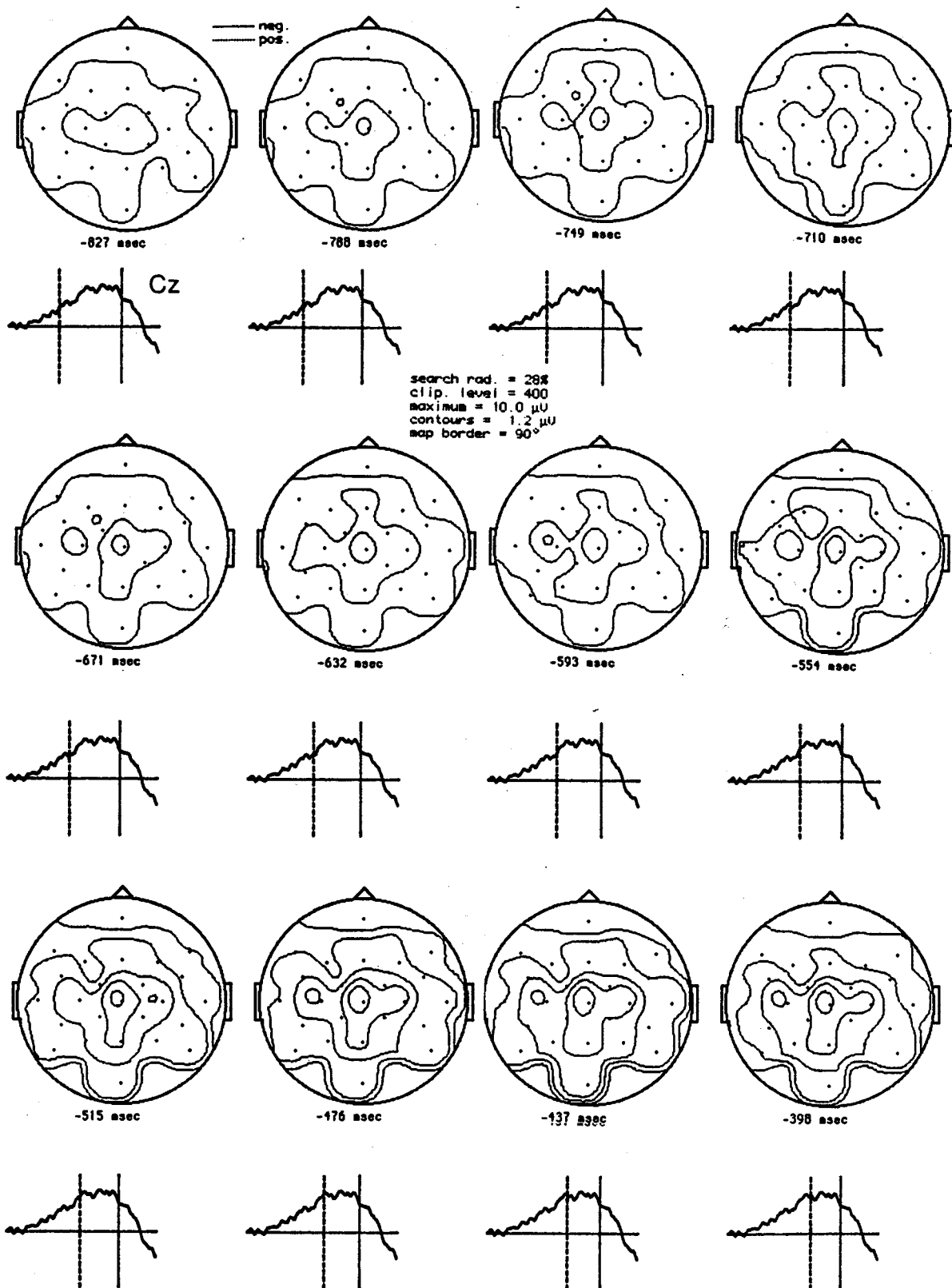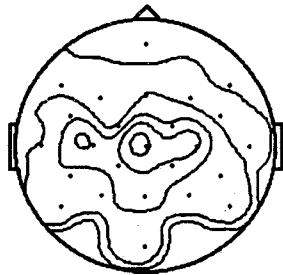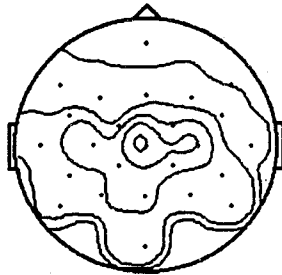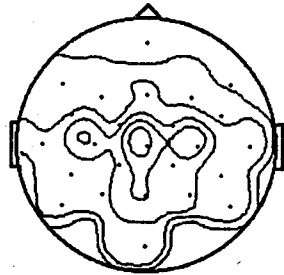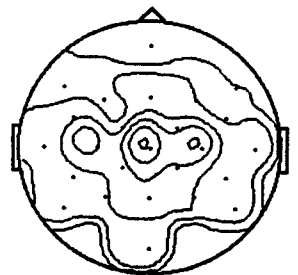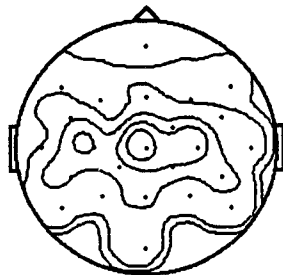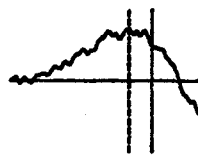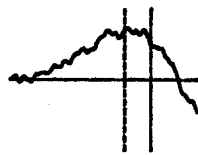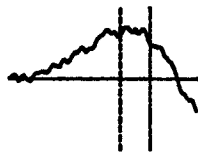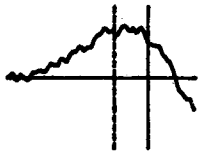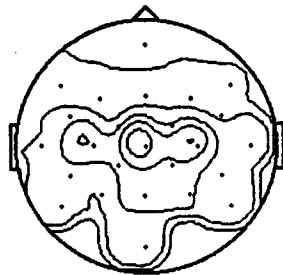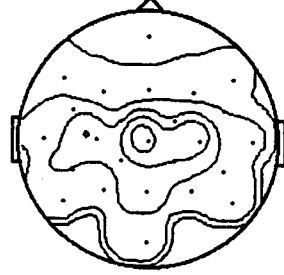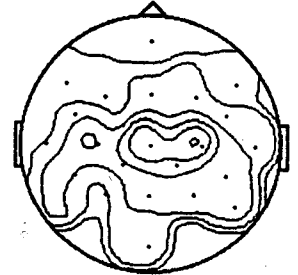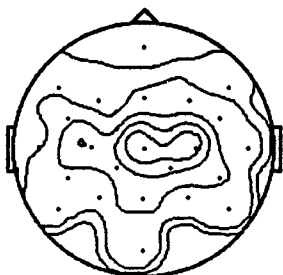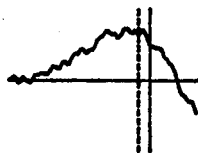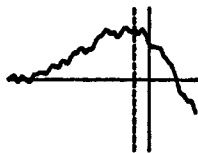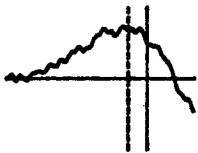
search rad. = 28%
clip. level = 400
maximum = 10.0 µV
contours = 1.2 µV
map border = 90°
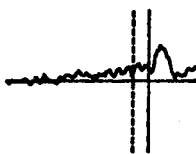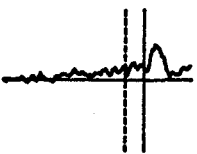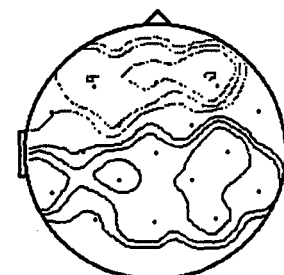
151

-359 msec   -320 msec   -281 msec   -242 msec

-203 msec   -164 msec   -125 msec   -86 msec

-17 msec   -6 msec   31 msec   70 msec

152

109 asec   148 asec   187 asec   226 asec

265 asec   304 asec   343 asec   382 asec

153
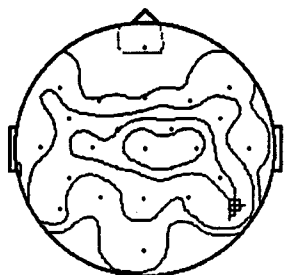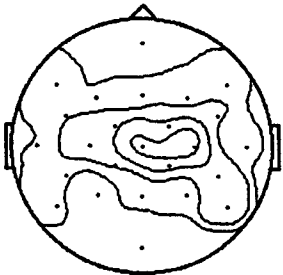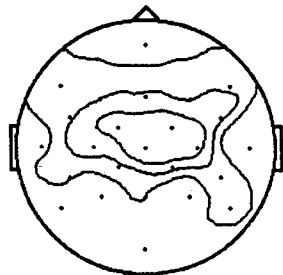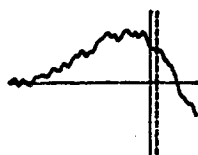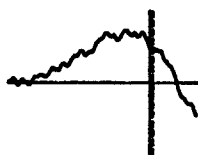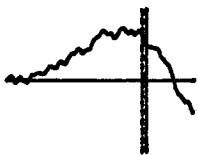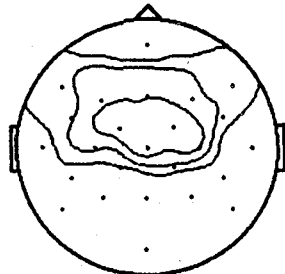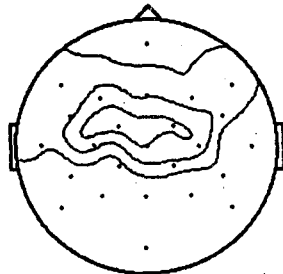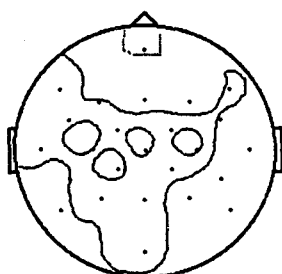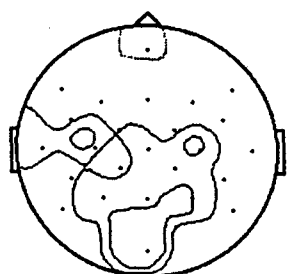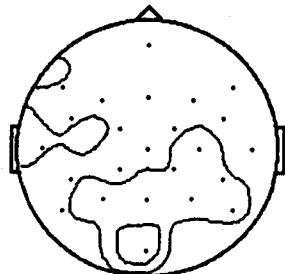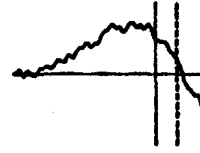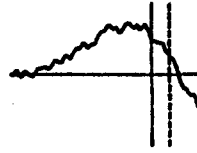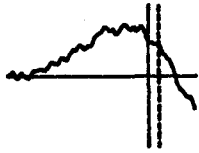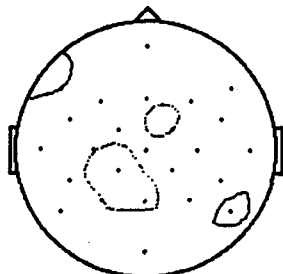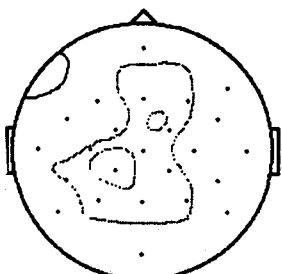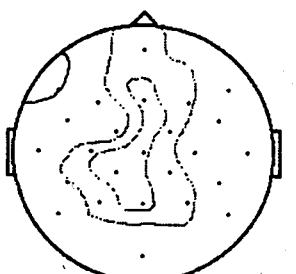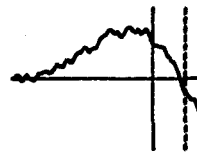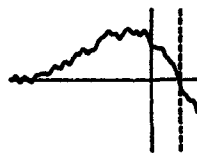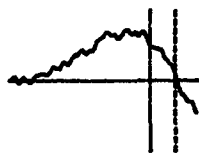
FIGURE 14.2.5. Isocontour maps of EEG (referential) - Left hand (H.W.)

search rad. = 28%
clip. level = 400
maximum = 10.0 μV
contours = 1.2 μV
map border = 90°

-359 msec   -320 msec   -281 msec   -242 msec

-203 msec   -164 msec   -125 msec   -86 msec
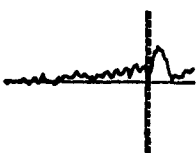
-47 msec   -8 msec   31 msec   70 msec

155

109 msec   148 msec   187 msec   226 msec

265 msec   304 msec   343 msec   382 msec

156
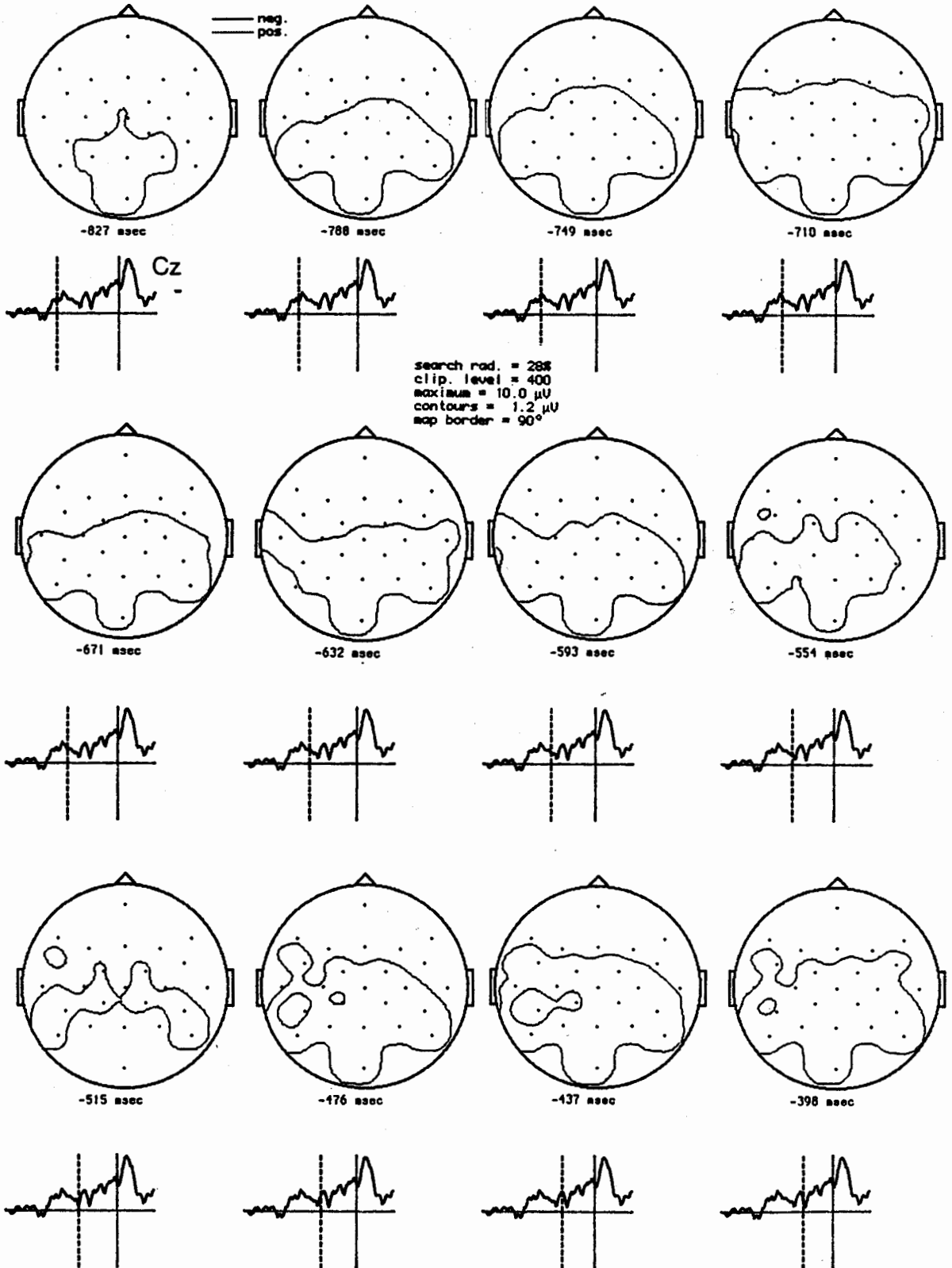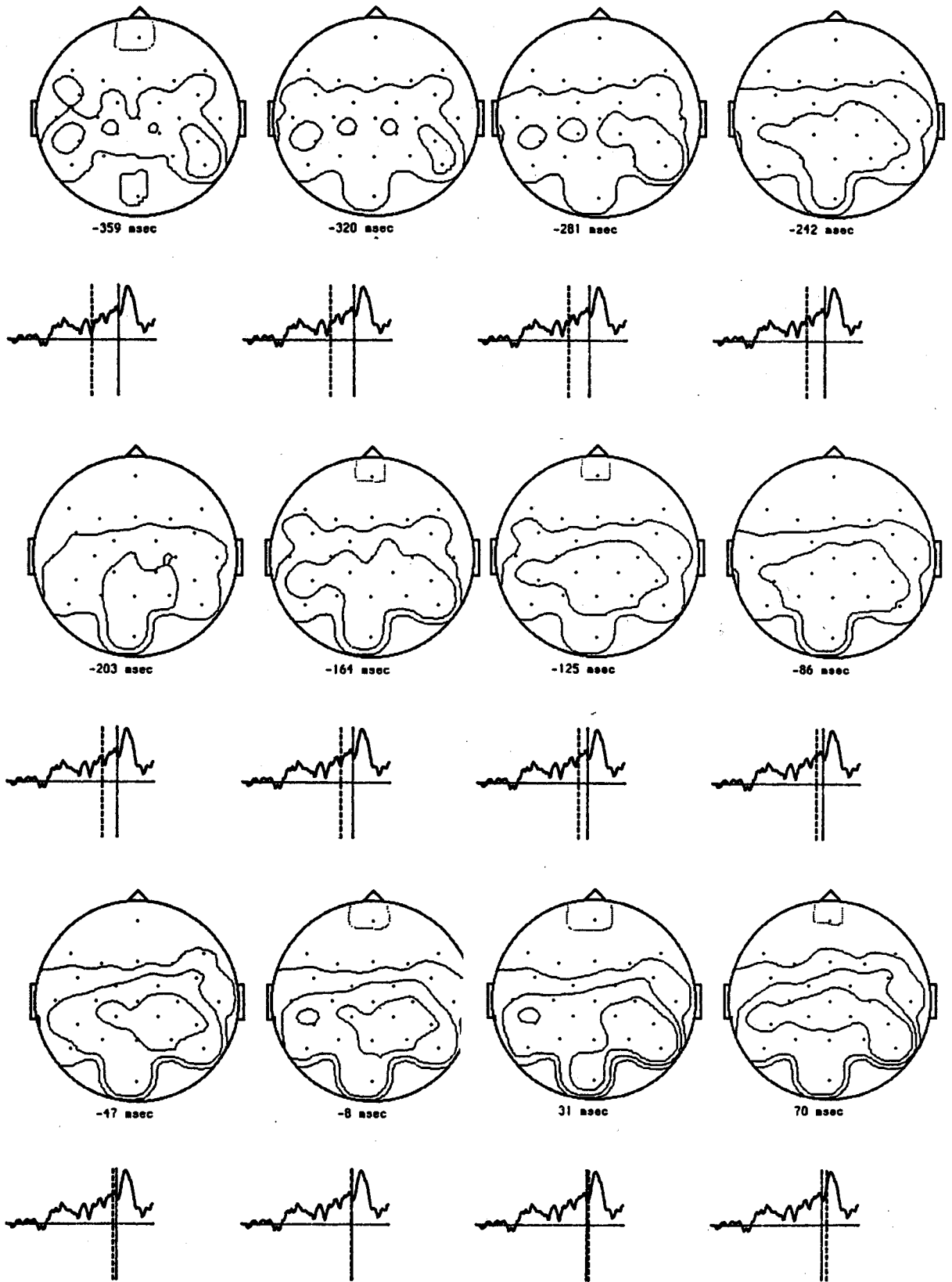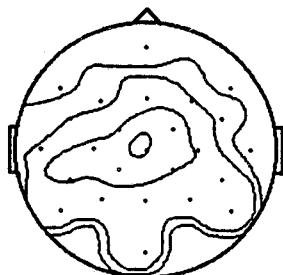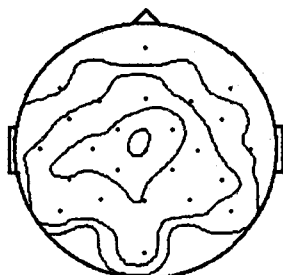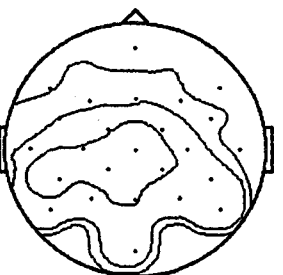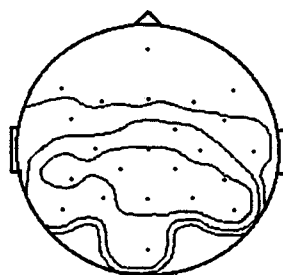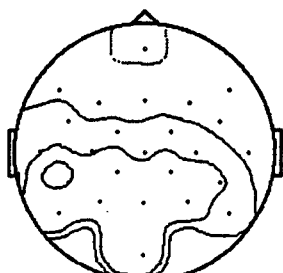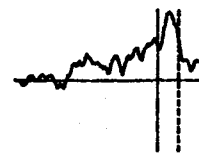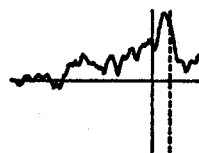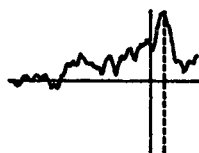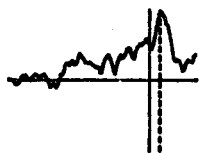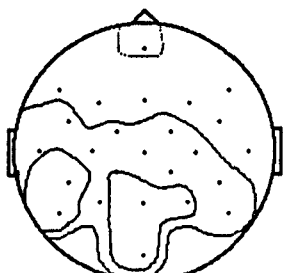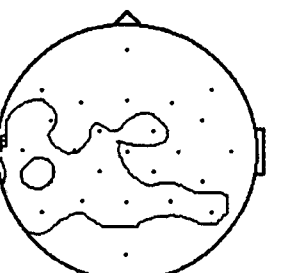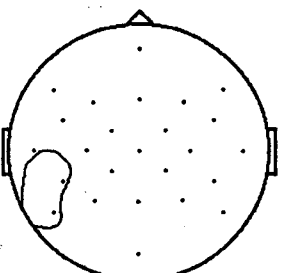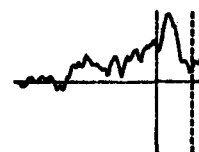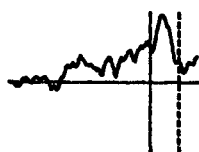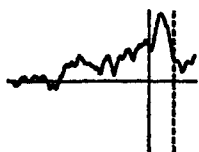
APPENDIX B: SPATIO-TEMPORAL ISOCONTOUR MAPS OF EEG (LAPLACIAN) ACTIVITY DURING UNILATERAL FINGER FLEXIONS.

FIGURE 15.1.1. Isocontour maps of EEG
(Laplacian) - Simple condition (T.R.)
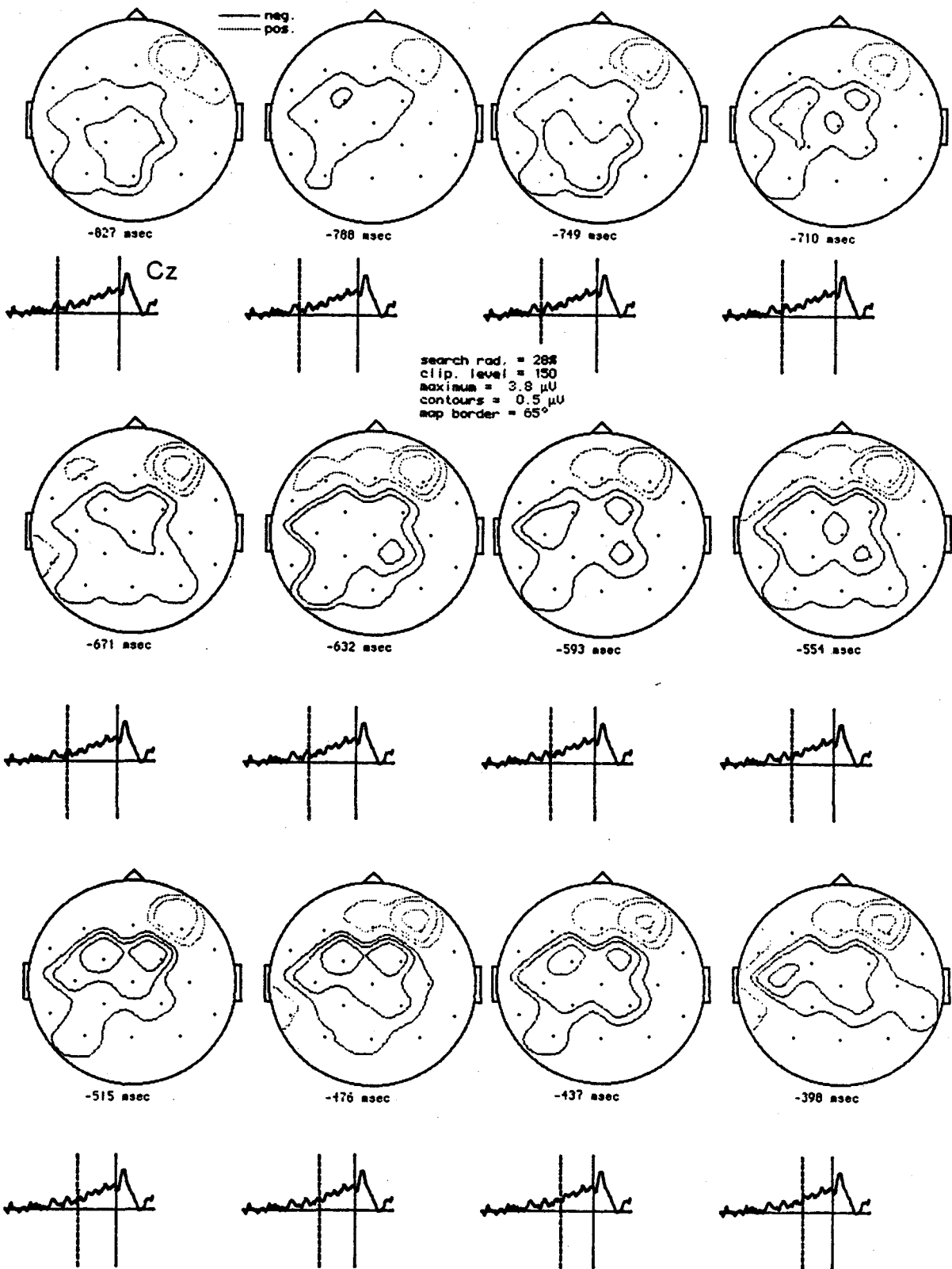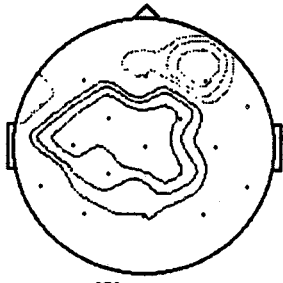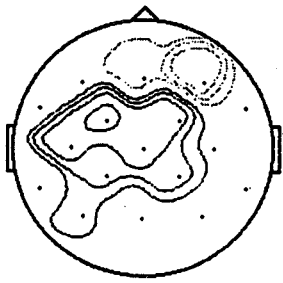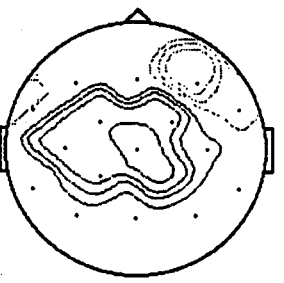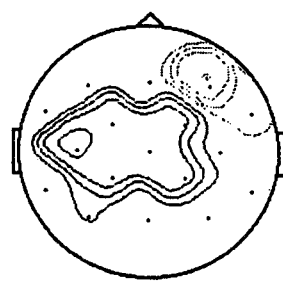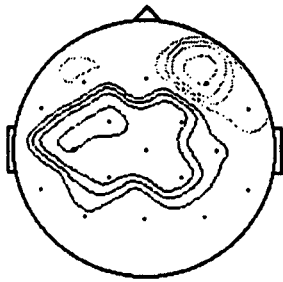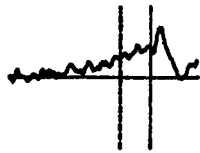
search rad. = 28%
clip. level = 150
maximum = 3.8 µV
contours = 0.5 µV
map border = 65°

-359 msec   -320 msec   -281 msec   -242 msec
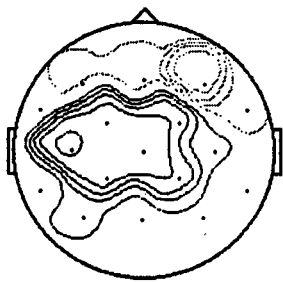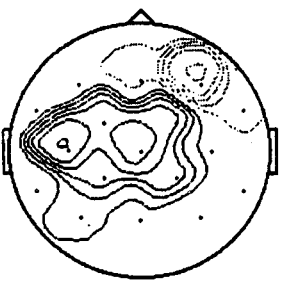
-203 msec   -164 msec   -125 msec   -86 msec
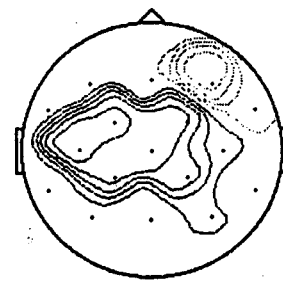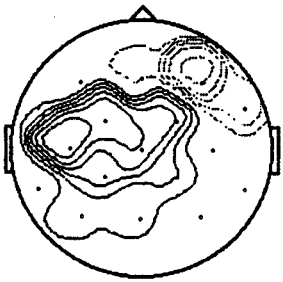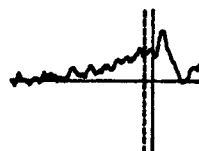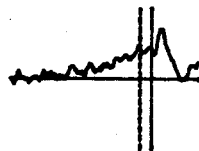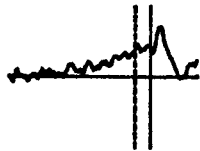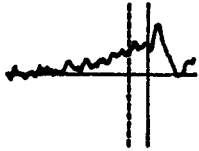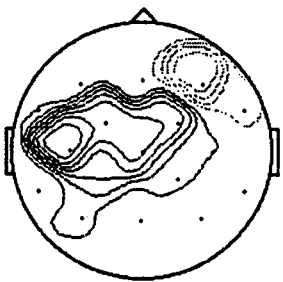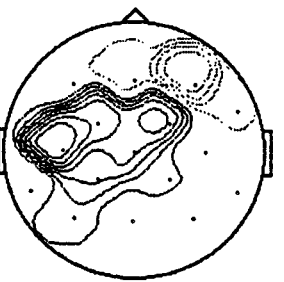
-47 msec   -8 msec   31 msec   70 msec
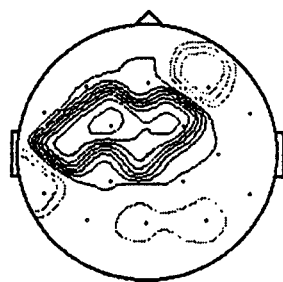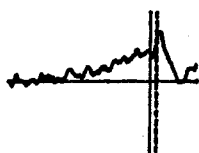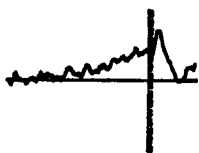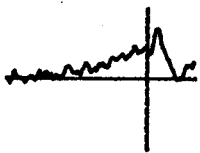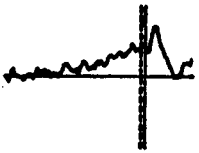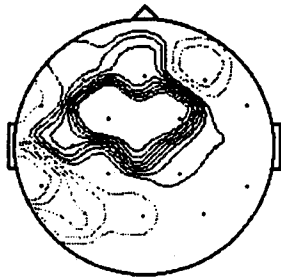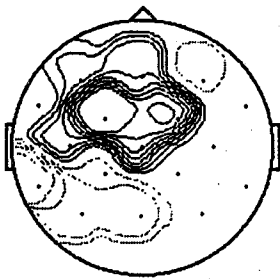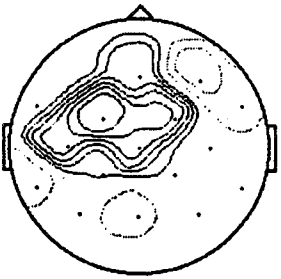
109 msec   148 msec   187 msec   226 msec
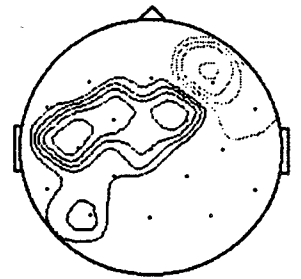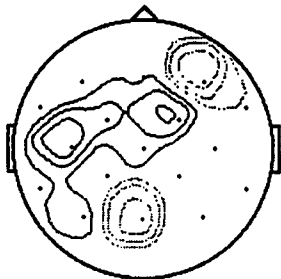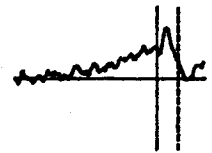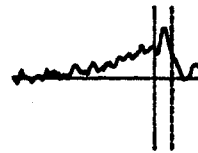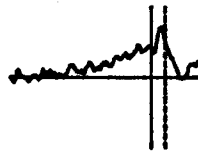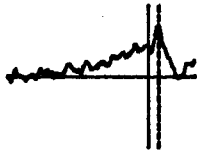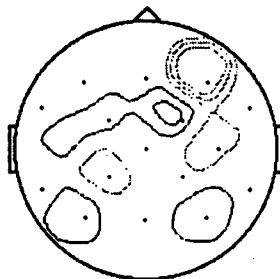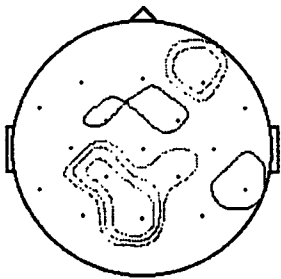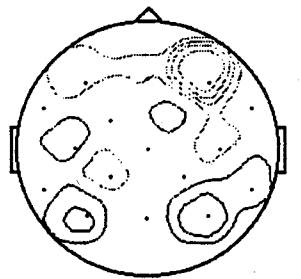
265 msec   301 msec   313 msec   382 msec
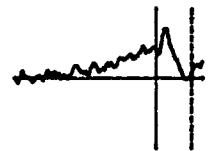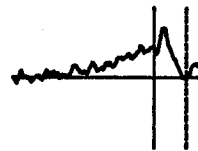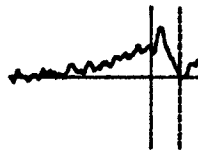
FIGURE 15.1.2. Isocontour maps of EEG
(Laplacian) - Simple condition (R.G.)

search rad. = 20%
clip. level = 150
maximum = 3.8 µV
contours = 0.5 µV
map border = 65°

-359 msec   -320 msec   -281 msec   -242 msec

-203 msec   -164 msec   -125 msec   -86 msec

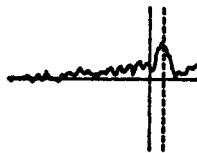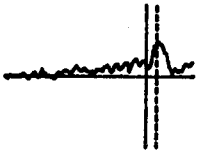-47 msec   -8 msec   31 msec   70 msec

162

109 msec   148 msec   187 msec   226 msec
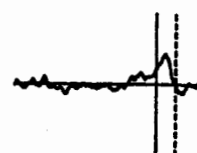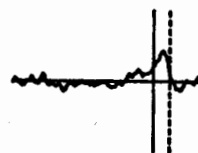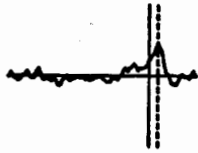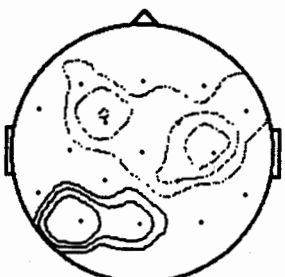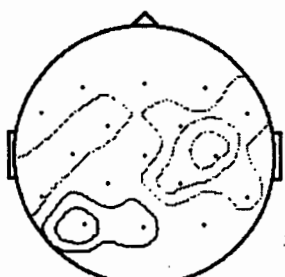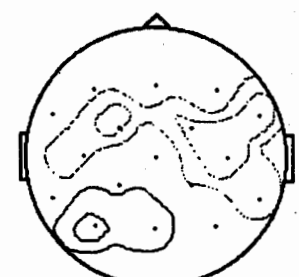
265 msec   304 msec   343 msec   382 msec
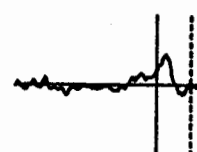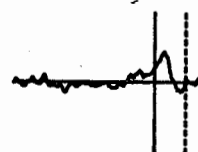
FIGURE 15.1.3. Isocontour maps of EEG (Laplacian) - Simple condition (B.J.)

164

-359 msec   -320 msec   -281 msec   -242 msec

-203 msec   -164 msec   -125 msec   -86 msec
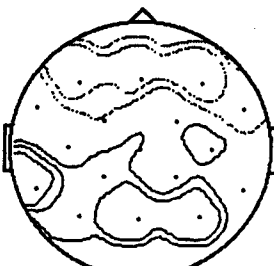
-47 msec   -8 msec   31 msec   70 msec

165
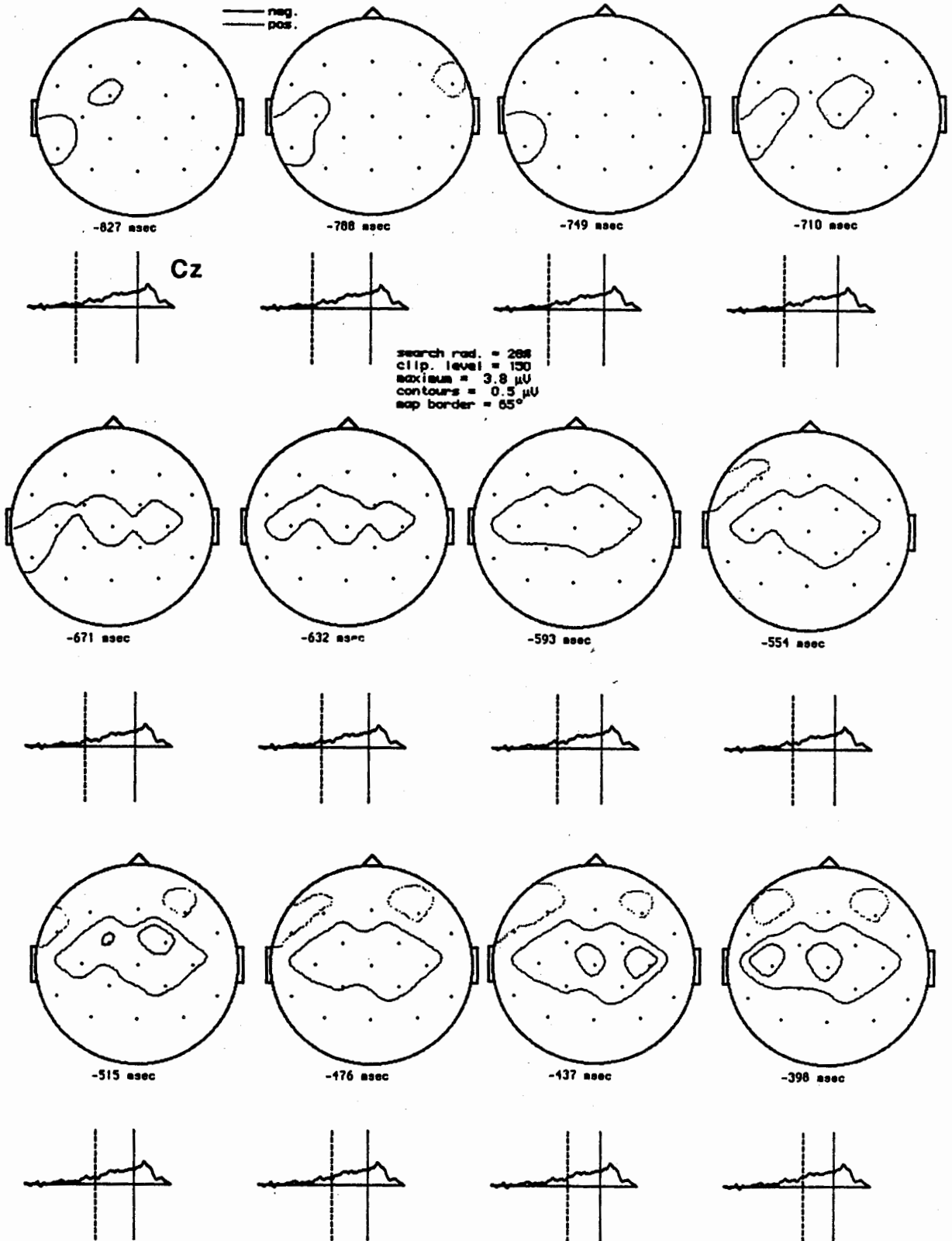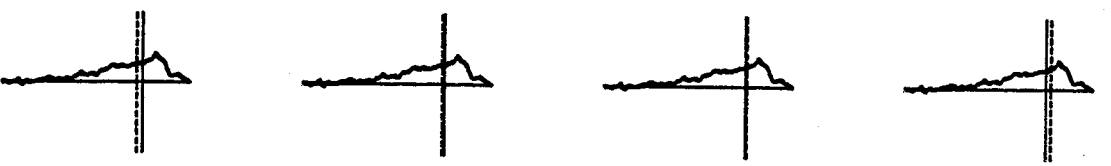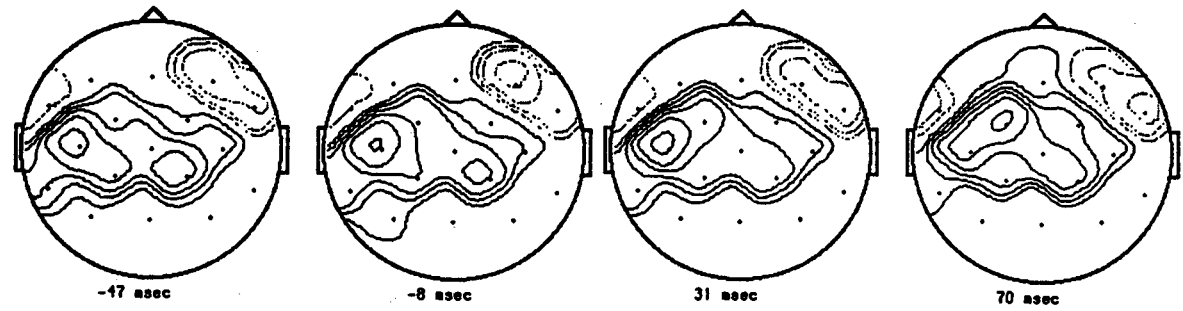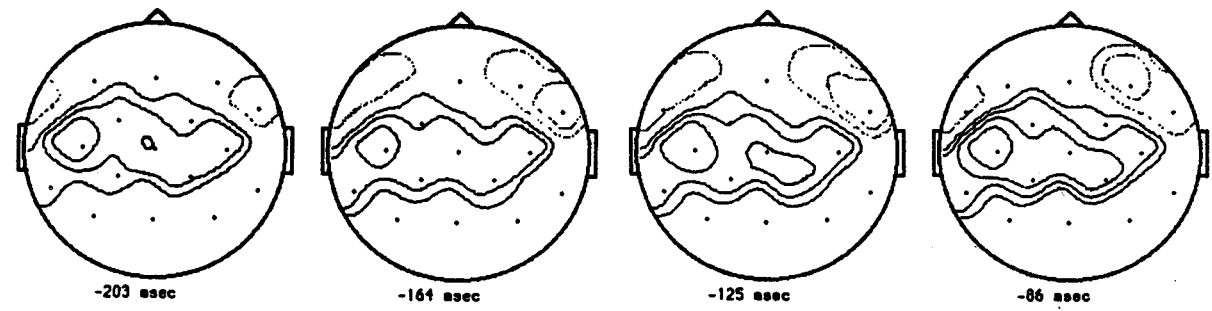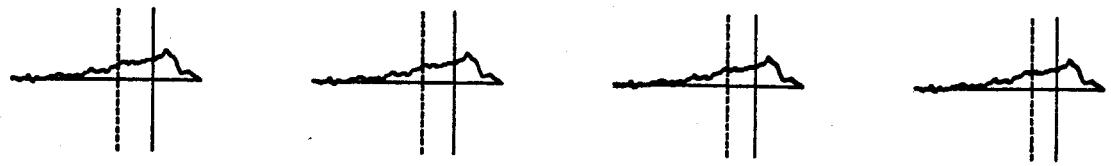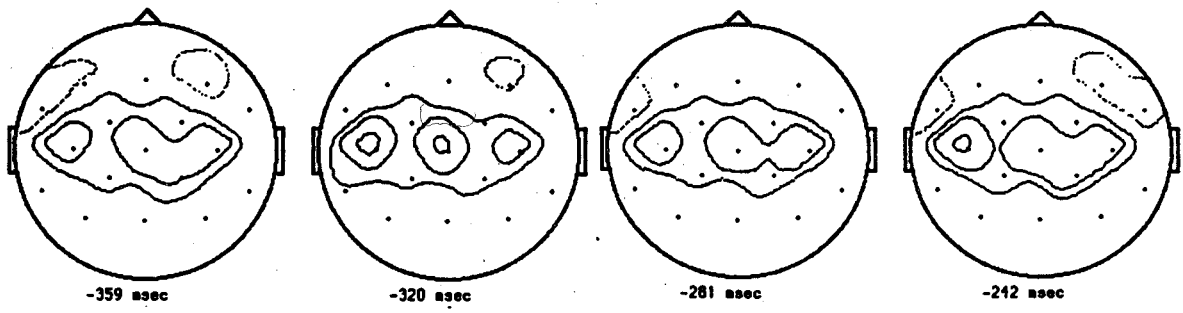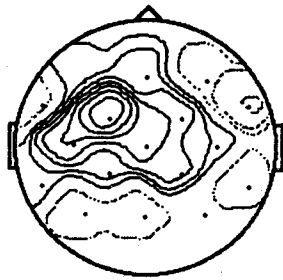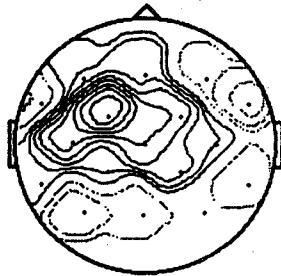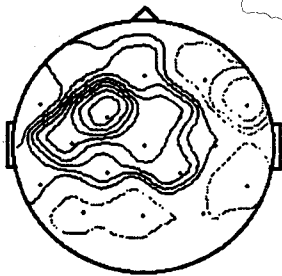
109 msec   148 msec   187 msec   226 msec
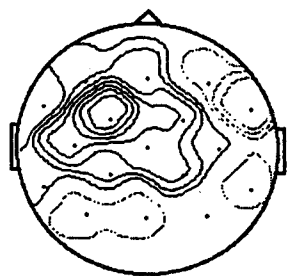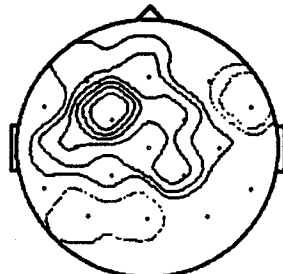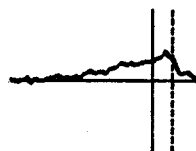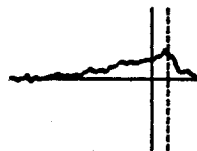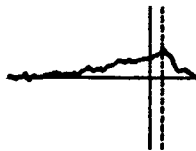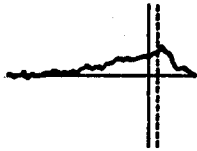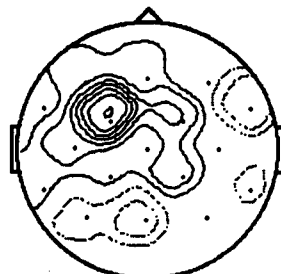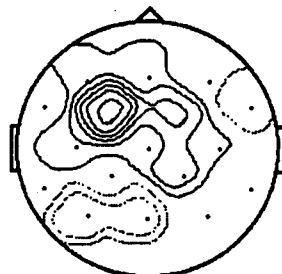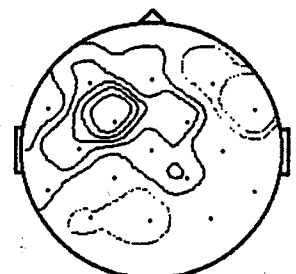
265 msec   304 msec   343 msec   382 msec
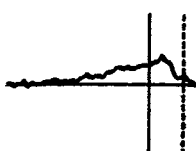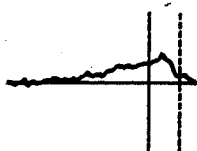
FIGURE 15.1.4. Isocontour maps of EEG (Laplacian) - Right hand (D.C.)

search rad. = 28%
clip. level = 150
maximum = 3.8 μV
contours = 0.5 μV
map border = 65°

-359 msec   -320 msec   -281 msec   -242 msec

-203 msec   -164 msec   -125 msec   -86 msec

-47 msec   -8 msec   31 msec   70 msec

168
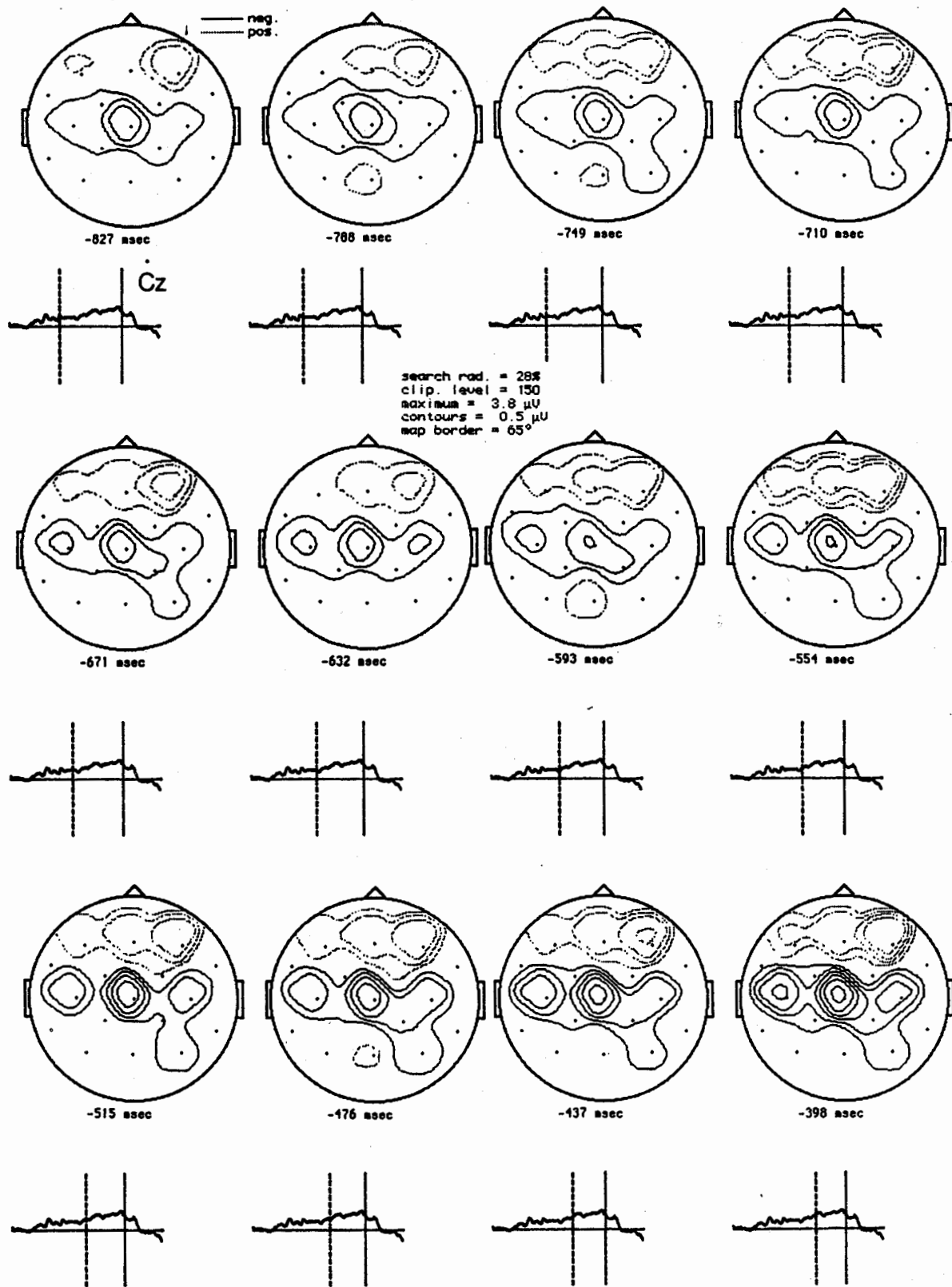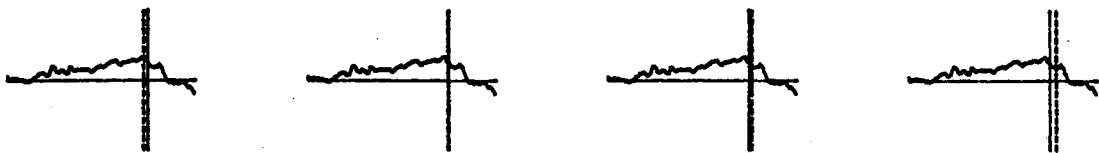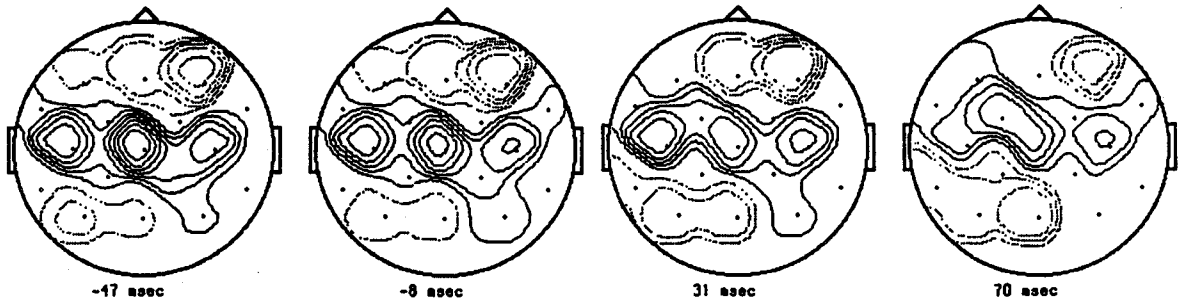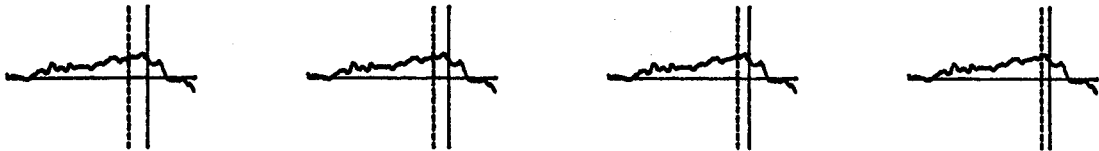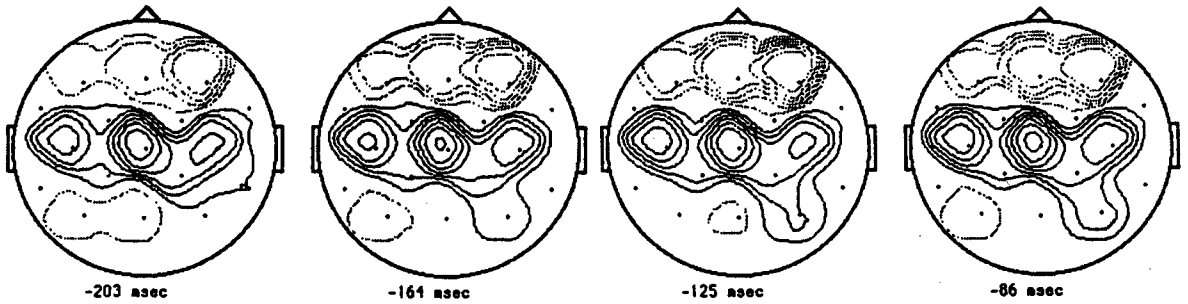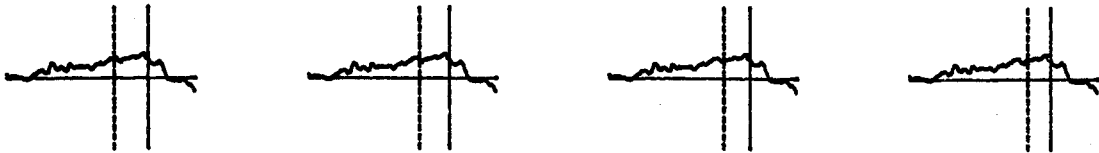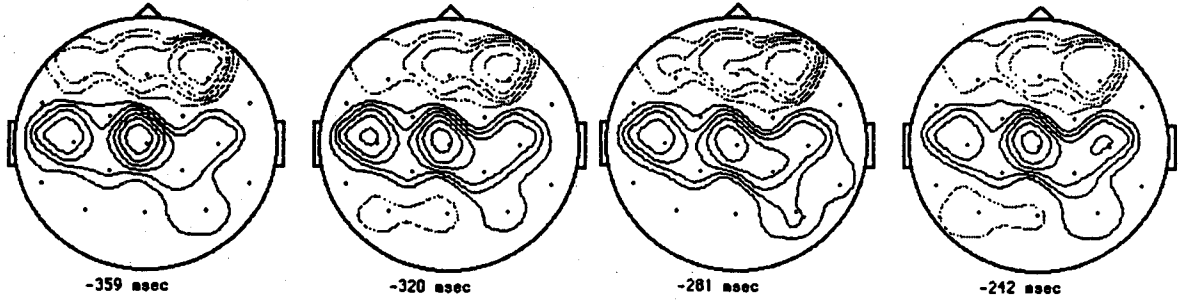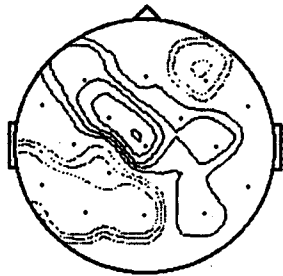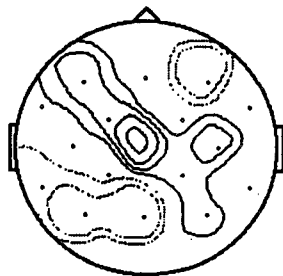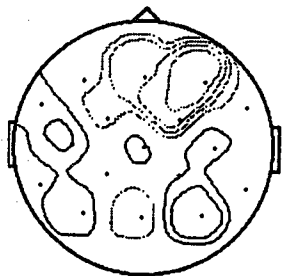
109 msec   148 msec   187 msec   226 msec
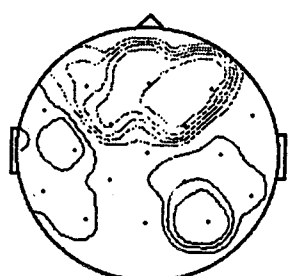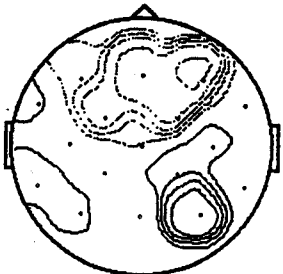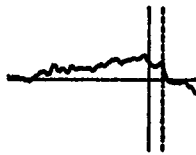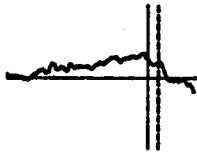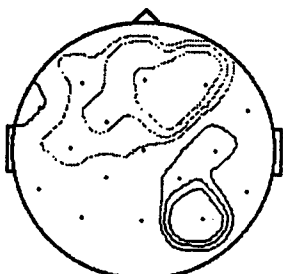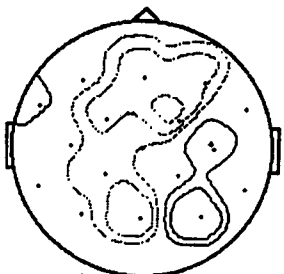
265 msec   304 msec   343 msec   382 msec
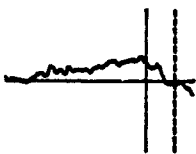
FIGURE 15.1.5. Isocontour maps of EEG
(Laplacian) – Right hand (H.W.)
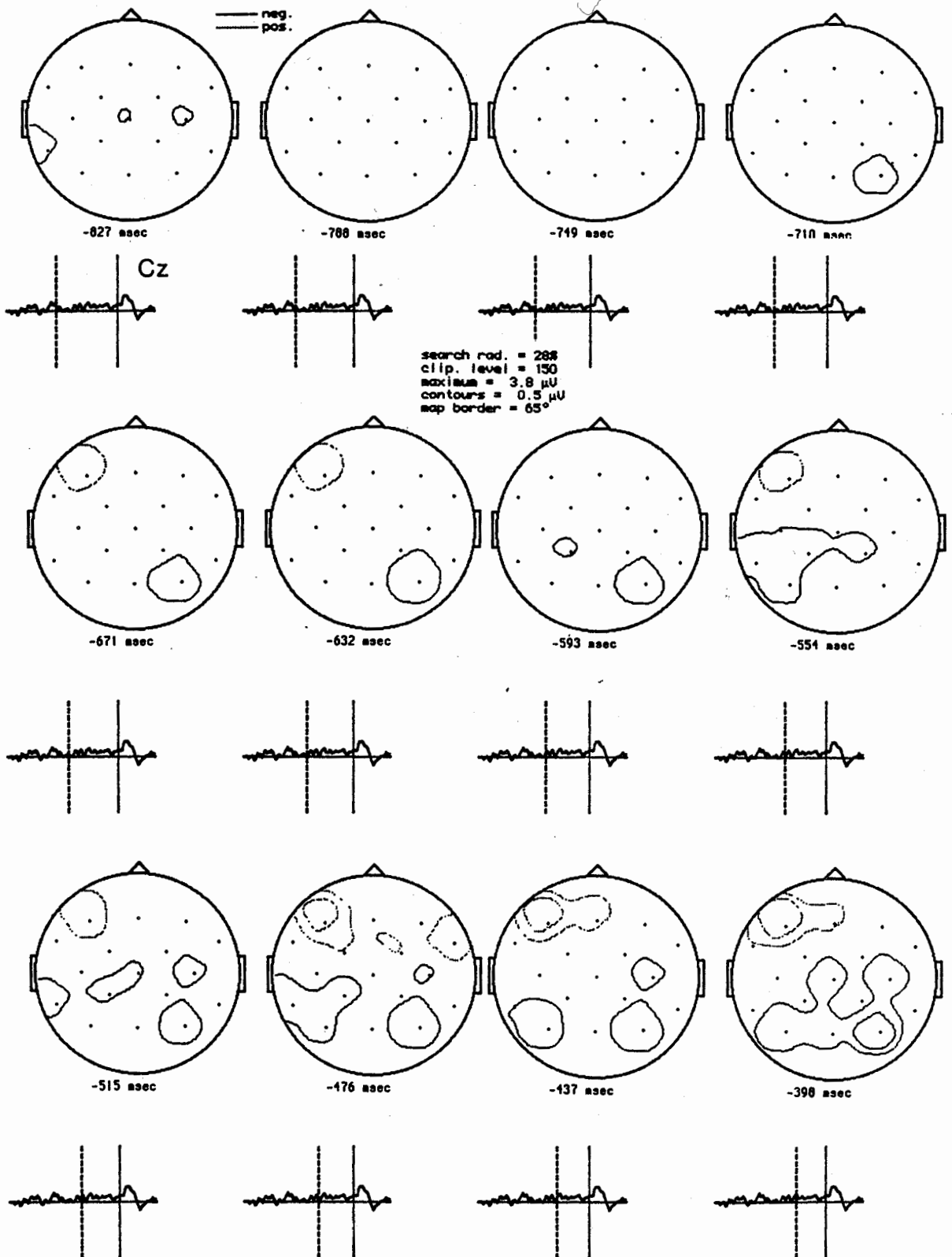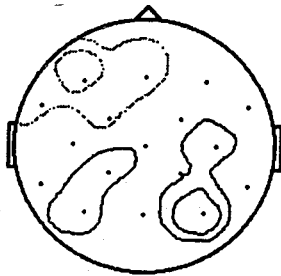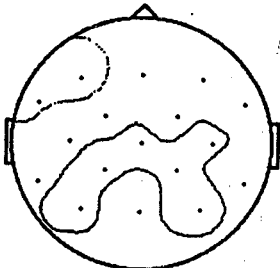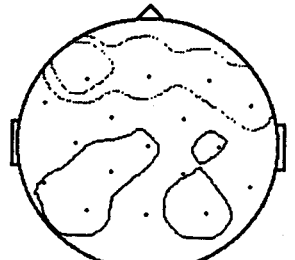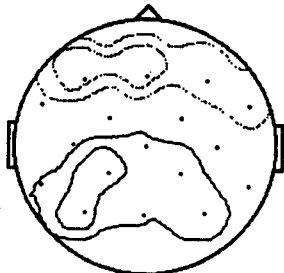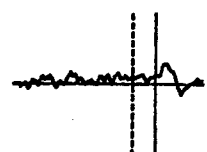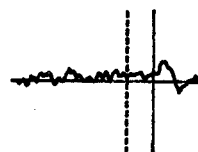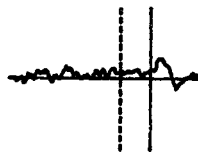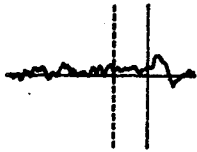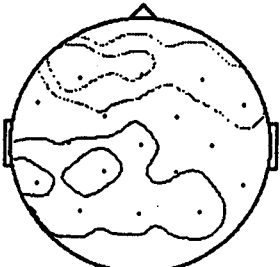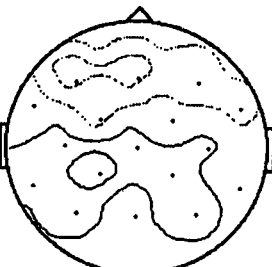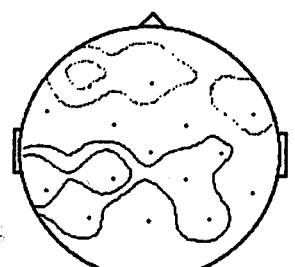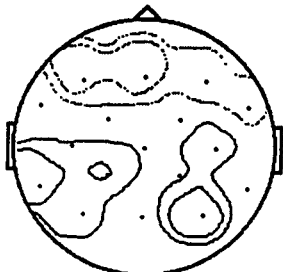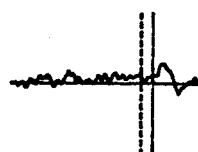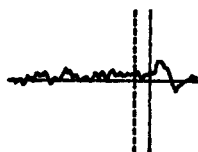
search rad. = 288
clip. level = 150
maximum = 3.8 μV
contours = 0.5 μV
map border = 65°

-359 msec   -320 msec   -281 msec   -242 msec

-203 msec   -164 msec   -125 msec   -86 msec

-47 msec   -8 msec   31 msec   70 msec

171
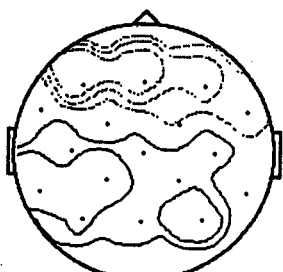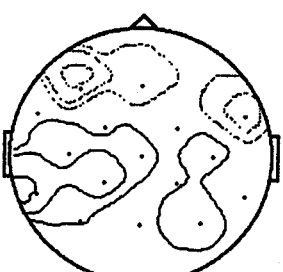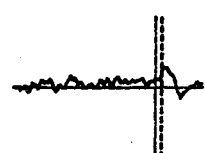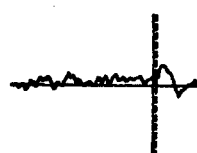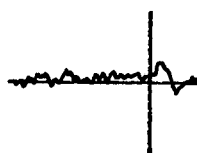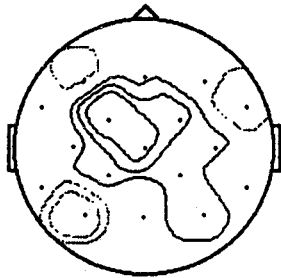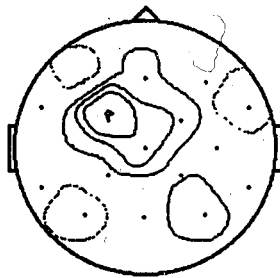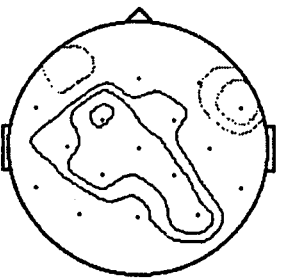
109 msec   148 msec   167 msec   226 msec
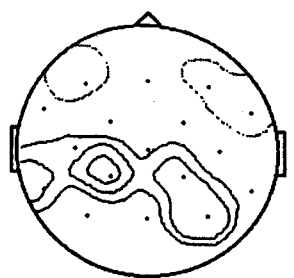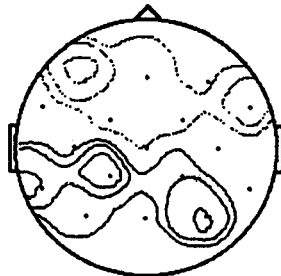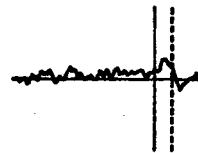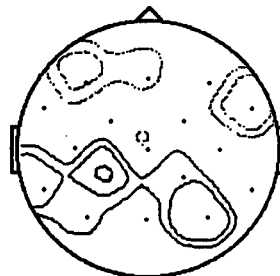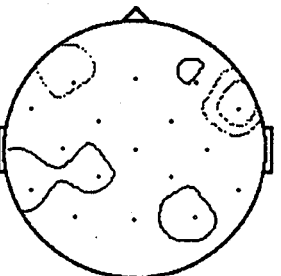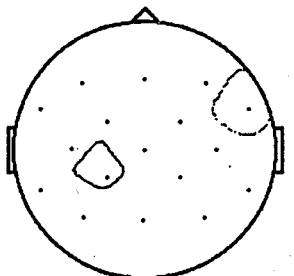
265 msec   304 msec   343 msec   382 msec
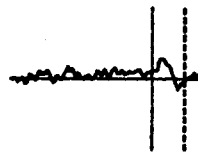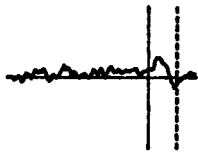
FIGURE 15.2.1. Isocontour maps of EEG
(Laplacian) - Pattern condition (T.R.)

173

-47 msec   -8 msec   31 msec   70 msec

109 msec   146 msec   187 msec   226 msec

265 msec   304 msec   343 msec   382 msec

174
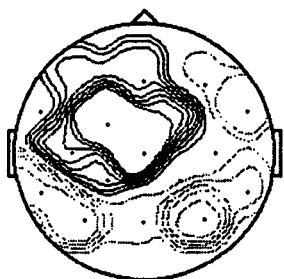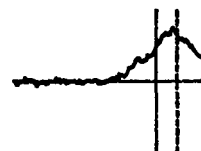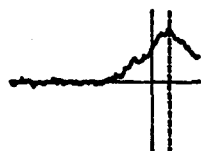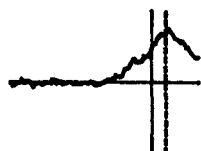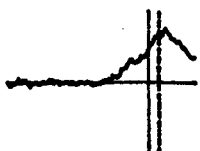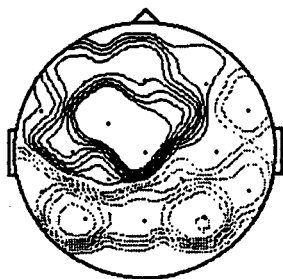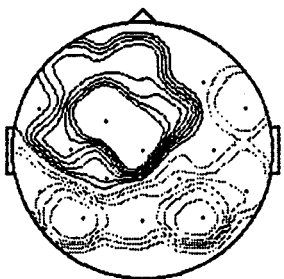
FIGURE 15.2.2. Isocontour maps of EEG (Laplacian) - Pattern condition (R.G.)
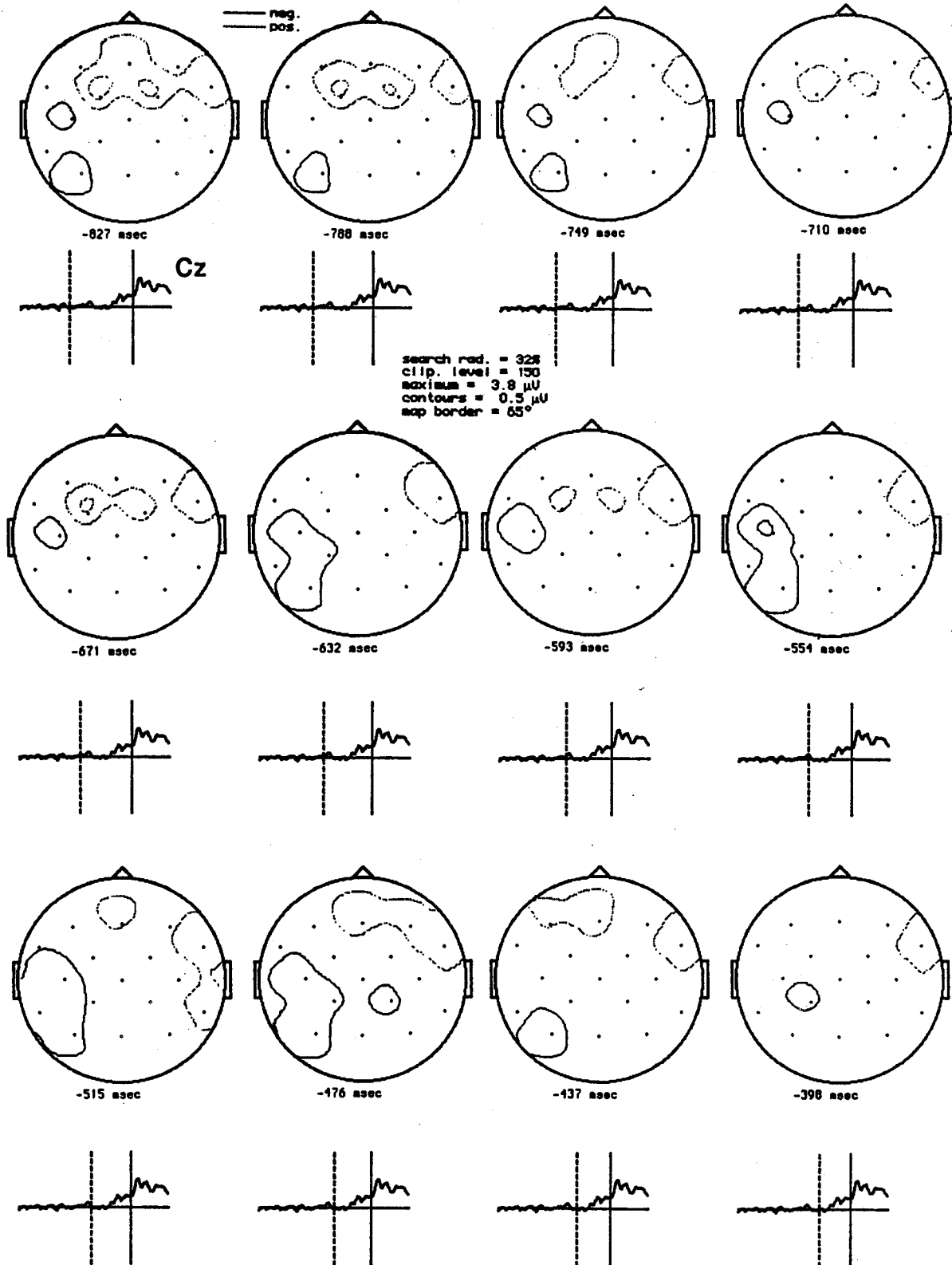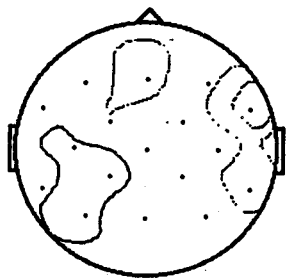
-359 msec   -320 msec   -281 msec   -242 msec
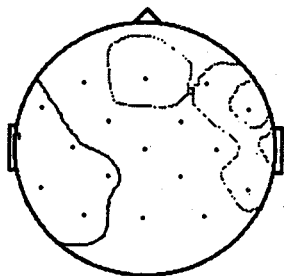
-203 msec   -164 msec   -125 msec   -86 msec

-47 msec   -8 msec   31 msec   70 msec

176
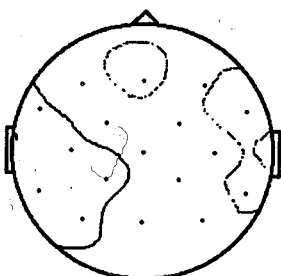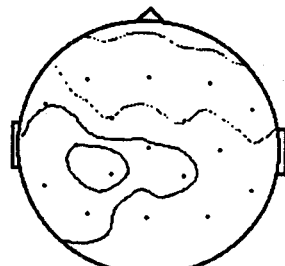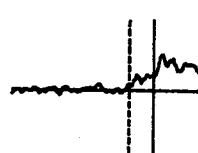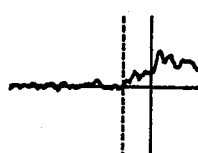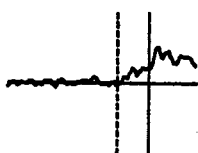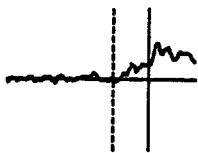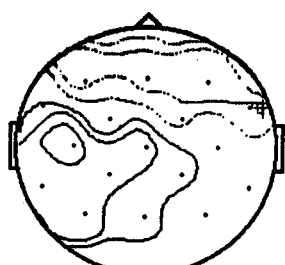
109 msec   148 msec   187 msec   226 msec
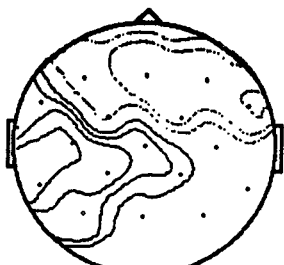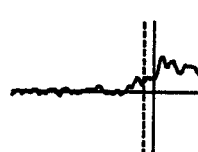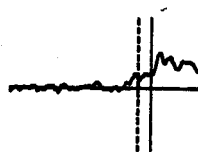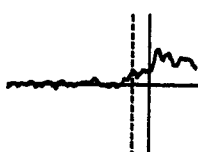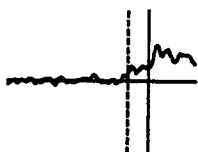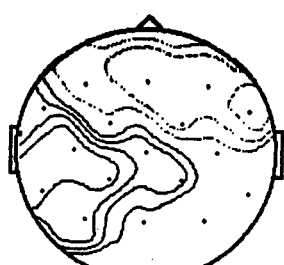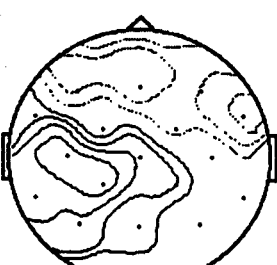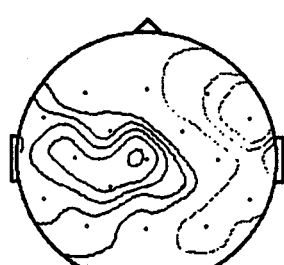
265 msec   304 msec   343 msec   382 msec
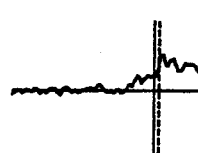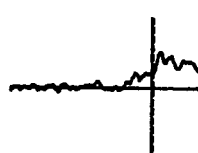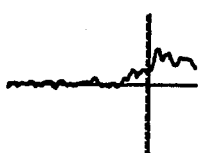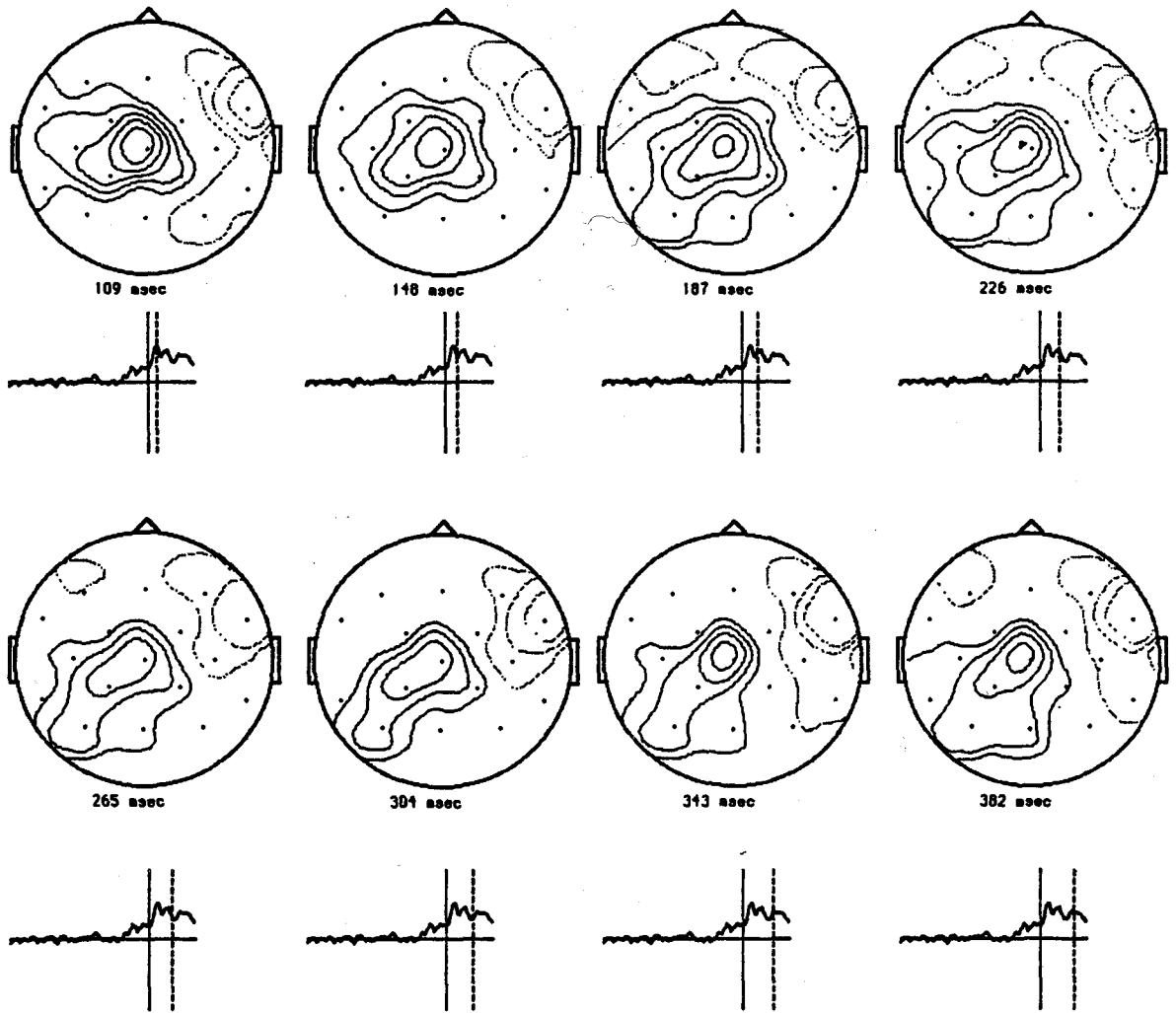
FIGURE 15.2.3. Isocontour maps of EEG (Laplacian) – Pattern condition (B.J.)

-359 msec   -320 msec   -281 msec   -242 msec

-203 msec   -164 msec   -125 msec   -86 msec

-47 msec   -8 msec   31 msec   70 msec

179

109 msec 148 msec 187 msec 226 msec

265 msec 304 msec 343 msec 382 msec

180
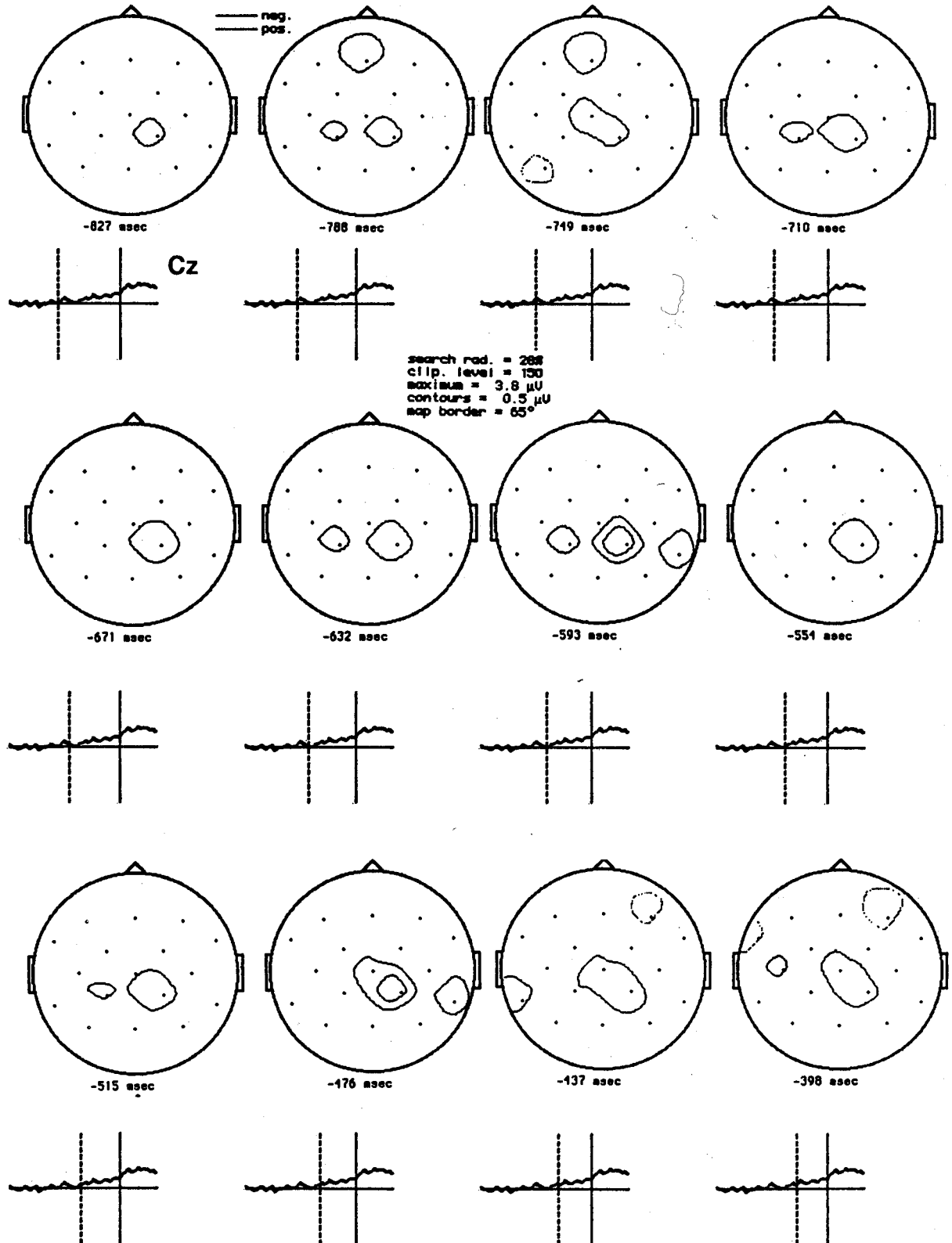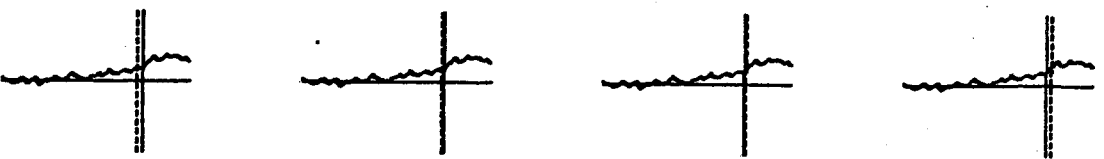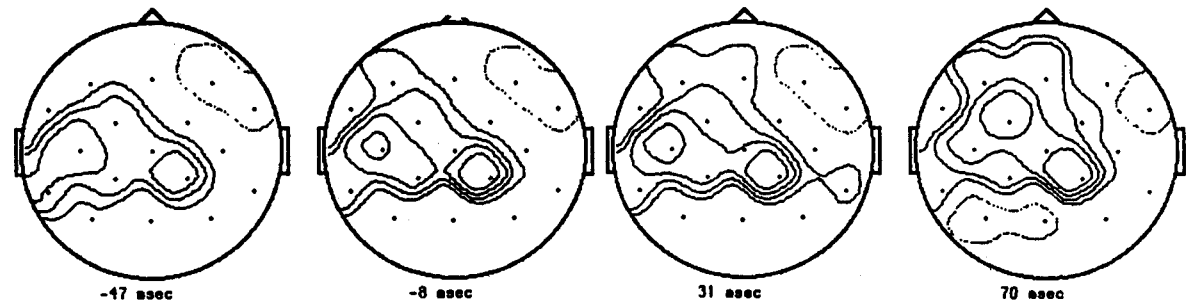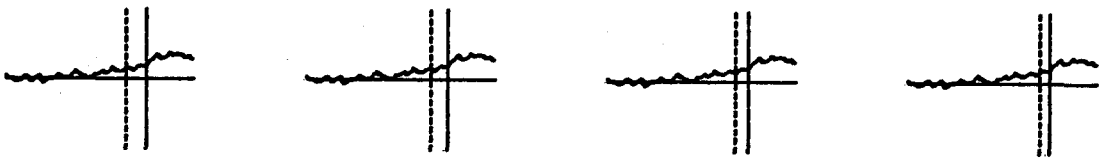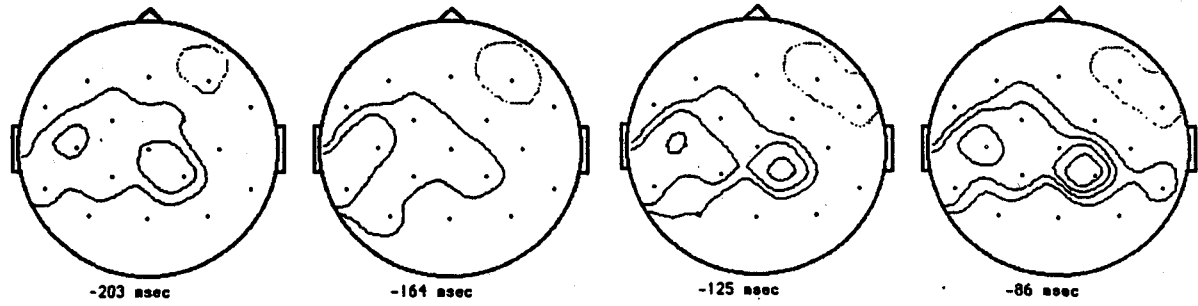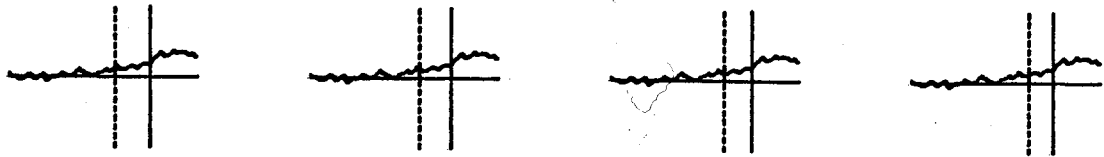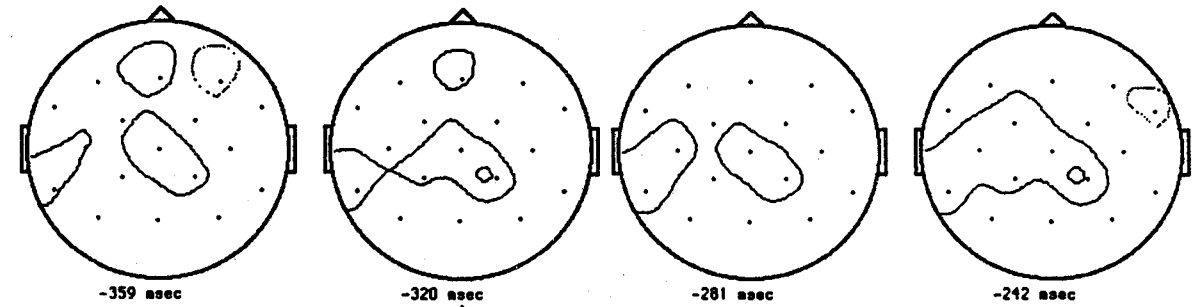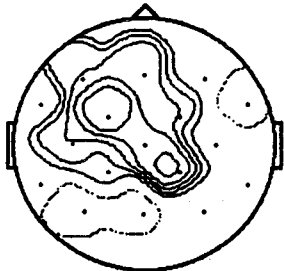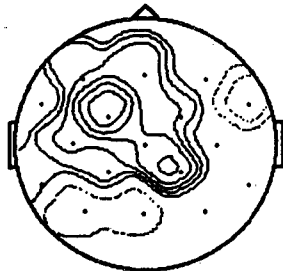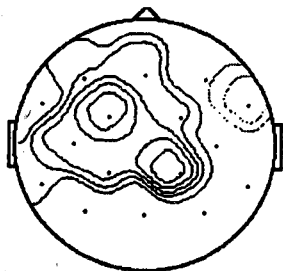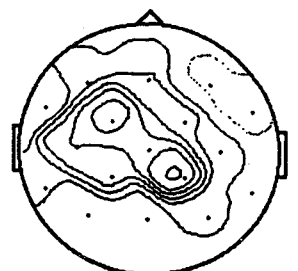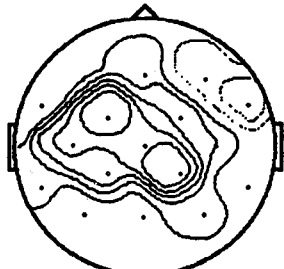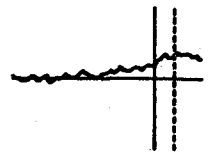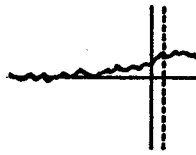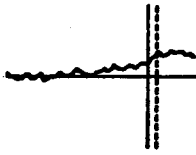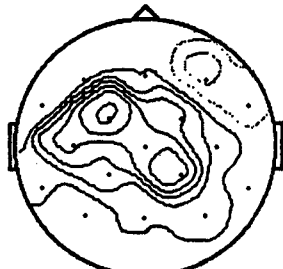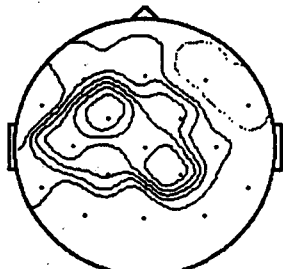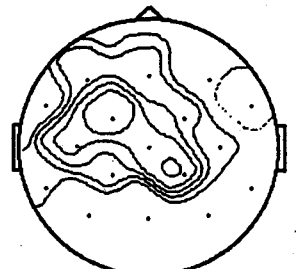
FIGURE 15.2.4. Isocontour maps of EEG (Laplacian) - Left hand (D.C.)
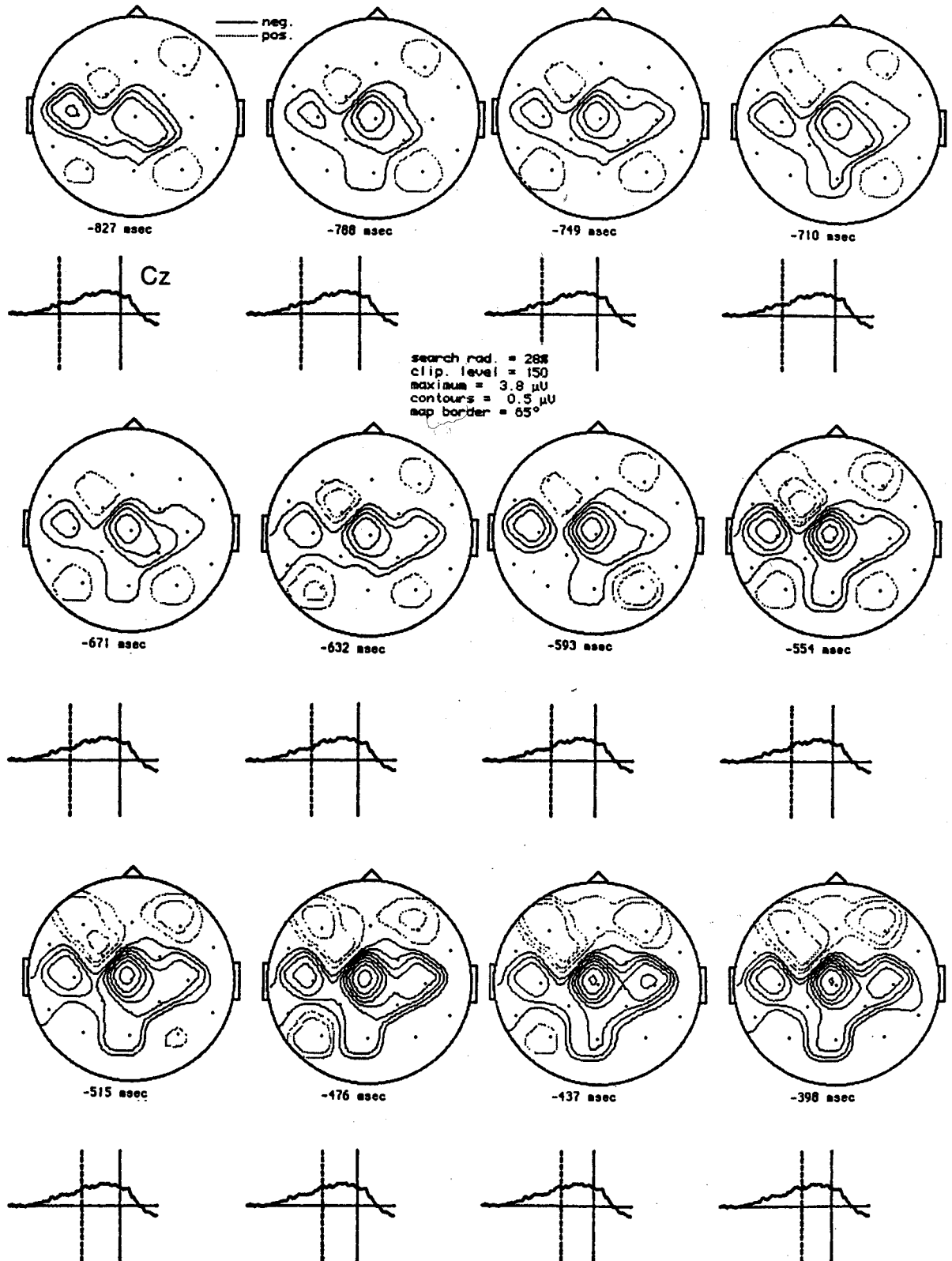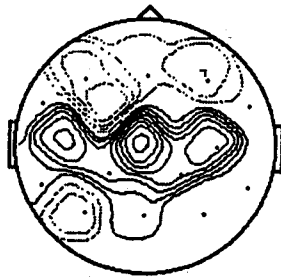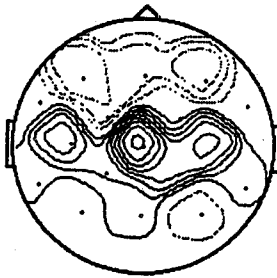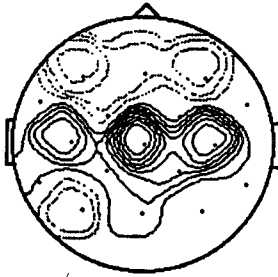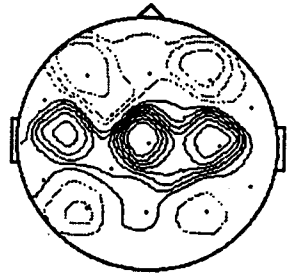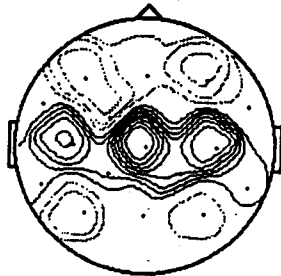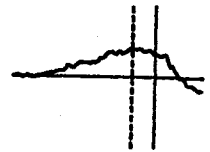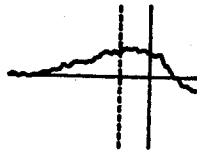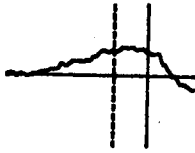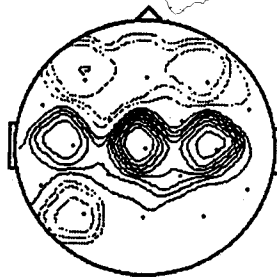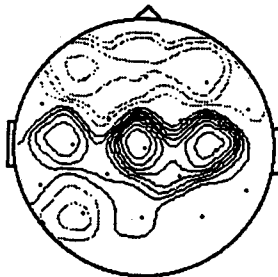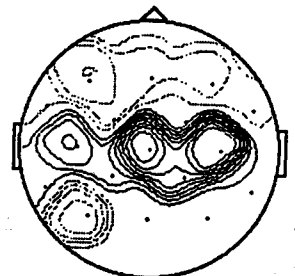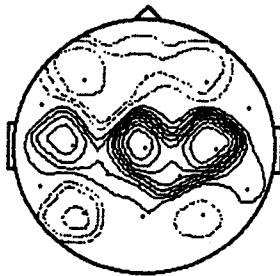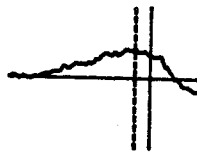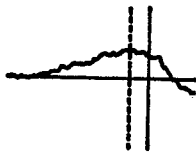
neg.
pos.

Cz

-827 msec   -788 msec   -749 msec   -710 msec

search rad. = 28%
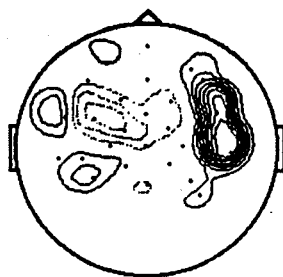clip. level = 150
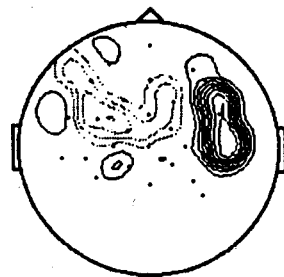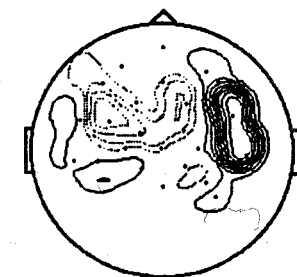maximum = 3.8 µU
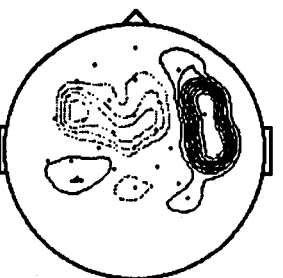contours = 0.5 µU
map border = 65°

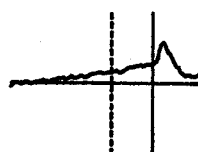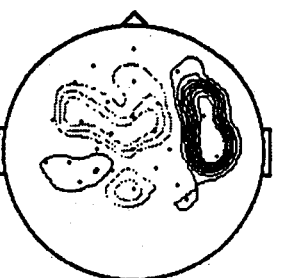-671 msec   -632 msec   -593 msec   -554 msec
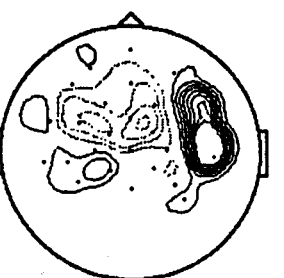
-515 msec   -476 msec   -437 msec   -398 msec

181

-359 msec   -320 msec   -281 msec   -242 msec

-203 msec   -164 msec   -125 msec   -86 msec

-47 msec   -8 msec   31 msec   70 msec

182
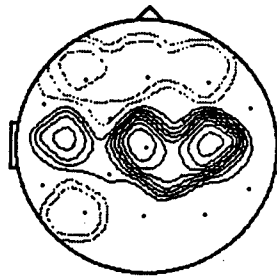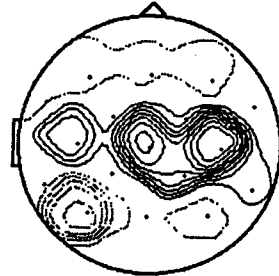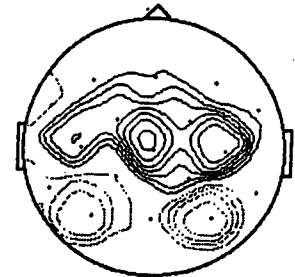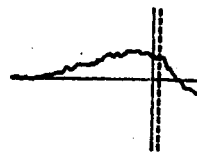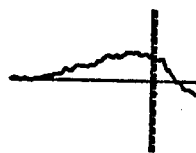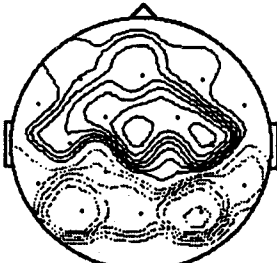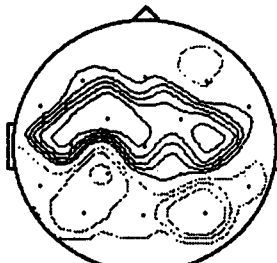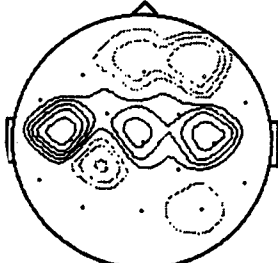
109 msec   146 msec   187 msec   226 msec
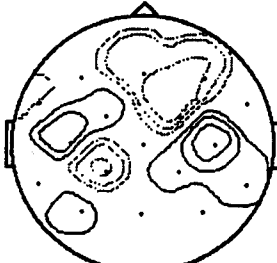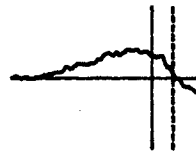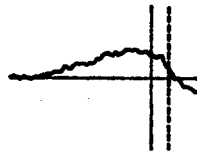
265 msec   304 msec   343 msec   382 msec

FIGURE 15.2.5.   Isocontour maps of EEG (Laplacian) – Left hand (H.W.)
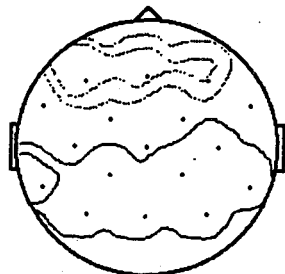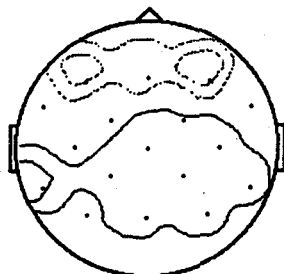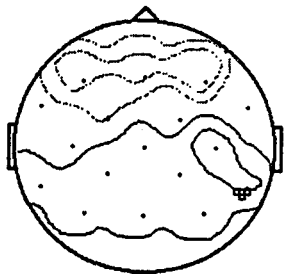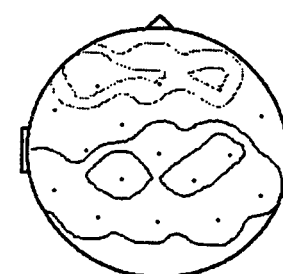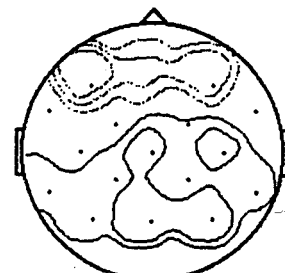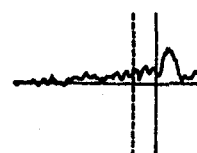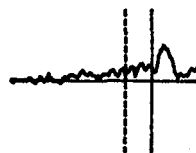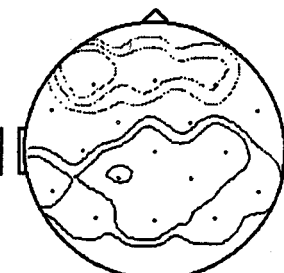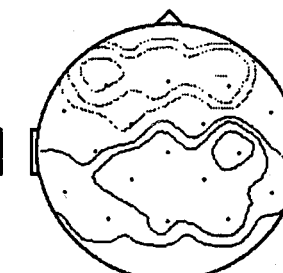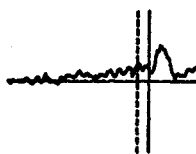
search rad. = 28%
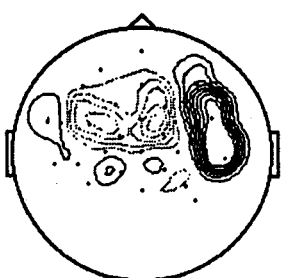clip. level = 150
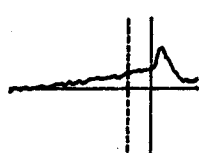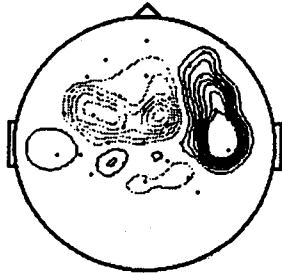maximum = 3.8 µV
contours = 0.5 µV
map border = 65°

184

-359 msec   -320 msec   -281 msec   -242 msec

-203 msec   -164 msec   -125 msec   -86 msec
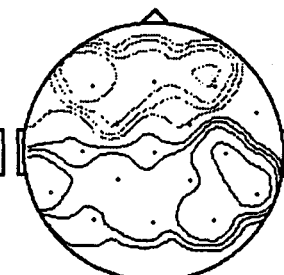
-47 msec   -8 msec   31 msec   70 msec
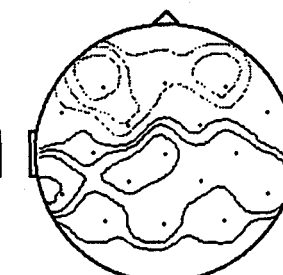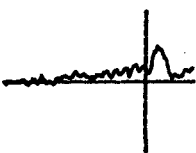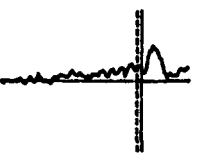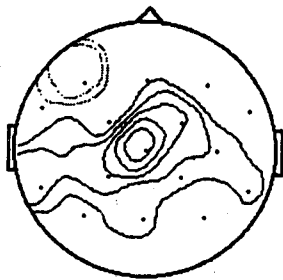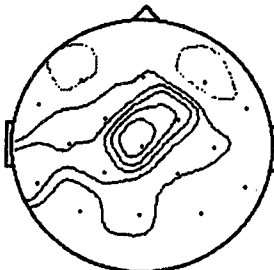
109 msec 148 msec 187 msec 226 msec
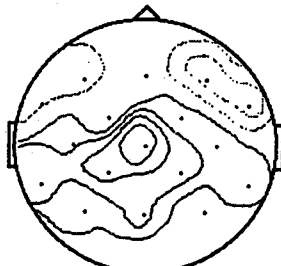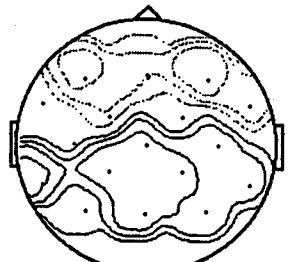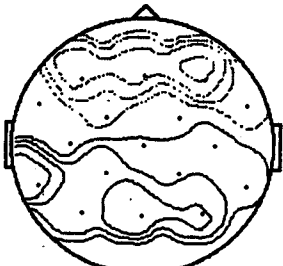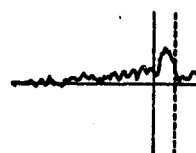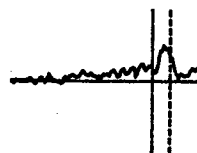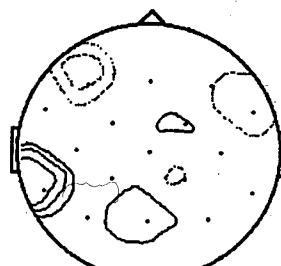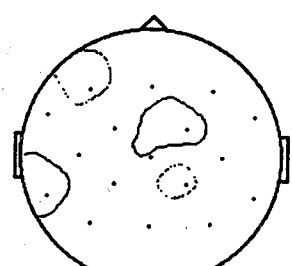
265 msec 304 msec 343 msec 382 msec
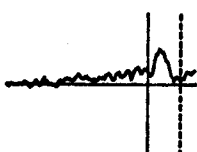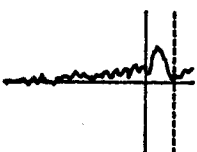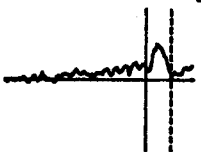
APPENDIX C: SPATIO-TEMPORAL ISOCONTOUR MAPS OF MEG ACTIVITY DURING UNILATERAL FINGER FLEXIONS.

FIGURE 16.1.1. Isocontour maps of MEG activity - Simple condition (T.R.)
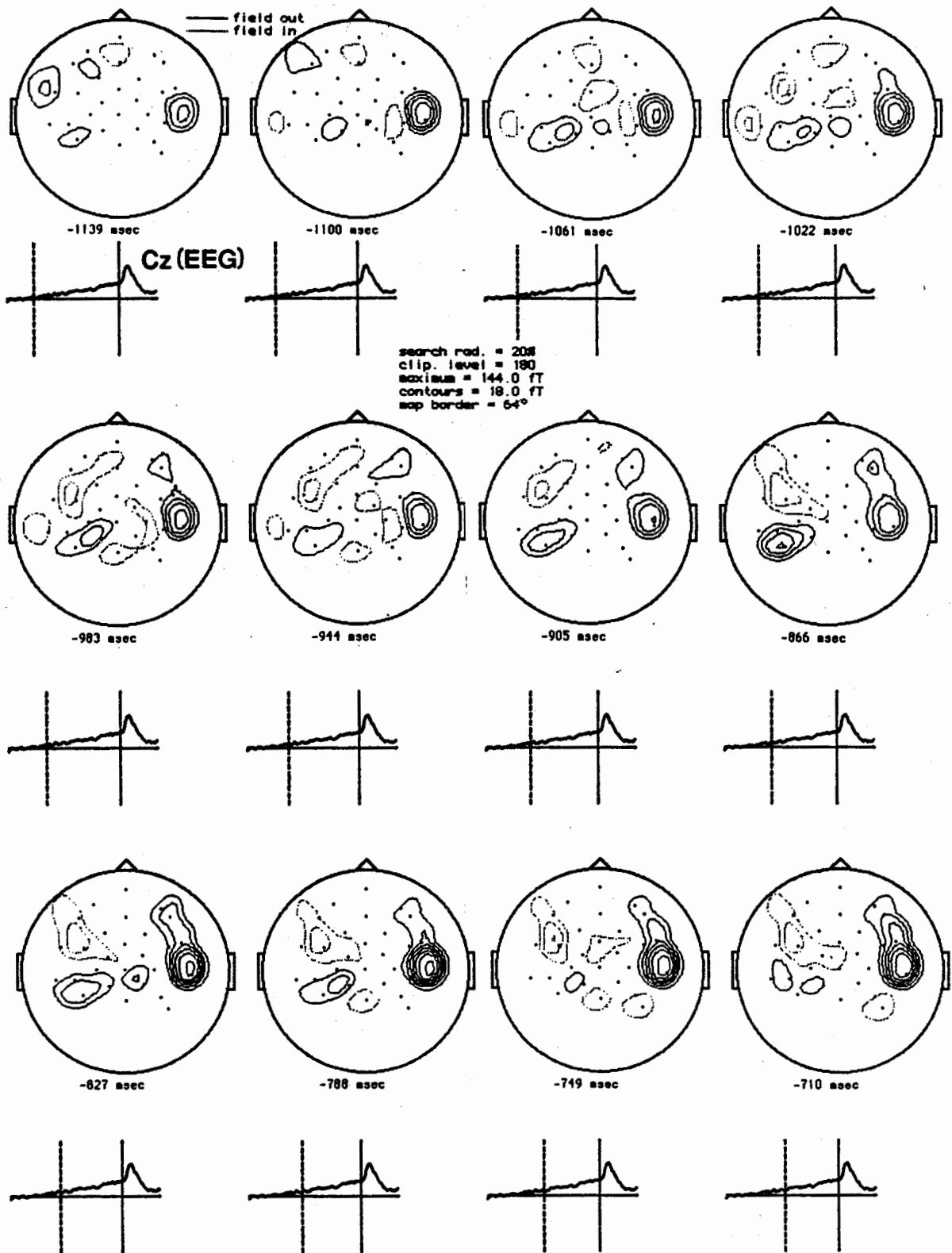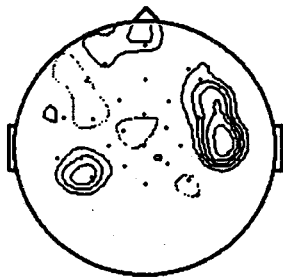
-671 msec   -632 msec   -593 msec   -554 msec
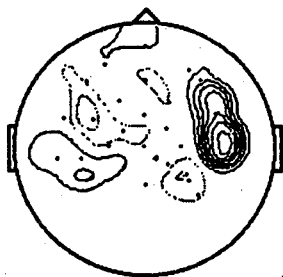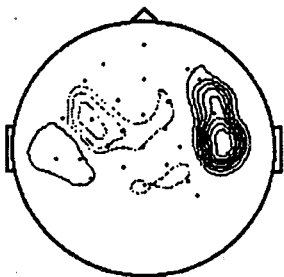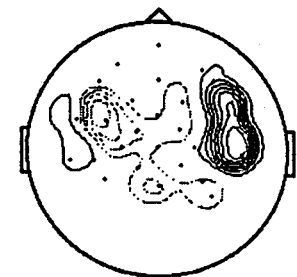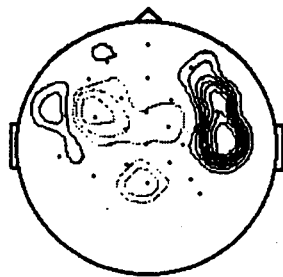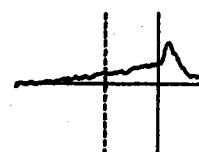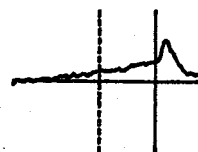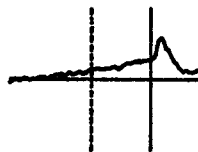
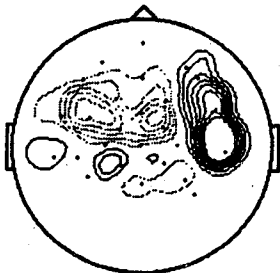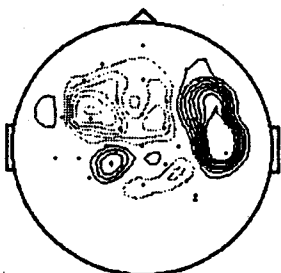-515 msec   -476 msec   -437 msec   -398 msec

-359 msec   -320 msec   -281 msec   -242 msec

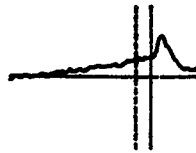-203 msec   -164 msec   -125 msec   -86 msec
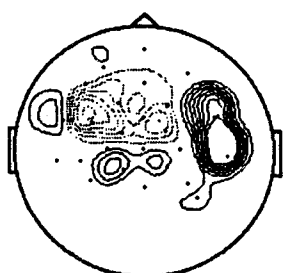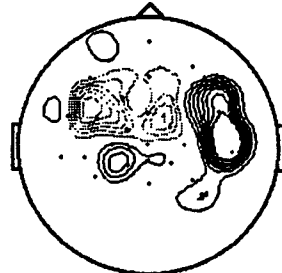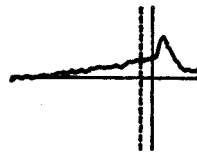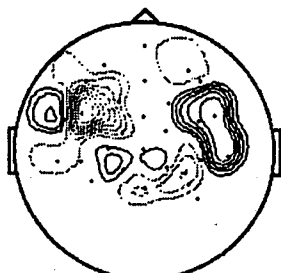
-47 msec   -8 msec   31 msec   70 msec
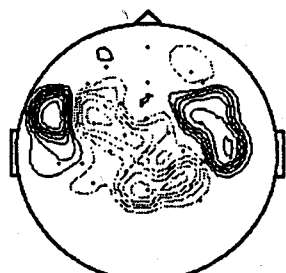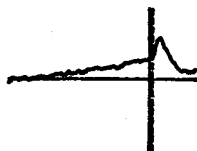
109 msec   148 msec   187 msec   226 msec

FIGURE 16.1.2 Isocontour maps of MEG activity - Simple condition (R.G.)

-671 msec   -632 msec   -593 msec   -554 msec

-515 msec   -476 msec   -137 msec   -398 msec
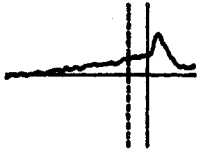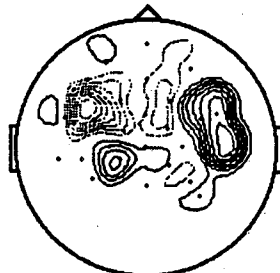
-359 msec   -320 msec   -281 msec   -242 msec
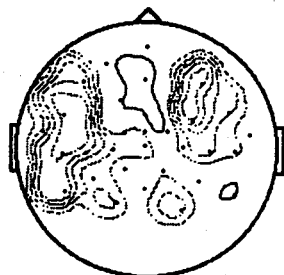
-203 msec   -164 msec   -125 msec   -86 msec
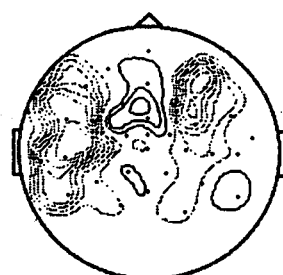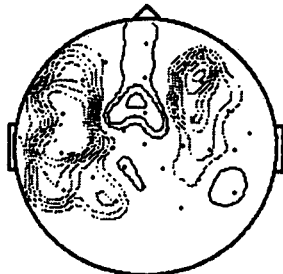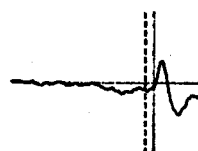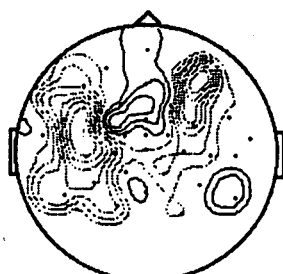
-47 msec   -8 msec   31 msec   70 msec
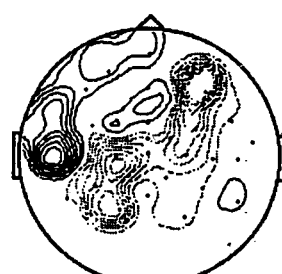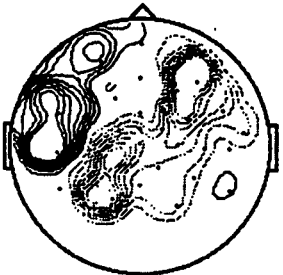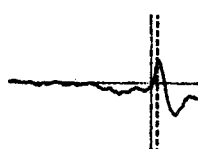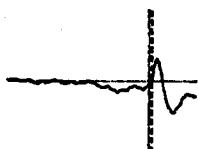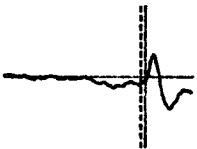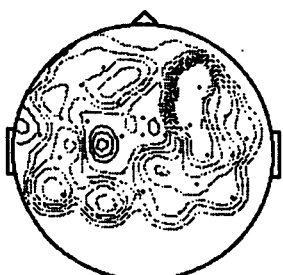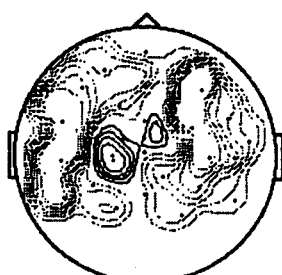
109 msec   148 msec   187 msec   226 msec
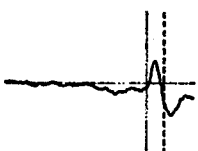
FIGURE 16.1.3. Isocontour maps of MEG activity - Simple condition (B.J.)
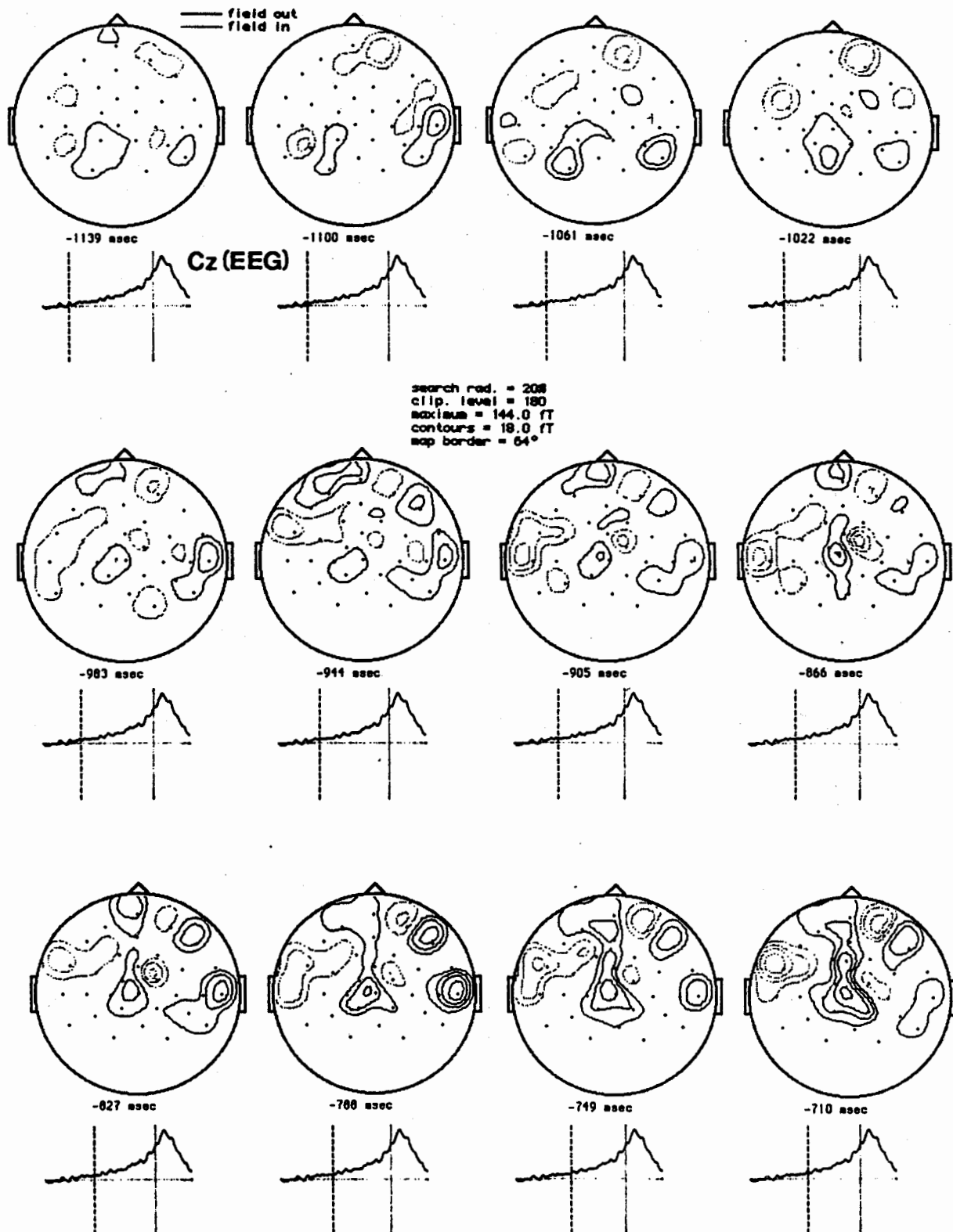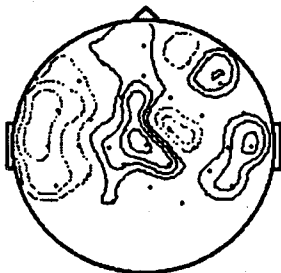
-671 msec   -632 msec   -593 msec   -554 msec
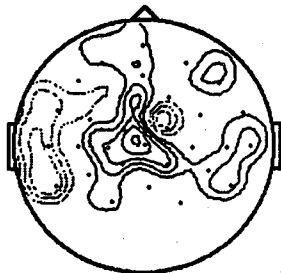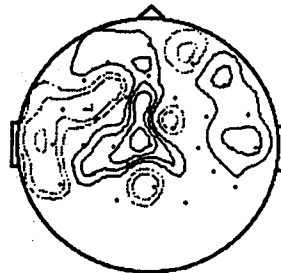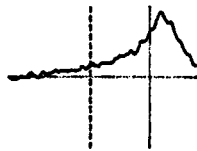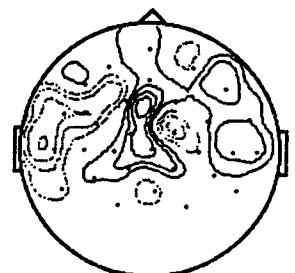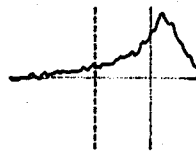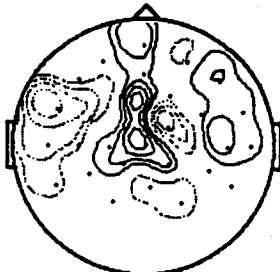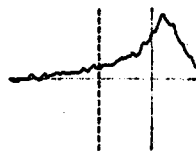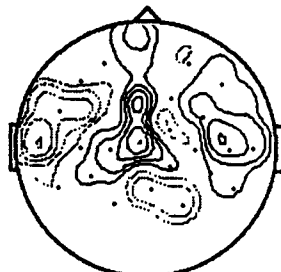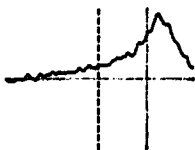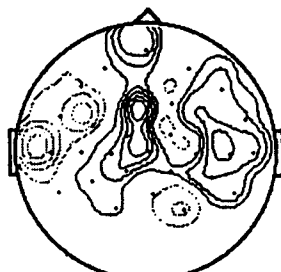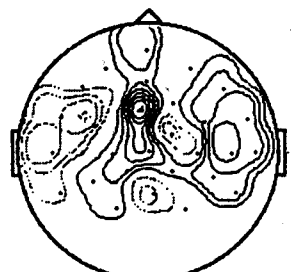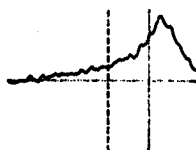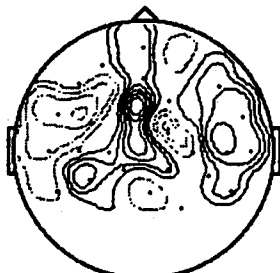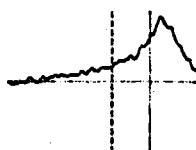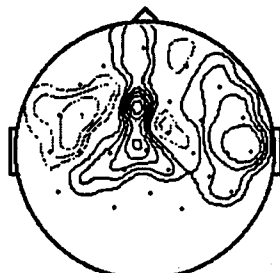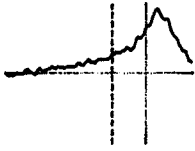
-515 msec   -476 msec   -437 msec   -398 msec

-359 msec   -320 msec   -281 msec   -242 msec

195
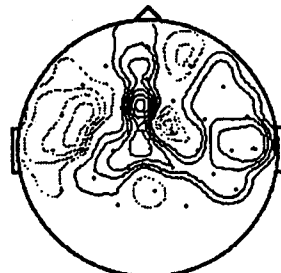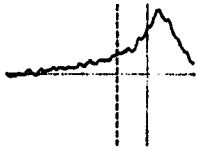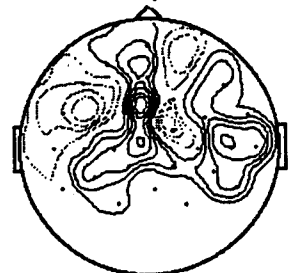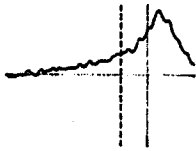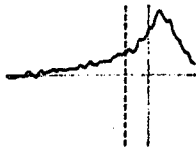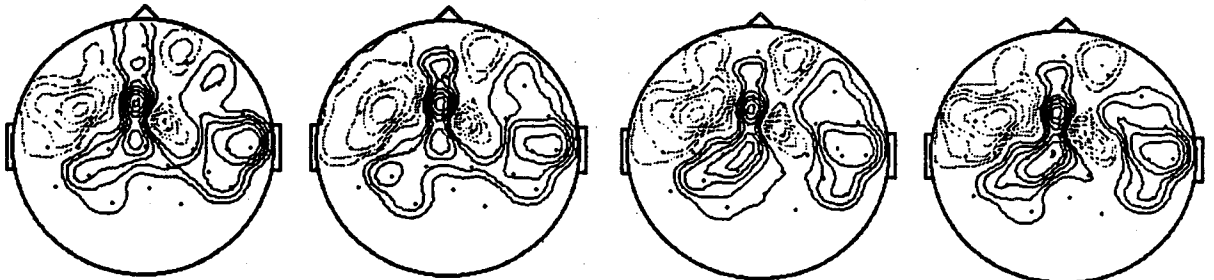
-203 msec   -164 msec   -125 msec   -86 msec
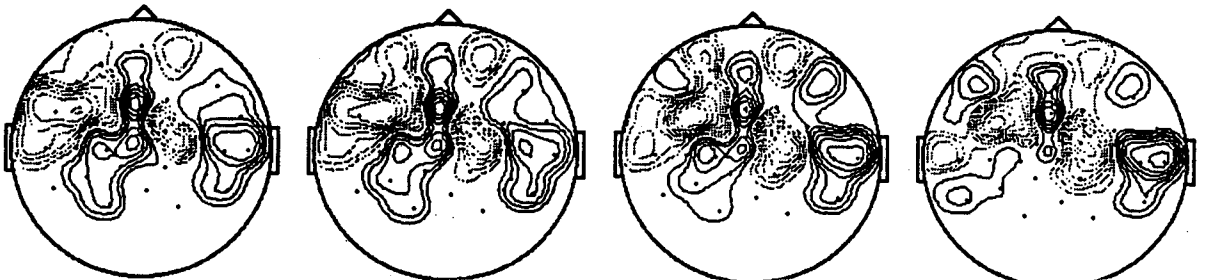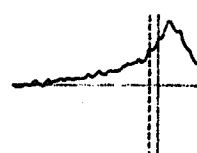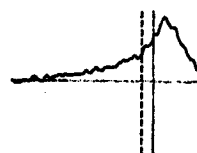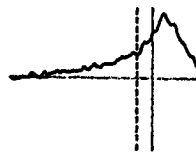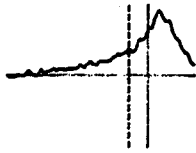
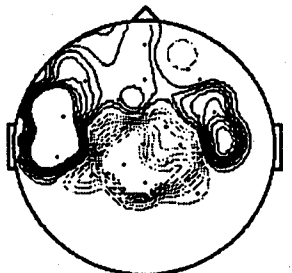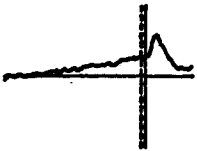-47 msec   -8 msec   31 msec   70 msec
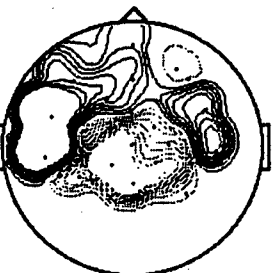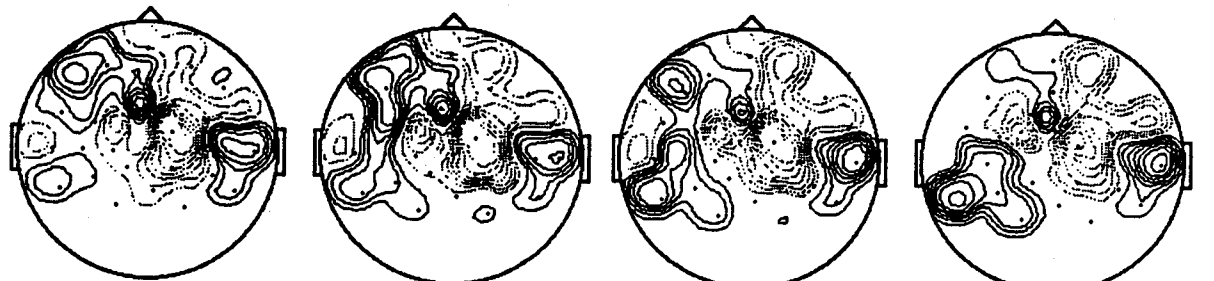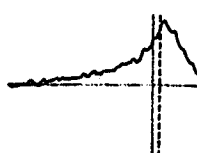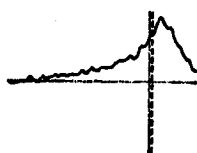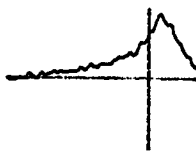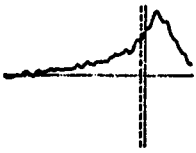
109 msec   148 msec   187 msec   226 msec
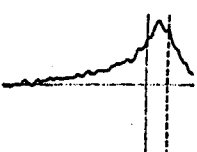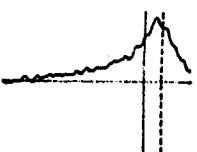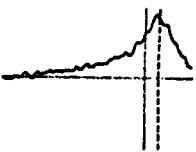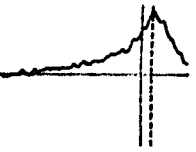
FIGURE 16.2.1. Isocontour maps of MEG activity – Pattern condition (T.R.)
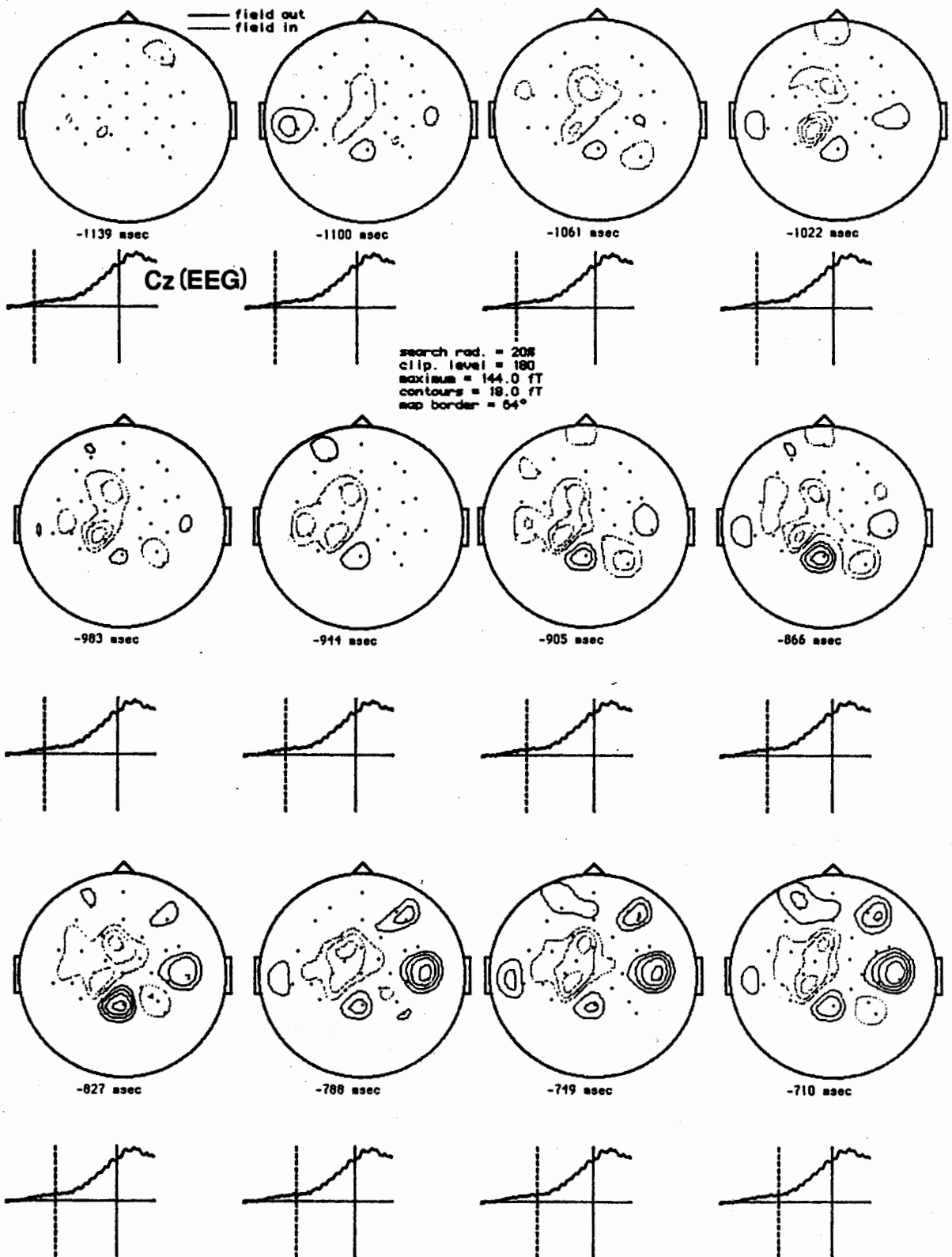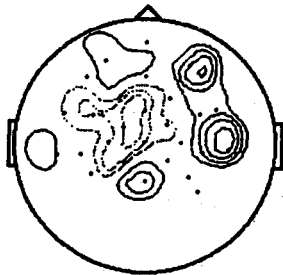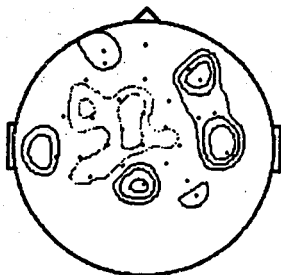
search rad. = 20%
clip. level = 180
maximum = 144.0 fT
contours = 18.0 fT
map border = 64°

-671 msec

-632 msec

-593 msec

-554 msec

-515 msec

-476 msec

-437 msec

-398 msec

-359 msec

-320 msec

-281 msec
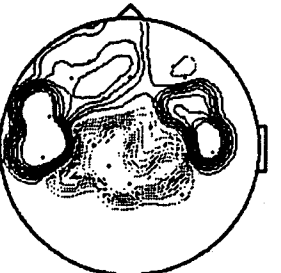
-242 msec

198

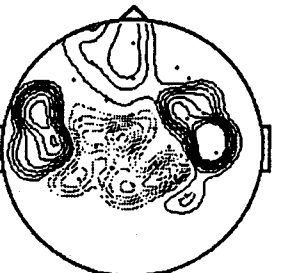-203 msec　　-164 msec　　-125 msec　　-86 msec
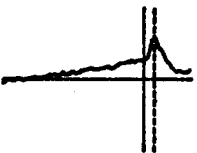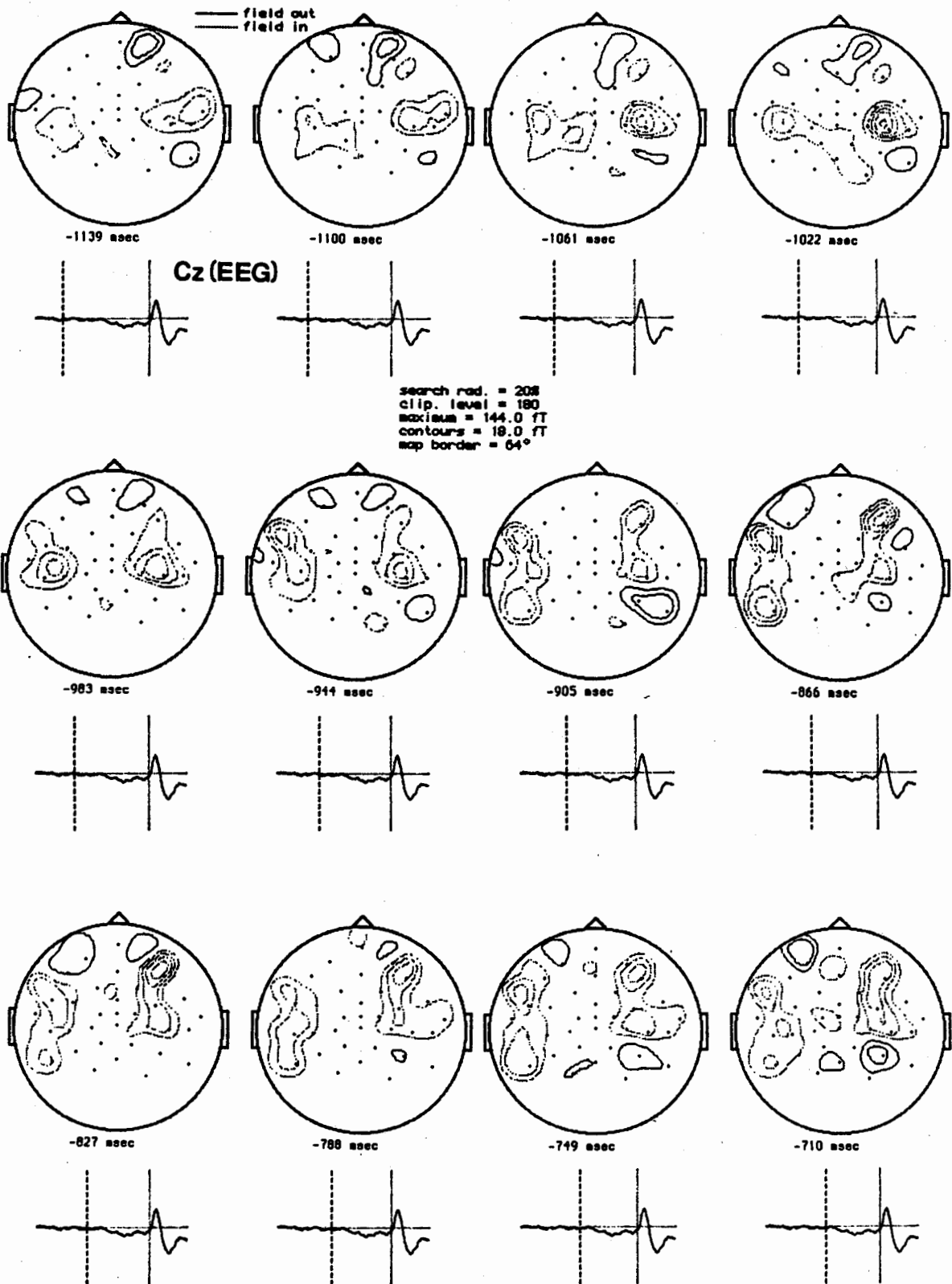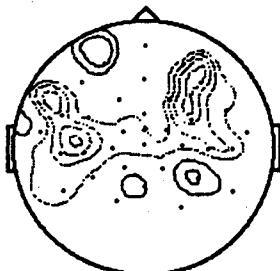
-17 msec　　-8 msec　　31 msec　　70 msec

109 msec　　148 msec　　187 msec　　226 msec

199

FIGURE 16.2.2. Isocontour maps of MEG activity - Pattern condition (R.G.)
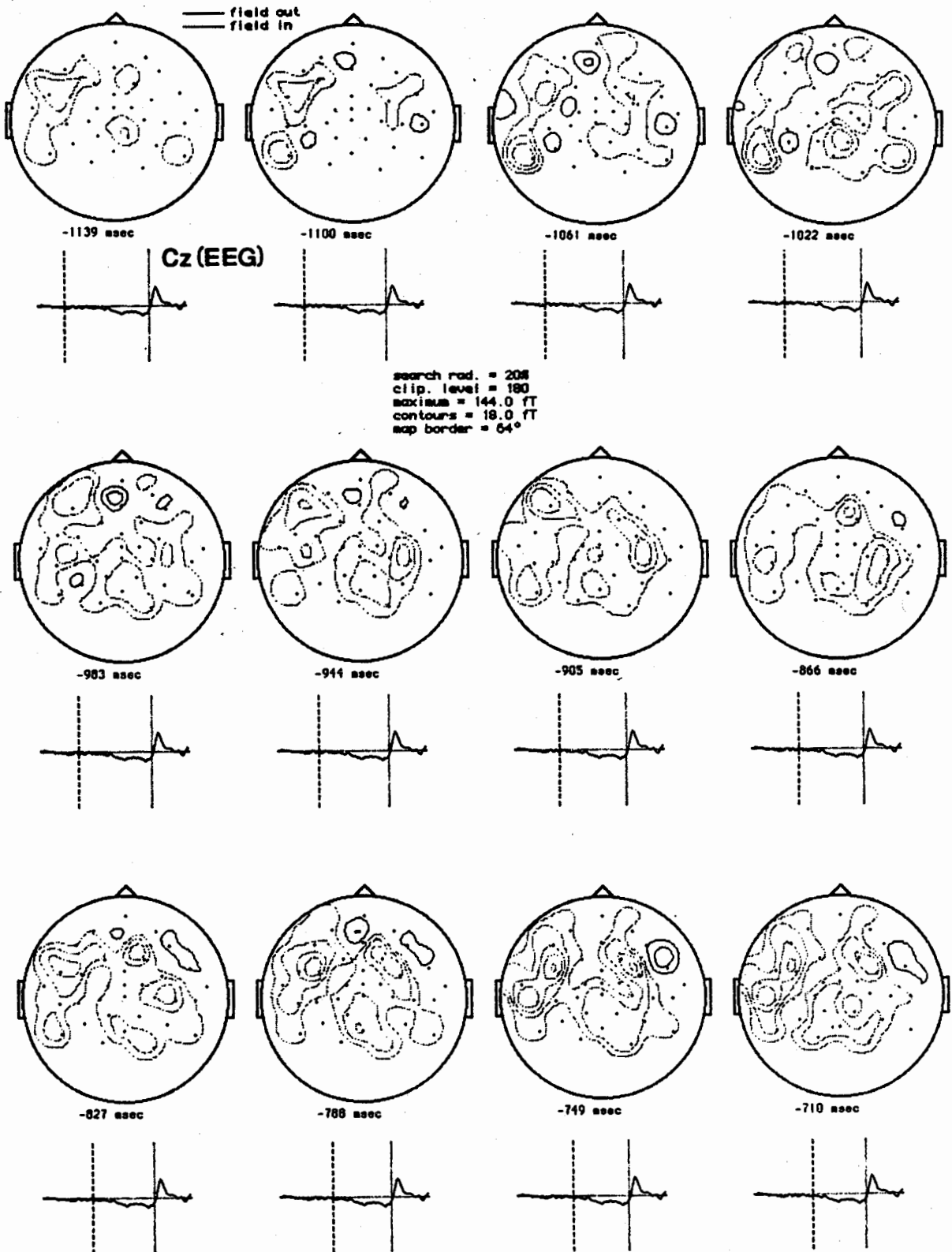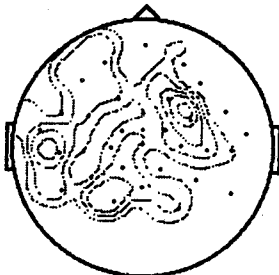
-671 msec   -632 msec   -593 msec   -554 msec
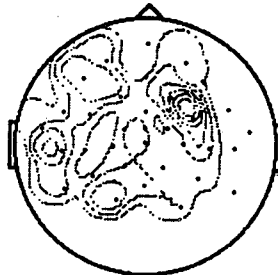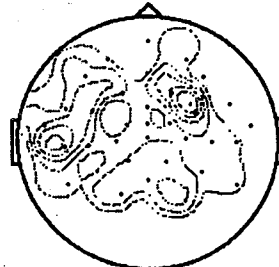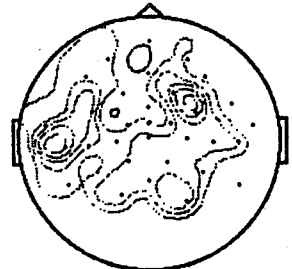
-515 msec   -476 msec   -137 msec   -398 msec

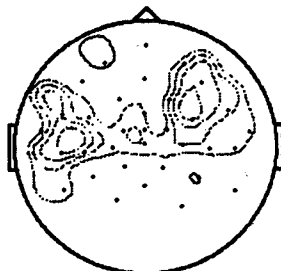-359 msec   -320 msec   -281 msec   -242 msec

201
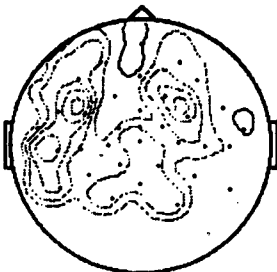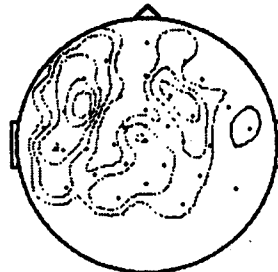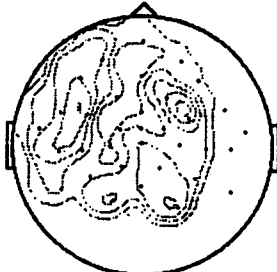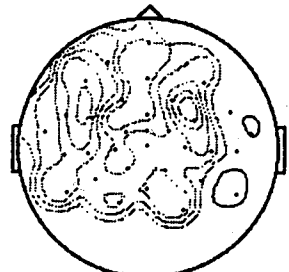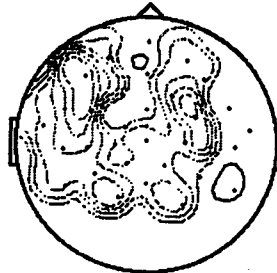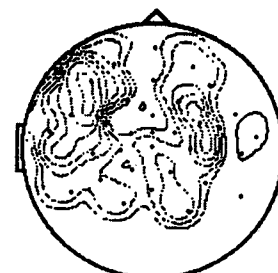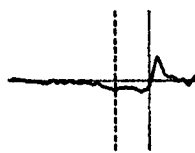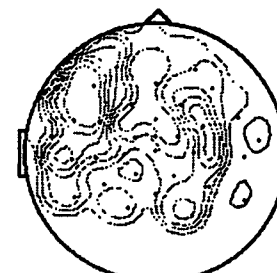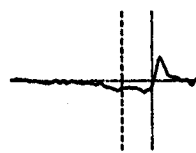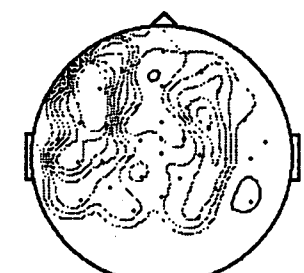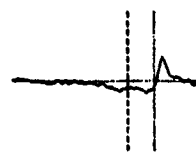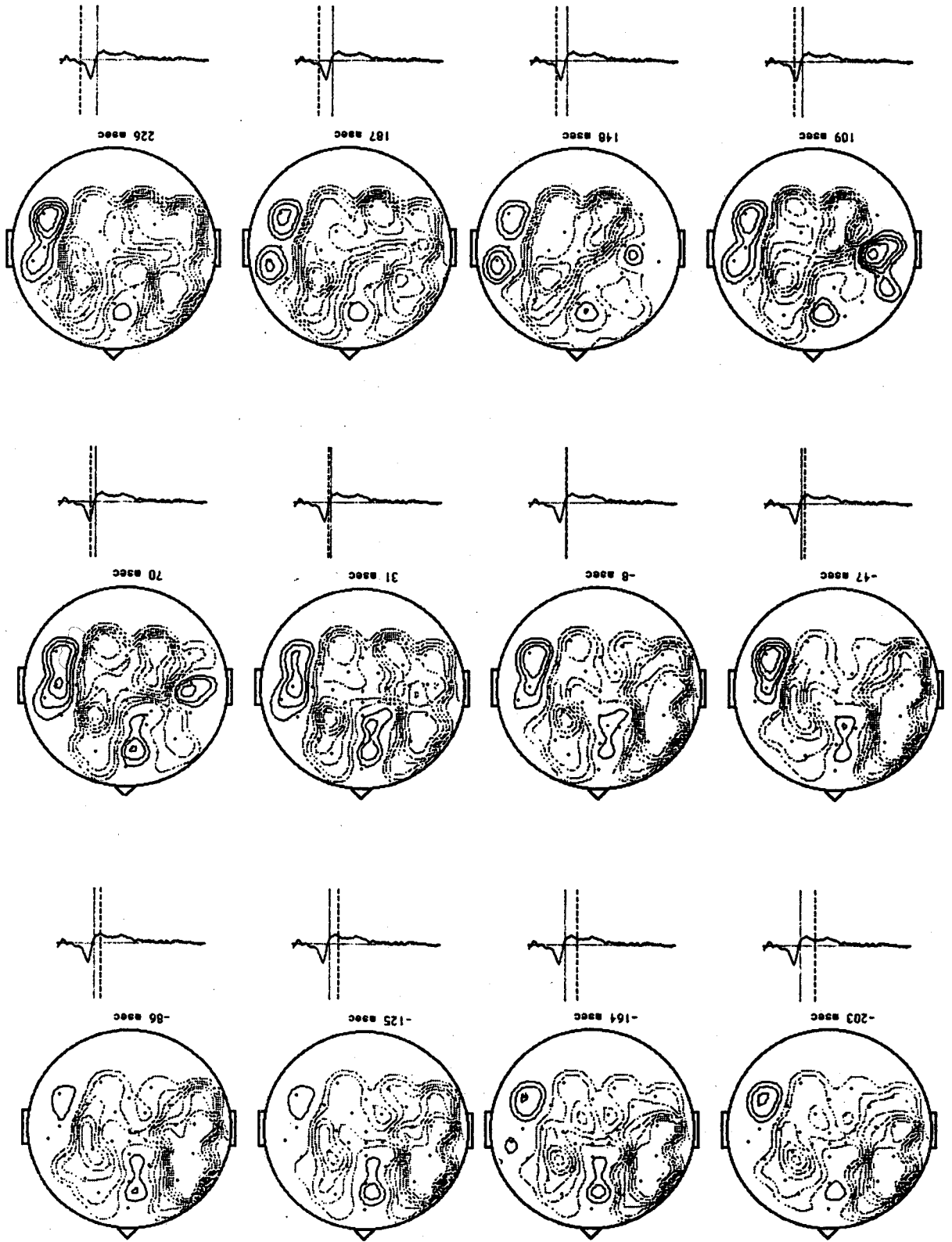
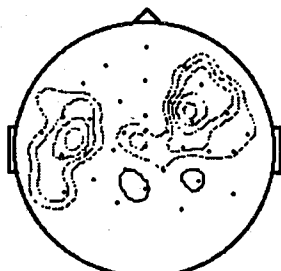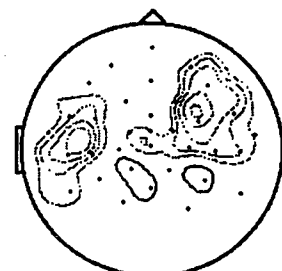FIGURE 16.2.3 Isocontour maps of MEG activity - Pattern condition (B.J.)
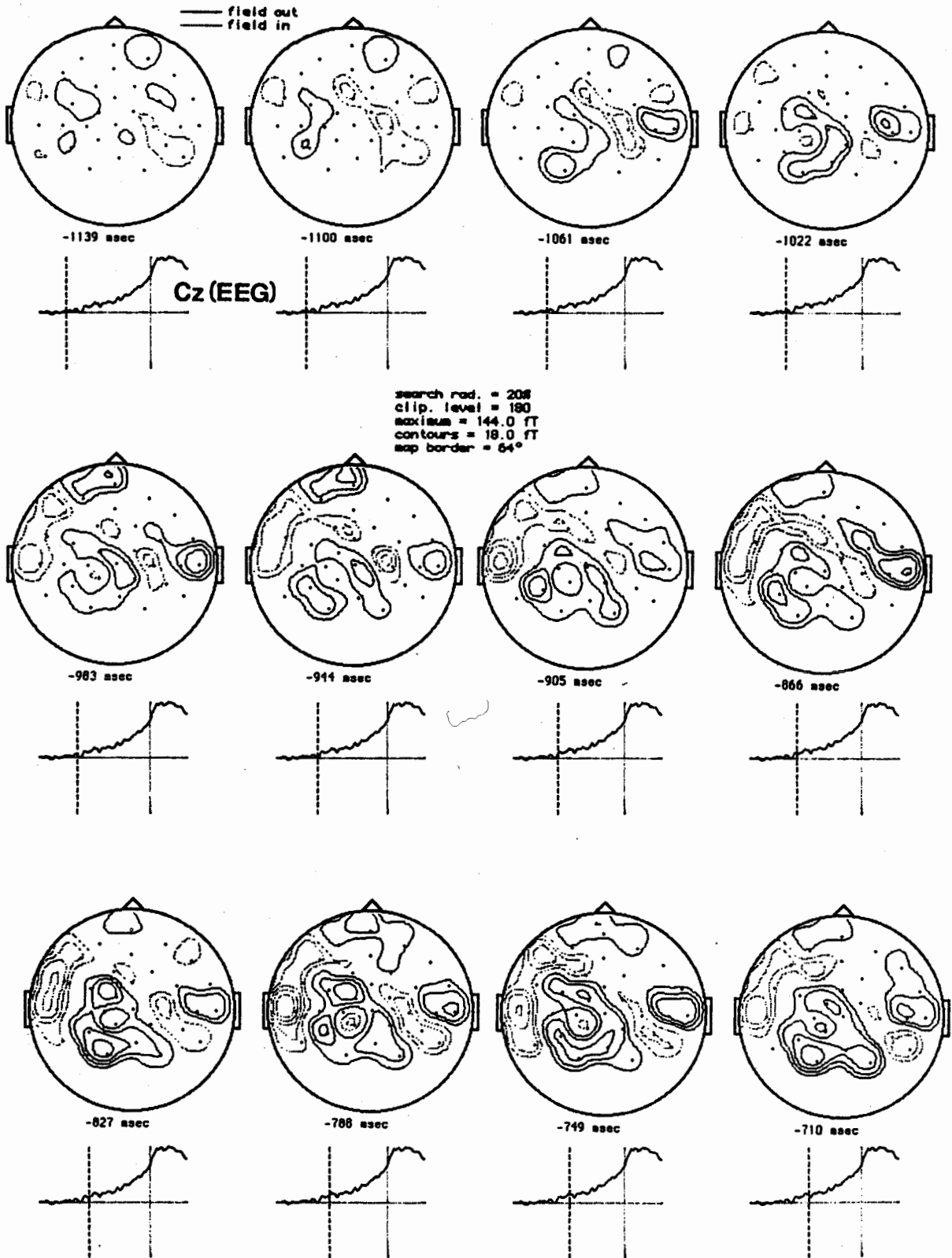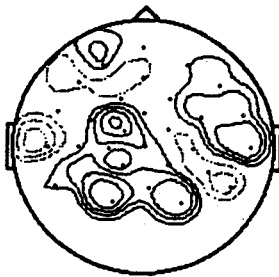
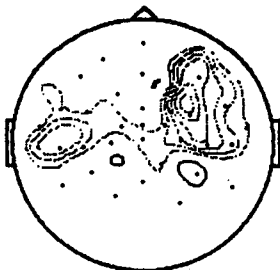-671 msec   -632 msec   -593 msec   -554 msec
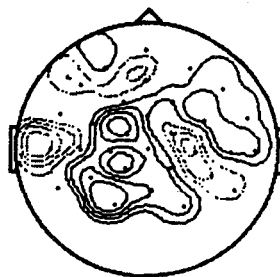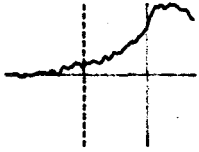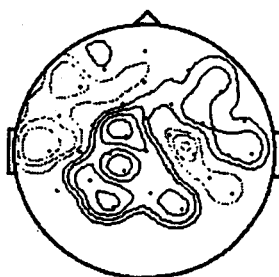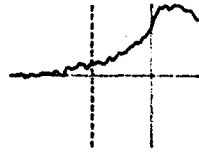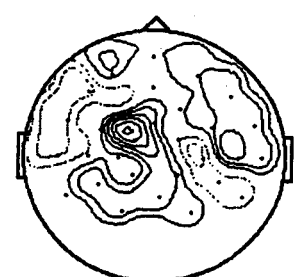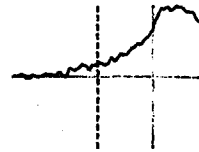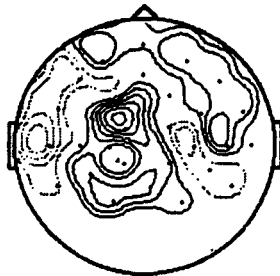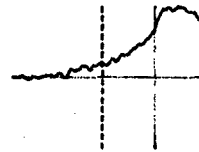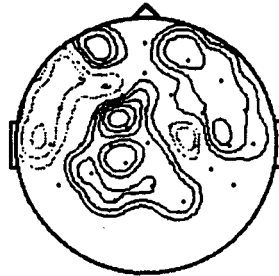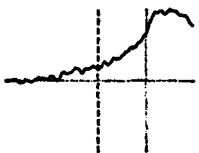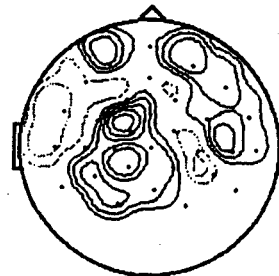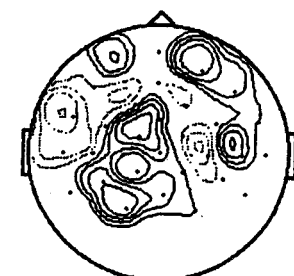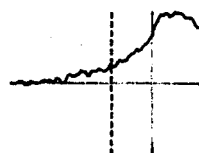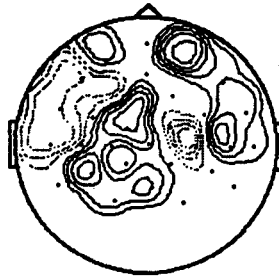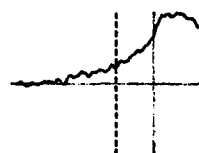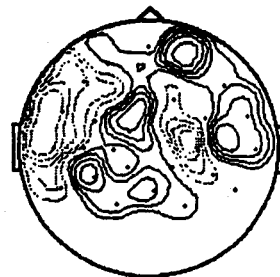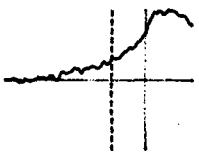
-515 msec   -476 msec   -437 msec   -398 msec

-359 msec   -320 msec   -281 msec   -242 msec

-203 msec   -164 msec   -125 msec   -86 msec

-47 msec   -8 msec   31 msec   70 msec

109 msec   148 msec   187 msec   226 msec

205
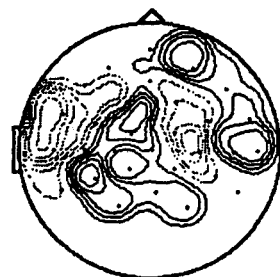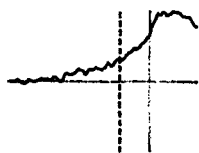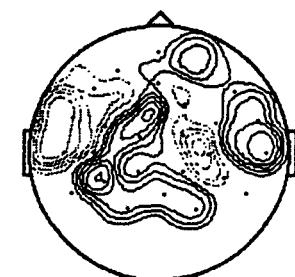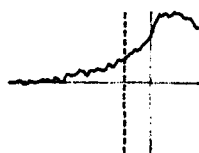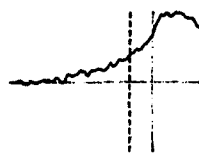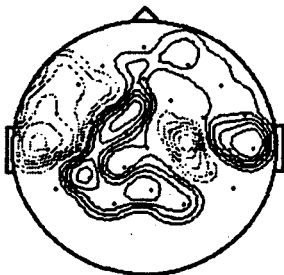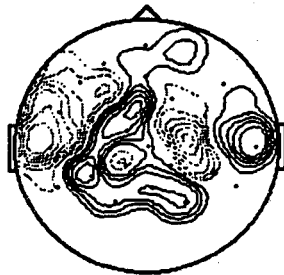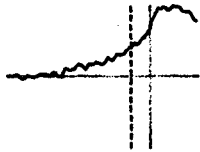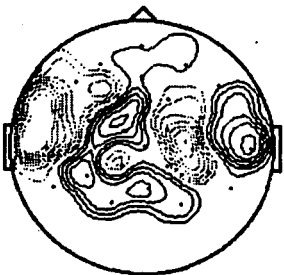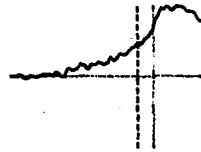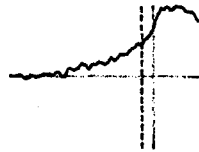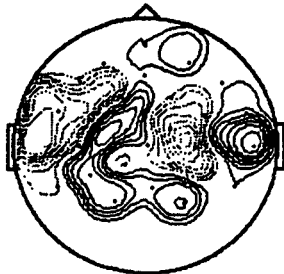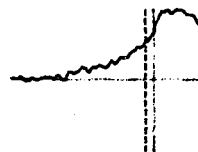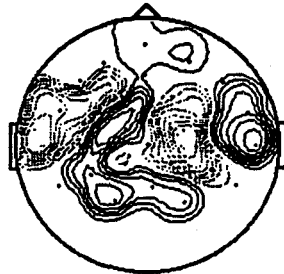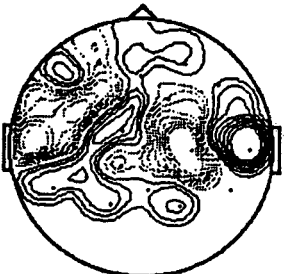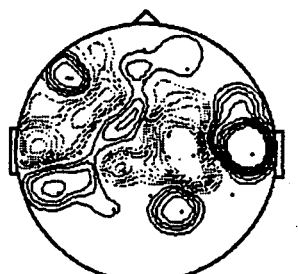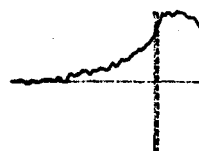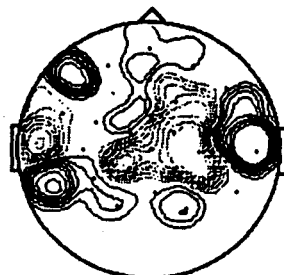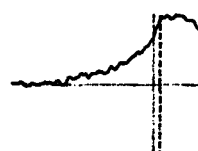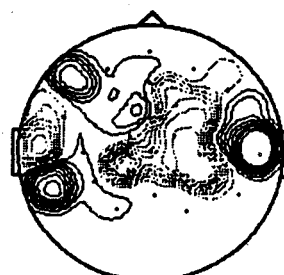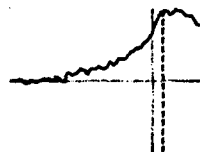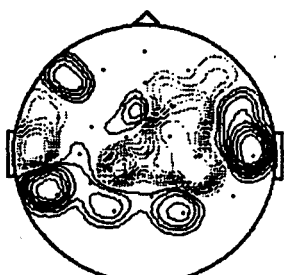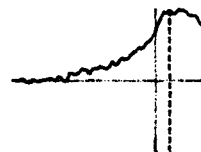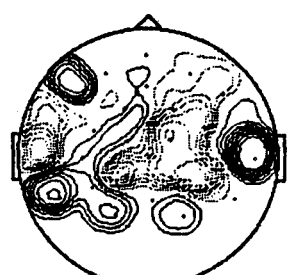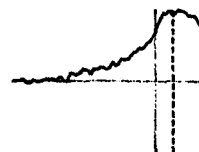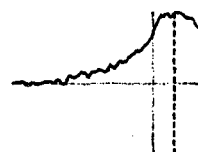
FIGURE 16.3.1. Isocontour maps of MEG activity - right finger flexion (D.C.)
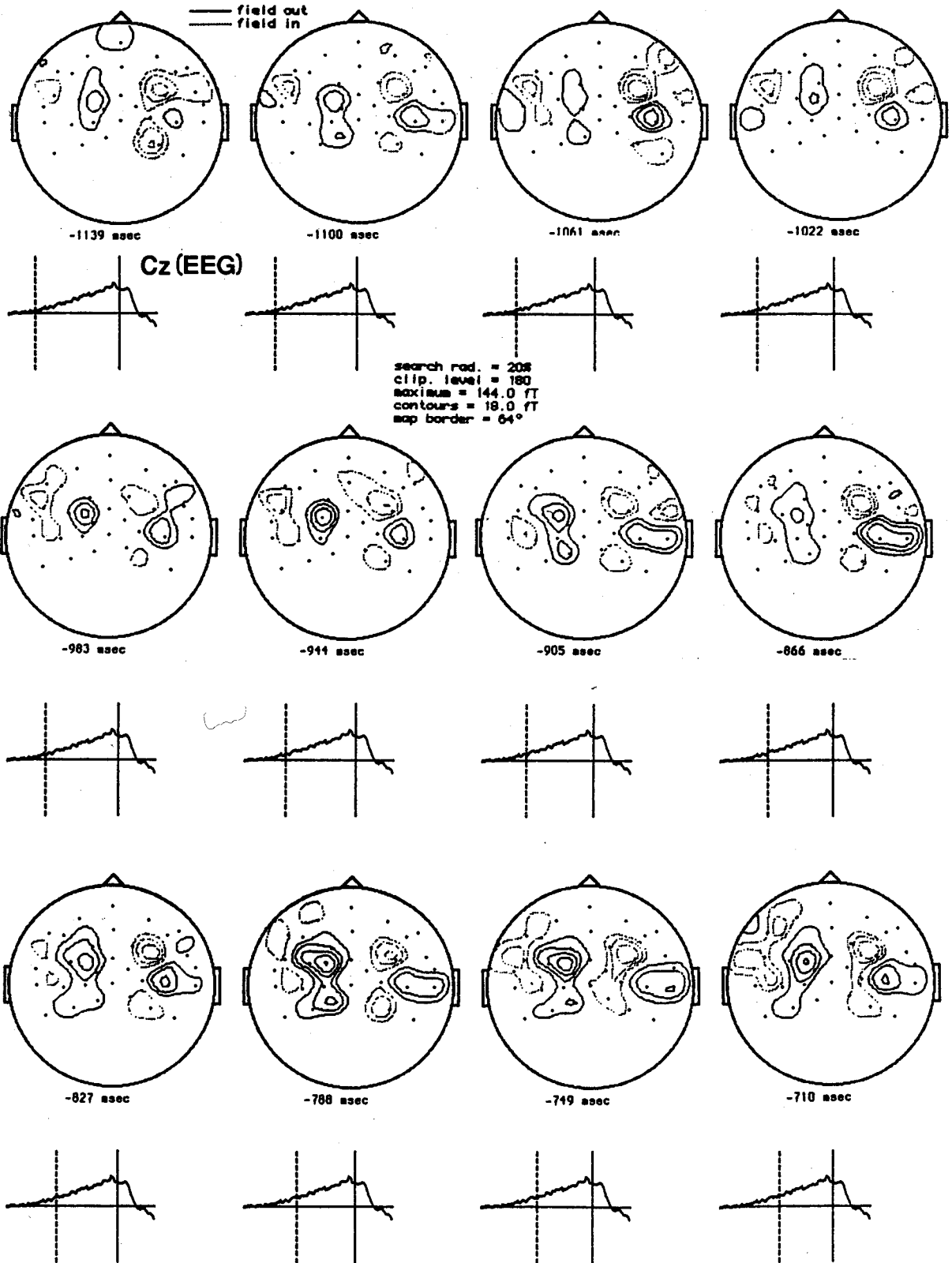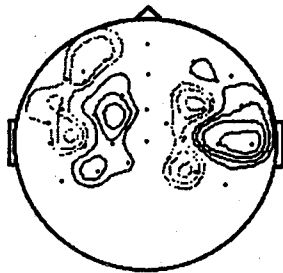
field out
field in

-1139 asec   -1100 asec   -1061 asec   -1022 asec

Cz (EEG)

search rad. = 20%
clip. level = 180
maximum = 144.0 fT
contours = 18.0 fT
map border = 64°

-983 asec   -944 asec   -905 asec   -866 asec

-827 asec   -788 asec   -749 asec   -710 asec
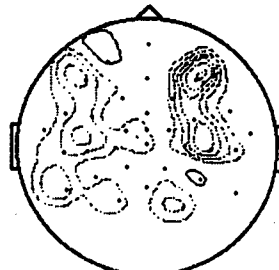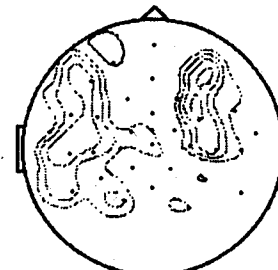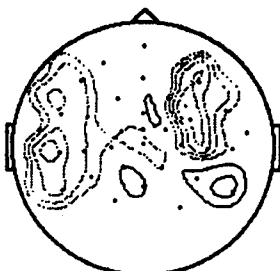
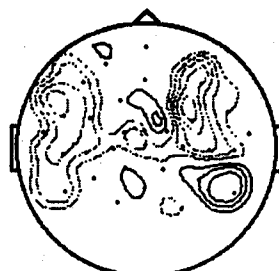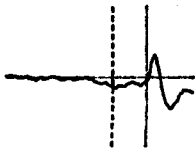-671 msec   -632 msec   -593 msec   -554 msec

-515 msec   -476 msec   -437 msec   -398 msec

-359 msec   -320 msec   -281 msec   -242 msec

-203 msec   -164 msec   -125 msec   -86 msec

-47 msec   -8 msec   31 msec   70 msec

109 msec   148 msec   187 msec   226 msec

FIGURE 16.3.2. Isocontour maps of MEG activity – right finger flexion (H.W.)
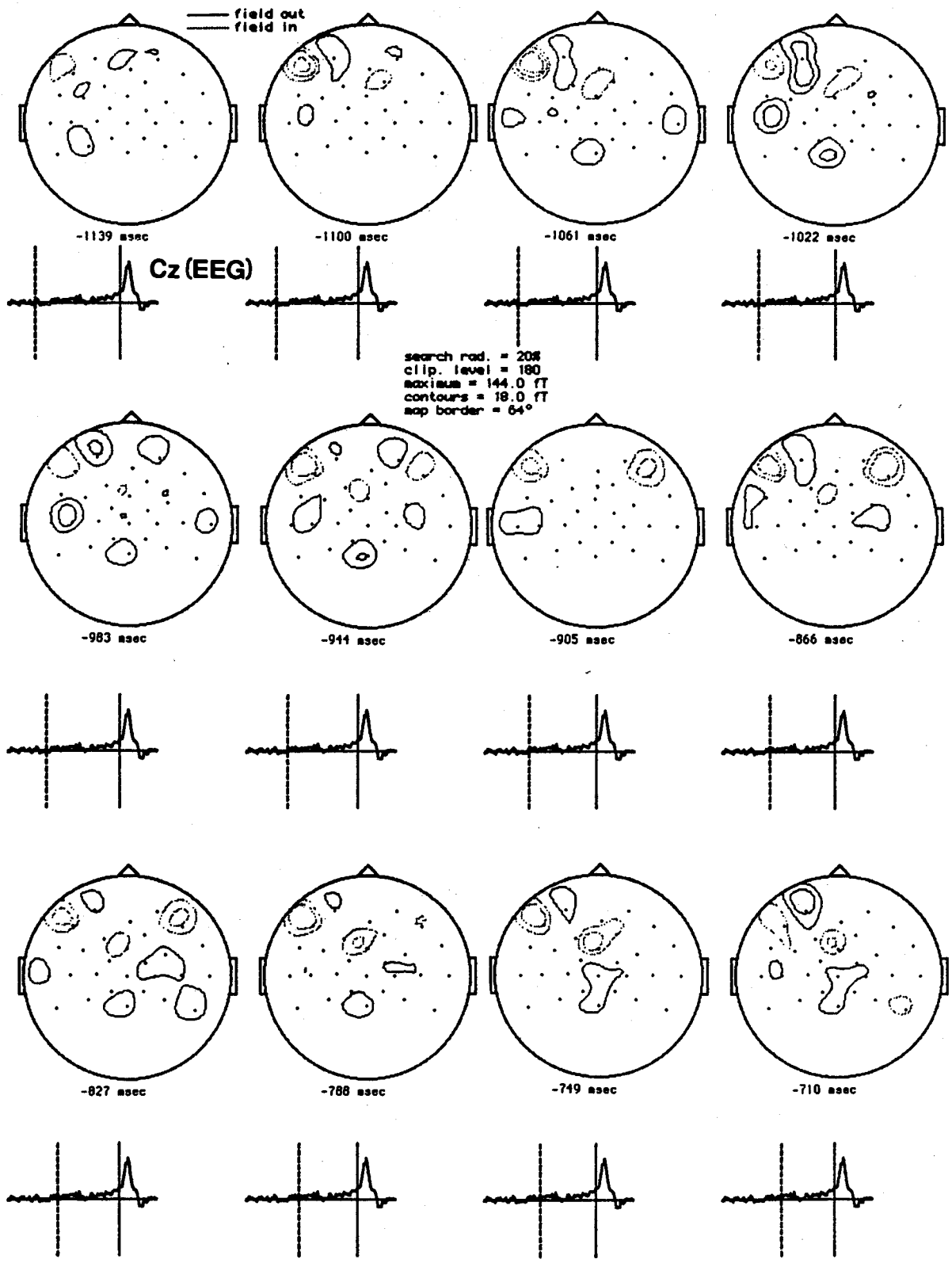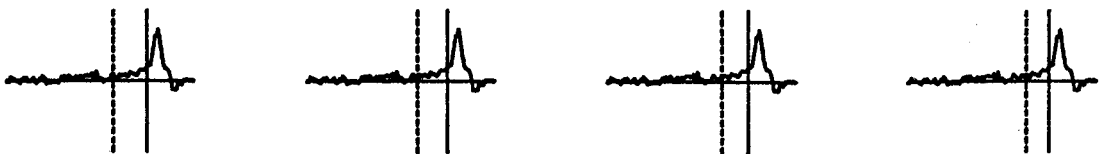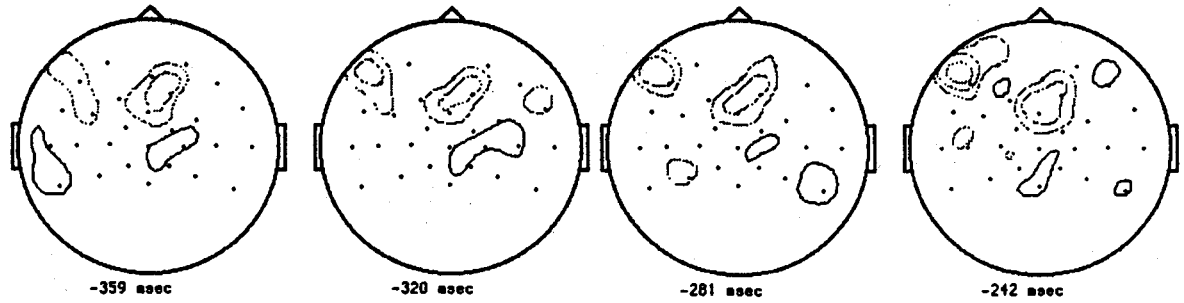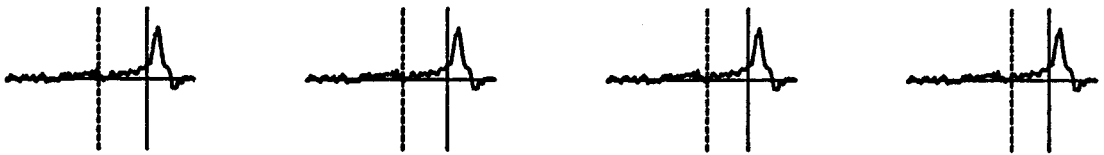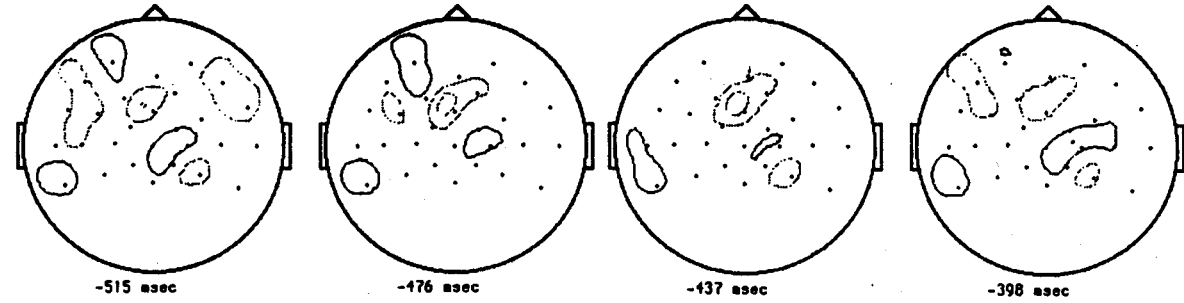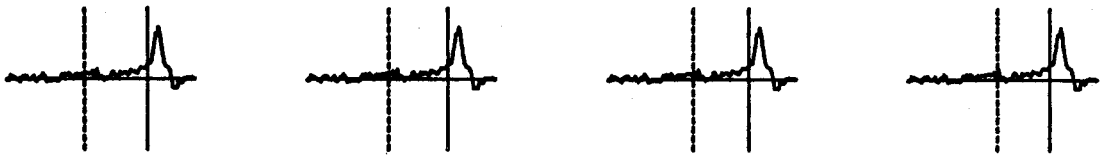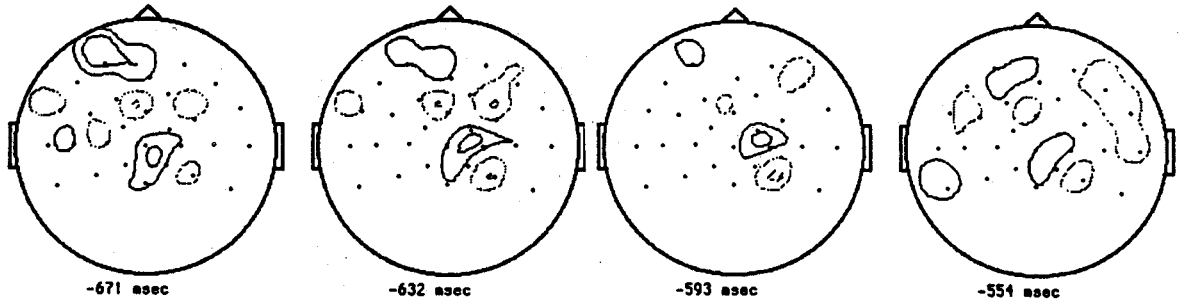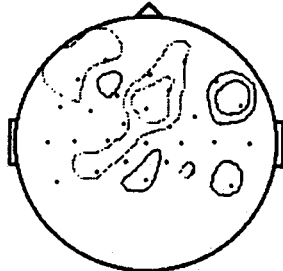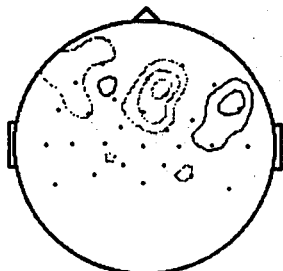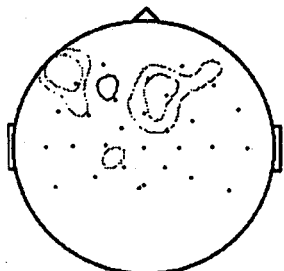
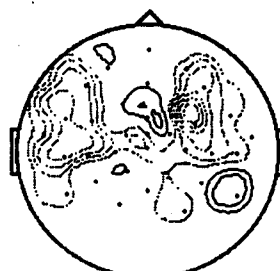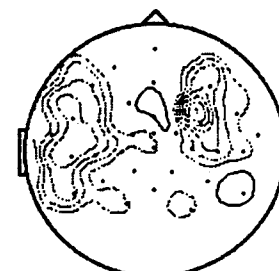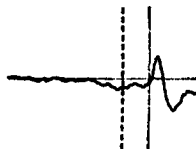-671 msec   -632 msec   -593 msec   -554 msec

-515 msec   -476 msec   -437 msec   -398 msec

-359 msec   -320 msec   -281 msec   -242 msec

-203 msec   -164 msec   -125 msec   -86 msec

-17 msec   -8 msec   31 msec   70 msec

109 msec   148 msec   187 msec   226 msec

211
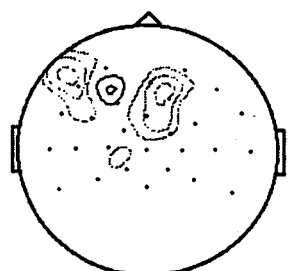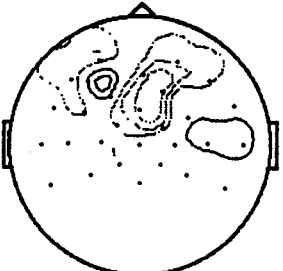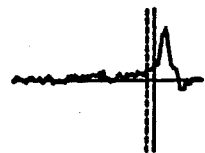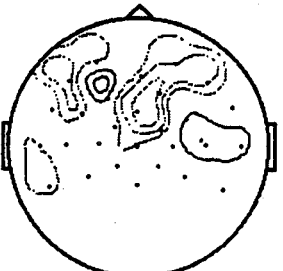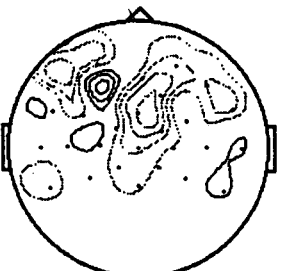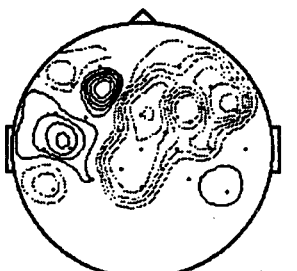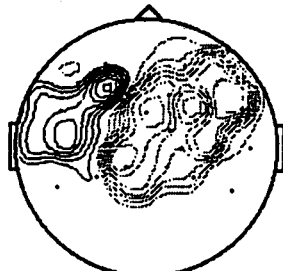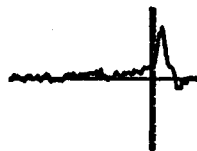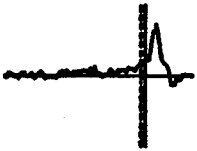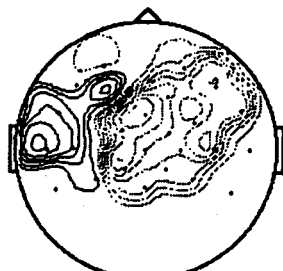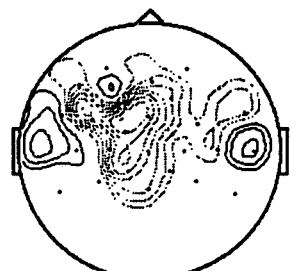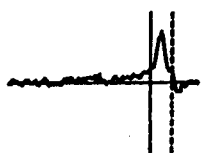
FIGURE 16.4.1. Isocontour maps of MEG activity - left finger flexion (D.C.)
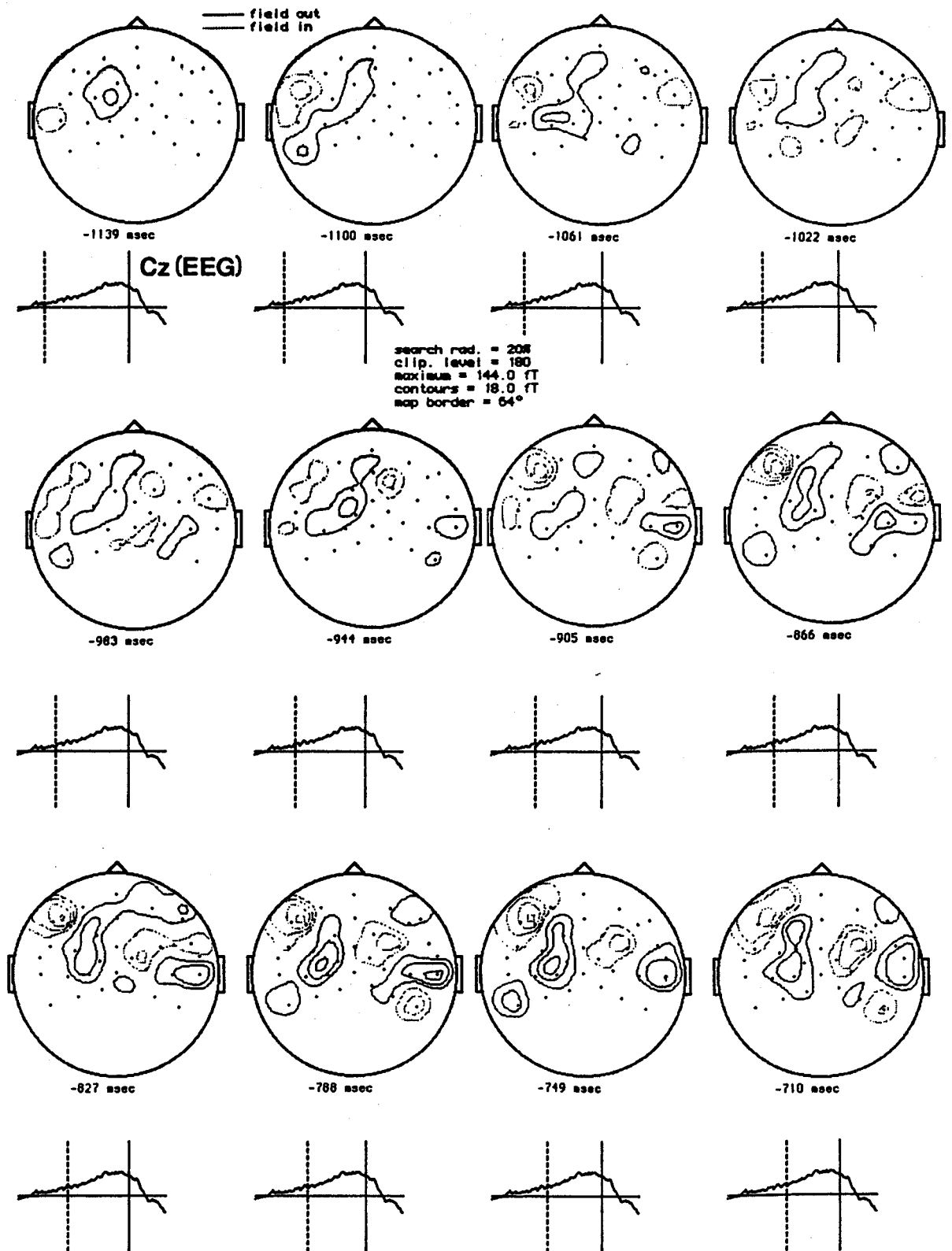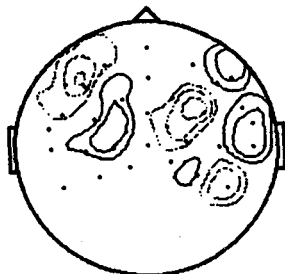
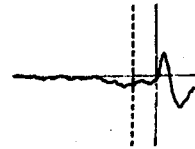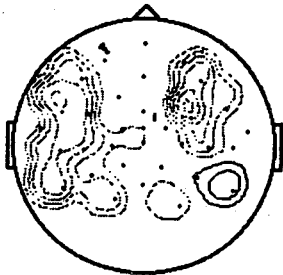-671 msec -632 msec -593 msec -554 msec
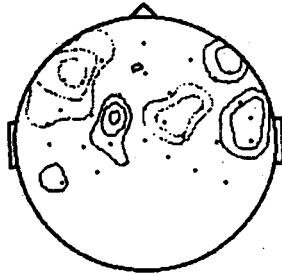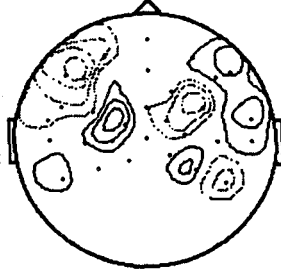
-515 msec -476 msec -437 msec -398 msec

-359 msec -320 msec -281 msec -242 msec

213

-203 msec   -164 msec   -125 msec   -86 msec

-47 msec   -8 msec   31 msec   70 msec
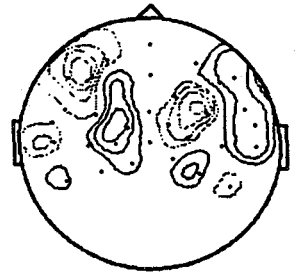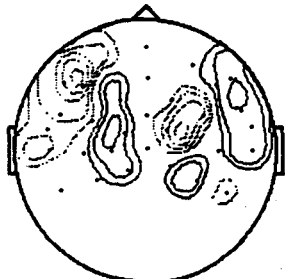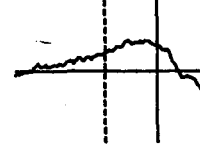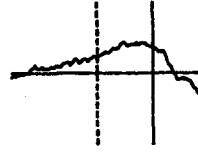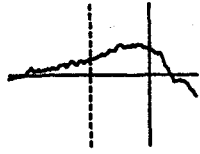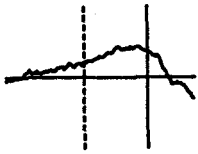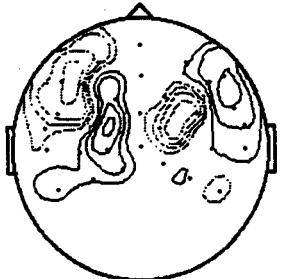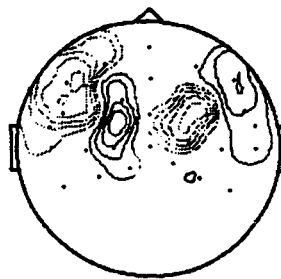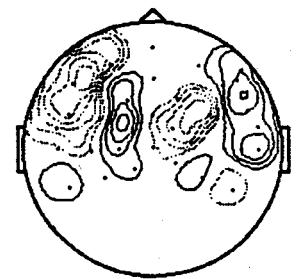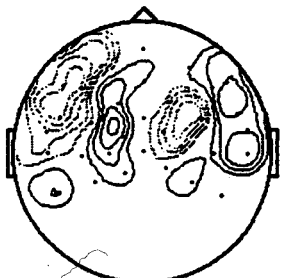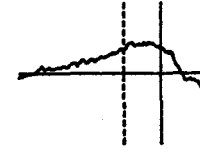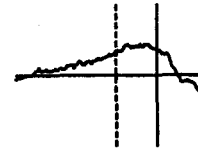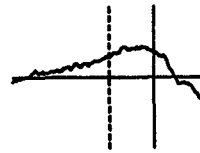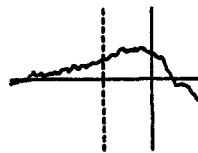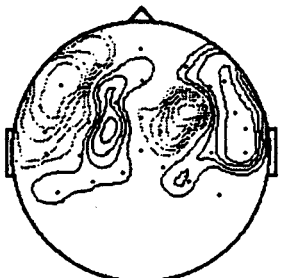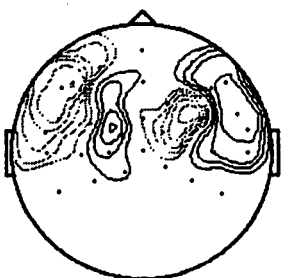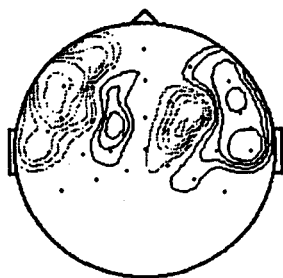
109 msec   146 msec   187 msec   226 msec
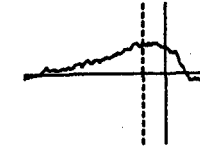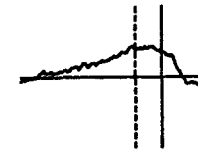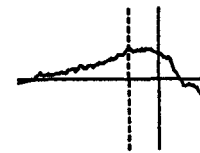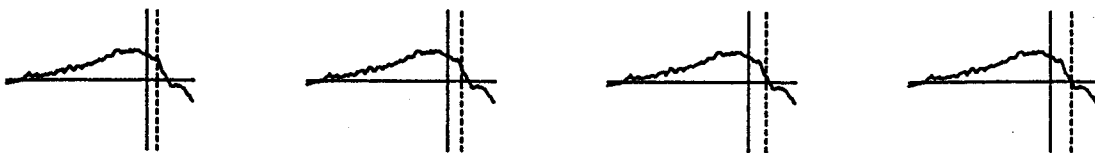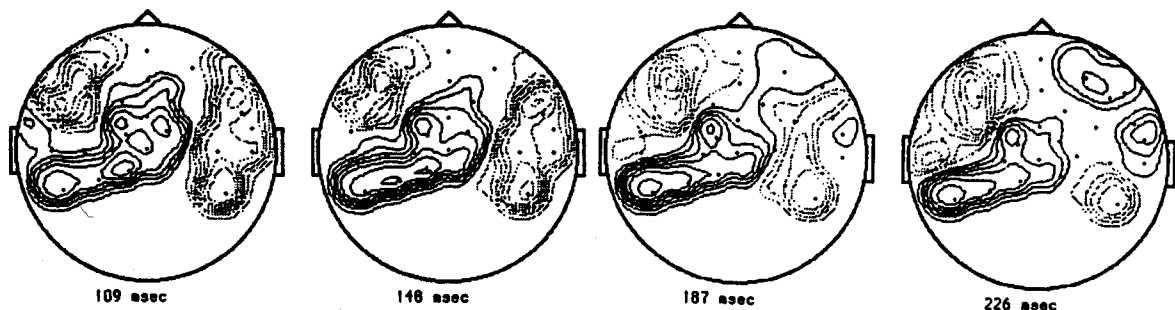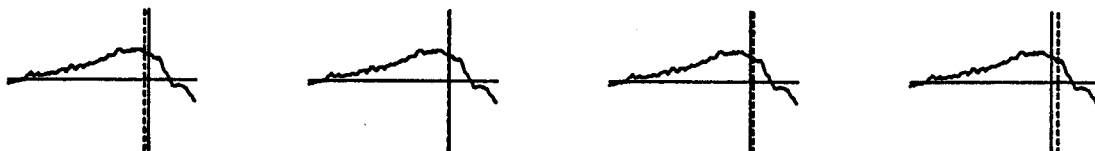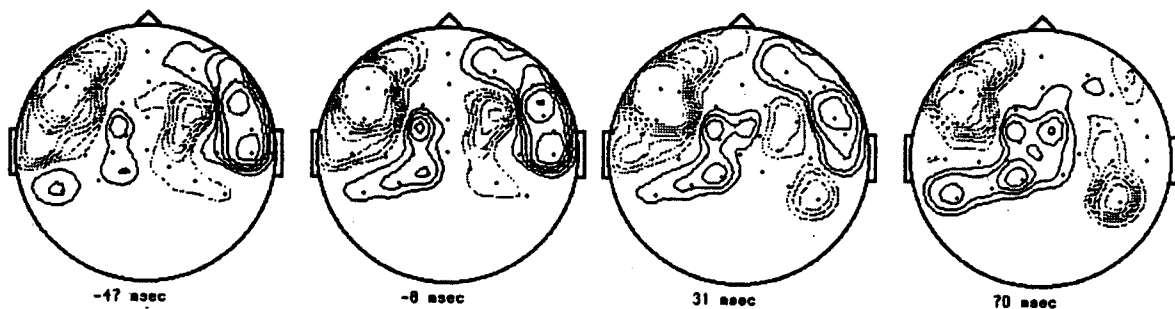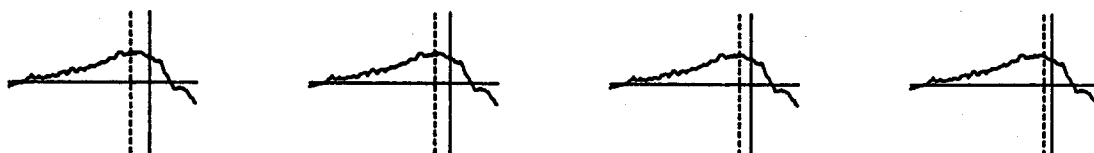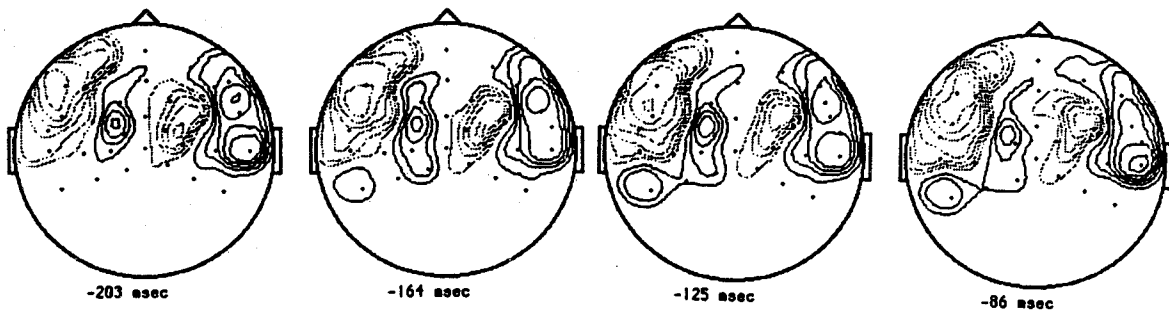
FIGURE 16.4.2. Isocontour maps of MEG activity – left finger flexion (H.W.)
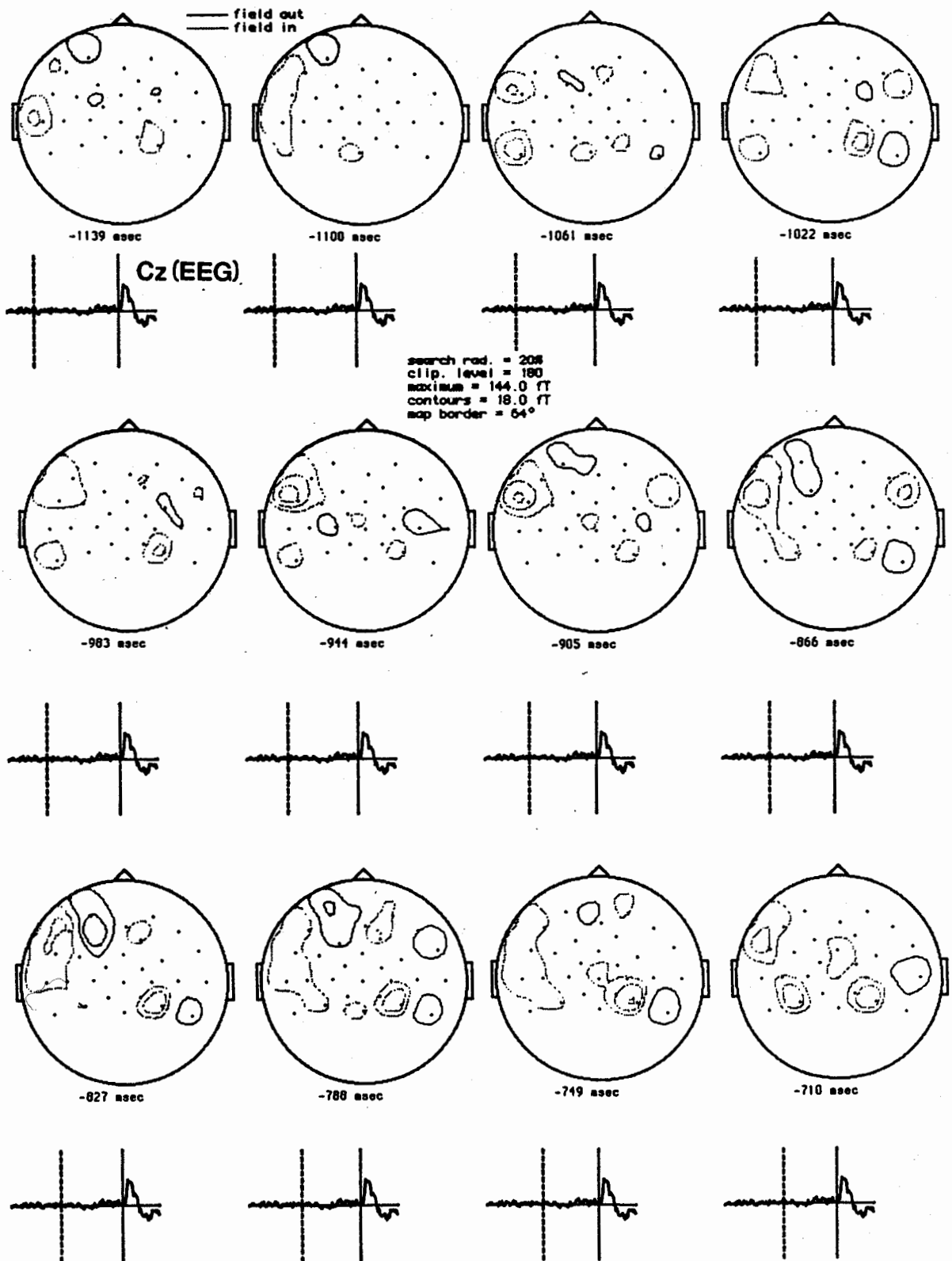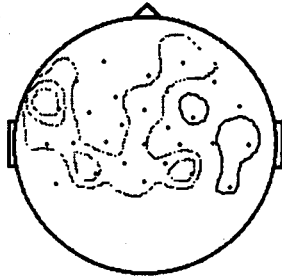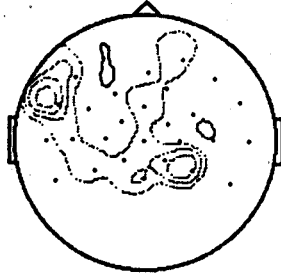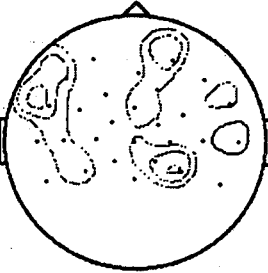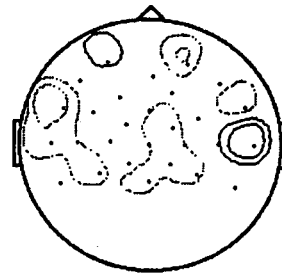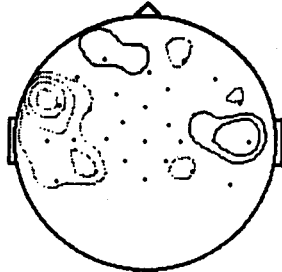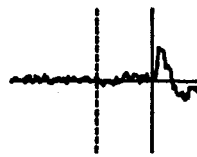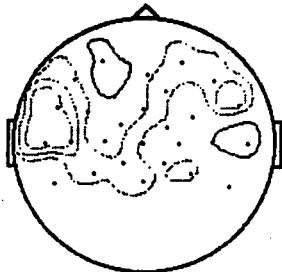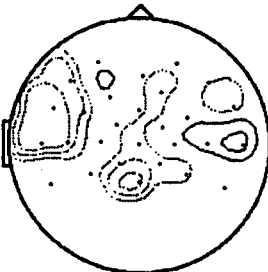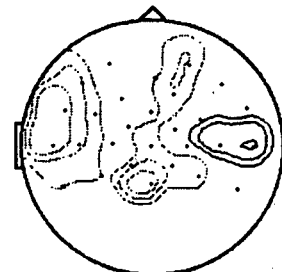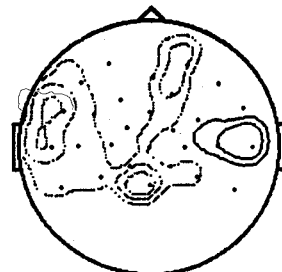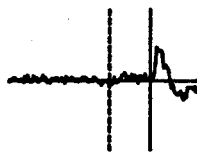
-671 msec   -632 msec   -593 msec   -554 msec

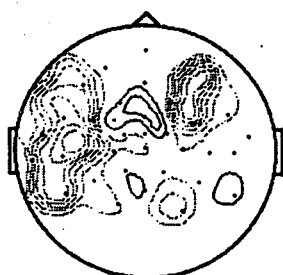-515 msec   -476 msec   -437 msec   -398 msec

-359 msec   -320 msec   -281 msec   -242 msec

216

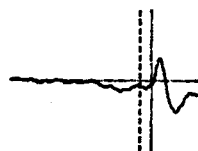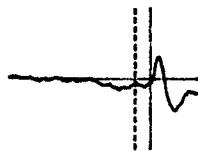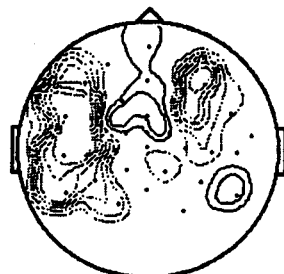-203 msec   -164 msec   -125 msec   -86 msec

-17 msec   -8 msec   31 msec   70 msec

109 msec   148 msec   187 msec   226 msec

217
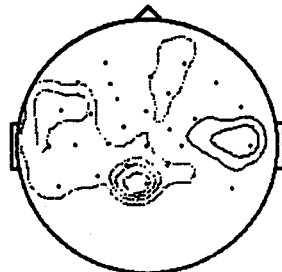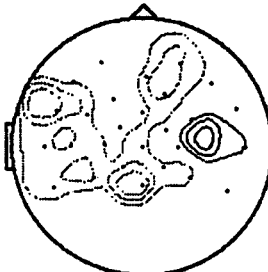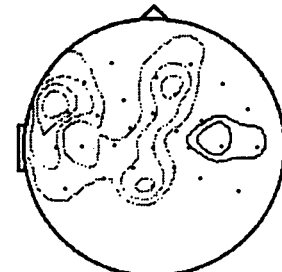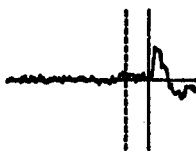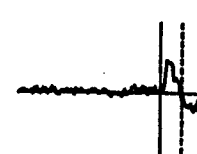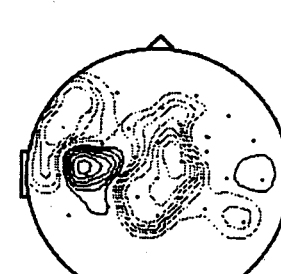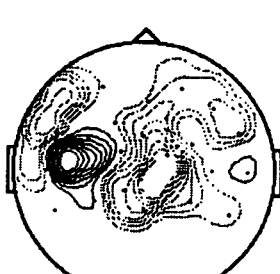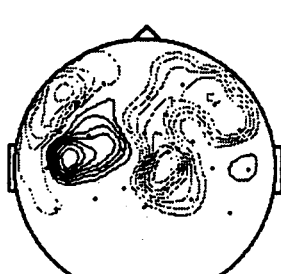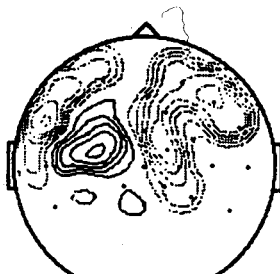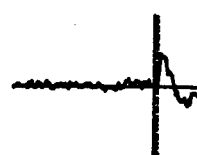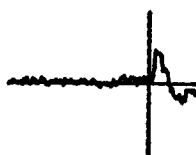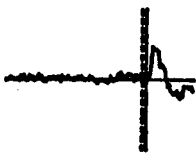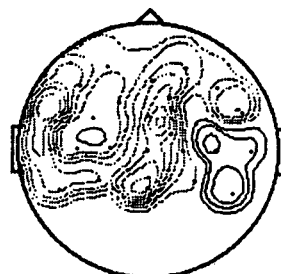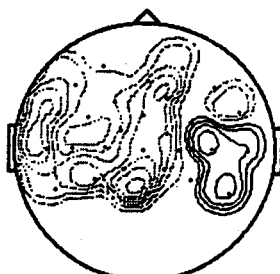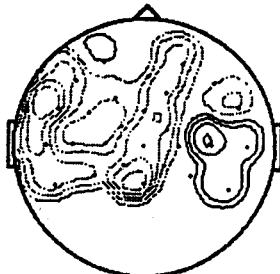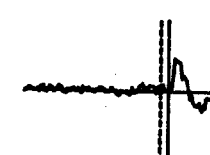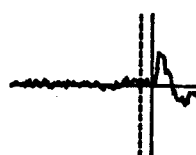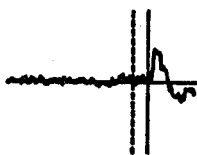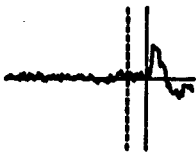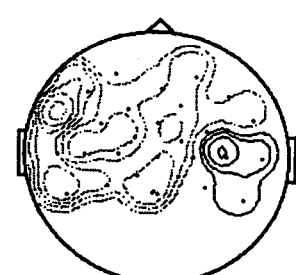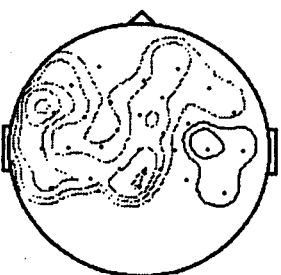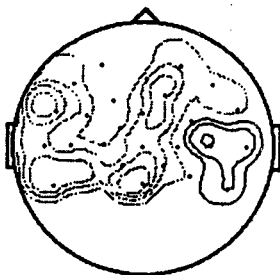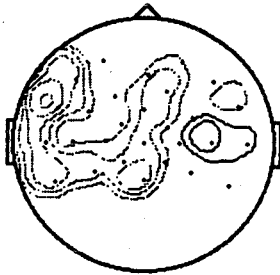
The use of the electroencephalogram to correlate changes in scalp-recorded electrical potential with sensory, motor or perceptual/cognitive events has been established as a widely used paradigm of non-invasive electrophysiological recording. The traditional application of this technique in psychophysiology has mostly involved the description of evoked "potentials", that is, waveforms that result from potential shifts between two electrodes. This involves the qualitative and quantitative analysis of waveform 'components' which appear as 'peaks' and 'troughs' (relative negativities and positivities) which occur with known latencies and amplitudes relative to some external (or covert) event. This approach has developed mainly as a result of the assumed indeterminancy with which electrical generators can be estimated from these sorts of potentials (see Appendix F) and many have favoured the use of analyses of variance in these components independently of hypothetical generators because of this purported inability to study the underlying "sources" of such potentials directly.

The analysis of potential waveforms derived between two electrodes -- the so-called active vs. referent (monopolar) derivation is a widely used, yet flawed technique, in that, there is no truly 'inactive' reference site on the body with which to compare the 'active' electrode. This seriously constrains the interpretation of "potentials" derived in this manner and can have serious consequences, particularly for cases where asymmetrical generators may be suspected or if polarity reversals are used simplistically as an indication of generator location (Nunez, 1981). However, the careful use of monopolar and bipolar EEG derivations has led

* For an extensive treatment of the concepts discussed here, see Nunez (1981).

to a number of interesting observations of event-related activity, albeit limited in their ability to estimate accurately the intracranial sources of that activity (except in the case where specific bipolar derivations can be used to infer relative differences across subjects,etc.). It is perhaps more accurate to consider the recordings taken from an EEG electrode montage as a measure of the electrical field in a volume conductor at various locations (observation points) which supposedly surround electrical generators within the volume -- all of these generators contributing to the observed field which is estimated from patterns of electrical current constrained to flow within the conductor. For activity in the range of frequencies of physiological interest, this field can be described according to electrostatic theory, provided certain assumptions are made (e.g., conductivity is linear, electric and magnetic fields are 'uncoupled'). An electrical generator (or generators) producing this type of field can be described as a <u>current</u> <u>dipole</u>, that is, a separation of charge forming a source and sink with current flow between each. The assumption of a current dipole source stems from both physiological models of current flux in neuronal columns and as a simplification of the total description of the electric field by the *multipole expansion* in which case the dipolar component best describes the source when observed at a distance (Nunez, 1981), since this decreases as the inverse of the smallest (2nd) power of distance from the dipole. This amounts to a mathematical abstraction of the source which may arise from a variety of hypothetical physiological mechanisms yet will account for most of the variance in the field.

EEG "Source Derivation" Techniques

As can be seen from the above discussion, the way in which current lines will form between the observation and reference electrodes will determine to a great extent the estimation of the electric "field" over the head. One attempt to overcome the effects of volume currents (which obscure source location) and the placement of the reference electrodes is the

application of spatial transformations to the referential recordings which eliminate the relativity to the potential at the reference electrode and the effects of current conducted through the scalp. Such transformations are sometimes referred to as "source derivation" or reference-invariant techniques. One reference-invariant application to the scalp-recorded electrical field that has been applied recently is that of the two-dimensional current source-density analysis, or Laplacian transformation. This involves estimating the change in potential gradient over the scalp (i.e., the 2nd spatial derivative of the electrical potential field using approximations of the Laplacian operator) performed on the potential at each electrode relative to some arbitrary common reference. This technique is similar to the use of current source-density analyses using in-dwelling electrodes in cortex which provide a method of estimating the strength of sources (or sinks) acting as the local generators of the field potentials around the electrode (for review see Mitzdorf, 1985). The modifications of this technique for scalp-recorded EEG data (e.g., Hjorth, 1975) provide estimates of the 'curvature' of the potential field over the scalp and therefore a better measure of "source" current flow vertically through the skull due to a cancelling-out of volume-conducted artifact currents flowing transversly through the scalp. There are limitations to this technique -- electrodes should be closely spaced and equidistant, and source estimates cannot be calculated for electrodes at the outer edge of the montage.

The analysis used for computing the Laplacian transformation of the EEG montage in the present study involves the numerical estimation of the spatial derivatives of electrical potential in two dimensions (ignoring curvature of the scalp) over the surface of the scalp recorded at one instant in time, using the finite differences method of solving partial derivatives for two independent variables. The common reference recordings provided by the EEG produce a scalar field of potential (Φ) over the head surface. The del operator (∇) applied to this scalar field (1st spatial

derivative) provides a vector field (rate of change with direction) termed the *gradient* of the potential, thus,

$$\nabla \Phi = \frac{\partial \Phi}{\partial x} i + \frac{\partial \Phi}{\partial y} j$$

Performing the del operation on this quantity, termed the *divergence* of the gradient (or the Laplacian) then provides a scalar field representing the 2nd spatial derivative of potential over the scalp as follows,

(EQ. 1)
$$\nabla \cdot \nabla \Phi = \nabla^2 \Phi = \frac{\partial^2 \Phi}{\partial x^2} + \frac{\partial^2 \Phi}{\partial y^2}$$

This is understood to represent the rate of change of the potential gradient in two orthogonal directions at each observation point which in turn may reflect current flow vertically through the scalp below each electrode (Hjorth, 1975; 1980, Nunez, 1981). Numerical approximations of the above partial derivatives have been employed taking into account the surrounding electrodes (Hjorth, 1980) or all electrodes in the montage, weighting each by the reciprocal of its distance (Doyle & Gevins, 1986; Thickbroom, Mastaglia, Carroll & Davies, 1984). Since a slightly non-equidistant montage was used, the derivation used by the latter authors was chosen to compute the Laplacian at each electrode location, normalized for distances providing a measure in units of potential measured, where,

the transformed potential, V_{Ti}, for n electrodes is given by,

(EQ. 2)
$$V_{Ti} = V_i - \left[\sum_{\substack{j=1 \\ i \neq j}}^{n} V_j/d_{ij} \Big/ \sum_{\substack{j=1 \\ i \neq j}}^{n} 1/d_{ij} \right]$$

d_{ij} = distance between electrodes i and j

(from Thickbroom *et al.*, 1984)

This transformation was implemented in a Pascal program (see Appendix G) on a microcomputer which could read in a file of electrode positions with known polar coordinates (these were derived trigonometrically and from known coordinates of the 10-20 system) and the inter-electrode distances derived approximating a spherical head surface with a mean radius of 10 cm).

APPENDIX E: TOPOGRAPHICAL ANALYSIS OF NEUROMAGNETIC FIELDS
(MAGNETOENCEPHALOGRAPHY)

The first recordings of magnetic activity of the brain were conducted by Cohen (1968) who was able to observe sinusoidal fluctuations in the magnetic field over the scalp resembling the electrical alpha rhythm using a measurement device constructed of a million-turn coil of copper wire and recording in a magnetically shielded room. Magnetic activity from the human brain had not been studied prior to this, since the fields produced by physiological activity, although relatively unaffected by intervening tissues, are extremely low in amplitude compared to the surrounding magnetic environment. Since then, the field of biomagnetism, including magnetoencephalography (MEG) has expanded rapidly into a large area of research into the magnetic fields produced by biological tissue, mainly as a result of the development of superconducting magnetometers and sophisticated noise-rejection techniques. There are a number of extensive reviews of the development and theoretical bases of biomagnetic measuring instruments. For detailed reviews see Reite and Zimmerman (1978), Williamson and Kaufman (1981), Erné (1983), Sato and Smith (1985) and Clarke (1986).

The magnetic fields produced by the brain are measured in terms of the quantity magnetic flux density and are on the order of 10^{-14} to 10^{-12} Tesla (T) (1 Telsa = 10^4 gauss). Since the surrounding magnetic environment of any measuring device is on the order of 10^{-7} T and the earth's steady field about 5×10^{-5} T (meaning that an angular vibration of the instrument of as much as 10^{-8} degrees will produce excessive noise) the activity produced by the brain can only be observed with a device with (1) extremely high sensitivity and (2) some form of common-mode rejection capability in order to achieve a suitable signal-to-noise ratio. The former is achieved by the use of a *S*uperconducting *QU*antum *I*nterference *D*evice or *SQUID* which is capable of measuring minute electrical currents or small

magnetic fields applied to such devices via superconducting coils. Superconductivity is the phenomenon whereby certain materials exhibit zero resistivity when supercooled below a critical temperature, making them very susceptible to induced current flow. Two such devices are presently being manufactured and employed in biomagnetic measurements, rf SQUID sensors and dc SQUID sensors, both of which involve conveying the field to be measured to a superconducting ring (usually constructed of a metal such as niobium which becomes superconducting when immersed in a liquid helium bath at approx. 4.2 °K or less) which has a 'weak link' or point contact in it referred to as a Josephson junction (for details see Erné, 1983; Clarke, 1986). As predicted by Nobel laureate Brian Josephson in 1962, the effects of this junction on a superconducting current induced in the ring by a magnetic field threading the ring are as follows. Normally, a current arises on the surface of the ring which prevents flux from passing through (the Meissner effect). However, an increase in the current beyond a level that can be tolerated by the weak link results in a loss of superconductivity and magnetic flux 'entering' the ring. This occurs in a stepwise manner since the superconducting current can only be mathematically described in terms of a macroscopic wavefunction whereby the magnetic flux threading the ring cannot take on arbitrary values but rather are 'quantized' in units of the ratio of Planck's constant to the charge of a superconducting electron (Cooper) pair (h/2e) known as the flux quantum Φ_0 (Φ_0 = 2.07 x 10^{-15} Wb). In addition to this 'flux quantization', a second phenomenon important to the function of SQUID sensors is that of 'Josephson tunnelling' where superconducting electron pairs pass through the high energy barrier of the weak link (thereby violating the laws of classical physics) in a manner such that an increase beyond the critical superconducting current that the junction can withstand causes a voltage and a phase difference across the junction produced by normal current flow which varies with respect to units of flux quanta. A bias current can thus be applied to the ring such that time-varying changes in the applied flux to the ring is reflected by the electronically

amplified bias current in units of flux quanta or 'phi noughts'(Φ_0). Such instruments are typically operated in a 'flux-locked mode' where the SQUID operates as a null detector in a negative feedback circuit which linearizes the output signal and increases the dynamic range of the instrument. This then allows one to obtain a linear output signal from the instrument which can be calibrated in units of tesla per phi nought. Rf SQUIDs utilize an alternating bias current in the radio frequency range (usually 20 MHz) applied to a ring with a single junction and are the most commonly used sensors at present, although dc SQUIDs are now being developed in which a dc bias current is applied to a ring containing two Josephson junctions. These devices have a ten-fold increase in sensitivity, limited only by the Nyquist noise of the electronics themselves (Clarke, 1986) and may eventually replace rf SQUIDs in biomagnetic applications.

The second requirement for the recording of MEG signals is the use of *gradiometers* (see Carelli, Modena and Romani, 1983). A single superconducting metal coil used to measure the magnetic flux passing through it and relayed to a SQUID is termed a 'flux transformer' and the entire device a 'magnetometer'. However, by turning the coil such that two loops or coils are wound in opposition, the currents induced by large fields passing through both coils will tend to cancel such that the device measures only the difference between flux at either coil, i.e., the 1st spatial derivative or gradient of the field. When one coil is placed close to the source of interest (e.g., over the scalp) the gradiometer measures primarily sources within the intercoil distance (sometimes referred to as the 'baseline') from the sensing coil. The other coil is referred to as the 'parasitic' coil and common-mode rejects the large ambient magnetic fields not produced by the source (and may also attenuate the source field to the extent it also reaches the second coil). Similarly, three sets of coils separated by some distance can be wound in opposition (the middle coil wound twice so that it has the same effective surface area as the other two coils) which measures the 2nd spatial derivative of the field.

Such devices are referred to as 2nd-order gradiometers and and are effective in producing adequate signal-to-noise ratios since magnetic noise sources, if considered as magnetic dipole sources, fall off as $1/d^3$, their gradients as $1/d^4$ and their 2nd-derivatives as $1/d^5$ (Reite and Zimmerman, 1982) therefore only sources close to the sensing coil will produce large changes in gradiometer output. 2nd-order gradiometers are the most commonly used at present, although a 3rd-order gradiometer design (Vrba *et al.*, 1982) has been found to have greater noise-rejection capability with somewhat reduced sensitivity (since an increase in the number of coils will attenuate the source field due to increased shared flux over all the coils). Obviously, various combinations of coil diameters, coil separations (baselines), and gradiometer configurations will affect the kinds of sources to which the instrument will be maximally sensitive (see Cuffin and Cohen, 1983). Basically, there is a trade-off between sensitivity to distant (deep) sources and noise-rejection with respect to baseline length and a trade-off between sensitivity to weak sources and spatial resolution with respect to sensing coil diameter. Large diameter sensing coils also make sources appear more distant than they actually are due to the spatially averaging of the coil with respect to the separation of peak ingoing and outgoing fields from some source (Williamson and Kaufman, 1981). Additionally, due to the bulkiness of the cryostatic containers necessary for these instruments, most MEG recordings to date have been conducted with single-sensor systems in which recordings must be taken one point at a time and moved sequentially over the surface of the head and the measurements repeated many times. Multiple-sensor biomagnetometers are now being developed and can improve the process of MEG data collection considerably.

Since the measurement of magnetic fields produced by the brain presents a technically difficult task one may question the interest in using biomagnetic measurements of physiological activity. There are two main characteristics of MEG measurements that make them attractive to the study of electrical sources of neural activity in the brain. (1) Magnetic fields are relatively unaffected by physical barriers such that they are not constrained by the conductivity of the surrounding media (aside from interactions with their associated electrical fields as described below). Magnetic fields 'enter' and 'exit' the head without the smearing or attenuation that occurs in electrical recordings and can actually be measured without physically touching the subject or applying conductive pastes and so on. (2) The magnetic fields can be detected by a sensor calibrated to record absolute values of magnetic flux density (or its spatial derivatives) without need of a 'reference'. Thus, MEG devices are inherently reference-free and therefore not subject to the difficulties in establishing appropriate references and baselines encountered in EEG measurements. In some cases, however, the above characteristics are problematic in that the penetrability of magnetic fields means that it is very difficult to shield the recording environment from noise (thus the need for careful gradiometer design). This also makes the instrument extremely susceptible to movement artifacts. Also, the low levels being measured by the SQUID makes it highly susceptible to so-called 1/f noise which increases dramatically at frequencies below 1 Hz. However, the main interest in using biomagnetic measurements is the increased ability to localize discrete electrical sources due to the lack of distortion of the field by overlying bone and tissues and the theoretically small contributions of diffuse volume currents to fields observed outside the head.

The measurement of magnetic flux from sources in the brain requires some detailed analysis of the kinds of fields produced by electrical
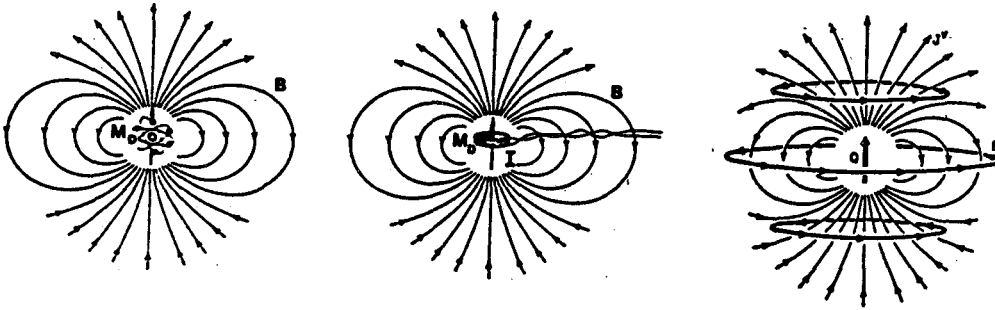
Figure A1. Magnetic field lines for three different sources. (1) Field lines for an atom having a magnetic moment M_d (left), field lines for a magnetic dipole produced by a current loop (center), and magnetic field lines and current lines (J) for a current dipole Q (right).

sources in volume-conducting media. As in the case of EEG measurements the principal magnetic field source in the CNS of functional significance is considered to be a current element which can be best modelled as the current dipole described previously. However, magnetic field sources can also be described as 'magnetic dipoles'. An important distinction between the two sources is that for magnetic dipoles the field falls off as $1/d^3$, whereas, for current dipoles it falls off as $1/d^2$ (ignoring angular dependencies) (Williamson and Kaufman, 1981). Magnetic dipoles can be produced by current 'loops' although the physiological basis of such sources is difficult to define. For current dipole sources the field strength B at any point some distance r from a current dipole vector Q is given by the Biot-Savart law as follows,

(EQ. 3) $$B = \frac{\mu_0 Q \sin\theta}{4\pi r^2}$$

$\mu_0 = 4\pi \times 10^{-7}$ N/A^2
θ = angle with respect to axis of current dipole

It should be noted that the dipole orientation for magnetic sources is

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speculated to be in the direction of in the *intracellular* currents. The extracellular (volume) currents which determine the direction of the dipole for electrical fields in this case would theoretically produce an equal but opposite field such that the net external field is zero. However, in inhomogeneous conducting media it has been shown that magnetic fields arising from electrical generators are subject to a much greater number of constraints than that of surface recorded electrical fields.

Firstly, it has been found that the transmembrane current in a neuron produces no field at large distances from the generator, most likely due to its axial symmetry and the thinness of the membrane (Swinney and Wikswo, 1980) nor do action potentials travelling down an axon since the repolarization phase follows closely the depolarization wave producing two dipoles of opposite orientation in close proximity (see Wikswo, 1983). Furthermore, the intracellular current density is measured to be two orders of magnitude greater than that of the extracellular current and except in cases where the extracellular current is constrained to flow in a manner that increases its density, it is postulated that the primary source of fields recorded from a distance is due to intracellular current (Plonsey, 1981; Okada, 1983). These so-called primary generators can then be modelled as synchronously active neuronal elements which may act as 'equivalent' (intracellular) current dipoles with opposite direction than that of the current dipoles modelled in the electrogenesis of electrical fields. Secondary sources of observed fields are postulated to arise at boundaries of conducting media with differing resistivities, as in the case of multiple concentric-sphere models of the head, due to perturbations of the volume currents (Tripp, 1981; Okada, 1983; Nunez, 1986b).

A second condition important to the observation of external magnetic fields is the effects of spherical conducting media on generators of various orientation. It has been shown that for a tangential dipole in a slab of infinite extent that intervening media between the current dipole and the point of measurement causes no distortion of the normal component

of the field (Baule and McFee, 1965). However, in cases of conducting volumes with spherical symmetry, a dipole which has axial symmetry produce no external field because the field from its volume currents cancels the field from the primary source itself (Baule and McFee, 1965; Geselowitz, 1970; Grynzspan and Geselowitz, 1973; Cuffin and Cohen, 1977). Also, small departures from a perfect sphere produce only small changes in the observed field patterns (Cuffin and Cohen, 1977; Tripp, 1979). Furthermore, it is assumed that secondary sources from volume currents due to tangential primary sources are radially oriented and therefore do not contribute to the radial (normal to the scalp) component of the external field but do contribute to the tangential component of the field (Cohen and Hosaka, 1976; Okada, 1983).

These lines of argument form the basis of a fundamental assumption in MEG measurement namely that, **the normal component of the magnetic fields measured at the scalp arises principally from the tangential component of primary generators in the brain which reflect intracellular current flow.** This of course differs from electrical fields which are due to both tangential and radial components of dipole sources. Thus, in recording the MEG the sensing coil is usually oriented normal to the scalp (i.e., normal to the spherical surface approximated by the head surface) such that the recorded field changes can be interpreted in terms of a simple generator or set of generators with minimal contribution from volume currents. Therefore, evoked or event-related magnetic fields (ERMFs) should, in theory, produce surface patterns which more accurately reflect the location and extent of discrete dipole sources. However, a significant limitation of these measurements is that *radially* oriented sources are not detected in MEG. Thus, the MEG technique is assumed to be maximally sensitive to neural sources which are tangential to the surface of the scalp or have a significant tangential component. Again, pyramidal cells in cortex provide the most likely candidate for sources of dense intracellular current flow with a uniform orientation for large numbers of cells. MEG field patterns

would therefore reflect active areas of cortex in sulci or gyri oriented
perpendicular to the scalp, for example, the anterior and posterior banks
of the central sulcus (areas 4 and 3b) or some regions of the superior
surface of the temporal lobe (e.g., Heschl's gyri). Estimates of the
strength of dipoles of this nature are in the range of dipole moments of 2
to 20 nA·m (Brenner *et al.*, 1978).

Given these simplifying assumptions of field generators and taking
into consideration the angular dependencies of the normal (radial)
components of fields produced by eccentric tangential dipoles based on the
Biot-Savart law, the field strength in the *radial* direction at any point P
on the sphere of radius R (as shown in Fig. A2) is given by the equation,

(EQ. 4)
$$B_r = \frac{\mu_0 Q}{4\pi d^2} \left[\frac{b/d\cos\phi\sin\theta}{1 + 2bR/d^2(1 - \cos\theta)} \right]^{3/2}$$

(from Williamson and Kaufman, 1981)

where, μ_0 is the permeability of free space, Q is the dipole moment and
the values b, d and R and angles ϕ and θ are as shown in Fig. A2. It can
be seen that the radial component of the field is zero directly over the
dipole ($\sin(0°) = 0$) so that a null region exists between two maxima which
occur on either side of the dipole where the radial component is greatest
at a fixed angle for a dipole of depth d. Also, the field from a

tangentially oriented dipole vanishes as the source approaches the center of the sphere (b/d → 0) and dipole at the center of the sphere produces no external field since it has axial symmetry in all orientations. Based on calculations by Okada (1986) it is suggested that deep sources (as much as 10% from the sphere center) should produce detectable fields if the (tangential) generator is of sufficient strength to produce an electrical maxima of about 10 μV at the surface of a 10 cm radius head. However, as can be seen from EQ. 1, such a field diminishes rapidly once the source is very near (e.g., 1 cm) to the center of the sphere.

APPENDIX F: SOURCE LOCALIZATION TECHNIQUES -- CURRENT DIPOLE MODELLING AND THE INVERSE PROBLEM

Recent studies using current source-density techniques provide some empirical support for the hypothesis that pyramidal cells activated in cortex can produce sources and sinks which would act as dipole moments producing homogeneous field potentials. Thus, generators of electrical potentials associated with this kind of cortical activation may be sought as likely candidates for the neural "sources" of evoked activity of the brain. Although the inhomogeneity and unique tropicity of the brain and skull present problems for the estimation of field potential patterns measured at the scalp, it can be stated, that based on limited experimental evidence that computed fields of this nature are relatively insensitive to variations of conductivity of the brain and its coverings (Vaughan, 1982; Henderson, Butler and Glass, 1975). It is acknowledged by the above authors, however, that there are three main factors affecting the localization of dipole sources based on their field potentials: (1) attenuation the fields by the skull (2) "smearing" of the potential gradients and (3) deviation of the skull shape from a perfect sphere. The attenuation effect has been mentioned above and the "smearing" of the field potential is thought to be due to the greater conductance of the skull bone laterally than through its thickness, causing the signal to 'spread out' over the surface of the head. It is stated that both attenuation and smearing will not affect accuracy of the estimated location of a dipole source but will increase the overall error between the computed field for a dipole and the observed field for that dipole (Henderson, Butler and Glass, 1975). Also, the skull is usually thinner at vertex and this might lead to the estimated dipole locations being displaced slightly 'upward'. The shape of the human head would indicate that it might be better modelled as a prolate sphere although this complicates the computation of sources greatly. Presently, no solutions to this problem have been devised and anatomical variability of head shape remains a persistent problem in the

analysis of electrical sources in the brain.

Given the above assumptions, generators of EEG potentials may be modelled as current dipoles arranged in planes such as to represent the sulci and gyri of the cortical surface of the brain. This can only be considered in cases where cortical activation is considered to be relatively 'focal' producing a well localized dipole source. Accordingly, a small 3-dimensional layer polarized across its thickness may be conceptualized as an "equivalent dipole" source. In cases where the area of cortex is larger and curved due to convolutions then the source may be modeled as a complex vector sum of dipoles of different orientations (Henderson, Butler and Glass, 1975; Wood, 1982). The physiological interpretation of equivalent dipole sources raises larger issues related to neurophysiological theory of brain function which must be addressed in the attempt to localize discrete neural generators of evoked potential activity. In the case of a number of distributed sources in the brain following from the principle of superposition, first described by Helmholtz in the mid-19th century, there is a theoretically infinite number of source configurations which can give rise to the same surface field pattern (Wilson and Bayley, 1950; Plonsey, 1963; 1969). Thus, in the attempt to localize a source or number of sources for a given distribution of potentials on the scalp surface, one runs head-on into the so-called "inverse problem" - the fact that source configurations determined from surface patterns are non-unique and therefore no one solution can be shown to be necessarily the "correct" one. For this reason, the inverse solution cannot be practically applied for the localization of dipole sources from field potentials. Alternatively, the approach that is used is that of the 'forward' or 'direct' solution, whereby, given an assumed electrical source of known location and magnitude, the surface field pattern can then be calculated and compared with the observed field. This involves using field equations from electrostatic and magnetostatic theory to calculate the surface potentials or fields for a hypothetical source (or sources), and

varying the location of the source in order to achieve a best-fit for the predicted data to the observed data. This can now be efficiently achieved using computerized iterative least-squares fitting routines. The use of these source localization methods for electrical data involves estimating the significant distortions of the surface field that occurs as a result of the varying resistivities of the tissues in the scalp, largely, the differences between brain tissue, meninges, skull, and scalp. In vitro modelling studies have further demonstrated that the effects of these differences are small and relatively symmetrical over the surface of the scalp, and can be adequately modelled as concentric layers in a spherical approximation of the head (Kavanagh et al., 1978). An important aspect of this method, however, is the need for some subjective estimation of the number of sources and their location that one would theoretically suspect for a given pattern of activity. This often involves a consideration of the paradigm being used (for instance, for visual hemifield stimulation, one would expect a unilateral generator in the vicinity of the contralateral primary visual cortex) and an examination of the pattern of activity corresponding to the event (for example, a single dipole source should produce a "dipolar" pattern on the scalp in many instances, depending on the dipole orientation). Thus, the usefulness of the source localization methods utilizing the forward solution depends on the ability to hypothesize a priori sources for a given pattern of activity and to then test these hypothetical sources for 'goodness of fit' to the observed data. The primary means of achieving these estimates therefore requires an accurate method of measuring patterns of current flow on the surface of the head related to underlying generators (and not due to tangential current flow through the scalp due to muscle artifact or other noise) and a means of displaying this information in order to estimate the number and location of these sources.

In the case of neuromagnetic measurements, the application of the forward solution shows even more promise since the fields are theoretically

undistorted and can be calculated by appropriate derivations of the
Biot-Savart law as described in Appendix E. Attempts to localize dipole
sources based on the separation of magnetic field maxima have been
initially attempted on the basis that, for a simple dipolar field produced
by a single generator, the depth can be deduce from the angular separation
of the field maxima such that,

$$depth = separation/\sqrt{2}$$

assuming a constant radius and normality of the sensing coil to a perfect
sphere (Willamson and Kaufman, 1981). The surface area of the sensing coil
produces some error since it spatially averages the field detected at the
scalp producing deeper and stronger dipole estimates. Corrections can be
applied for this error (Williamson and Kaufman, 1981, p. 371) for a known
gradiometer configuration. Errors are found to be about 6% when the coil
diameter is 1/2 the maxima separation distance and increases sharply as the
diameter approaches this distance. Dipole localization methods have more
recently been applied based on the forward technique using least-squares
fitting routines (Okada, 1985; Weinberg, Brickett, Coolsma and Baff, 1986;
Romani and Leoni, 1985; Hämäläinen, Ilmoniemi, Knuutila and Reinikinen,
1985). The method described by Okada (1985) estimated a surface position
and orientation for the dipole based on maxima separation and then used a
least-squares fitting routine for estimates of depth and strength of the
dipole. This technique found goodness-of-fit estimates for single dipole
fits for data showing relatively simple field patterns. More complex
fitting routines have been applied which take into acount the varying radii
of each observation point and performing iterative least-squares fits for
five parameters specifying dipole location (Romani and Leoni, 1985;
Weinberg, Brickett, Coolsma and Baff, 1986). The advantage of this
technique is that it does not require the subjective localization of two
"peaks" or field maxima in the scalp distribution in order to fit a single
dipole, moreover, more complex field patterns (two or more dipoles
patterns) can be computed and assessed in terms of 'goodness of fit'
criteria. The study by Weinberg, Brickett, Coolsma and Baff (1986) found

good agreement between observed fields and fields calculated using a least-squares fitting routine for current dipoles implanted in a simulated head model filled with a uniform conducting medium. The least-squares method provided greater accuracy than the 'peak-location' method using maxima separation when varying radii of each recording position were included in the calculations (using a multi-sphere model of the head) and was able to provide good localization estimates when the "peaks" were excluded from the data set, whereas, a large increase in error occured for this condition using the peak location method.

APPENDIX G: PASCAL PROGRAMS

```
PROGRAM LTransform (input, output);

{program to read position file and perform Laplacian transformation on the number of data points}
{specified in the menu - reads ASCII data files with contiguous time points for up to 30 sequential}
{ positions (averages) and stores them in the same format. The position file should specify the number}
{of positions followed by the polar coordinates for each position, declination angle followed by azimuth}
{in degrees in the same order as in the data files.}

{written in LightSpeed Pascal V1.11 by D. Cheyne}

  CONST
    pi = 3.1415926;
    dtor = 0.01745327;
    MaxNumPts = 30;
  TYPE
    datArray = ARRAY[1..512, 1..30] OF integer;
    datArrayPtr = ^datArray;
  VAR
    npos, npoints : integer;
    dname, outfilename : STRING;
    posarray : ARRAY[1..MaxNumPts, 1..2] OF real;
    darray : datArrayPtr;
    tdarray : datArrayPtr;
    weightarray : ARRAY[1..MaxNumPts, 1..MaxNumPts] OF integer;
    key : char;

  FUNCTION ArcLength (theta1, phi1, theta2, phi2 : real) : integer;
  {computes arc length for sphere, radius = 10 cm}
    VAR
      a, b, c, d, gamma : real;
  BEGIN
    a := cos(theta1) * cos(theta2);
    b := sin(theta1) * sin(theta2) * cos(phi1 - phi2);
    c := a + b;
    d := -c * c + 1;
    IF d = 0 THEN
      d := 0.0000001;  {avoid SANE floating point error}
    gamma := -arctan(c / sqrt(d)) + 1.5708;  {arccosine of c}
    ArcLength := trunc(gamma * 100);
  END;

  FUNCTION Laplacian (thePoint, thePosition : integer) : integer;
    VAR
      j : integer;
      num, denom, numsum, denomsum, weight : real;
  BEGIN
    numsum := 0;
    denomsum := 0;
    BEGIN  {summation}
      FOR j := 1 TO npos DO
        BEGIN {loop}
          IF j <> thePosition THEN
            BEGIN
              IF j > thePosition THEN
                weight := weightarray[j, thePosition] / 10    {weights stored in }
              ELSE                   {triangular matrix}
                weight := weightarray[thePosition, j] / 10;
              num := darray^[thePoint, j] / weight;
              denom := 1 / weight;
```

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```
              numsum := numsum + num;
          denomsum := denomsum + denom;
        END;
      END; (loop)
    END; (summation)
    Laplacian := round(darray^[thePoint, thePosition] - (numsum / denomsum));
END;

PROCEDURE Calltext;
  VAR
    window : Rect;
BEGIN
  SetRect(window, 1, 270, 512, 350);
  SetTextRect(window);
  Showtext;
END;

PROCEDURE ReadPositions;
  VAR
    r, phi, theta, d : real;
    pname : STRING;
    k : integer;
    posfile : text;
BEGIN (read positions)
  pname := OldFileName('');
  IF pname = ' ' THEN
    ExitToShell;
  open(posfile, pname);
  read(posfile, npos);
  FOR k := 1 TO npos DO
    BEGIN
      read(posfile, theta, phi);
      posarray[k, 1] := theta;   (declination angle)
      posarray[k, 2] := phi;     (azimuth angle)
    END;
  close(posfile);
END;

PROCEDURE CallMenu;
BEGIN
  Calltext;
  writeln('enter position file');
  ReadPositions;
  Calltext;
  writeln(npos : 1, ' positions entered');
  writeln('enter data file name');
  dname := OldFileName('');
  IF dname = ' ' THEN
    ExitToShell;
  Calltext;
  writeln('enter * of sequential time points in file');
  readln(npoints);
  writeln('enter name for output file');
  readln(outfilename);
END;

PROCEDURE GetDistanceWeights;
  VAR
    i, j, idist : integer;
```

```
        theta1, theta2, phi1, phi2 : real;
BEGIN
 writeln('calculating interelectrode distances ');
 FOR i := 1 TO npos DO
   FOR j := 1 TO npos DO
     BEGIN
       IF j < i THEN
         BEGIN {loop}
           theta1 := posarray[i, 1] * dtor;
           theta2 := posarray[j, 1] * dtor;
           IF theta1 = 0 THEN          {check for special cases}
             idist := trunc(theta2 * 100)   {arclength in mm, R=10 cm}
           ELSE IF theta2 = 0 THEN
             idist := trunc(theta1 * 100)
           ELSE
             BEGIN   {compute arc length}
               phi1 := posarray[i, 2] * dtor;
               phi2 := posarray[j, 2] * dtor;
               idist := ArcLength(theta1, phi1, theta2, phi2);
             END;
           weightarray[i, j] := idist;
         END; {loop}
     END;
END;


PROCEDURE ReadDataFile;          {read transposed files}
 VAR                {ie., points are contiguous variable}
   i, j : integer;
   datafile : text;
   afloat : real;
BEGIN
 open(datafile, dname);
 writeln('Reading data from file ', dname);
 FOR j := 1 TO npos DO
   FOR i := 1 TO npoints DO
     BEGIN
       read(datafile, afloat);
       darray^[i, j] := round(afloat);  {to handle real data files}
     END;
 close(datafile);
END;


PROCEDURE WriteDataFile;          {points are contiguous}
 VAR
   outfile : text;
   i, j, linecount : integer;
BEGIN
 open(outfile, outfilename);
 writeln('');
 writeln('Writing transformed data to file ', outfilename);
 linecount := 0;
 FOR j := 1 TO npos DO
   FOR i := 1 TO npoints DO
     BEGIN
       IF linecount = 8 THEN
         BEGIN
           writeln(outfile, ' ');
           linecount := 0;
         END;
```

```pascal
          write(outfile, tdarray^[i, j]);
          linecount := linecount + 1;
        END;
    writeln(outfile, ' ');   {avoid eof error}
    close(outfile);
  END;

  PROCEDURE MainLoop;
   VAR
     i, j : integer;
  BEGIN
   Calltext; {clear screen}
   writeln('calculating value for point: ');
   FOR i := 1 TO npoints DO
     BEGIN {a time point}
       writeln(i : 3);
       FOR j := 1 TO npos DO
         BEGIN {do transform}
           tdarray^[i, j] := Laplacian(i, j);
         END;
     END;   {a time point}
  END;

BEGIN {main program}
 HideAll;
 CallMenu;
 GetDistanceWeights;
 REPEAT
   BEGIN
     new(darray);
     new(tdarray);
     ReadDataFile;
     MainLoop;
     WriteDataFile;
     dispose(darray);
     dispose(tdarray);
     writeln('Recycle for same positions [r] or exit [e] ? ');
     readln(key);
   END;
 UNTIL key = 'e';
END.
```

```
PROGRAM Map (input, output);

(************************************************************)
(   This program creates interpolated maps from data read from disk files created)
(   for further display on screen as colour, gray scale or line isocontour  projections)
(   using linear interpolation of data found within a specified search radius.)


(   Written in Lightspeed Pascal (version 1.11) by D. Cheyne , 1987)
(   Interpolation algorithm by Dr. P. Brickett)
(   Line Contour Drawing routine adapted from P. D. Bourke. BYTE, June 1987)


{Program Input :)
{npos:    number of positons)
{theta (1..n):   angles of declination from vertex of map (in degrees))
(phi (1..n): azimuthal angles, counterclockwise from top of map (in degrees))
(data file (1..n): sequential data for each positions in integer or floating point)
(Position file format — ASCII   with number of positions followed by coordinates)
(           eg.,npos theta1 phi1   theta2  phi2 ...... etc.)


(Data file format  -- ASCII file  of sequential data for above points)


(************************************************************)



(main routine should call the following procedures )

   PROCEDURE InitData;
    VAR
     k : integer;
     d : real;
   BEGIN
    IF mnum = 1 THEN
      BEGIN (open data file)
       open(datafile, dname);
      END;
    FOR k := 1 TO npos DO
      BEGIN
       read(datafile, d);
       darray[k] := (d / dmax) * 1000; (normalize data)
      END;
    IF mnum = nmap THEN
      close(datafile);
   END;

   PROCEDURE InitGrid;  (convert positions to integer for interpolation)
    VAR
     i, j : real;
     k : integer;
   BEGIN
    FOR k := 1 TO npos DO
      BEGIN
       i := posarray[k, 3] * mapscale;  (grid = mapSize x mapSize, radius = 25, origin=25,25)
       j := posarray[k, 4] * mapscale;
       intarray[k, 1] := trunc(i * mapradius + xmaporigin);
       intarray[k, 2] := trunc((-j) * mapradius + ymaporigin);
      END;
   END;

   PROCEDURE Interpolate;    (Paul's algorithm)
```

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```pascal
VAR
  delx, srSqr, dely, point, i, j, k : integer;
  wsum, weight, weightPt : real;
  di, di2 : integer;
  startTime : longint;
  passFlag : boolean;
BEGIN (search by columns then rows on virtual integer grid)
  startTime := TickCount;
  srSqr := sqr(sr);
  FOR i := 1 TO mapSize DO
    FOR j := 1 TO mapSize DO
      BEGIN
        passFlag := false;
        wsum := 0;
        weight := 0;
        FOR k := 1 TO npos DO (check positions)
          BEGIN
            dely := j - intarray[k, 2];
            delx := i - intarray[k, 1];
            IF (abs(dely) < sr) AND (abs(delx) < sr) THEN
              BEGIN
                di2 := sqr(delx) + sqr(dely) + 1;
                IF di2 < srSqr THEN    (include this position in weighting)
                  BEGIN
                    passFlag := true;
                    weightPt := (sr / sqrt(di2)) - 1; (weight by inverse of dist)
                    wsum := wsum + weightPt;
                    weight := weight + (weightPt * darray[k]);
                  END;
              END;
          END; (positions)
        IF NOT passFlag THEN
          BEGIN
            dplane[i, j] := 0;
          END
        ELSE
          BEGIN
            weight := weight / wsum;
            IF weight > 32767 THEN
              weight := 32767
            ELSE IF weight < -32767 THEN
              weight := -32767;
            dplane[i, j] := trunc(weight);
          END;
      END;(i,j)
  startTime := TickCount - startTime;
  writeLn('Interpol. time = ', startTime DIV 60 + 1, ' sec');
END;

PROCEDURE Filter;        (2-d spatial, brick-wall filter )
  VAR              (3 points, 2 passes)
    pass, i, j, sum : integer;
    pstring : STRING;
BEGIN
  FOR pass := 1 TO 2 DO
    BEGIN (pass)
      pstring := StringOf(pass : 1);
      writeln('filtering - pass ', pstring);
(filter columns)
```

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```
        FOR i := 1 TO mapSize DO
          FOR j := 2 TO mapSize - 1 DO
            IF dplane[i, j] <> -5000 THEN
              BEGIN
                sum := dplane[i, j] + dplane[i, j + 1] + dplane[i, j - 1];
                dplane[i, j] := sum DIV 3;
              END;
{filter rows}
          FOR j := 1 TO mapSize DO
            FOR i := 2 TO mapSize - 1 DO
              IF dplane[i, j] <> -5000 THEN
                BEGIN
                  sum := dplane[i, j] + dplane[i + 1, j] + dplane[i - 1, j];
                  dplane[i, j] := sum DIV 3;
                END;
      END;  {pass}
   END;
```

{**** Maplane is rectangular array MapSize X MapSize which contains the interpolated }
{values. The resolution of interpolation is specified by MapSize (50x50 is suggested) and}
{can by passed to the appropriate drawing routines to produce maps on screen or other }
{output devices. ClipData clips values to a 16 level integer scale for gray scale or colour}
{map. Contour data save the full range of values for contour drawing routines.}

```
  PROCEDURE clipData (count : integer);  {clip data for colour/gray scale}
    CONST
      scale = 1000;         {clipping level}
      max = 16;             {0..16 levels}
    VAR
      i, j, icn : integer;
      cn, halfMax : real;
  BEGIN
    halfMax := max / 2;
    FOR i := 1 TO mapSize DO
      FOR j := 1 TO mapSize DO
        BEGIN
          cn := ((dplane[i, j] / scale) * halfMax) + halfMax;
          icn := trunc(cn);
          IF icn < 0 THEN
            icn := 0
          ELSE IF icn > max THEN
            icn := max;
          MapPlane[count]^[i, j] := icn;
        END;
  END;

  PROCEDURE ContourData (count : integer);  {save full range for contours}
    VAR
      i, j : integer;
  BEGIN
    FOR i := 1 TO mapSize DO
      FOR j := 1 TO mapSize DO
        BEGIN
          MapPlane[count]^[i, j] := dplane[i, j];
        END;
  END;
```

```
{contour drawing segment for interpolated data - uses stored array of data points }
{stored in MapPlane() which is MapSize X MapSize in dimension. Data should }

{written in LightSpeed Pascal V 1.11  for Macintosh/Macintosh II by D. Cheyne}
{- adapted from QuickBasic version by P.D. Bourke (1987) }

FUNCTION getdmin (i, j : integer) : real;
 VAR
  min : real;
BEGIN               {find lowest vertex}
 IF d^[i, j] < d^[i, j + 1] THEN
  min := d^[i, j]
 ELSE
  min := d^[i, j + 1];
 IF d^[i + 1, j] < min THEN
  min := d^[i + 1, j];
 IF d^[i + 1, j + 1] < min THEN
  min := d^[i + 1, j + 1];
 getdmin := min;
END;


FUNCTION getdmax (i, j : integer) : real;
 VAR
  max : real;
BEGIN               {find the highest vertex}
 IF d^[i, j] > d^[i, j + 1] THEN
  max := d^[i, j]
 ELSE
  max := d^[i, j + 1];
 IF d^[i + 1, j] > max THEN
  max := d^[i + 1, j];
 IF d^[i + 1, j + 1] > max THEN
  max := d^[i + 1, j + 1];
 getdmax := max;
END;


FUNCTION cross_prod (a, b, c, d : real) : real;
BEGIN
 cross_prod := (a * d - b * c) / (a - b);
END;


PROCEDURE drawcontour;  {(x1, y1, x2, y2 : real;  pentype : integer);}
 VAR
  h1, h2, v1, v2 : integer;
BEGIN
 CASE pentype OF
  1 :
   PenPat(black);
  2 :
   PenPat(ltGray);
  3 :
   PenPat(gray);
 END;
 h1 := trunc(x1);
 v1 := trunc(y1);
 h2 := trunc(x2);
 v2 := trunc(y2);
 MoveTo(h1,  v1);
 LineTo(h2,  v2);
```

```
    PenNormal;
END;

PROCEDURE InitContourRoutine;   {called once}
  VAR
    i : integer;
BEGIN
  xub := mapSize;
  yub := mapSize;

  im[0] := 0;          {mapping from i,j to rectangle offsets}
  im[1] := 1;
  im[2] := 1;
  im[3] := 0;
  jm[0] := 0;
  jm[1] := 0;
  jm[2] := 1;
  jm[3] := 1;

  LUT[0, 0, 0] := 0;          {contour case look-up table}
  LUT[0, 0, 1] := 0;
  LUT[0, 0, 2] := 8;
  LUT[0, 1, 0] := 0;
  LUT[0, 1, 1] := 2;
  LUT[0, 1, 2] := 5;
  LUT[0, 2, 0] := 7;
  LUT[0, 2, 1] := 6;
  LUT[0, 2, 2] := 9;
  LUT[1, 0, 0] := 0;
  LUT[1, 0, 1] := 3;
  LUT[1, 0, 2] := 4;
  LUT[1, 1, 0] := 1;
  LUT[1, 1, 1] := 3;
  LUT[1, 1, 2] := 1;
  LUT[1, 2, 0] := 4;
  LUT[1, 2, 1] := 3;
  LUT[1, 2, 2] := 0;
  LUT[2, 0, 0] := 9;
  LUT[2, 0, 1] := 6;
  LUT[2, 0, 2] := 7;
  LUT[2, 1, 0] := 5;
  LUT[2, 1, 1] := 2;
  LUT[2, 1, 2] := 0;
  LUT[2, 2, 0] := 8;
  LUT[2, 2, 1] := 0;
  LUT[2, 2, 2] := 0;
  BEGIN {contour levels}
    FOR i := 0 TO numcontours DO
      BEGIN
        z[i] := (i - (numcontours / 2)) / (numcontours / 2);
      END;
  END;              {contours levels}
END;

PROCEDURE Initialize;       {initilize coordinates for contours}
  VAR
    i, xoffset, yoffset, blocksize : integer;
BEGIN
  blocksize := 4;
```

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      xoffset := trunc(xscreenorigin - screenradius - (blocksize / 2));
      yoffset := trunc(yscreenorigin - screenradius - (blocksize / 2));
      BEGIN
        FOR i := 1 TO xub DO
          x[i] := (i - 1) * blocksize + 2 + xoffset;
        FOR i := 1 TO yub DO
          y[i] := (i - 1) * blocksize + 2 + yoffset;
      END;
    END;

PROCEDURE GetData;   (uses count: integer)
  VAR
    i, j : integer;
  BEGIN
    FOR i := 1 TO mapSize DO
      FOR j := 1 TO mapSize DO
        BEGIN                    (puts data into real array)
          d^[i, j] := MapPlane[count]^[i, j] / 1000.0;   (forces float  -1 to +1)
        END;
  END;

PROCEDURE DoContours;

  VAR
    i, j, k, m, n, icase, linetype : integer;
    dmin, dmax, x1, x2, y1, y2 : real;
    m1, m2, m3 : integer;
    h : ARRAY[0..4] OF real;
    ish : ARRAY[0..4] OF integer;
    xh : ARRAY[0..4] OF real;
    yh : ARRAY[0..4] OF real;

BEGIN
  Initialize;
  BEGIN
    writeln('computing  contours');
    FOR j := 2 TO mapSize - 1 DO
      FOR i := 2 TO mapSize - 1 DO
        BEGIN (main loop)
          dmin := getdmin(i, j);
          dmax := getdmax(i, j);
          IF dmin + dmax <> 0 THEN
            BEGIN   (contour routine)
              IF (dmax >= z[0]) AND (dmin <= z[numcontours - 1]) THEN (in contour range)
                BEGIN (draw contour for this box)
                  FOR k := 0 TO numcontours DO
                    IF k <> (numcontours DIV 2) THEN    (don't show zero line)
                      BEGIN
                        IF (k > -1) AND (k < (numcontours DIV 2)) THEN
                          linetype := 1;
                        IF (k > (numcontours DIV 2)) AND (k < numcontours + 1) THEN
                          linetype := 3;
                        BEGIN
                          IF (z[k] >= dmin) AND (z[k] <= dmax) THEN (check again?)
                            BEGIN (some in triangle)
                              FOR m := 4 DOWNTO 0 DO
                                BEGIN
                                  IF m > 0 THEN
                                    BEGIN
```

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```
            h[m] := d^[i + im[m - 1], j + jm[m - 1]] - z[k];
            xh[m] := x[i + im[m - 1]];
            yh[m] := y[j + jm[m - 1]];
          END;
        IF m = 0 THEN
          BEGIN
            h[0] := (h[1] + h[2] + h[3] + h[4]) / 4;
            xh[0] := (x[i] + x[i + 1]) / 2;
            yh[0] := (y[j] + y[j + 1]) / 2;
          END;
        IF h[m] > 0 THEN
          ish[m] := 2
        ELSE IF h[m] < 0 THEN
          ish[m] := 0
        ELSE
          ish[m] := 1;
      END;[ downto]
    FOR m := 1 TO 4 DO
      BEGIN [scan each triangle]
        m1 := m;
        m2 := 0;
        m3 := m + 1;
        IF m3 = 5 THEN
          m3 := 1;
        icase := LUT[ish[m1], ish[m2], ish[m3]];
        CASE icase OF
          0 :
            ;  [do nothing]
          1 : [line between vertices n1 and n2]
            BEGIN
              x1 := xh[m1];
              y1 := yh[m1];
              x2 := xh[m2];
              y2 := yh[m2];
              drawcontour(x1, y1, x2, y2, linetype);
            END;
          2 : [line between vertices m2 and m3]
            BEGIN
              x1 := xh[m2];
              y1 := yh[m2];
              x2 := xh[m3];
              y2 := yh[m3];
              drawcontour(x1, y1, x2, y2, linetype);
            END;
          3 : [line between vertices m3 and m1]
            BEGIN
              x1 := xh[m3];
              y1 := yh[m3];
              x2 := xh[m1];
              y2 := yh[m1];
              drawcontour(x1, y1, x2, y2, linetype);
            END;
          4 :[line between vertex m1 and side m2-m3]
            BEGIN
              x1 := xh[m1];
              y1 := yh[m1];
              x2 := cross_prod(h[m3], h[m2], xh[m3], xh[m2]);
              y2 := cross_prod(h[m3], h[m2], yh[m3], yh[m2]);
              drawcontour(x1, y1, x2, y2, linetype);
```

```
                                    END;
                        5 : (line between vertex m2 and side m3-m1)
                           BEGIN
                             x1 := xh[m2];
                             y1 := yh[m2];
                             x2 := cross_prod(h[m1], h[m3], xh[m1], xh[m3]);
                             y2 := cross_prod(h[m1], h[m3], yh[m1], yh[m3]);
                             drawcontour(x1, y1, x2, y2, linetype);
                           END;
                        6 : (line between vertex m3 and side m1-m2)
                           BEGIN
                             x1 := xh[m3];
                             y1 := yh[m3];
                             x2 := cross_prod(h[m2], h[m1], xh[m2], xh[m1]);
                             y2 := cross_prod(h[m2], h[m1], yh[m2], yh[m1]);
                             drawcontour(x1, y1, x2, y2, linetype);
                           END;
                        7 : ( line between sides m1-m2 and m2-m3)
                           BEGIN
                             x1 := cross_prod(h[m2], h[m1], xh[m2], xh[m1]);
                             y1 := cross_prod(h[m2], h[m1], yh[m2], yh[m1]);
                             x2 := cross_prod(h[m3], h[m2], xh[m3], xh[m2]);
                             y2 := cross_prod(h[m3], h[m2], yh[m3], yh[m2]);
                             drawcontour(x1, y1, x2, y2, linetype);
                           END;
                        8 : (line betwen sides m2-m3 and m3-m2)
                           BEGIN
                             x1 := cross_prod(h[m3], h[m2], xh[m3], xh[m2]);
                             y1 := cross_prod(h[m3], h[m2], yh[m3], yh[m2]);
                             x2 := cross_prod(h[m1], h[m3], xh[m1], xh[m3]);
                             y2 := cross_prod(h[m1], h[m3], yh[m1], yh[m3]);
                             drawcontour(x1, y1, x2, y2, linetype);
                           END;
                        9 : (line between sides m3-m1 and m1-m2)
                           BEGIN
                             x1 := cross_prod(h[m1], h[m3], xh[m1], xh[m3]);
                             y1 := cross_prod(h[m1], h[m3], yh[m1], yh[m3]);
                             x2 := cross_prod(h[m2], h[m1], xh[m2], xh[m1]);
                             y2 := cross_prod(h[m2], h[m1], yh[m2], yh[m1]);
                             drawcontour(x1, y1, x2, y2, linetype);
                           END;
                       END;(case)
                     END;(scan/ next m)
                   END;(in triangle/ next k)
                 END;(for this box)
               END  (contour routine )
           END;  (for case k of)
       END;(routine)
     END;(i,j loop)
  END;(main loop)
END;
```

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