EVOKED RESPONSE PATTERN AND RECOVERY CYCLES IN HUMAN SUBJECTS

by

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I INTRODUCTION

By definition evoked potentials are "the detectable electrical changes in the brain in response to deliberate stimulation of any part of the nervous system" (16). The importance of recording human brain responses to controlled sensory stimuli is well recognized. These responses represent, in fact, the end product of a long series of events in the nervous system from the peripheral receptor organs, through many interneurones and relay stations, up to the cortical neurones which participate in their production. Any change, physiological, chemical or pathological, occurring anywhere along their paths may be reflected in the recorded evoked responses. It is conceivable, therefore, that the study of these electrophysiological data can yield useful information about the functional state of the nervous system. They can also, when correlated with behavioural and mental changes in the individual, become of considerable value in psychophysiological investigations. W. Grey Walter rightly said in 1950 that:

> "The future of applied electrophysiology lies not so much in the elaboration and standardisation of recording technique, nor yet in the accretion of overwhelming statistics; but in the combination of these with carefully planned experiments designed to evoke in the central nervous system activity of a known or

predictable extent and modality" (21).

The evoked responses are so small in relation to the "spontaneous" background activity of the brain that they are difficult or impossible to detect in the usual electroencephalogram. With the new averaging techniques, however, these responses can be extracted from other existing potentials and recorded from scalp electrodes. Various systems for the extraction of brain signals have been developed and described in the last few years. Many of these can process the evoked neuroelectric signals with great speed and a high degree of precision but are, however, very complex and costly. Contributions to the development of relatively less complicated and less expensive averaging systems have been made recently in the Electrophysiology Laboratory of the Allan Memorial Institute (26), (27).

A considerable amount of work on the average responses to various sensory modalities in man has accumulated over the last few years. This work has been directed mainly toward the study of the morphology of the average responses, their distribution, and their relation to changes in the parameters of the stimulus or to changes in the subject's psychophysiological state. This neurophysiological technique has also found some clinical application.

Shagass and Schwartz (71), (72) have measured the recovery cycles of the early components of the somatosensory evoked responses both in normal and in psychiatric patients. They found that the recovery cycles in certain psychiatric diagnostic categories differed from normal, and that the recovery cycles of "psychotic" depressive patients differed from those of "neurotic" depressive patients. The methods and procedures used by these workers in reaching their results were laborious and impractical for use in a large patient population. Their results, however, opened new issues for further psychophysiological investigations of cerebral responsiveness in mental illness.

Other aspects of the evoked sensory responses seem also to be correlated with the subjective state of the individual. In fact, some studies have indicated that the late components of the sensory evoked responses were related to psychological phenomena (41), (66), (57), (23). The late components of the average somatosensory evoked responses have been less studied in comparison to the late components of responses evoked by other sensory modalities, particularly, the visual responses (20), (22), (9), (23).

This study has several aims, including an extensive review of the literature on evoked responses in relation not only to the present work, but also to provide a basis for future studies in this field.

The purpose of the experiments themselves is to investigate certain aspects of the average somatosensory evoked responses such as their pattern, their distribution and the recovery functions of their early components. This will provide us with data about these aspects of the responses in normal subjects, and will constitute a useful basis for the comparison of data obtained from psychiatric patients in later investigations. Other aims are to investigate the relation of these responses to artifacts as well as to some evoked phenomena in the normal electroencephalogram. We further propose to compare our results with the results obtained in recent studies by Shagass and Schwartz (69), (71), Allison (3), and Goff *et al.*(45). In order to make this comparison we have used various recording techniques, including those used in the above stated studies.

II REVIEW OF THE LITERATURE

1. Animal studies on evoked responses

a. Methods and aims of such studies

The introduction of the cathode ray oscillograph has given impetus to the study of the electrical activity of the nervous system. The early studies were performed on acute preparations or deeply anaesthetized animals. With progressive refinement in the recording techniques, the brain's electrical activity could be studied in the non-anaesthetized unrestrained animal, and correlated simultaneously with the animal's behaviour under various conditions. The recording with macro-electrodes directly from the exposed cortex or from sub-cortical structures can now also be supplemented by intracellular recordings with implanted microelectrodes in the intact conscious animal. The early experiments were carried out on animals under deep barbiturate anaesthesia which causes the depression of the "spontaneous activity" (background noise) of the brain, thus improving the signal-to-noise ratio (33), (35), (1), (60).

The technique of evoked response recording has been used to study: i) the effect and action of drugs and anaesthetics (33), (1), (40), (12), (53); ii) the anatomical and functional organization of the nervous system (13), (53), (2); iii) the topographical organization of the sensory cortex (60), (62), (1), (77); iv) the cerebral responsiveness and the effect of different states of alertness (8), (49), (40), (53), (34), (67); v) the electrical correlates of conditioning, learning, sensory performance and different mental states such as habituation, attention, etc. (38), (51); vi) the electrical behaviour of single cortical cells to peripheral stimulation (4), (5).

It is, however, important to recognize in evaluating these studies that the responses obtained depend greatly on a number of experimental parameters, e.g. the type and depth of anaesthesia, the site of recording, the nature of the stimulus, etc.

Most of the sensory modalities have been used to evoke responses in the brain, however, the best studied sensory systems are the visual, somesthetic and auditory. Since in this study electric shocks to peripheral nerves have been exclusively employed, we shall mainly restrict our historical review to findings related to the somesthetic system and the somatosensory cortex.

b. Somatosensory evoked responses recorded from the primary projection area

Among the first workers who recorded evoked responses from the somatosensory projection area were Marshall *et al*.(60), Forbes and Morison (35), Adrian (1), Marshall *et al*. (62). Their experiments were carried out on deeply or moderately anaesthetized animals. Several mammalian species were investigated but the cat and monkey brain have been the most studied. In these experiments either a cutaneous stimulation in the form of a single touch (60), (62), or an electrical stimulation applied to a superficial peripheral nerve (35), (63) were used to evoke activity which was directly recorded from the brain with gross electrodes. The response obtained under these conditions was a short latency, localized, usually surface positive potential called the primary response. This response was known since the early part of the century but it was only in 1937 that Marshall _et al_. (60) made use of it to study the functional organization of the sensory cortex. Since then, many workers have endeavoured to localize and map the sensory receiving areas of the cortex for different sensory modalities in different species of animals. Since this early component is quite stable and of sufficiently high amplitude to be detected, it was found amenable to study, and its characteristics are now well known.

This response is usually surface positive and monophasic. When chloralose anaesthesia is used it may become initially surface negative and diphasic (74). Its latency in the cat or the monkey varies between 5-20 msec., according to the areas of the body stimulated (60), (35), (1), (12). Its amplitude ranges up to 0.5 millivolt (1) and its duration is about 10-30 msec. (1), (2).

With a somesthetic stimulation it is recorded from the contralateral somatosensory area. The tactile representation of the body was found to correspond roughly to the motor points on the precentral gyrus by Marshall _et al_.(60), except for a small part of the face, which is represented in the ipsilateral somatosensory area (79). A somatic area II has also been described; it is less well organized topographically and it responds to bilateral peripheral stimulation (1), (77), (78), (79).

On the primary receiving area the response is less localized under light anaesthesia than under deep anaesthesia, and is occasionally associated with a repetitive after-discharge of 10 to 20 cycles per sec. which progressively diminishes in amplitude (1).

The primary response recorded from the cortex can follow a peripheral stimulation frequency up to 5 per sec. according to the degree of anaesthesia, and it disappears at a frequency of 12-15 per sec. (63), (60). Its characteristics, particularly its short latency, localization, stable pattern, rapid recovery and relative resistance to barbiturates suggested that it was carried to the cortex through the specific ascending pathways (1), (63). In fact, it can be recorded or elicited along any part of these pathways up to the specific cortex.

The mechanisms by which the surface positive wave is produced are not yet definitely known. Chang considers the primary response as consisting of presynaptic and postsynaptic potentials. The former, of very short duration, are due to activity in thalamocortical fibres and the latter, constituting the main part of the surface positive wave, are due to "the propagation of nerve impulses along the vertically oriented apical dendrites of different sized cortical pyramids." (16).

It is important to recognize the action of central regulatory mechanisms and background states on evoked cortical responses. In fact, upon arrival at the cortex, an afferent impulse can be modified in relation to the spontaneous cortical activity (8), the cortico-thalamic excitability (16), (15), or the influence of other afferent stimuli (nociceptive) (44). The effect of reticular stimulation has been demonstrated by King *et al*. (53), Bremer (10), Gauthier *et al*. (42), Schwartz and Shagass (68). All pointed out that such stimulation will depress a peripherally evoked primary response.

In addition to the short latency response (primary response), and the repetitive after-discharge, long latency responses are also recorded from the specific primary projection area. Schwartz and Shagass (67), using an averaging technique, recorded both short and long latency responses from the somatic and auditory areas in response to peripheral electric shocks and clicks respectively. Torres and Warner (73) recorded in the cat both early and late responses to photic stimuli from the primary visual area. Buser and Borenstein (12) demonstrated on non-anaesthetized, curarized cats, that late components ("secondary responses") evoked by stimuli belonging to a different sensory modality could be recorded in the auditory and visual cortex but not in the somatic cortex. Brazier (9) recorded from the primary visual area of the cat both early and late components in response to photic stimuli but found that the late components were not diffuse and could be recorded only from the primary visual area.

c. Somatosensory evoked responses recorded from areas other than the primary projection area

There is a fair agreement about the nature and characteristics of the early component of the evoked potentials which is localized in the primary receiving areas and carried up to the cortex through the "classic" specific sensory pathways. It is generally designated as the primary response. On the other hand, different types of later components have been described by various authors and no definite agreement has yet been reached as to their physiological nature and functional significance. Several names, some well established, have been applied to describe them, however, they share in common longer latencies, a widespread distribution and greater lability than the early component.

In 1936, Derbyshire _et al_. (33) first described in the deeply anaesthetized cat, following sciatic nerve stimulation, a long latency widespread cortical potential. It could only be obtained when the level of anaesthesia was deep enough to abolish the spontaneous cortical activity. This response was termed by Forbes and Morison (35) the "secondary discharge" to distinguish it from the primary response. It is characterized by a latency of about 40-80 msec., a similar or somewhat longer duration and a recovery time of greater than one sec. It disappears with a stimulation frequency greater than 3 per sec.

French, Verzeano and Magoun (36), (37), by stimulating the medial brain stem reticular formation, recorded a similar diffuse cortical response which was, however, diminished or abolished by anaesthetics. These authors also contrasted the properties of the medially and laterally situated ascending sensory pathways, by recording from these sites responses evoked by various peripheral stimuli. They found that "the medially conducted potentials exhibited slower conduction, common transport for all modalities and distribution to wide areas of the cortex by way of the diffuse thalamic projection system". The medial but not the lateral pathways were found to be sensitive to anaesthetics. The characteristics of the long latency secondary discharge, as well as the selective action of the anaesthetics on the medial system were attributed in part to the multisynaptic nature of this system.

Purpura (64) studied further the "secondary discharge" in anaesthetized cats and found that it could be evoked by peripheral electrical shocks or by stimulation of the medial brain stem reticular formation. This response was found to be rather diffusely distributed with its maximal amplitude occurring bilaterally in the anterior lateral gyrus. It was predominantly surface positive, its pattern changing according to the cortical area from which it was recorded.

In 1954, Amassian (5), experimenting on cats under chloralose anaesthesia, recorded from the somesthetic association area a positive wave of 15-32 msec. latency, in response to stimulation of any limb. This response showed blocking interaction between afferent impulses from different parts of the body as well as between afferent impulses belonging to various sensory modalities. Amassian's "association area positive responses" seem, however, different from the responses recorded from Purpura, as they are dependent on sensorimotor cortical relay and are abolished by barbiturates. Single unit analysis in this area revealed that the same cell responded to stimulation at various peripheral sites and of various sensory modalities, but with different discharge patterns.

Buser and Borenstein (12) revealed the true complexity of the late components which they designated as "secondary responses". Their experiments were conducted on unanaesthetized, curarized cats using a photographic superimposition technique. The responses they recorded were widespread but maximal in the "associative" cortex comprising the suprasylvian area and anterior lateral gyrus. They could be evoked by different sensory modalities, and showed great variation in their form, latency, and amplitude, in contrast to the primary response. These authors also demonstrated under curarization or light chloralose anaesthesia that there were three distinct cortical areas where dynamic interactions occurred between responses to somesthetic, auditory or visual stimuli when applied in pairs, simultaneously or successively. These interaction areas were situated between the primary projection areas of the respective paired modalities. In an interaction area the "secondary response" to a particular stimulus was either inhibited or augmented by a stimulus of the complementary modality according to the experimental parameters.

In another study (13) the same workers found that barbiturates depressed the secondary responses while chloralose augmented them. They also demonstrated the independent nature of the secondary responses in that the destruction of the primary receiving area did not affect them.

Albe-Fessard <u>et al</u>. (2) demonstrated in the monkey, under chloralose anaesthesia using electric shock stimuli, "non-specific" responses both in the superior frontal gyrus and the superior parietal region. These responses had a long latency of 50-80 msec., occurred bilaterally and showed blocking interaction when elicited from different parts of the body. Responses with similar properties were recorded in the centrum medianum and zona incerta. Stimulation of the centrum medianum evoked similar responses of relatively long latency in the frontal area. The authors suggested the centrum medianum as a relay along a secondary somesthetic pathway.

It is evident from the above discussion that the late components of the evoked response show complex features and at times contradictory results have been reported by different authors regarding their distribution, or behaviour to the action of anaesthetics and different experimental conditions. Recently, Torres and Warner (73), using photic stimulation in unanaesthetized cats, distinguished two types of "delayed responses": "Type I" was always topographically associated with the primary response, and resistant to barbiturate anaesthesia and brain stem section; "Type II" was not topographically associated with the primary response and was sensitive to light anaesthesia and brain stem section. It is suggested that the first type is "in many aspects similar to though not identical with the secondary discharge of Forbes and Morison", while the second type would correspond to the responses described by French <u>et al</u>.(36), (37) and by Buser and Borenstein (12).

The effects of the reticular formation and different states of arousal on the late components have been studied by several authors. Buser and Borenstein (13) found that their "secondary responses" were related to the "level of vigilance" of the animal and the pattern of the electrocortical activity. They were best developed when the cortical activity showed an alternation of rapid and slow rhythm; and tended to disappear during cortical "arousal" whether spontaneous, due to peripheral nociceptive stimulation, or due to stimulation of the reticular formation. They disappeared during the electrocortical pattern that corresponded to "deep sleep". Bremer (10) also reported the depression of the late components of the evoked responses after thalamic or mesencephalic reticular formation stimulation. Schwartz and Shagass (67), (68) noted the relation of the late components to the spontaneous cortical activity and their depression with states of alertness whether spontaneous, due to the effect of drugs, or due to stimulation of the mesencephalic reticular formation.

2. Animal studies on cerebral recovery cycles

Like a peripheral nerve, a neuronal aggregate in the central nervous system, when activated either directly or synaptically, undergoes a series of changes in its excitability consisting of periods of absolute unresponsiveness, relative unresponsiveness and full responsiveness (40), (16). The stage of full responsiveness or recovery is sometimes followed by a cyclic variation in excitability demonstrated by phases of supernormality and subnormality (40), (53), (34), (67). Cortical responsiveness can be measured by the technique of paired stimulation. This technique consists of applying pairs of "conditioning" and "test" stimuli separated by various intervals, and by plotting the ratio of the amplitudes of the second to the first response as a function of the separation between the stimuli. In 1933, Bishop (8) was the first to postulate the presence of a spontaneous cortical excitability cycle when he found that repeated constant stimuli to the optic nerve did not evoke similar responses in the contralateral visual cortex. In 1936, Bartley (7) was the first to plot an excitability curve of the visual cortex of the rabbit by applying the technique of paired stimulation to the optic nerve.

Several workers have studied the recovery functions of various sensory systems in animals. The recovery time of the somatosensory cortex in the cat was found by Jarcho (49) to range between 50-100 msec. Marshall (61) reported that the recovery time of the visual cortex of the cat ranged up to 1-4 sec. Tunturi (75) reported a recovery time of up to 350 msec. for the auditory cortex of the dog. Other authors, however, have found different recovery values than the ones quoted. The wide range of values reported by any one author, as well as the disagreement between authors, shows that the recovery time of the brain depends on many factors. The following are some of these factors:

i) the type and dosage of drugs and anaesthetics (40).

ii) the intensity of stimulation (65).

iii) the locus of recording (34).

iv) the state of alertness of the experimental animal (34).

v) the influence of the reticular formation (53).

We shall comment in greater detail on the effects of drugs, the influence of the reticular formation, and the varying states of sleep and alertness.

Regarding the action of barbiturates, there is general agreement that they lengthen the recovery time. With light doses of barbiturates which tended to cause synchrony in the resting electrocortical activity, King _et al_. (53), recording from the thalamus and internal capsule, found an increase in the facilitation peaks (supernormal excitability) of the recovery cycle. With large doses of barbiturates, they reported a reduction in amplitude and a prolongation of the recovery time of the responses recorded rostral to the thalamus but no effect was found on the responses recorded from the medial lemniscus. These authors concluded that barbiturates act on the thalamus. Ether also increased the recovery time but less than barbiturates (40), (62). Amphetamine was reported by Gastaut (40) to shorten the absolute refractory period but Schwartz and Shagass (67) could not confirm this and found that it only depressed the facilitation peaks of the recovery cycles. The latter workers showed also that chlorpromazine increased the facilitation peaks of the recovery cycles. They concluded that the pattern of the recovery cycles depended on the accompanying spontaneous cortical electric activity.

Electrocortical arousal, whether spontaneous or caused by reticular formation stimulation, is associated with a depression of the facilitation peaks of the recovery cycles (53), (67). Sleep, on the other hand, causes an increase in the facilitation peaks (34).

Recently, Schwartz and Shagass (68) investigated the effect of reticular stimulation on the somatosensory cortical recovery in the cat. They found that such stimulation produced an early recovery peak at about 30 msec., which was not reported in previous studies (49), (67).

3. <u>Techniques of recording average evoked responses</u>.

One of the difficulties encountered in recording an evoked response from the human scalp is that its amplitude is so small in relation to the background "ongoing" activity that it is difficult or impossible to detect in the usual electroencephalogram. Some of the existing activity, like the alpha rhythm, cannot be filtered out because parts of the response which require amplification lie in the same frequency band.

An evoked response consists of a predictable series of electrical events bearing a definite relationship to the onset of the stimulus. Such an activity is time-locked to the stimulus in distinction to the background activity which occurs in a random fashion. Since any system of averaging is essentially based on the principle of integration, upon repetition of the stimulus the time-locked activity will tend to add in the same direction while the random activity will average out. Thus, a small signal previously hidden in a large background activity will build up and become detectable.

Many averaging systems, some of great complexity, are now available for averaging evoked responses. For the description of the individual devices, the original sources should be consulted. Recently, Davis and Ferris (25), Goldstein (46), Goldstein *et al*.(47), and Brown *et al*. (11) have reviewed the commonly used systems and have discussed their underlying principles.

The first method used was that of Dawson (29) in which he synchronized the sweeps of the cathode ray oscilloscope to the stimulus delivery and photographed a number of responses on the same plate. Through this photographic superimposition technique, he could separate the evoked responses from the background noise. The method, however, lacked accuracy in that the response had to be higher than the noise level and no fine details could be obtained. In 1951, Dawson (31) devised an electromechanical averager based on the principle of adding the successive potentials of the waveform following the stimulus. This system had great sensitivity and could detect potentials much smaller than the background noise but on the other hand, there were several limitations on account of its mechanical design. In most of the recent systems the computation is performed entirely electronically which adds greatly to the rapidity and flexibility of these systems.

Though different methods may be employed in different devices, the computation of the average responses is basically the same. It consists of measuring the signal voltages of the response at different points following each stimulus; the samples taken at the same points are stored and added together and when the desired number of responses has been added, an average response is given. "Thus the amplitude of any point in the average response waveform is the average of amplitudes of points at corresponding latency in the individual responses." (46). The different systems used for computation belong to one of two groups, either analog or digital.

The system employed in this study will be described later (27).

4. Sensory evoked responses in man.

As previously pointed out, it is difficult to detect the evoked responses in man with the standard electroencephalographic methods. This is particularly true of the early components of the responses, which have smaller amplitudes and shorter durations in comparison to the later ones. As early as 1939, Davis (28), and Davis *et al*. (24) described long latency responses to various sensory stimuli both in awake and sleeping subjects. Other workers subsequently described somewhat similar responses under various names. However, it was only after Dawson (29) introduced his photographic superimposition technique, and especially after the development of the electronic methods of averaging, that the evoked responses in man lent themselves to study.

Generally speaking, early and late components can be distinguished; the latter being sometimes followed by recurring rhythmic waves. There is agreement that the early components are relatively simpler and more stable than the later ones. These various components have been studied with respect to their differential distribution on the scalp, their recovery times, and their correlations with changes in the stimulus parameters or in the psychophysiological state of the subject. We shall briefly review some of the findings on the visual and auditory responses and then summarize the data on somatosensory responses relevant to the present work.

a. Visual and auditory evoked responses.

Among the recent studies of visual evoked responses is the work of Calvet *et al*. (14) who used an averaging technique and recorded the responses from the occipital region. They found that the early components consisted of small potentials of varying polarity which were difficult to detect. These early components had a latency of 40-50 msec., and were followed at 100-150 msec. after the stimulus by one or two negative waves, each about 100 msec. in duration. The late components were sometimes followed by rhythmic waves recurring at a frequency of about 10 cycles per sec. and decreasing rapidly in amplitude.

Brazier (9), using a cross-correlation technique, recorded the first 100 msec. of the responses following a flash stimulus, and was able to detect small occipital potentials as early as some 20 msec. after the stimulus.

Ciganek (17), (18), (19), employing the photographic superimposition technique described the complex pattern of the evoked visual responses up to 600 msec. after a photic stimulus, and studied the effect of the stimulation frequency on its components. The earlier components could follow a much higher frequency than the later ones. In 1961, Ciganek (20) constructed an average summary curve of his previous individual curves and after complementing his previous test observations with the study of the effect of sleep, both natural and following barbiturates, gave his final views and conclusions. He considered the responses to consist of a series of 7 waves ranging from 28 to 135 msec. followed by a "rhythmic after-discharge" at about 240 msec. after the stimulus. He called the first three waves "the primary response" on account of: i) its short latency; ii) its resistance to an increase in the stimulation frequency; iii) its resistance to sleep. The part of the responses following wave 3, he called the "secondary response" and suggested that it was produced by non-specific diffuse pathways because of the following characteristics: i) its long latency (over 90 msec.); ii) its decrease or disappearance on increasing the rate of stimulation; iii) its non-specificity with regard to modality (it was evoked also by sound during sleep); iv) its lability to sleep. Following the secondary response, a "rhythmic after-discharge" sometimes appeared which had approximately the same frequency as the alpha rhythm; it had a fusiform pattern and gradually decreased in amplitude.

Cobb and Dawson (22) studied the latency and form of the visual evoked responses using the more sensitive averaging technique described by Dawson (32). They demonstrated that the initial occipital electric change was a positive deflection 1-1.5 microvolts in amplitude occurring at 20-25 msec. after the stimulus. The further sequence of the responses they obtained consisted of a negative wave with a peak latency at 40-50 msec., a larger positive wave with its peak at 55-65 msec. and a negative wave with its peak at 90-100 msec. The latter was followed by a series of rhythmic deflections of about 10 cycles per sec. These authors studied the effect of a change in the intensity of the stimulus, and found that a reduction in intensity led to a decrease in the amplitude and an increase in the latency of the responses. Investigating the effect of visual attention, they reported that "fixation on a detail of the visual field between flashes may lead to an increase in the second, negative, component of the response and a shortening of the initial positive deflection".

In a recent study, Contamin and Cathala (23) recorded average evoked visual responses simultaneously from different scalp locations. They demonstrated the complexity and the change in the pattern of the responses with different placements. They differentiated between the responses obtained in the occipital regions and those obtained from more anterior positions up to the nasion. They subdivided further the occipital responses into: i) early components, ("primary responses"), which had a triphasic waveform starting with a positive deflection at 50 msec. These components were localized in their distribution and seemed to depend on the intensity of the stimulus. ii) the "secondary responses", which consisted of a diphasic component (negative-positive) starting at 135 msec. and ending at about 260 msec. They were found to be more diffuse in their distribution and seemed to be more related to the psychophysiological state of the subject. They decreased in amplitude when the eyes were closed or when the subject was not fixating the source of light. iii) "late rhythmic waves" which started at 260-350 msec. and lasted about 200-500 msec.; they were prominant on closure of the eyes.

It is generally appreciated that the early part of the auditory evoked responses (corresponding to the primary response found in animals) is difficult to detect from the scalp even when an averaging technique is employed, because the auditory cortex is buried in the Sylvian fissure. Calvet _et al_.(14) recorded auditory evoked responses somewhat similar to the somatosensory evoked responses they obtained. They found early inconsistent deflections starting at about 15-25 msec. and lasting 30-40 msec. They were followed by later components consisting of negative and positive phases, the durations of which were less than those of the corresponding phases of the somatosensory responses. These were sometimes followed by rhythmic waves of relatively shorter period than noted in the somatosensory recording.

Geisler (43) studied the "short latency components" of the responses to click stimuli with a special-purpose digital computer (ARC-1). He recorded monopolarly from different placements and found that the most consistent response was a bilateral negative deflection with a peak latency at 30 msec. This wave was of "fairly widespread" distribution and its maximal amplitude was in the occipital regions. An inconsistent positive wave with a peak latency at 20 msec. was recorded in some subjects. Geisler concluded on the basis of their latencies and distributions that these responses were "secondary". In this study he also investigated their behaviour under different experimental conditions; including the alteration of stimulus rate and intensity, and the effects of sleep and varying psychophysiological states.

b. Somatosensory evoked responses recorded from the scalp.

Though probably the earliest study on the average sensory evoked responses (29) was performed on the somatosensory system, it was only recently that the somatosensory evoked responses have been studied in detail. Table I summarizes the techniques and results obtained by various workers who have recorded somatosensory evoked responses.

Dawson (29), (30), using his superimposition technique and electric shock stimulation to peripheral nerves, recorded a highly localized surface positive deflection over the contralateral somatosensory area. It began at 22-23 msec. after the stimulation of the ulnar nerve at the wrist, and had a peak latency of about 25 msec. The focus of maximal amplitude was

Table I Comparison of the findings and techniques of various authors in recording average somatosensory evoked responses from the human scalp.

Authors	Components Described	Localization	Surface polarity and latencies in msec.					Methods and set up.
				50	100	150	200	
Dawson, 1947 1950	"Primary wave"	Contralateral. Highly localized.	+					System: Photographic superimposition. Leads: Monopolar and bipolar. Stimulation: Ulnar nerve at wrist 1 per sec. 50 shocks. Subjects: Supine, awake, neck muscles relaxed.
Larsson, 1953 1956	"Primary response"	Contralateral. Highly localized.	−+−					System: Photographic superimposition. Leads: Bipolar over somatosensory area, and mid-line locations. Stimulation: Ulnar nerve at wrist 1 per sec. 50 shocks. Subjects: Sitting, awake.
	"Non-specific responses"	Bilateral and widespread.		−	+		+	
Dawson, 1954	Early and late components	Contralateral over somatosensory area.	−+−+	−+				System: Electromechanical averager. Leads: "Monopolar" 6 cm. lateral to mid-line, reference electrode on forehead. Stimulation: Ulnar nerve at wrist 1 per sec. 220 shocks. Subjects: Awake.
Calvet *et al.* 1956	Early components	Contralateral. Localized.	++ or −+−+					System: Analog computer. Leads: Monopolar, active electrode over sensory area, reference electrode frontal or occipital. Stimulation: Peripheral nerves. 50 - 150 shocks.
	Late components	Widespread.		−+				
	Total response		−+−+	−+				
Geisler, 1960	Early components	Contralateral on described "central locations". Bilateral on occipital locations.	−+ or −++					System: Digital computer (ARC-1). Leads: Monopolar from different placements 4 cm. apart, reference electrode on nose. Stimulation: Median nerve at wrist 1 per 5 sec. 100 responses averaged. Subjects: Awake and alert, reading during experiment.
Shagass and Schwartz, 1961 1962	"Primary response"	Contralateral over somatosensory area.	−+					System: Analog computer. Leads: Bipolar, one electrode 7 cm. lateral to mid-sagittal plane and 2 cm. behind ext. audit. meatus; the other electrode 5 cm. anteriorly. Stimulation: Ulnar nerve at wrist 1 per 1.3 sec. 50 - 150 shocks. Subjects: Awake.
Allison, 1962	"Component I"	Contralateral.	+−+					System: Special-purpose analog computer. Leads: Monopolar from different placements, reference electrode on nose. Stimulation: Median nerve at wrist 1 per 3-4 sec. 40 shocks. Subjects: Sitting, "alert" monitoring their own EEGs.
	"Component II"	Contralateral.	+					
	"Component III"	Contralateral.	+					
	"Component IV"	Widespread.		−+				
	"Component V"	Widespread.			−		+	
	Total response		+−+++	−+	−		+	
Goff *et al.* 1962	"Component I"	Posterior contralateral quadrant.	+−+					System: Special-purpose analog computer. Leads: Monopolar from different placements, reference electrode on nose. Stimulation: Median nerve at wrist 1 per 4.5 - 6.0 sec. Subjects: Sitting, "alert" monitoring their own EEGs.
	"Component II"		+					
	"Component III"	Contralateral.	+					
	"Component IV"	Widespread.		−+				
	"Component V"	Widespread.			−		+	
	Total response.		+−+++	−+	−		+	
Uttal and Cook 1962	"M wave"	Posterior contralateral quadrant.	−+					System: Analog-digital converter. Leads: Monopolar from contralateral and ipsilateral somatosensory areas. Stimulation: Median nerve at wrist 1 per 2.5 sec. 80 shocks. Subjects: Sitting "attentively observing their EEGs." Hand immobilized in plaster cast.
	"N wave"		+					
	"O wave"	Widespread.			−	+		
	Total response		−++		−	+		

located at the surface marking of the central sulcus; the potential gradients were found to be steeper anterior than posterior to this focus (30).

Larsson (55), (56) confirmed Dawson's findings regarding the latency and high localization of the early positive deflection which he considered as corresponding to the primary response in animals. He also found that this deflection was sometimes preceded by an inconstant small negative deflection and was followed by a diphasic wave. Larsson also described a "non-specific response" consisting of a negative wave commencing at 50-90 msec. and a positive wave commencing at 100-120 msec. each with a duration similar to its latency. This response was found to be widespread in its distribution and had the same characteristics as the late components of the responses to visual or auditory stimuli.

Dawson (32) produced clearer records of the different components with his electromechanical averager. The other workers, like Calvet _et al_. (14), Geisler (43), Shagass and Schwartz (69), (72), Allison (3), Goff _et al_. (45) and Uttal and Cook (76), all used electronic techniques for averaging their responses. Shagass and Schwartz (69) studied the recovery cycles of the early negative-positive waves with peaks of latency respectively at about 20 and 25 msec. They demonstrated a statistically significant difference between its recovery in normal subjects and psychiatric patients.

Allison (3) described the total response up to 500 msec. following the stimulus and subdivided it into five components on the basis of differential recovery times. He suggested a functional significance for each of the components.

Goff _et al_. (45) studied systematically the distribution of the somatosensory evoked responses on the scalp and used Allison's classification.

Uttal and Cook (76) used a still different terminology by applying the letters "M", "N" and "O" to waves described by the previous authors.

Repetitive waves, following the late components similar to those elicited by visual or auditory stimulation, have been found in response to a somesthetic stimulus (55), (14), (3). However, these are less prominant than those following a visual stimulus.

c. _Somatosensory responses recorded directly from the cortex_.

Woolsey and Erickson (80), using a six-channel electroencephalograph, recorded somatosensory evoked potentials directly from the cortex of neurosurgical patients under ether or pentothal anaesthesia. These evoked potentials were initially surface positive and varied in pattern depending on the depth of anaesthesia. The initial surface positive wave was localized to the posterior margin of the central sulcus and its amplitude ranged from 50-150 microvolts. With a "quiet cortex", the positive wave was easily detected and served to locate the post central gyrus.

Jasper _et al_.(50), using a multi-beam cathode ray oscilloscope, recorded simultaneously from different points on the exposed cortex single tracings of somatosensory potentials evoked by electrical stimulation of the ulnar nerve at the elbow. By varying the time constant of the recording amplifiers, these authors could emphasize the early and late components of the evoked potentials. The initial deflection of the "primary complex" was a surface positive wave with a latency of about 18 msec. and an amplitude ranging up to 100 microvolts. They found that "the primary complex seems very stable, either with or without anaesthesia, and is restricted to a cortical area consistent with the sensory responses to stimulation".

Hirsch _et_ _al_. (48), using an averaging technique, recorded evoked responses to peripheral nerve stimulation directly from the cortex in neurosurgical patients under different types of anaesthesia. The maximum amplitude of the responses was found in the post central gyrus but they were present as well in front of and behind this area. These authors pointed out that there was a satisfactory similarity between the responses they recorded from the cortex and those recorded from the scalp (14).

In conclusion, there is qualitative agreement among the various authors as to the differential characteristics and the factors which affect the early and the late components of the sensory evoked responses in man. Some of the differential characteristics of the two major components are summarized in Table II, while some of the factors affecting them are summarized in Table III.

Table II Differential characteristics of the early and late components of the sensory evoked responses in man.

Characteristic	Early Components	Late Components
Pattern	Less complex and less variable	Complex and variable
Latencies	Short	Longer
Distribution	Localized	Widespread
Duration	Short	Longer
Sensory modality	Modality specific	Modality non-specific
Recovery time	Short	Longer

Table III Factors affecting the early and late components of the sensory evoked responses in man.

Factor	Early Components	Late Components
State of alertness	Less affected	More affected
Degree of attention to stimulus	Less affected	More affected
Stimulus frequency	Can follow higher frequencies	Disappears at relatively lower frequencies
Anaesthetics	Less affected	More affected.

5. Psychological and behavioural correlates of sensory evoked responses and cortical excitability.

Evoked cerebral responses have been studied in relation to behavioural manifestations in waking, unrestrained animals, and in relation to certain psychological phenomena in man. We shall now review some of the data derived from these studies.

Galambos (38) recorded in cats evoked responses to clicks from chronically implanted electrodes in the cortex and in subcortical structures. He found that the amplitude of the responses varied from one click to another. The responses "being large when attention is directed toward the stimulus and small when the animal is distracted, habituated or attending to something else". Thus, when the cat was "attending" to food, a reduction in the amplitude of the responses occurred at all recording sites. Galambos also studied the electrical correlates of conditioned learning, finding that the responses increased in amplitude when conditioning was established and that they decreased in amplitude during the extinction procedure. Further analysis of the responses showed that they were large and protracted in time in the conditioned state and that they were relatively small and of shorter duration in the extinguished state. In the light of these results, Galambos concluded that the variations of the brain responses were related to the "significance" of the stimulus rather than to its physical characteristics. Jouvet and Hernandez-Peon (51) had previously shown that the amplitude of the click responses recorded from the dorsal cochlear nucleus of the cat was greatly reduced after habituation or when the cat's "attention" was diverted to non-auditory stimuli. This diminution in the amplitude of the evoked responses was attributed to a centrifugal inhibitory action exerted by the reticular formation. The authors discussed this controlling mechanism in relation to habituation, attention and conditioning.

Lindsley (59) reviewed the literature concerning the role of the reticular formation in behaviour and in psychological phenomena. He also studied perception and sensory discrimination in relation to temporal factors. Applying this approach in the investigation of the perceptual processes, he determined the critical flicker frequency in human subjects and found that it was about 42 flashes per sec. When he applied the same light flashes to curarized or acute preparations, he found that the subcortical visual pathways could follow a flash frequency above 100 per sec., while the cortex could only follow a frequency of about 40-50 flashes per sec. In this way, he demonstrated that there was "one parallelism or correspondence between limits of human discrimination of flicker and electrophysiologic response in the visual pathways and cortex of the cat".

It is clear that these studies of the evoked responses in animals have provided valuable electrophysiological correlates to some psychological phenomena and some aspects of behaviour. It should be stressed, nevertheless, that it is impossible to assess the subjective state of the experimental animal.

The effects of attention, distraction and habituation on the sensory evoked responses in man have been studied and findings similar to those obtained in animals were demonstrated. Thus, Garcia-Austt et al. (39), who recorded average visual evoked responses from different scalp locations observed the following changes in the responses: when the subject became habituated to the flashes, i) the amplitude of the evoked responses diminished; ii) their waveforms became more complex; iii) the distribution of the responses became restricted to the occipital region; iv) an after-discharge appeared in the records. When the subject's attention was distracted from the flashes by asking him to perform a mental calculation, the amplitude of the responses diminished also. When the subject's attention was, on the other hand, focused on the flashes by asking him to count them, features opposite to those present under habituation became apparent, viz.: i) the amplitude of the responses increased; ii) their waveforms became more simplified; iii) the distribution of the responses became more diffuse; iv) the after-discharge disappeared.

Jouvet and Courjon (52) recorded visual evoked responses from the optic radiation in conscious neurosurgical patients. The diminution of the amplitude of the responses "during states of distraction" was accompanied by alpha blocking. Of particular interest is the finding reported by these authors in the case of a patient suffering from conversion hysteria with generalized body anaesthesia. They found that a painful stimulus did not disturb the patient's attention, that there was no diminution of the evoked responses to photic stimulation, and that no alpha blocking appeared. When, however, the patient was asked an emotionally loaded question the amplitude of the evoked responses diminished and the alpha blocking appeared.

Contamin and Cathala (23) found that the early components ("primary responses") of the visual evoked responses in man were related to the physical characteristics of the stimulus, while the late components ("secondary responses") were related to the psychophysiological state of the subject. These late components, in fact, varied according to the subject's degree of visual attention. Larsson (57) reported that the late components of the somatosensory responses were related to the "significance" of the stimulus.

The effect of sleep on the evoked responses to different sensory modalities was investigated and found to be a complex one. Most authors, however, agree that the late components are those which are most affected by sleep (20), (43), (76).

Of interest is the close correspondence demonstrated between the psychophysical threshold of a sensory stimulus and the electrophysiological threshold of the averaged evoked responses. This correspondence was pointed out for somatic and auditory stimuli by Shagass and Schwartz (69) and Geisler (43). Attempts are being made to use this correlation to measure the psychophysical threshold in children and to differentiate between organic and non-organic disorders of sensation.

Psychological and psychiatric relationships to cortical excitability cycles have been also reported. The concept of a spontaneous cortical excitability cycle was first formulated in 1933 by Bishop (8). This concept which implies a waxing and waning excitability was used again by Lindsley (58) and Lansing (54) and correlated with psychological phenomena.

Lansing studied the relationship between the reaction time to a visual stimulus and the phases of the occipital and motor alpha cycles. A significant relationship was found - the shortest and longest reaction times being in opposite phases of the alpha cycle.

Recently, Shagass and Schwartz (70), (71), (72) measured the cortical recovery cycles of the early components of the somatosensory responses both in normal controls and in the following psychiatric groups: i) neurosis with anxiety and depression; ii) psychotic depression; iii) schizophrenia; iv) various personality disorders. They found that there was no significant difference in the early recovery peak of the cortical excitability cycles between the neurotic group and the normal controls. However, all other groups showed a diminution of early recovery. Clinical improvement tended to be associated with a restoration of normal early recovery.

III INSTRUMENTATION AND EXPERIMENTAL PROCEDURES

1. Data recording system.

All the experiments were conducted in a moderately illuminated room which was maintained at a constant temperature. The usual sounds originating from outside the room could not be heard. The evoked responses were averaged by means of a one-channel analog averager (SARA) developed at the Electrophysiology Laboratory of the Allan Memorial Institute by Davis and Ross (27). This is essentially an analog averager in which information is stored on a short loop of magnetic tape. It has a resolution of one millisecond and reads out continuously the result of the integration. The build up of the averaged response can, therefore, be observed and the computation is "on-line". The result of integration is recorded continuously with the ink writer of an Offner recorder type 542 and is displayed more clearly on the screen of a cathode ray oscilloscope. See Fig. 1 . When the desired number of stimuli has been given, the averaged response is photographed from the screen of the oscilloscope by means of a polaroid camera and thus obtained in a permanent form. The other ink writer of the Offner recorder displays the raw data of the brain's electrical activity under the same scalp electrodes from which the response is averaged. The noise level of the system normally was masked by the biological "noise" of the background activity of the electroencephalogram.

This averaging system has obviously some limitations,

Fig. 1. The upper ink tracings of each pair, A and B, show the build up of the averaged responses between the 15th and 20th stimuli and between the 40th and 45th stimuli respectively. The lower tracings show the spontaneous brain activity recorded from the same electrodes with the individual evoked responses hidden in the "background noise". The amplitude scale refers to the non-averaged brain activity.

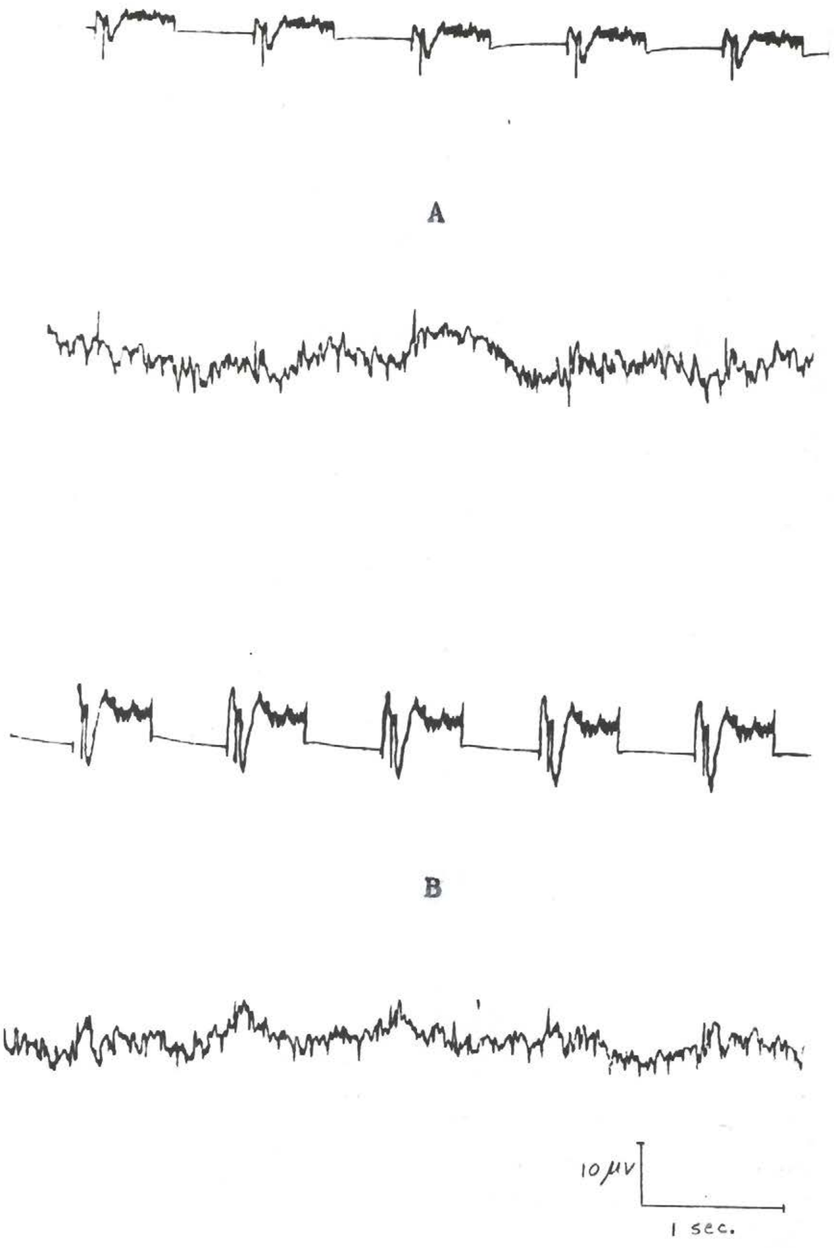


Fig. 1.

viz.: i) it possesses only one averaging channel so that simultaneously evoked responses from different scalp placements cannot be obtained under the same experimental conditions; ii) due to the analog nature of the system any slight unbalance would tend to produce a cumulative drift.

Large artifacts, as with any averaging system, tend to contaminate the data accumulated in any run, resulting in a certain amount of the data being rejected. The subsequent repetition of a run in order to obtain a clean record may, if it occurs too often, prolong the recording session to the extent that a limit is placed upon the usefulness of a single channel analyzer to survey large areas of the scalp. This limitation is particularly troublesome with a non-cooperative subject.

Silver electrodes attached to the scalp with bentonite paste were used to pick up the brain potentials. The placements of the recording electrodes will be described under experimental procedures. The electroencephalographic signals were amplified by a Tektronix type 122 preamplifier and then fed to the input of the averager.

2. <u>Stimulation system</u>.

Electric stimulation of the ulnar nerve at the wrist was exclusively used in this study. The stimuli were 1 msec. pulses delivered to the subject from a Grass S4 stimulator through an isolation unit. When paired stimuli were used, the interval between each stimulus of the pair was determined by the dial settings of the stimulator. Stimulation was triggered from the averager and the frequency of presentation controlled by the length of the magnetic tape loop. The frequency of stimulation varied from 1 per sec. to 1 per 4 sec., being varied from one run to another but remaining constant within any one run. Only repetitive regular stimuli were given and no random stimuli were used. Stimuli were repeated 50 times in order to obtain the average of the subject's responses. The stimulus intensity was adjusted from the voltage dial of the stimulator to produce a twitch of the ulnar side of the hand, without being painful or uncomfortable to the subject. The voltage settings used varied between 70-120 volts with the actual voltage at the electrodes being somewhat less than this, due to the internal impedance and non-linearity of the isolation unit. There was no indication of the actual voltage, current, or energy acting upon the nerve. The stimulating electrodes were taped, the cathode on the ulnar nerve at the wrist, and the anode on the palm of the hand. To minimize the stimulus artifact, a grounded lead sheet was applied on the subject's arm. Stimulus parameters were checked by means of an oscilloscope.

3. Subjects.

Nineteen subjects served in this study; all were either hospital staff members or medical students in apparently good health. Their ages were between 20-35 years and thirteen subjects were males. During the experiment, they lay comfortably on a bed with their head on a pillow to keep the neck muscles relaxed. The subjects were required to keep their eyes open and to stay alert except when stated otherwise. Most of the subjects were interested by the experimental procedure and reported about their subjective state between recordings. When a monopolar technique was used with the reference electrode on the bridge of the nose, the subjects were specifically asked to relax their facial muscles during the recording. Furthermore, the tracing of the normal electroencephalogram gave an idea about the degree of alertness and muscle potentials present at the time of recording.

4. Experimental procedures.

The procedures used in this study aimed at: i) studying the latencies, pattern and distribution of the somatosensory evoked responses; ii) measuring the recovery cycles of the early components of the responses; iii) studying the effects of different recording techniques and of changes in the stimulus parameters; iv) excluding sources of artifacts, mainly muscle potentials.

Nineteen subjects were tested in this study. Recovery cycles were measured in nine and data concerning the remaining aspects of the study were obtained from all the subjects. Each experimental session lasted 2 - 3 hours; the sessions for recording recovery cycles being the longer. Six of the subjects served for more than one experiment and a total of 31 experiments were performed.

Recovery cycle procedure:

We have used the method described by Shagass and Schwartz (71) in order to compare our results with their findings. To obtain the recovery function, pairs of "conditioning" and "test" stimuli were given separated by varying intervals and the ratio of the amplitudes of the second to the first response was plotted against the time intervals. The separation between each stimulus of a pair varied from 2.5 msec. up to 170-190 msec. The increase in the interval was made in steps of 2.5 msec. up to 20 msec., in steps of 5 msec. up to 30 msec. and then in steps of 10 msec. up to the end of the series. The pairs of stimuli were repeated 50 times at a rate of 1 per 1.3 sec. to obtain the average of their responses. Usually, three tracings of average responses due to unpaired stimuli were taken during an experimental session to compare the repeatability of the responses and to use in the computation of the recovery cycles. The intensity of the stimulus was adjusted so as to produce a twitch of the ulnar side of the hand without being painful to the subject. The range of voltages used varied between 70-105 volts. The evoked potentials were recorded bipolarly from both contralateral and ipsilateral somatosensory areas. Two different time scales were used exhibiting either about 100 msec. or about 250 msec. of the time-locked activity. The former was used for time intervals between each stimulus of the pair up to 50 msec.; for greater time intervals, the longer length of activity was recorded. The recording electrodes were placed, one 7 cm. lateral to the midline and 2 cm. behind the interaural plane, and the other 5 cm. anterior on the same parasagittal plane. Relative positivity of the posterior electrode was made to produce an upward deflection in the tracings.

In this series of experiments, we also recorded bipolarly from two other placements in order to detect any time-locked activity occurring within the time limits of the early components used in the computation of the recovery cycles. A pair of electrodes was placed on the midline, one at the vertex, the other 6 cm. behind it; and another pair placed some distance above the left eye on positions Fp 1 - F 7 (standard ten twenty system).

For the calculation of the recovery cycles, only the first two most constant deflections of the contralateral somatosensory evoked potentials were considered. These are negative-positive peaks occurring at latencies of about 19.50 ± 1.50 and 31 ± 5 msec. respectively.

In the tracings due to paired stimulation the response to the second stimulus was usually clearly seen and its peak latencies as well as its duration resembled largely those of the first response. In those tracings where the second response was not well defined these characteristics were used to locate it. Since the deflections produced by the second stimulus frequently coincided in time with those due to the first stimulus, it was necessary to deduce the true amplitude of the former deflections. This was done by assuming, as Shagass and Schwartz did (71), that the recorded response was the algebraic summation of the responses to the individual stimuli. Hence, the peak amplitudes following unpaired stimuli were subtracted from the deflections in the paired stimulus records at the times corresponding to the peaks due to the second stimulus. This correction was made for intervals between each stimulus of a pair up to 50 msec.

Distribution procedure:

Information regarding the distribution of the responses was derived from the tracings of the average responses due to unpaired stimuli made during the recovery cycle procedure. For the study of the distribution of the late components, however, it was found preferable to use a monopolar recording technique with the reference electrode on the bridge of the nose and a slower stimulation frequency of 1 per 4 sec. A longer duration of the responses (about 450 msec.) following the stimulus was also filmed by using a slower sweep rate of the oscilloscope. The monopolar technique presented the advantage of being associated with less variability of the responses but tended to pick up muscle potentials which in turn tended to disrupt the averaging system. Combined with a stimulation frequency of 1 per 4 sec. this technique, though useful, could not be used for extensive surveys because of the above mentioned difficulty and because of being time consuming. Responses of 450 msec. duration were recorded both bipolarly and monopolarly from three of the four placements used in the recovery cycle procedure, namely the contralateral, ipsilateral and midline placements. To study more systematically the distribution of the various components, responses were also recorded monopolarly from points each 4 cm. from the other, starting from the vertex, as illustrated in Fig. 6 p. 54. The vertex point (#4 in Fig. 6) was defined here as the intersection of the mid-sagittal plane and the interaural circle. The responses were recorded on two different time scales of 100 and 450 msec. to show clearly the early and late components respectively. In two subjects (D.M and T.R.), this survey was carried out more extensively. In subject D.M. a total of 60 average responses were recorded from 37 different scalp locations over three experimental sessions each lasting about two hours. Of these responses, 35 were recorded on the 100 msec. time scale using a stimulation frequency of 1 per 1.3 sec. and 25 responses were recorded on the 450 msec. time scale using a stimulation frequency of 1 per 4 sec. in order to show the late components. In subject T.R., we recorded the responses from 14 and 6 locations respectively using the above time scales and frequencies.

Other procedures:

The procedures used in the remaining aspects of this study will be discussed with the results under the appropriate headings.

IV RESULTS

1. Description of the somatosensory evoked responses.

The average cerebral responses evoked by ulnar nerve stimulation consisted of a series of complex waveforms which lasted about 500 msec. The components of these responses showed certain variations in their latencies, patterns, and amplitudes when recorded in the same subject as well as in different subjects. However, despite these variations the somatosensory evoked responses were quite stable and repeatable when recorded in the same subject under the same experimental conditions. These responses showed some common features in different individuals which allowed a general description. Fig. 2 shows the patterns of the contralateral somatosensory evoked responses recorded monopolarly in six subjects.

It is convenient to divide the somatosensory responses into components simply for descriptive purposes without attaching a special functional significance to any of the components. This classification of the responses into components was based on the following considerations: i) the latency ranges of the components; ii) the distribution of the components on the scalp; iii) the recovery characteristics of the components under different stimulation frequencies.

Several terminologies and labels were used in the literature to describe the components of the somatosensory evoked responses. Since our results coincide with those of Allison (3),

Fig. 2. Patterns of the monopolar somatosensory evoked responses of six subjects. The active electrode was 8 cm. lateral to the mid-line on the contralateral interaural coronal plane and the reference electrode was on the bridge of the nose. Relative positivity of the active electrode is indicated by an upward deflection in these and the following tracings. Vertical scale = 5 μv.

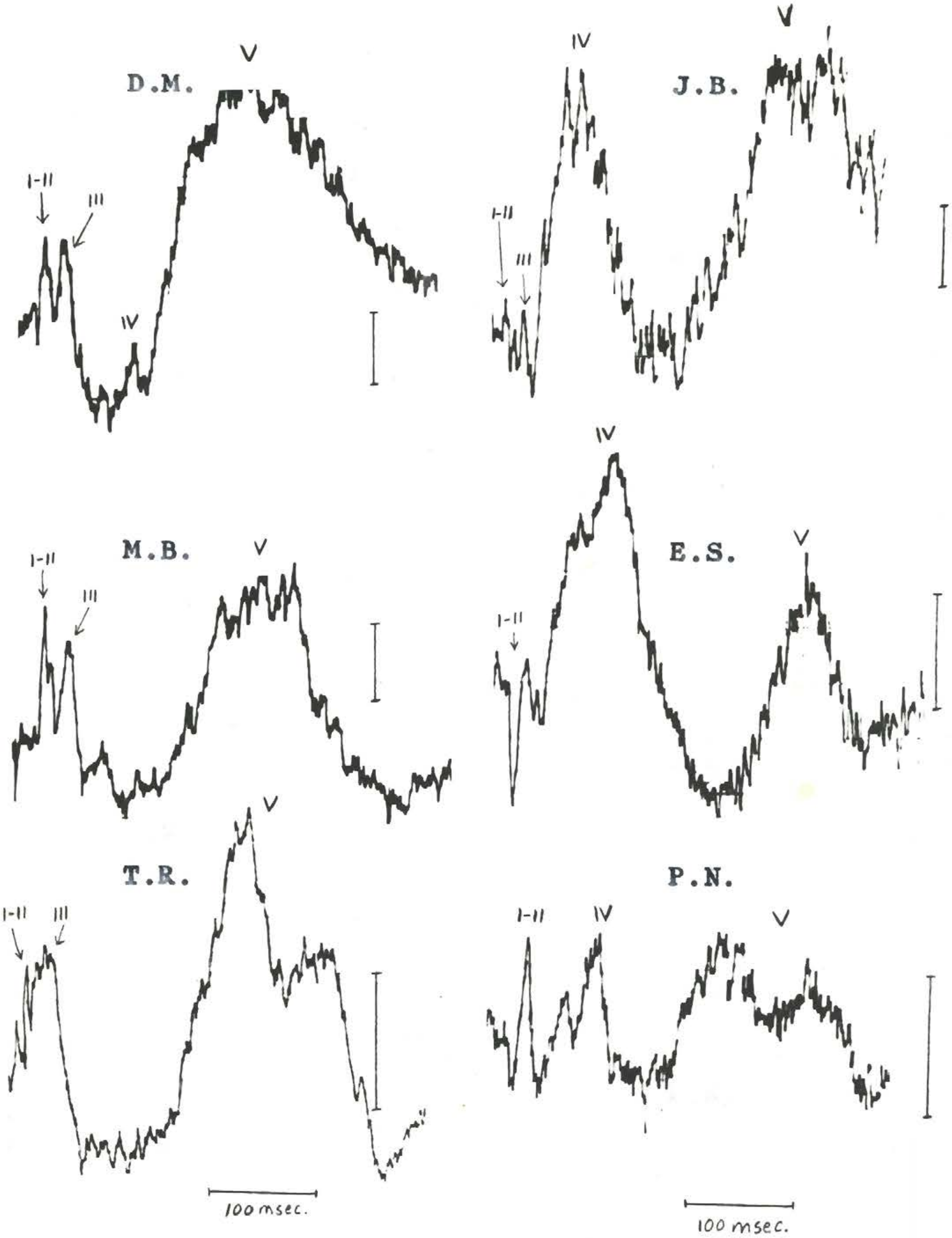
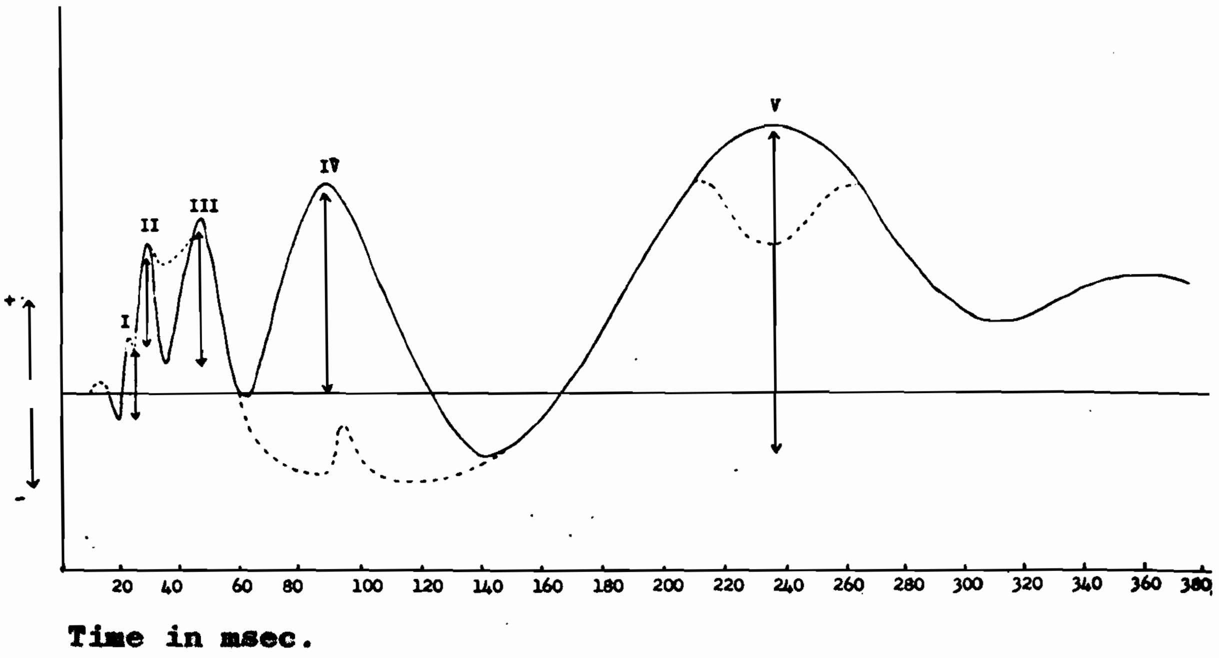

D.M.
I-II
III
IV
V
J.B.
I-II
III
IV
V
M.B.
I-II
III
V
E.S.
I-II
IV
V
T.R.
I-II
III
V
P.N.
I-II
IV
V
100 msec.
100 msec.

Fig. 2.

we have followed his classification which divided the somatosensory responses into five components. Fig. 3 shows a schematic representation of the contralateral somatosensory evoked responses recorded monopolarly with an active electrode 8 cm. lateral to the mid-line on the interaural plane and a reference electrode on the bridge of the nose. Relative positivity of the active electrode is indicated by an upward deflection in this diagram and in subsequent tracings.

The results concerning the patterns and the peak latencies of the components were based on data collected during all the experimental sessions. A total of 905 measurements of peak latencies of the various components were calculated from the tracings of the 19 subjects tested. These 905 measurements represent 568 latency measurements of components I and II in 19 of the subjects; 82 measurements of component III in 13 subjects; 123 measurements of component IV in 17 subjects; and 132 measurements of component V in 18 subjects. Each measurement represented the peak latency of a component of the average cerebral responses to 50 electric stimuli applied to the ulnar nerve at the level of the wrist.

Component I consisted of a triphasic wave (positive-negative-positive). The early positive deflection was inconstant and of small amplitude; its peak latency occurred at about 16 ± 2 msec. It was followed by a sharp, very constant negative peak occurring at about 19.50 ± 1.50 msec. The latency and pattern of this deflection were very stable in any


+
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I
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III
IV
V
20
40
60
80
100
120
140
160
180
200
220
240
260
280
300
320
340
360
380
Time in msec.

Fig. 3.

Fig. 3. Schematic representation of the contralateral somatosensory evoked responses. Dashes indicate either inconstancy of a component or a possible variation in pattern.

one of the subjects tested. The last part of the first component is an inconstant positive wave which may appear as a "notch" anywhere on the rising limb of the next component.

Component II consisted of a constant positivity with its peak latency at 31 ± 5 msec. This deflection was also stable in its appearance and in its latency in any one subject tested. Component II was followed by a series of complex and variable, usually positive waves which constituted component III. The peak latency of this component was about 50 ± 9 msec. At times, this third component was absent or was separated from the preceding wave by a negative deflection.

Component IV was an inconstant, diphasic (negative-positive) wave which showed great variation of amplitude and pattern; its peaks occurred respectively at 63 ± 22 msec., and 89 ± 31 msec.

Component V is also a diphasic (negative-positive) wave; its peak latencies occurred respectively at 145 ± 35 msec. and 240 ± 50 msec. This component was constant in its occurrence and diffuse in its distribution. Its amplitude tended to be as high as components I and II combined together; it was even higher when the stimulation frequency was 1 per 4 sec.

Sometimes following component V, repetitive rhythmic waves in the alpha frequency range were recorded. These waves had a sinusoidal appearance and their amplitudes decreased gradually. They were not detected beyond 500 msec. in our series.

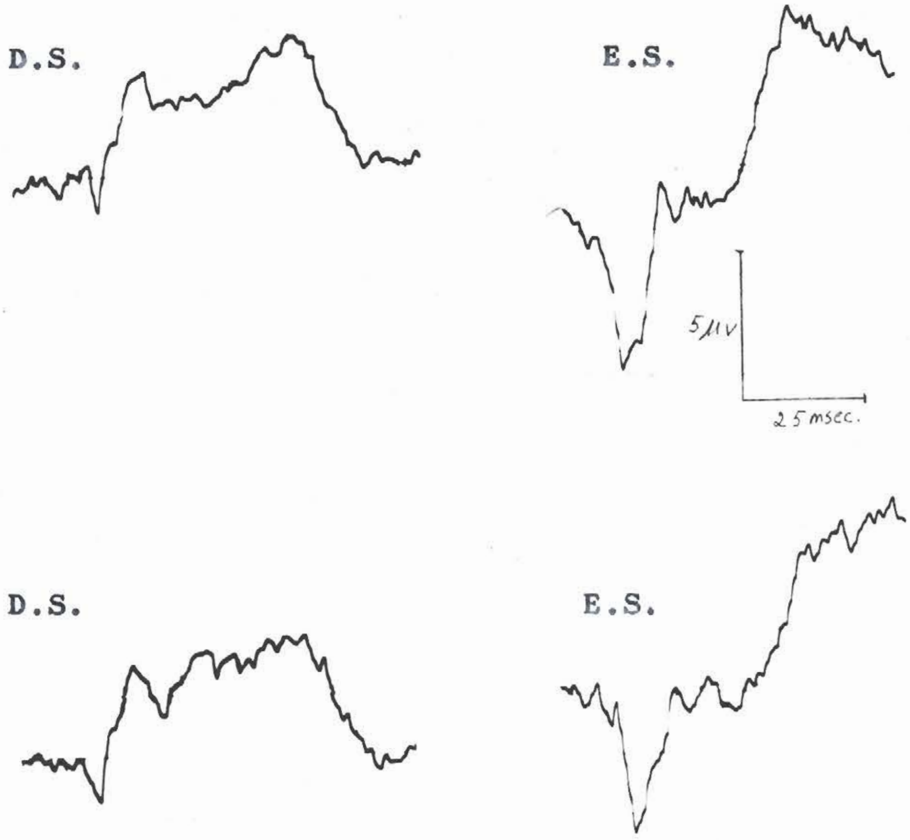
Table IV summarizes the peak latencies and the degree of constancy of the various components of the responses. The peak latencies of the inconstant deflections of component I were omitted because of the difficulty in their measurements. The table shows that the late components have greater ranges of peak latencies and overlap with each other to some extent. The early components, on the other hand, are relatively more stable regarding their latencies and patterns. In fact, we could obtain almost identical contralateral responses (100 msec. time scale) for each of two subjects we retested after a 6 month interval under the same experimental conditions. (See Fig. 4). In most of the other subjects where we recorded the early responses more than once during the same experimental session, similar results were obtained.

In three subjects, we filmed the build up of the responses after 10, 25, and 50 stimuli to the ulnar nerve. The output of the averager was adjusted each time before filming the tracings in order to obtain the same amplitude scale (See Fig. 5). It is noticed that the average responses to 10 stimuli resemble in their general pattern those obtained after 25 and 50 stimuli. The late components of the responses show relatively more variations in their build up than the early components I and II. In general, with a greater number of stimuli, the responses became clearer in their details and the random "background noise" was more efficiently averaged out.

Table IV Peak latencies and constancy of the different components of the somatosensory responses recorded in 19 subjects.

Component and Polarity		Constancy	Peak Latency ± its Variability
Component I	+	inconstant	---------
	-	constant	19.5 ± 1.5 msec.
	+ (notch)	inconstant	---------
Component II	+	constant	31 ± 5 msec.
	-	inconstant	40 ± 8 msec.
Component III	+	inconstant	50 ± 9 msec.
Component IV	-	inconstant	63 ± 22 msec.
	+	inconstant	89 ± 31 msec.
Component V	-	constant	145 ± 35 msec.
	+	constant	240 ± 50 msec.
Late rhythmic waves		inconstant	rate 8-12 per sec.

Fig. 4. Tracings from two subjects showing the high repeatability of the early components of their respective contralateral somatosensory responses after a period of six months.

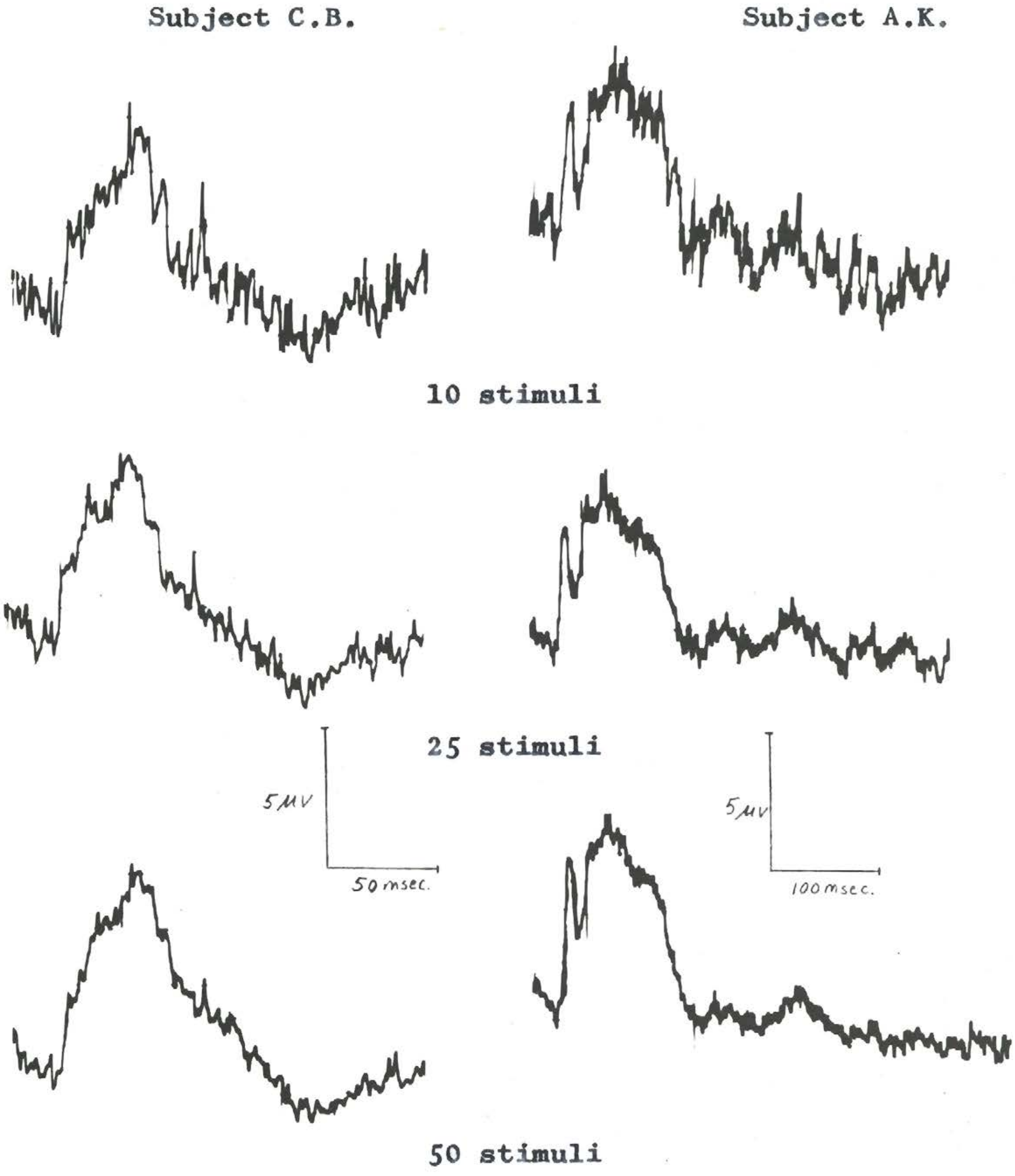


after six months

after six months

Fig. 4.

Fig. 5. Tracings from two subjects showing the build up of their averaged contralateral somatosensory evoked responses after a repetition of the stimulus 10, 25, and 50 times respectively. The output of the averager was adjusted for each tracing in order to maintain a constant voltage scale.


Subject C.B.
Subject A.K.
10 stimuli
25 stimuli
5µV
50 msec.
5µV
100 msec.
50 stimuli

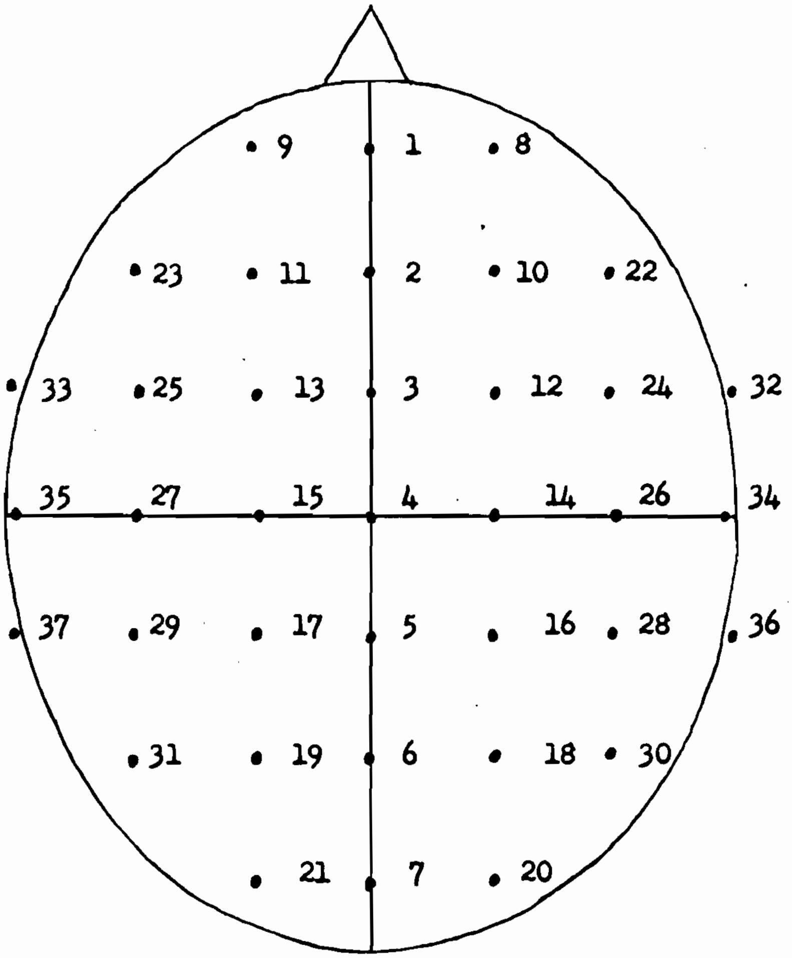
<u>Fig. 5.</u>

2. Distribution of the responses.

In the study of the distribution of the responses we relied on the amplitude measurements of the components recorded from different scalp locations. The amplitudes of all the components varied between 0.88 microvolts and 26.40 microvolts. The lower limit of this range was sufficiently high to be separated from the noise level. In most subjects, the responses were recorded from the placements used in the recovery cycle procedure, i.e. from contralateral, ipsilateral and midline placements. The responses were recorded from these placements bipolarly, monopolarly or both. Stimulation frequencies ranging from 1 per 1.3 sec. to 1 per 4 sec. were used in order to show clearly the early and late components respectively.

In two subjects, D.M. and T.R., the distribution of the responses was studied more extensively by recording monopolarly from 37 locations on the scalp. Each of these locations was separated 4 cm. from the other, after the vertex-point was determined as previously described and illustrated in Fig. 6 . The right side of the diagram with the even numbers indicates the locations contralateral to the ulnar nerve stimulation. In subject D.M., we recorded the responses from 35 locations with a fast sweep rate of the oscilloscope to show the first 100 msec. of the responses, and from 25 locations with a slow sweep rate to show the first 450 msec. In subject T.R., we recorded the responses from 14 positions with the fast sweep rate and from 6 positions with the slow sweep rate.

Fig. 6. Schematic diagram of the placements of active electrodes in monopolar recordings. These placements were spaced 4 cm. apart after determination of the vertex-point (#4). The reference electrode was placed on the bridge of the nose. The right side of the diagram with the even numbers is contralateral to the ulnar nerve stimulation.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15
4
14
26
34
37
29
17
5
16
28
36
31
19
6
18
30
21
7
20

Fig. 6.

In our amplitude measurements, components I and II were considered together because of their similar distribution on the scalp and because of the inconstancy of the last positive deflection of component I. We thus measured the amplitude of these components from the peak of the sharp negative deflection of component I to the peak of the positive deflection of component II. The amplitude of the positive deflection of component III was measured either from the peak of a preceding negative deflection when this was present or otherwise from the base line (See schematic diagram in Fig. 3). The amplitudes of components IV and V were measured from the peaks of their negative deflections to the peaks of their positive deflections.

The data obtained from the two subjects studied more extensively and from the remaining 17 subjects showed that components I and II were relatively more localized in their distribution than all the other components of the responses. These early components were recorded from the posterior contralateral quadrant of the head, and their maximal amplitude was found on the locations 4 or 8 cm. behind the contralateral interaural plane. Positive deflections falling within the latency ranges of components I and II were also found on the mid-line locations mostly posterior to the vertex. These components were present to a lesser extent anterior to the interaural coronal plane. Their amplitude gradient showed a much steeper decrement anterior to this plane than posterior to it. In some subjects small positive deflections appeared on the ipsilateral somatosensory region.

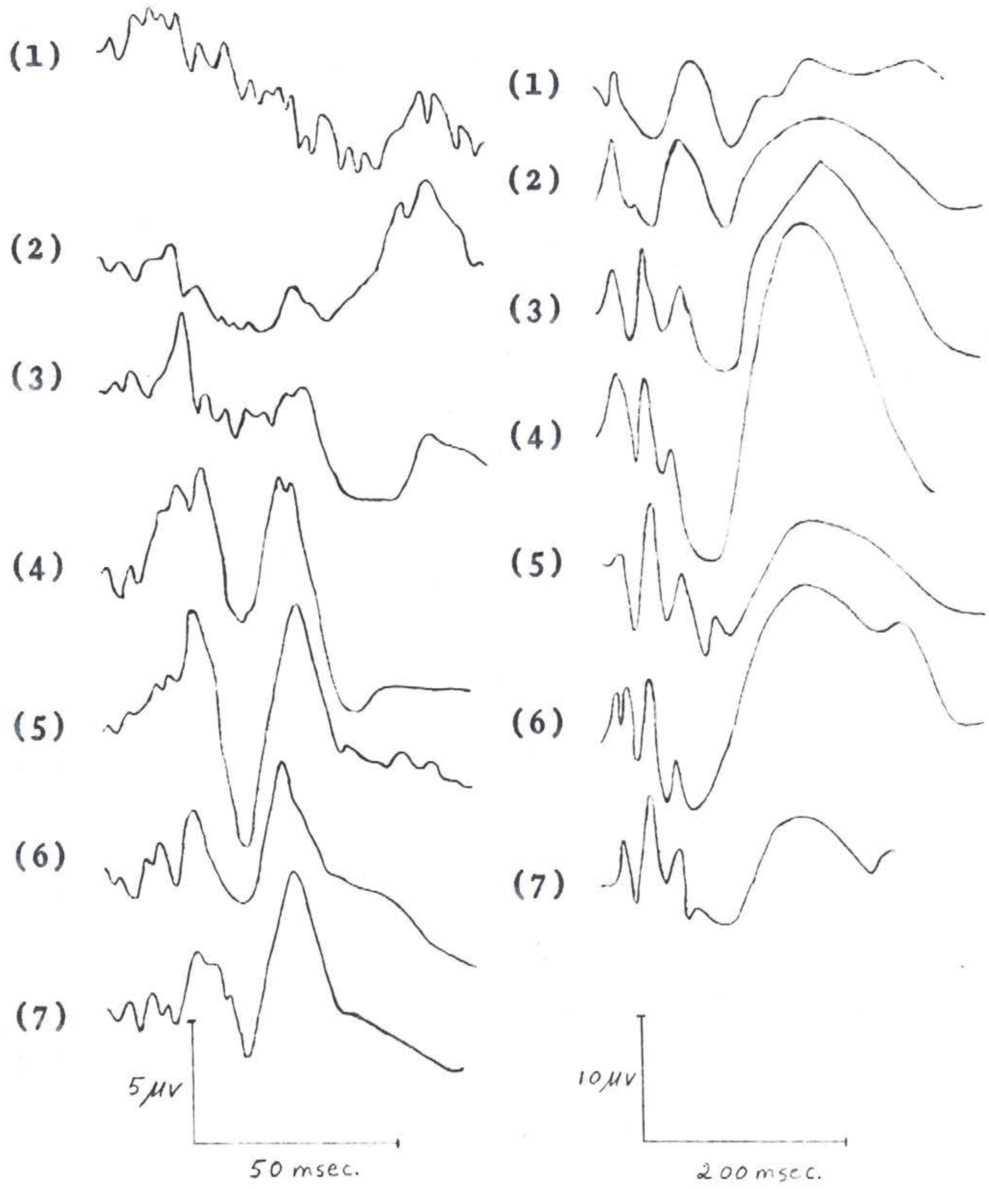
Component III was more diffuse in its distribution than I and II. It was more pronounced on the contralateral locations on the head; its maximal amplitude seemed to be on the contralateral interaural plane. Its amplitude gradient, like components I and II, decreased more rapidly anteriorly than posteriorly.

Component IV was more diffuse in its distribution than the previous components, and also showed greater variations of latencies and patterns. It could not always be clearly detected. Its amplitude was smaller than that of component V.

Component V was very diffuse in its distribution, being picked up from all locations. Its positive deflection was highest at the vertex where it appeared as a tall narrow peak. On both sides of the vertex the base of this component broadened and its peak sometimes became bifid. Figs. 7 and 8 show the distribution of the responses recorded in subject D.M. from the placements on the mid-line and interaural plane.

Although components I and II in this study were not always found to be very localized over the somatosensory region, there is evidence that they spread from a focus in this area. Thus, in one subject (R.B.) where we used bipolar leads, these early components failed to appear where we had previously recorded them, although the later components were present. However, a displacement of both electrodes 1 cm. anteriorly was enough to reveal the early components. This was interpreted as due to the electrodes being placed in the first case on an isopotential line (See Fig. 9).

Fig. 7. Tracings from subject D.M. showing the distribution of the somatosensory responses recorded from mid-line placements. The tracings on the left side of the figure were recorded with a fast sweep rate while those on the right side were recorded with a slow sweep rate in order to show the later components of the responses. Numbers refer to the electrode placements as shown in Fig. 6.



<u>Fig. 7.</u>

Fig. 8. Tracings from subject D.M. showing the distribution of the somatosensory responses recorded on the interaural coronal plane. The tracings on the left side of the figure were recorded with a fast sweep rate while those on the right side were recorded with a slower sweep rate. Numbers refer to the electrode placements as shown in Fig. 6.

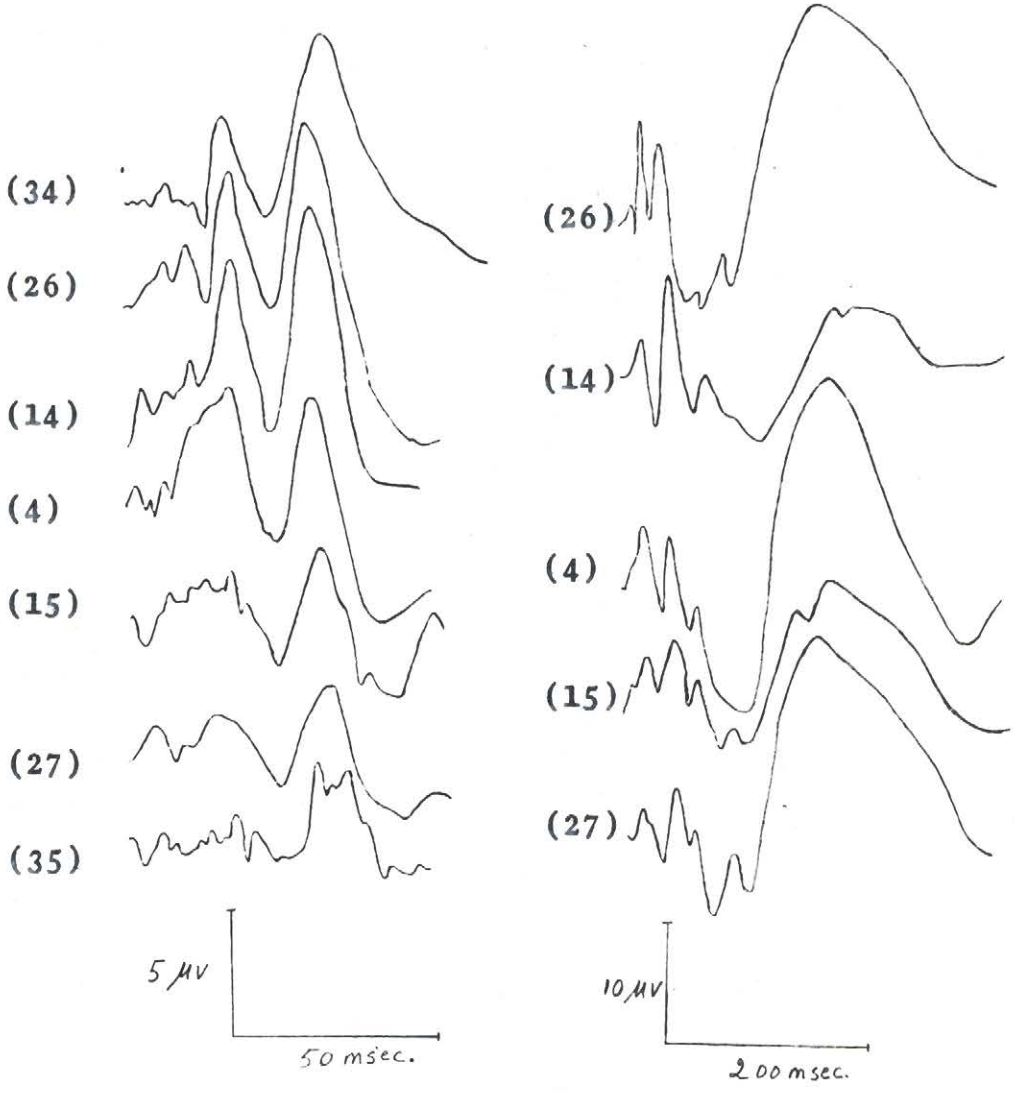


Fig. 8.

Fig. 9. Bipolar tracings showing the effect of a slight displacement of the recording electrodes on the early components. Tracings A and B were recorded from the same contralateral placements with a fast and slow sweep rate respectively. Only long latency components are seen in B. Tracing C, recorded with the slow sweep rate, exhibited short latency components after displacing each electrode 1 cm. anteriorly. (See text.)

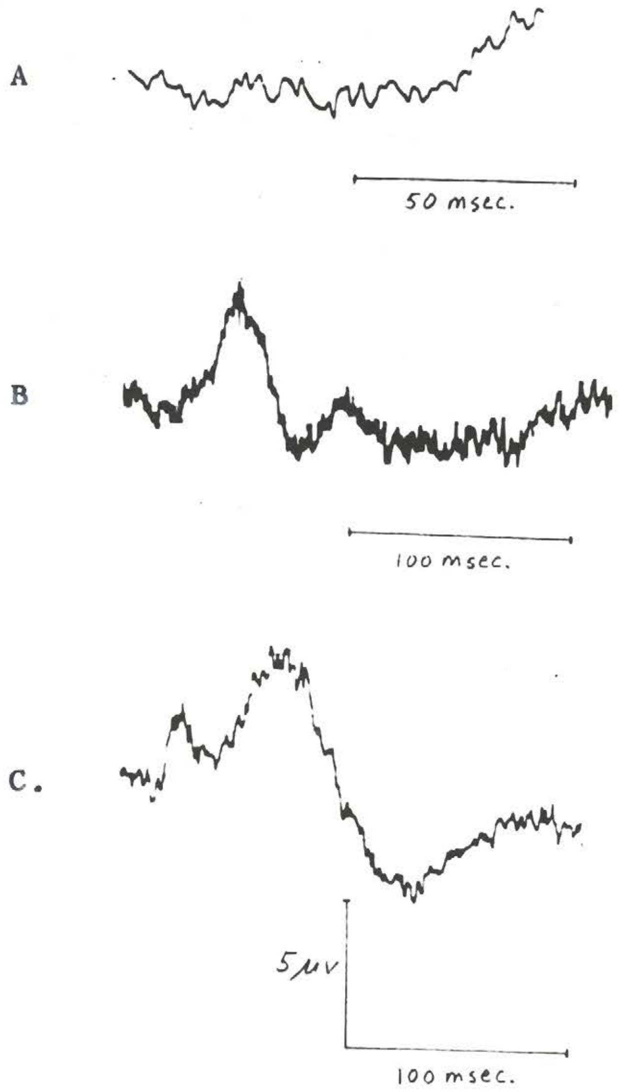


Fig. 9.

3. Recovery cycles of the early components of the responses.

The procedure of administering pairs of "conditioning" and "test" stimuli separated by varying intervals and the method of computing the recovery cycles have been described in the previous section. The degree of recovery of the early components has been expressed as a percentage of the ratio of the amplitude of the second response (R2) in relation to the first response (R1) for interstimulus intervals ranging between 2.5 msec. up to 170-190 msec. Full recovery is reached when R2 = R1, i.e. when the second response has reached the value of R1. When this occurs, the recovery curve is at the level of the line which indicates 100% recovery (See Fig. 10). The values of R1 have been found quite constant during any one experimental session. The amplitude measurements were made from the peak of the sharp negative deflection of component I to the peak of the positive deflection of component II which, in the subjects tested for recovery cycles, occurred respectively at latencies of 19.50 ± 1.00 msec. and 31 ± 5 msec.

Nine subjects were tested for their recovery cycles. Figs.11 & 12 show samples of responses to paired stimuli from which the recovery cycles were plotted. The variations in the amplitudes of R2 in relation to R1 can be observed at the different interstimulus intervals shown.

In general, the pattern of the recovery cycles measured were characterized by oscillations both below and above the line of full recovery, denoting periods of subnormal and supernormal excitability, as well as fluctuations in the level of excitability

Fig. 10. Recovery cycles of the early components of the somatosensory responses illustrated for two subjects. Recovery level of 100% indicates that full responsiveness has returned.

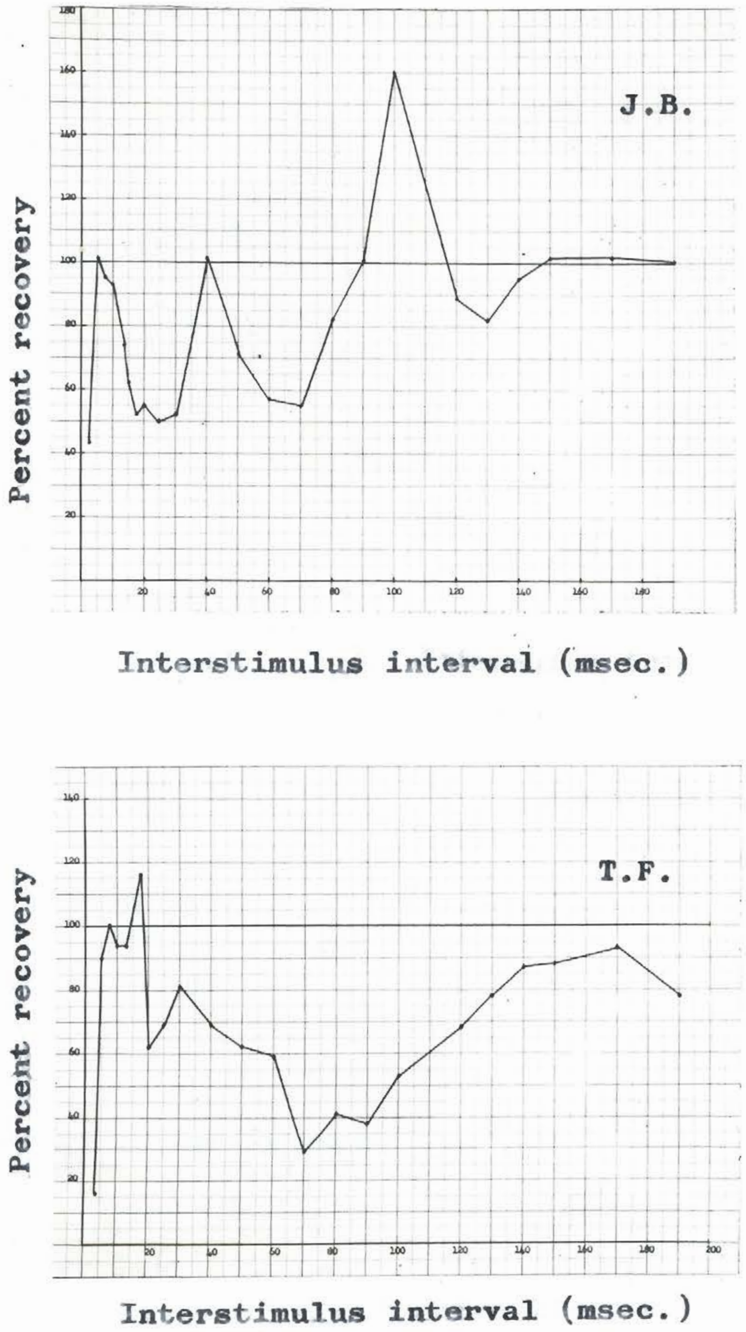

J.B.
Percent recovery
180
160
140
120
100
80
60
40
20
20
40
60
80
100
120
140
160
180
Interstimulus interval (msec.)
T.F.
Percent recovery
140
120
100
80
60
40
20
20
40
60
80
100
120
140
160
180
200
Interstimulus interval (msec.)

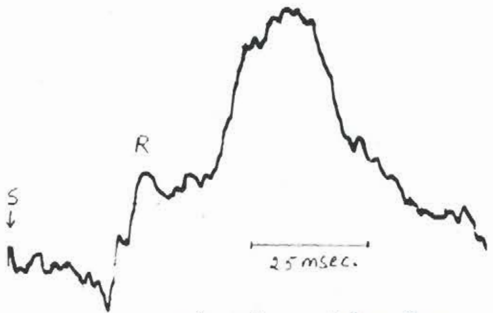
Fig. 10.

Figs. 11 and 12. Samples of responses to unpaired and paired stimuli illustrated for two subjects, J.B. (Fig. 11) and T.F. (Fig. 12). The method of calculating the true value of the response to the second stimulus (R2) is described in the text.

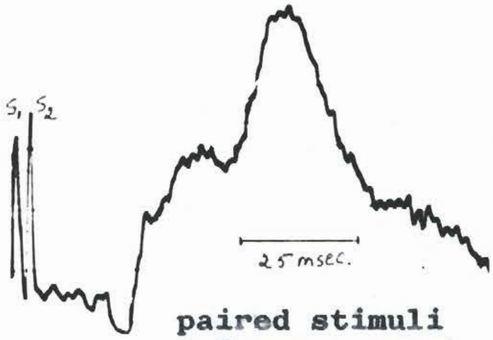
S1 and S2 = first and second stimulus artifacts.

R1 = response to first stimulus.

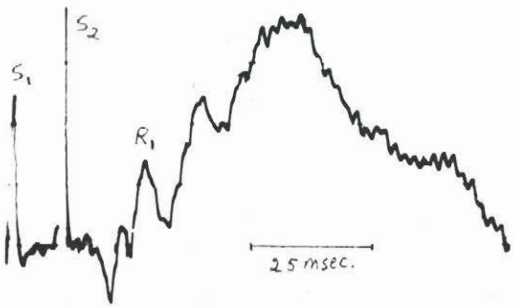
R = response to unpaired stimulation.



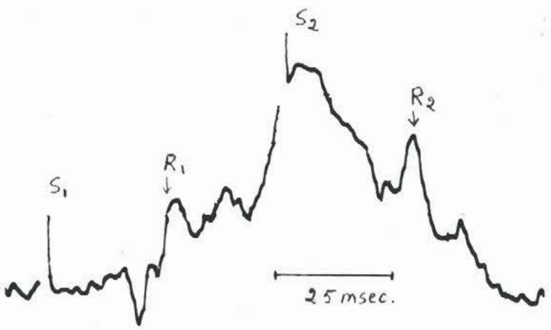
single stimulus



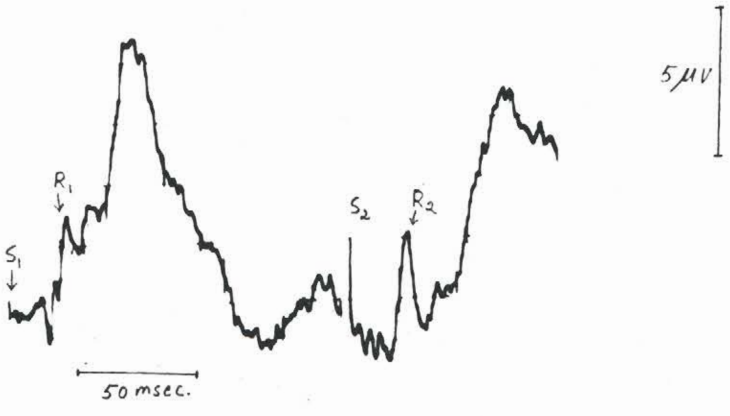
paired stimuli
2.5 msec. apart



10 msec. apart

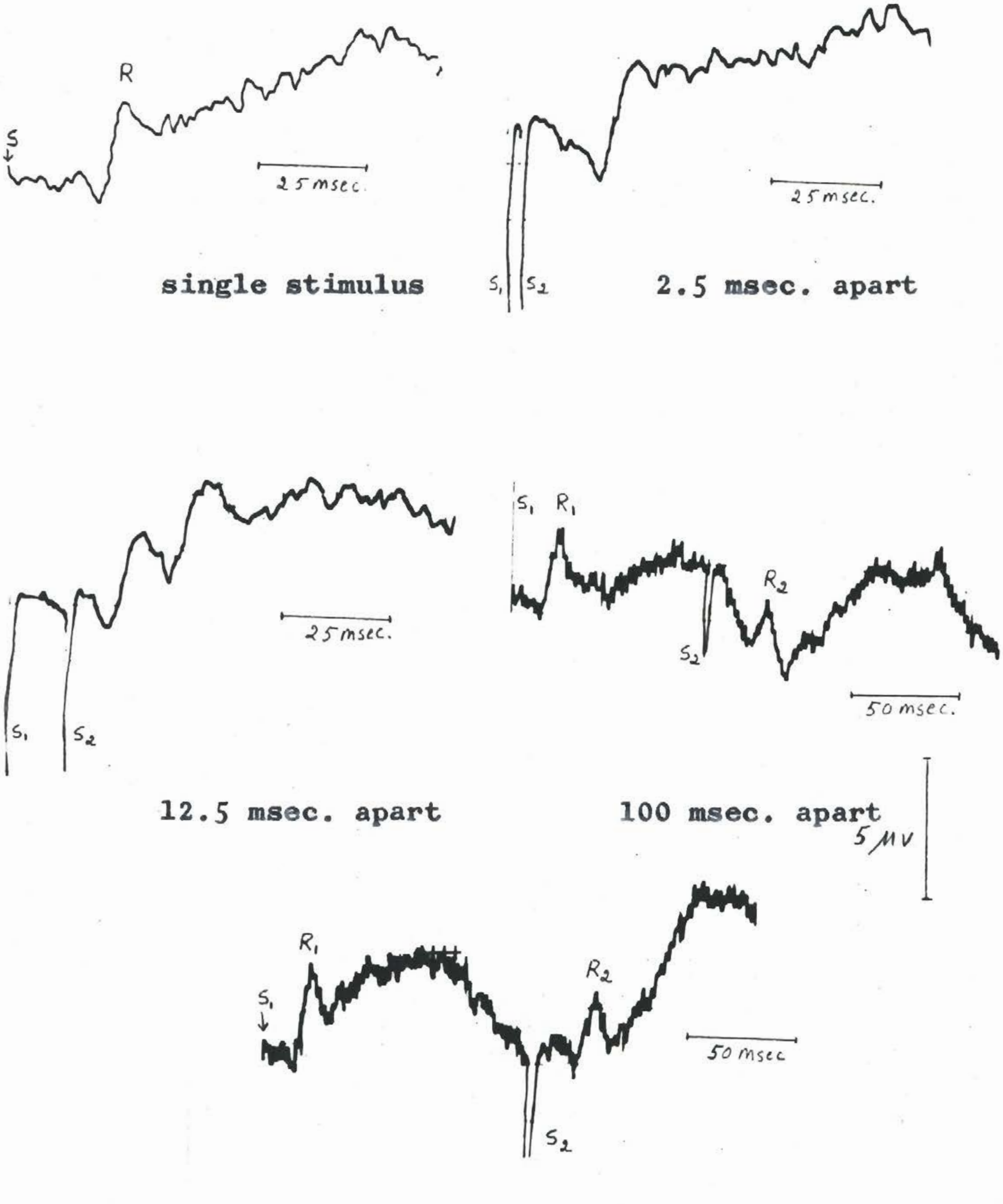


50 msec. apart



150 msec. apart

Fig. 11.



single stimulus

2.5 msec. apart

12.5 msec. apart

100 msec. apart

130 msec. apart

Fig. 12.

within each period (See Fig. 10). Although the recovery cycles differed in their individual forms, they seemed to conform to a general pattern. All cycles, in fact, showed a recovery peak or a tendency for recovery within the first 20-30 msec. and another peak at about 130-150 msec. The first peak of recovery appeared, however, to be a more constant feature, since other facilitation peaks occurred before 130 msec. All subjects but one (M.M.) showed at least one recovery peak during the duration of the recovery cycle. Seven subjects showed either full recovery or a facilitation peak within the first 20-30 msec. of the cycle. The two subjects (M.M., A.K.) who did not show an early recovery peak each attained a recovery level of 80% during the first 30 msec. and then their recovery cycles followed subsequently the general pattern of recovery described. Six subjects showed recovery or faciliation peaks at about 130-150 msec. and the subject (A.K.) reached full recovery for the first time during this period. Three subjects showed a third facilitation peak at about 80-100 msec. Table V summarizes the findings regarding the patterns of the nine recovery cycles mentioned.

In only one subject (M.M.) was a period of absolute unresponsiveness found at the beginning of the recovery cycle. It is of interest that this is the same subject whose curve did not recover at all during the whole duration of the cycle. All the other subjects started their recovery cycles at about 30% of full recovery.

The recovery cycle of one subject (D.S.) was measured after a six month interval using both monopolar and bipolar

Table V Summary of the patterns of the somatosensory recovery cycles measured in 9 subjects.

Recovery patterns observed	Number of subjects
Recovery or facilitation peaks within the first 20-30 msec.	7
Absence of full recovery within the first 20-30 msec.	2
Recovery or tendency for recovery within the first 20-30 msec.	9
Recovery or facilitation peaks between 130-150 msec.	7
Absence of full recovery between 130-150 msec.	2
Recovery or tendency for recovery between 130-150 msec.	9
More than two facilitation peaks	3

recording techniques; the other experimental parameters were the same. The trends of recovery were found to be repeatable but the quantative values differed somewhat. The cause of these differences requires further investigation which could not be pursued in this study.

4. Effects of some experimental changes.

During the course of this study, we studied the effects of changing the parameters of the stimulus on the recorded responses. In six subjects we decreased the stimulation frequency to 1 per 4 sec. instead of the usual 1 per 1.3 sec. We found that under this condition the later components (IV and V) tended to appear more clearly and assumed higher amplitudes, especially with the monopolar recording technique. The early components on the other hand did not change appreciably in size or pattern (See Figs. 13 & 14).

The intensity of the stimulus was also varied in 4 subjects. We determined first the sensory threshold in each of the subjects. Its value ranged between 24-28 volts. When the stimulus was at threshold value, we could not determine exactly whether a response was present or not in the tracings, as it could have been smaller than the noise level. Responses usually began to show when the intensity of the stimulus was around 40 volts. It was also found that the twitch threshold was always higher than the sensory threshold and that cortical evoked responses appeared before the occurrence of the twitch. All components of the response seemed to grow in amplitude and

Fig. 13. Effect of a lower stimulation frequency on the late components of the contralateral somatosensory responses. Both tracings were recorded bipolarly. The stimulation frequency was 1 per 1.3 sec. in A and 1 per 4 sec. in B.

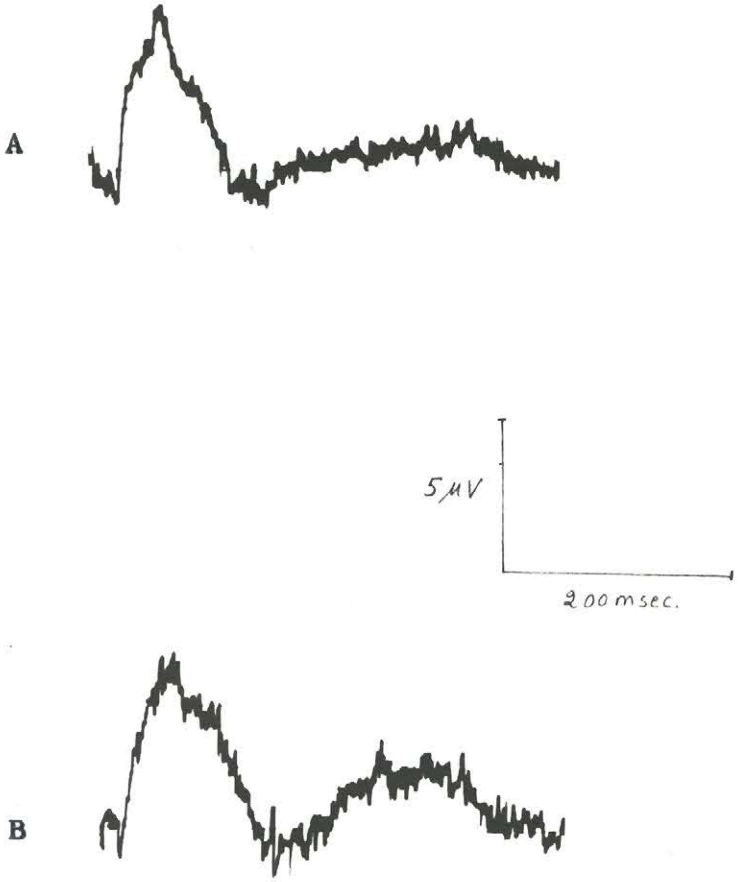


Fig. 13.

Fig. 14. Effect of a lower stimulation frequency on the late components of the contralateral somatosensory responses. Both tracings were recorded monopolarly. The stimulation frequency was 1 per 1.3 sec. in A and 1 per 4 sec. in B.

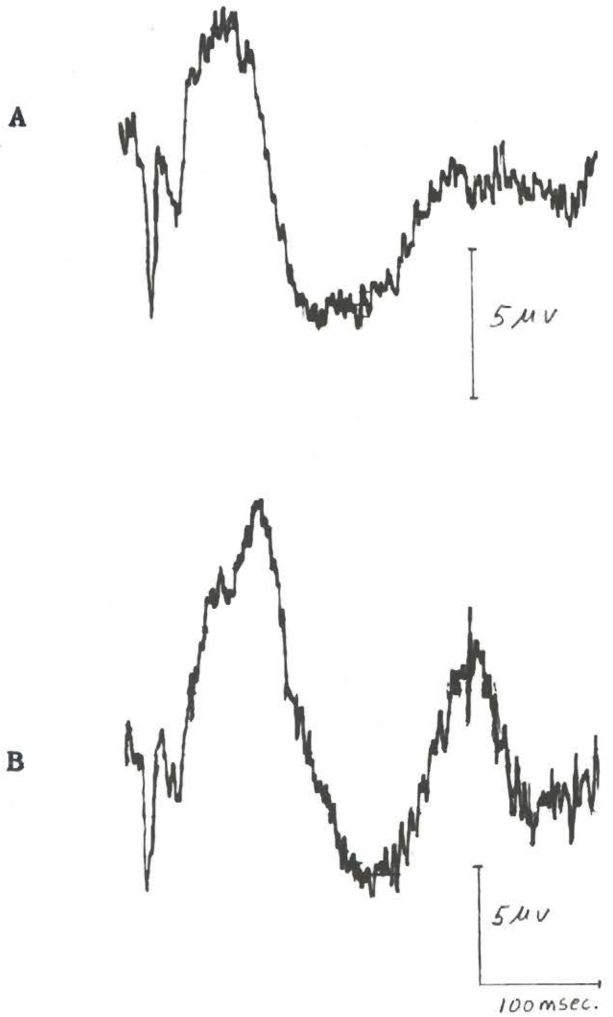


Fig. 14.

complexity as the intensity of the stimulus was increased (See Fig. 15).

5. Electrophysiological nature of the recorded potentials and exclusion of artifacts.

In recording electrical potentials from scalp electrodes, it is a legitimate question to ask whether the recorded signals do reflect the brain's activity or are of an artifactual origin. Some of the artifacts that may be mistaken for brain activity can originate from the recording system, the scalp musculature, eye blinks and eye movements, or from distant electrophysiological sources. In this study, we had firstly to guard against time-locked activities other than the evoked cerebral responses and secondly against non time-locked activities which can contaminate the averaged cerebral responses. As to the latter possibility, this applies to any averaging system and as mentioned before, the system used in this study was easily disrupted by excessive muscle potentials. These muscle artifacts could be detected as soon as they were produced while monitoring the build up of the response on the screen of the cathode ray oscilloscope and the run was then restarted.

That no artifact was produced by the averaging system itself could be shown by having the system function for the entire duration of the run but without applying the recording electrodes on the scalp. In this instance, no signals appeared on the screen of the oscilloscope.

To test the effectiveness of the averaging technique in

Fig. 15. Effect of increasing the stimulus intensity on the various components of the contralateral somatosensory responses. Tracings were recorded bipolarly. The sensory threshold was 28 volts in this subject. Voltages shown refer to dial settings of Grass S4 stimulator.

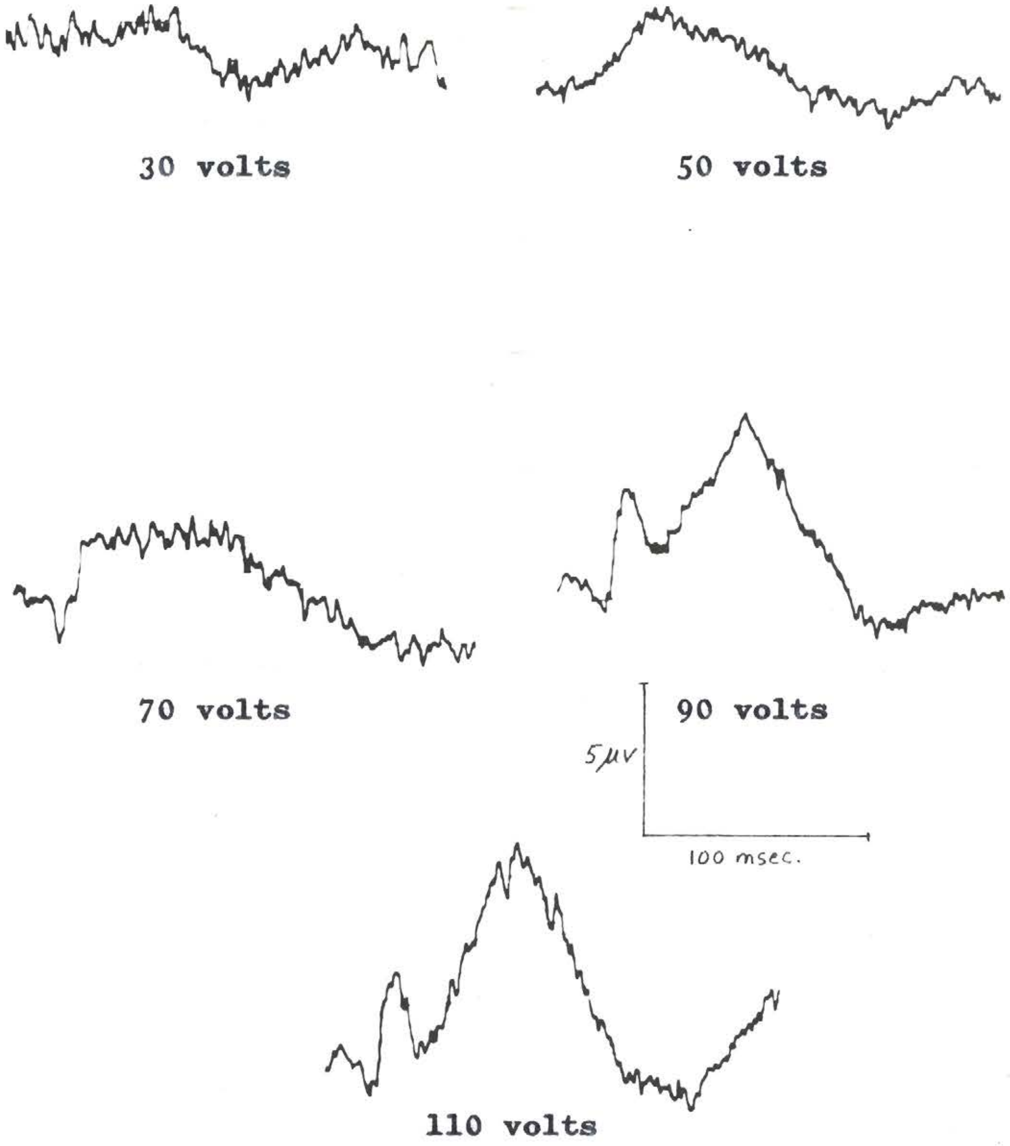


Fig. 15.

reducing the level of normal background activity, we recorded in 4 subjects up to 900 msec. samples under the usual experimental conditions but without applying stimuli to the ulnar nerve. In the seven tracings obtained in this way any components which were encountered were predominantly within the alpha frequency band, with peak to peak deflections of about 0.5 microvolts (See Fig. 16).

In order to test the possibility of very late components carrying over and contaminating the initial components of the response to the following stimulus, we also conducted these long term recordings (900 msec.) with stimulation. The recording system has an inherent minimum repetition rate of 1.3 sec., yet most of the major components were found to have died out before the end of the 900 msec. (0.9 sec.) recording. This indicates that there was no contamination from the carrying over of later components.

Other important sources of artifacts that had to be taken into consideration were the eye blinks and the associated eye movements. Eye blinks can occur as part of a muscular startle reaction (56), (57) associated with peripheral stimuli, or they may occur spontaneously. In 9 subjects, we recorded bipolarly some distance above the eye from positions Fp1 - F7 (standard ten twenty system), and in 4 other subjects, we recorded monopolarly either just above or below the eye. The time scales of the tracings extended up to 450 msec. to cover the duration of the early and late components of the somatosensory responses. In almost all the subjects the sensitivity of the averager had

Fig. 16. Absence of responses when no shocks were applied to the ulnar nerve. Tracings were recorded from the contralateral somatosensory areas with fast and slow sweep rates. Note the presence of a low amplitude activity within the alpha frequency band.

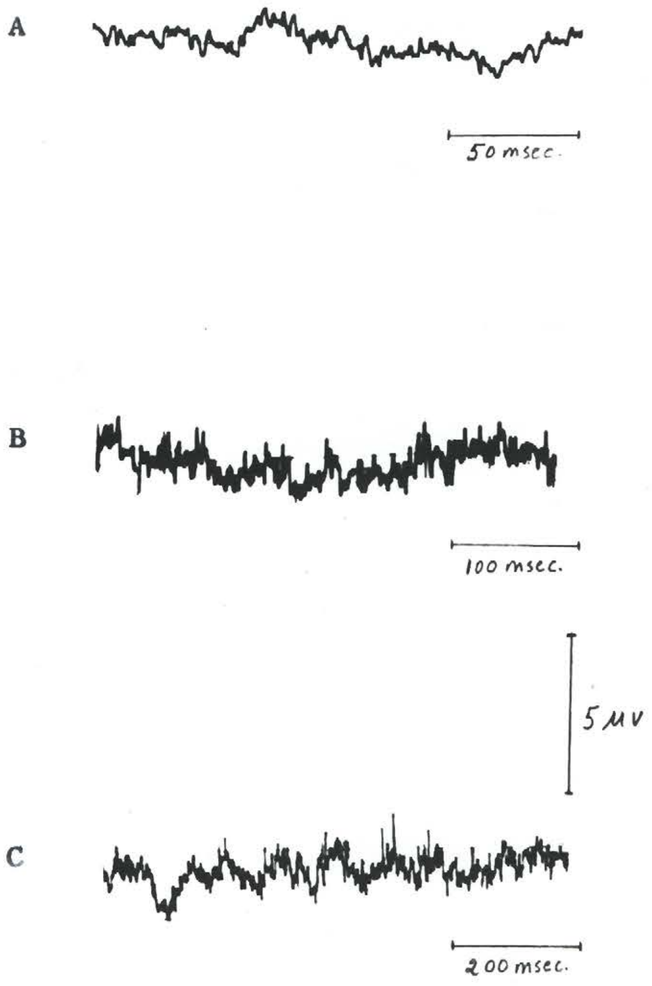


Fig. 16.

to be cut to one-half the usual gain in order to prevent extreme saturation of the raw record. Although the sensitivity was still high enough to detect normal evoked responses, blink artifacts were not found in the averaged record of any subject up to 450 msec. (See Fig. 17). We also recorded the eye blinks in 3 subjects with the ink writer of the Offner recorder. The electric pulse of the stimulator was fed into the Offner recorder to show the relation of the blink to the stimulus. In two of these subjects, the blinks occurred randomly without apparent relation to the stimuli, and with a frequency similar to their spontaneous occurrence during a control period in which they were recorded without applying shocks. In the third subject, we started recording his eye blinks at the beginning of the experimental session before the possible occurrence of habituation. The shock intensity was within the usual range. It was found that this subject blinked after each of the first four stimuli but these blinks varied in their latencies and patterns. Subsequently, the subject blinked 20 times during a period of time in which he received 72 shocks at a rate of 1 per 2 sec. These later series of blinks occurred randomly without apparent relation to the stimuli and varied in their latencies, amplitudes and patterns. It was concluded that the blinks were not time-locked to the stimuli except possibly the first few, and that the stimulus intensity used was not sufficient to produce blinks as part of a startle reaction or that if these blinks occurred, they became rapidly habituated.

The high degree of repeatability of some components

Fig. 17. Monopolar tracings recorded just below the eye in A and above the eye in B. There is no evidence of blink artifacts or other time-locked activity up to about 450 msec. after the stimulus.

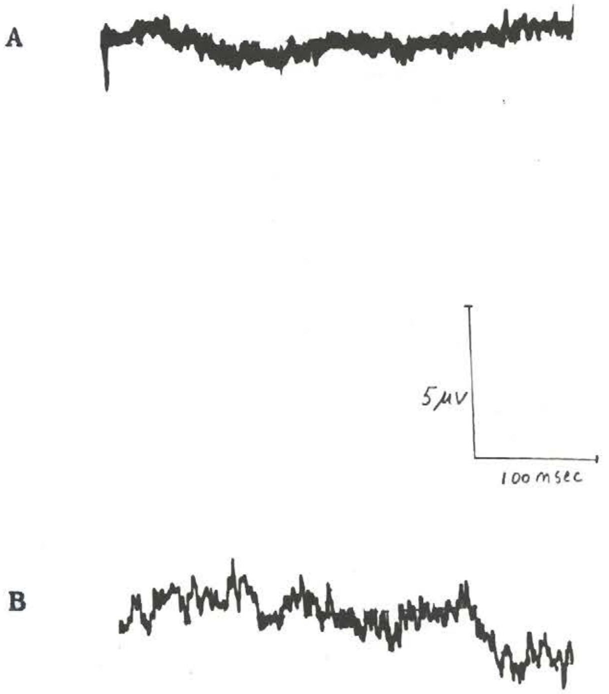


Fig. 17.

within the same subject after a long interval of time, their conformity to a general pattern in all subjects tested, and their differential distribution on the scalp are all in favour of their neurophysiological origin. Further evidence that the average responses recorded from the scalp reflect average responses detectable on the underlying cortex has been presented by Geisler (43). This author recorded in the monkey evoked responses to clicks from points lying each directly underneath the other on the different coverings of the brain, from the scalp to the pia mater. He demonstrated the effects of the different conductivities of these layers on the evoked potentials, and concluded that the "average responses recorded from the pial surface of monkey cortex are faithfully reflected at the surface of the scalp, as long as the potential fields evoked by the stimuli are not too sharply localized....we therefore expect that average responses obtained from the scalp of human subjects will indeed reflect activity existing in the brain beneath". Furthermore, the responses recorded in this study were similar to the responses recorded directly from the surface of the brain in man both with averaging (48) and non-averaging techniques (50).

V DISCUSSION

1. Description and distribution of the responses.

The cerebral responses to somatic stimulation do not differ essentially in their general pattern from the cerebral responses to other sensory modalities. As pointed out in the review of the literature, this general pattern consists of: i) short latency components; ii) long latency components; iii) late repetitive rhythmic waves. The characteristics of these major components have been described.

We have found as noted by Goff *et al*.(45), that a monopolar recording technique with the reference electrode on the bridge of the nose yielded less variability in the recorded responses than the bipolar technique. The latter technique tended to accentuate the inter-subject variations of the late components, and would be therefore less useful for the study of the form and distribution of the responses. The difficulties associated in averaging the responses of a monopolar recording have been discussed.

Our results on the latencies and the waveforms of the somatosensory evoked responses extending up to 500 msec. were found to agree, generally, with Allison's findings as well as with his classification of the responses into five components (3). The literature shows that there exists a fair agreement among the authors regarding the early part of the responses extending up to about 60 msec., corresponding to the first three of these five components. These similar results were obtained by different workers whether a photographic superimposition technique (29), (30), (55), (56), (57) or an electronic summation technique was used (32), (14), (69), (3), (45), (43), (76). See Table I. Direct recording from the surface of the brain also yielded early responses similar to those recorded from scalp electrodes (80), (50), (48).

These rather stable responses correspond to the negative deflection of component I and to the positive deflection of component II whose peaks occurred respectively at latencies of 19.50 ± 1.50 msec. and 31 ± 5 msec. in our subjects. The smaller values (25 ± 5 msec.) given to the positive deflection by some authors (55), (29), (69) seem to correspond to the last positive deflection of component I. This wave was found in our tracings, but it was not included in Table IV because of its inconstancy. Deflections similar to wave III, which occurred at 50 ± 9 msec., have been described by Larsson (55), Calvet <u>et al</u>. (14), Dawson (32), and Geisler (43). The wave labelled "N" by Uttal and Cook (76) falls within this range of latency.

Regarding the distribution of the responses, it is to be noted that we recorded from different scalp locations successively rather than simultaneously, because of the availability of only one averaging channel. It was found that components I and II were distributed more widely than was reported in earlier studies (29), (55) and were mainly present in the posterior contralateral quadrant of the scalp. The potential gradient of components I and II which was found to be steeper anterior to than posterior to the surface marking of the central sulcus has also been reported by Dawson (30) and Goff et al. (45).

Our findings on the distribution of component III, though scanty, compare with those of Goff et al.(45) who studied systematically the distribution of the somatosensory evoked responses from 21 locations in each of 6 subjects. The fusion of components II and III noted in this study have been reported in recent studies. The reason for this fusion is not clear; however, it does not seem to be related to the electrode placement (76). The implication of this fusion on the measurements of the recovery cycles will be discussed subsequently.

The late components are exemplified by the diphasic waves IV and V. These components occurred with peak latencies ranging from 63 ± 22 msec. to 240 ± 50 msec. (See Table IV and Fig. 3). They showed some overlap in their latencies and their distribution was widespread over the scalp. Component V was constantly present and reached its highest amplitude at the vertex.

On account of their higher amplitudes and longer durations, the late components of the responses have been recorded in the electroencephalogram using standard procedures. In 1939, Davis (28) recorded a diphasic or triphasic "on-effect" to auditory stimulation in waking subjects. This response lasted about 300 msec. and was highest at the vertex. Its amplitude ranged up to 100 microvolts. Davis et al. (24) described the "K-complex" in sleeping subjects and related its slow component to the "on-effect" observed in waking subjects. Gastaut (41) and Bancaud et al. (6) described simultaneously in 1953 under the names of "vertex spike" and "V-potential" a prominent negative wave with a phase reversal at the vertex. When this wave was not monophasic, its initial deflection was always negative. In 1956, Roth et al. (66) described a long latency response to various stimuli both in waking and sleeping subjects under the name of "K-complex". They disagreed with previous workers (41), (6), (55) about the polarity of its initial deflection, stating that "though the most prominent deflection is sometimes surface negative, careful examination has in our cases almost invariably revealed a small surface positive deflection preceding it". They reported also that "the form of the response is influenced by its voltage". Among the workers who used averaging recording techniques, Larsson (55), (56) described the "non-specific" response. This response was widespread in its distribution and consisted of a negative wave occurring between 50-90 msec. and a positive wave occurring between 100-120 msec. Calvet et al. (14) recorded two biphasic (negative-positive) waves with similar latencies to components IV and V. The wave labelled "O" by Uttal and Cook (76) seems also to correspond to components IV and V. The results given by Allison (3) and Goff et al. (45) are close to those obtained in this study.

Late repetitive rhythmic waves were at times recorded in our series. They have also been reported by other workers and seem to be less prominent after a somatic stimulus than a visual one (55), (14), (23), (3).

2. Recovery function of the early components.

A tentative general pattern for the recovery cycles of the early components of the somatosensory responses was described previously as noted above. This pattern consisted of a facilitation peak or a tendency for recovery within the first 20-30 msec. of the cycle and similarly another peak at about 130-150 msec. Other peaks of supernormal excitability or full recovery also occurred in the intervening part of the cycles. It should be stressed, however, that beyond the tendency to conform to this general pattern, the prominent feature of the recovery cycles that we measured was rather their phasic variations and oscillations within each phase so that no two cycles were found to follow exactly the same course of recovery.

The recovery functions of the early components of the somatosensory evoked responses have been studied recently by Shagass and Schwartz (69), (71), Allison (3), and Uttal and Cook (76). Our findings concerning the early peak of recovery agree with those obtained by Shagass and Schwartz. Allison reported a U-shaped recovery function for component I. He found that the recovery level of this component was about 60% at 3 msec.; it then decreased to about 20% between 5-20 msec. and it reached 90% at approximately 200 msec. Allison reported also that "the recovery function of 2, like that of 1, tends to be U-shaped, although 2 showed a greater degree of subnormality than did 1" (3). The discrepancy between our findings and those of Shagass and Schwartz on the one hand and those of Allison on the other hand regarding the early peak of recovery may be related to the different procedures used by the latter worker. Allison, in fact, employed a monopolar recording technique and had fewer intervals between 10 and 20 msec. He also used a different computation technique whereby he could obtain directly the amplitude of the second response by "programming the computer to cancel the conditioning response while summating the test response" (3). To test the effect of a monopolar recording technique on the pattern of the recovery cycles we repeated the recovery cycle of subject D.S. both monopolarly and bipolarly during the same session, and found that the general pattern of recovery was the same in either case, though they differed quantitatively.

Uttal and Cook (76) measured in two subjects the recovery cycles of the "M" wave. This wave seems to correspond to either component I or to a combination of I and II. The early course of the recovery cycles measured by these authors cannot however be assessed from their curves which started at 25 and 40 msec. In one of their subjects, the recovery level was 90% at 25 msec. and in the other subject, it was about 55 % at 40 msec.

In our series, the average level of recovery at the shortest time interval (2.5 msec.) of the recovery cycles was found to be about 30% in 8 of the 9 subjects. In only one subject (M.M.) was an initial period of absolute unresponsiveness present. It is of interest to note that this is the same subject whose curve did not recover during the whole duration of the cycle. Shagass and Schwartz on the other hand have shown "normal" recovery cycles which started at the zero level of recovery (absolute unresponsiveness) (69). Our findings on the pattern of the recovery cycles agree otherwise with those of the latter authors who also described facilitation peaks between 20 and 100 msec.

The absence of full recovery in M.M. (80% in the first 30 msec.) may be merely a normal variation or be due to the state of alertness of the subject during experiment. It may also be accounted for by a fusion of components II and III of his responses. The positive peak of his component II occurred at 35 msec. and it was immediately followed by another positive peak occurring within the latency range of component IV. It is to be noted in this regard that Allison reported a recovery time of about one sec. for component III.

The cyclic variations observed in the cortical recovery cycles of our subjects have been reported in previous studies both in man and in animals (40), (65), (34), (69). The mean values of the facilitation peaks which occurred within the first 30 msec. and between 120-150 msec. of the recovery cycles have been calculated for all the subject except M.M. These values showed a mean recovery level of 107% and 105% for the respective facilitation peaks. This degree of facilitation slightly above the level of full recovery seems to be related to the fact that our subjects were instructed to keep alert during the experiment. Evarts et al. (34) and Schwartz and Shagass (67) have pointed out the relatianship between states of alertness and cortical recovery cycles in cats with chronically implanted electrodes. These authors demonstrated that states of alertness characterized by an electrocortical pattern of arousal tended to be associated with low facilitation peaks in the cortical recovery cycles, and that sleep tended to be associated with higher facilitation peaks.

SUMMARY

A study of certain aspects of the cerebral responses evoked by ulnar nerve stimulation has been made on 19 normal subjects. A single-channel analog averager was used to separate these evoked potentials from the ongoing background activity of the brain.

1. The recorded average responses were found to consist of complex waveforms which lasted up to about 500 msec. For descriptive purposes these responses were divided into five components and the pattern of each component was detailed. The early components of the responses showed relative stability in their latencies and patterns, and were highly repeatable; the late components showed greater variations in these parameters, and were less repeatable.

2. The study of the differential distribution of the components on the scalp revealed that components I and II were relatively more localized. They were recorded from the posterior contralateral quadrant of the head and seemed to spread from a fairly circumscribed focus. Component III seemed to be more pronounced over the contralateral placements on the scalp. Component IV was diffuse and showed a great variation in its distribution. Component V was constant and widespread, reaching its maximum amplitude at the vertex.

3. The recorded potentials were discussed in terms of their neurophysiological nature and the elimination of possible sources of artifacts.

4. The recovery cycles of components I and II were measured in 9 normal subjects. The patterns of these recovery cycles were studied and described in view of the reported changes which can occur in certain psychiatric patients.

5. The findings obtained in this study were compared to and discussed in relation to the results obtained in some recent works.

6. The literature on evoked responses and the relationship of these responses to some behavioural and psychological phenomena have been reviewed with regard to this work.

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