SPECIFIC AND NONSPECIFIC ACTIVITIES OF THE VISUAL SYSTEM IN RABBITS

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Although it has been shown that the rises in cortical activities by 3 and 5/sec flash stimulations verified in the frequency response of the visual cortex of unanesthetized rabbits (MIMURA and SATO, 1965) can be correlated with the excitability changes of 5/sec (BISHOP, 1933) or 4-5/sec (PEARLMAN, 1963) in the visual cortex of the rabbit, it was not ascertained whether these excitability changes originated from the cortex itself or from subcortical structures nor was it ascertained whether it was from the specific or the nonspecific system. The present study is an attempt to solve the above problems through observations on the pattern of response to repetitive flash stimulations in the specific and non-specific systems of the cortex and subcortical structures of anesthetized and unanesthetized rabbits.

METHOD

Ten anesthetized and eleven unanesthetized rabbits weighing about 3 kg were used. The anesthetized experiments were carried out under an intraperitoneal administration of sodium pentobarbital at a rate of 15 mg/kg/2 hrs. The animal was mounted on the Johnson type stereotaxic instrument. Intubation to the trachea under ether anesthesia was done in unanesthetized experiments and the animal was immobilized after opening the skull by intraperitoneal administration of Flaxedil throughout the experiment, which necessitated artificial respiration with oxygen-mixed air.

Stainless steel electrodes of 0.5 mm and/or 80 μ diameter, insulated except at the tip, were inserted stereotaxically into the brain according to the atlases of SAWYER et al. (1954), MONNIER and GANGLOFF (1961) and FIFKOVÁ and MURŠALA (1962). Surface records from the cortex were taken with 0.5 mm diameter silver ball tipped electrodes. ERGs were recorded by placing the same silver ball electrode on the cornea. All recordings were monopolarly taken in relation to a reference electrode on the neck muscle. The location of the electrodes were checked histologically by the KLÜVER-BARRERA staining techniques (1953) after each experiment.

The exposed cortical surface was covered with warm mineral oil. The temperature

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of the shielded room was maintained at 28–29°C and sometimes a rubber bag filled with hot water was placed beneath the abdomen to keep the animal in good condition. The pupils were dilated with a 0.5% solution of atropine.

Stimulation was delivered by a photic stimulator to both eyes. A flash of 6000°K, 100 μ sec duration and 1 watt/sec energy from a strobo-flash bulb (Mazda, FT 100), which had been placed 50 cm away from the eyes, was used. The flash was passed through a 10 cm diameter iris and was further diffused through a frosted glass plate and a white curtain. Subcortical structures were stimulated by rectangular waves of 4–6 Volts intensity and 0.1–0.5 msec duration through bipolar depth electrodes (distance between electrodes 0.5 mm).

Ink records in the anesthetized animals and magnetic records on 1/4 inch tape monitoring ink records in the unanesthetized animals were obtained simultaneously through a 8-channel polygraph (RM-150, Nihon Kohden, Tokyo) and 8-channel data recorder (SPRA-48, Shiroyama Tsūshin, Tokyo), respectively. The average response time-contours to flash and electrical stimulations were computed by the simplified method of SATO et al. (1962) in anesthetized experiments. Though the stimulation was delivered for 30–60 sec, ten evoked responses from the tracings between 3–10 sec after the onset of the repetitive stimulation were selected to average the relatively constant amplitude of the evoked potentials. In the unanesthetized experiments, magnetic records of the responses were summed up thirty times to eliminate irrelevant background fluctuations over an analysis time of 500 msec through the Digital Computer for Data Processing (ATAC-401, Nihon Kohden, Tokyo).

RESULTS

PART I. EVIDENCES IN THE ANESTHETIZED RABBITS

1. *Repetitive flash stimulation.* A part of the tracings during repetitive flash stimulation and the average responses are shown in FIG. 1 and 2. The average evoked response in each brain site was found to consist of two or three components, in which the first and second components were marked here. In the cortex, the initial surface positive wave (peak latency: 60–95 msec) and the following surface positive (95–208 msec); in the lateral geniculate body (GL), the initial (peak latency: 52–86 msec) and the following upward deflections (112–172 msec); in the midbrain reticular formation (RF, P+9 L+2.5 H–3 in the atlas of SAWYER et al.), the initial (peak latency: 35–65 msec) and the following downward deflections (108–155 msec); in the superior colliculus (CS), the initial (peak latency: 43–65 msec) and the following downward deflections (99–146 msec) were studied. The primary response or the corresponding response is equal to the above initial potential. In this paper, the initial and the following deflections in each site except RF were assigned the name potentials A, A', B and B' respectively, whereas A, B, B' and B'' in RF. An example of the amplitudes of these potentials in relation to the flash frequencies (the amplitudes-frequency diagrams) is presented in FIG. 1Z and 2Z. Peak(s) appeared in the curves from almost all sites. In GL, peaks appeared at 2 f/sec in the A and B potentials, and at 2 and 5 f/sec in the A' potential. In RF,

FIG. 1. Examples of the brain masspotential ink records (X), the average response time-contours (Y) and the amplitude-frequency diagrams (Z). X: Ink records from the visual cortex (Cv), lateral geniculate body (GL) and midbrain reticular formation (RF) during 1 to 10/sec flash stimulations. Y: Average response time-contours to various flash frequencies. Z: Diagrams to depict the relation between the amplitude of each component (ordinate) and flash frequencies (abscissa). A, A', B and B' or B'': A, A', B and B' or B'' potentials respectively. Upward deflection in the time-patterns in all figures of this paper is negative.

FIG. 1.

maximum amplitudes were observed at 1 and 4 f/sec in the A and B potentials, at 1 and 3 to 5 f/sec in the B' potential and at 2 f/sec in the B'' potential. In the visual cortex, enhanced responses were seen at 2 and 5 f/sec in the initial surface positive A potential, at 1 and 5-6 f/sec in the following negative A' deflection and at 2 and 4 f/sec in the second positive B and negative B' potentials. The GL activity in this instance was characterized by the 2/sec acti-

FIG. 2. Patterns of response in the superior colliculus (CS) to various flash frequencies. X: Ink records. Y: Average response time-contours. Z: Amplitude-frequency diagrams of each component.

vity and the slight 5/sec activity, while the RF was characterized by the 1 or 2 and 4/sec activities. Cortical response patterns appear to be a mixture of both GL and RF, since the enhanced activities at 2 f/sec in the A, B and B' potentials and at 1 f/sec in the A' potential seem to be reflections of the characteristic activities of corresponding frequencies in GL and RF, while those at 5/sec in the A and A' potentials and at 4/sec in the B and B' potentials of the cortex seem to correspond with the characteristic activity of GL and RF, respectively.

Fig. 3. Typical response amplitude-frequency diagrams of each response component in various brain sites. Each curve was obtained by taking the average of five cases in the cortex, three cases in GL and RF and two cases in CS obtained under the same experimental conditions. A, A', B, B' and B'' indicate the response component. See text for details.

but it was enhanced at 1 and 8 f/sec. Enhanced activities in RF, the non-specific system, were elicited by stimulations of 1 and 4 f/sec in the B potential, by 1 and 3-5 f/sec in B', and by 2 f/sec in B''. Though both activities in GL and RF were characterized in common, therefore, by enhanced activity at 1 or 2/sec in the four potentials, distinct differences were revealed in such A potential activities that appeared a monotonous deterioration in GL and approximately flat trough at 3-7/sec following enhancements at 1 and 8/sec in RF and also in such B potential activities that followed a slight hump at 5-6/sec in GL and a distinct one at 4/sec in RF.

In the cortical responses, maximum amplitudes were obtained at 1 and 5 f/sec in the A potential, at 3 f/sec in A', and at 1 and 4 f/sec in B. As noted above, the most parts of the cortical activity may be a reflection or a mixture of the subcortical activities, since the 1/sec activity may be qualified by both GL (A and B') and RF (A, B and B'), while the 5 and 4/sec activities in the A and B potentials may be affected by B potential in GL and RF respectively. The cortical 5/sec activity may possibly be due to the cortical activity itself, at least in part, since it was one of the predominant activities in the diagram while that in GL was subdominant one. This evidence suggests that the 5/sec activity in the early response A of the cortex is partly influenced by the specific activity, whereas the later ones such as B and B' are affected by the nonspecific activity. The amplitudes of the A and A' potentials of GL and CS decayed with increasing frequency though there were some variabilities. This tendency was very similar to that of the retina (MIMURA and SATO, 1965), indicating little modification in the information from the retinal activity. Other responses in CS were observed as enhancements at 5 f/sec in the A' and/or A potential and at 3 and 5-6 f/sec in B, which may correspond with the patterns of the specific system, whereas 1/sec in A and A' may be related to both the specific and nonspecific systems.

2. *Repetitive electrical stimulation of GL and RF.* Nervous impulses originated from the retina will be transmitted to the cerebral cortex via mainly two routes, i.e. the specific and nonspecific pathways. In order to elucidate their frequency characteristics in the cortex which originate from GL or RF, the response patterns induced by stimulation to GL and RF, respectively, were studied. By this means, the cortical activity via GL or RF among the photically induced activities can be observed separately.

a) *GL stimulation.* Definite responses in the visual cortex and feeble responses in RF were produced by electric GL stimulation (FIG. 4X). The former were augmented distinctly by 3 and 5-6/sec GL stimulation, whereas no augmentation was observed in the motor cortex (FIG. 4X, Cm). Hence, these slow responses in the visual cortex may be considered as the augmenting response. The average time-contours of these responses in relation to the

FIG. 4. Patterns of response in the cortex and RF evoked by repetitive electrical stimulation to GL. X: EEG ink records. Responses in the motor cortex (Cm) were highly contaminated, while the augmenting responses were very remarkable in the visual cortex (Cv), especially at 3 and 5/sec stimulations. Y: Average response time-contours in the visual cortex (CORTEX) and RF. In order to eliminate stimulus artifacts, there are short blanks immediately prior to the potentials. Arrows denote stimulus pulse. Z: Amplitude-frequency diagrams. I, I', II and II' indicate the activity patterns of potential I, I', II and II' respectively.

FIG. 4.

stimulating frequency are illustrated in FIG. 4Y. The cortical response exhibited two remarkable components, i. e., a surface negative potential with 34-39 msec peak latency, which corresponds to the fifth wave elicited by stimulation of the optic pathway of cats (CHANG, 1952; MALIS and KRUGER, 1956), and a long-lasting surface negative shift with a 164-173 msec peak latency. These two waves and the following deflections to each potential were provisionally called potentials I, I', II and II' respectively (FIG. 4Z). In RF, a slow upward deflection (52-61 msec peak latency), followed by a downward deflection accompanying a small upward deflection, was elicited. The amplitudes of these response components were plotted in relation to the stimulating frequencies (FIG. 4Z). It was observed in the cortical activity via GL that the I potential was enhanced by a 3-4/sec and 8/sec stimulation, I' was enhanced markedly by 5/sec and slightly by 2 and 8/sec stimulation, II was enhanced by 2-3/sec, and II' was increased by 1-2/sec stimulation. The enhanced activity at 3-4/sec in the I potential and that at 5/sec activity in I' correspond respectively to those in A' potential, and in A and A' (FIG. 3). These correspondences suggest that the cortical activity via GL is attributable mainly to the short latency components with characteristic frequencies of 3 and 5/sec in response to the flash stimulation.

RF activities via GL, however, were characterized by 4/sec activity only in the I' potential since other components were not conspicuous in their patterns.

b) *RF stimulation.* Part of the electroencephalographic ink records made during repetitive electric RF stimulation at various frequencies and the aver-

age response time contours in the motor cortex and GL are shown in FIG. 5X and Y respectively. In the cortex, a long-lasting, large and surface negative potential with 86-103 msec peak latency was preceded by a small, surface negative one of short duration with 22-26 msec peak latency, which sometimes

FIG. 5. Patterns of response in the cortex and GL to repetitive RF stimulation. X: EEG ink records of the visual cortex (Ctx) and GL during 1 to 10/sec RF stimulation. Numerals on the left indicate the stimulating frequency. Y: Average response time-contours. Z: Amplitude-frequency diagrams in GL, visual (Vis) and motor cortex (Mot).

could not be readily shown on the figure. In GL, a sharp and upward deflection followed by a small upward deflection was observed with peak latencies of 17-26 and 65-78 msec respectively. These potentials that preceded or followed in the cortex and GL were named provisionally as potential I and II respectively, while the surface positive one in the cortex and the downward deflection in GL, which followed I and II, were named as I' and II' (FIG. 5Z). Their average amplitudes with respect to the stimulating frequencies were depicted in FIG. 5Z. The responses in the visual cortex were only slightly enhanced respectively by 3-5 and 1/sec RF stimulation in the I' and II' potentials, and a trace of elevation by a 4/sec in I and small II' was observed, though in the motor cortex the II potential showed more outstanding enhancement by a 4/sec stimulation than in the visual cortex and the II' potential did a raised activity at 3/sec. The 4/sec activity was distinct in I of unanesthetized animal (FIG. 14, Vc) and was similar in frequency to that of the B and B' potentials of the anesthetized cortex brought out by flash stimulation (FIG. 3), whereas the 1/sec activity appeared in the A and B potentials. It seems, therefore, that the cortical activities via RF are mainly related to the late component in the visual response, and that their characteristic frequencies are 1 and 4/sec, though the activity of the former frequency is related also to the early component.

GL activities via RF were characterized by 2 and 5/sec in I', 2-3/sec in II', and, though slightly, 1 and 6/sec in I. Some of these activities were the same in their frequencies to those associated with the GL and visual cortex activities elicited by photic stimulation, which are, therefore, inherently specific ones.

PART II. EVIDENCES IN THE UNANESTHETIZED RABBITS

1. *Repetitive flash stimulation.* Responses evoked by flash stimulation of varying low frequencies (1-15/sec), contaminated by the background activities, were traced in the motor (Mc), visual (Vc) and limbic cortex (Lc), lateral geniculate body (GL), optic radiation (OR; 2 mm beneath the cortical surface), mid-brain reticular formation (RF), Pulvinar (Pul), superior colliculus (CS) and, in a few cases, in the optic tract (OT). ERG was also recorded as an index of retinal activity. An example of the ink records and average response time-contours analyzed by ATAC-401 are depicted in FIG. 6X and Y, respectively. Typical wave forms of these potentials evoked by low frequency flash stimulations of 1 or 2.5/sec are illustrated in FIG. 7. The amplitudes of the waves, indicated as A, A', B, B' and C respectively were measured at each frequency. Here, the A potentials in GL, OR and Vc correspond to the primary response via the visual specific pathway. The response amplitude-frequency diagrams for various brain sites, illustrated in FIG. 8, were obtained by averaging eight

FIG. 6. An example of ink record during 1/sec flash stimulation (X) and average-time-patterns obtained by the Computer (ATAC-401) at various flash frequencies at various recording sites (Y). X: r; right, Mc; motor cortex, Lc; limbic cortex, RF; mid-brain reticular formation, Vc; visual cortex, OR; optic radiation, OT; optic tract, ERG; electroretinogram, sig; flash stimulus. Time scale: 1 sec. Y: numerals on the left indicate flash frequency. Thirty responses were averaged for each response over the analysis time of 500 msec.

FLASH

FIG. 7. Typical wave forms of responses evoked by flashing light. A, A', B, B' and C indicate the components of the evoked potentials. The amplitudes indicated by the broken line were measured for every average response at each flash frequency. In CS, two responses to successive stimulus of 2.5/sec stimulation were seen.

experiments in b-wave, five in GL, eight in OR and Vc, four in RF, two in Pul, three in CS and seven in Lc. The amplitude of the electroretinal b-wave was found to monotonously decrease with increasing flash frequency as has already been verified in the previous report (MIMURA and SATO, 1965). However, almost all components of the recordings from the various sites showed peaks in the diagrams.

In the specific system, the A potential of GL was augmented at 4.5-6/sec, and the C potential was enhanced at 2 and 3.5/sec stimulations, while the B potential did not show any appreciable enhancement except at 10/sec. In Pul, the specific elaborative nucleus, the activities of the B and C potentials were similar, respectively, to those of the A and C potentials of GL, although no pronounced periodic changes of the activities were brought out in the A and B' potentials.

On the contrary, in the nonspecific system, such as RF, no augmentations like those in GL were observed in either the A or C potential, except for a small hump at 1-2 and 3.5/sec in the A potential. Augmentative activity was brought out only at less than 6/sec in the B potential. In view of the similarity in the activity changes, the activities in the cortical area appear to be dependent upon both the specific and nonspecific subcortical structures. That is, there were striking similarities of the A potential of GL with the A poten-

FIG. 8. Response amplitude-frequency diagrams of various components to flashing light. A, A', B, B' and C: wave components of the evoked potential shown in FIG. 7. Ordinates: amplitude. Abscissae: flash frequency. Absence of diagram for B' of GL and RF means that this potential was not recognizable. Where only the scale is shown for B' of Vc and Lc indicates that this component was too weak to measure. See text for details.

tials of OR and Lc. Furthermore, the A potential of Vc seemed to show characteristics which were a mixture of the A potentials of both GL and RF, since the A potentials of Vc, GL and RF all demonstrated the highest activity at 1 or 2/sec stimulation and summation of the enhanced A potential activity of GL at about 4.5-6/sec and the diminutive one of RF at about 4-7/sec will form a plateau-like activity similar to that in Vc at about this same frequency range. Augmentations in the B potential of OR and Vc at such low frequencies as 3.5 and 4.5/sec seem to be a reflection of the activities in the B potential of RF at the corresponding frequency, and the peaks in OR at 5.5/sec may be due in part to the enhanced activity of GL at 4.5-6/sec. Thus, the B potentials of OR and Vc were more intensely affected by the nonspecific activity. The enhanced activities of the B potential in Vc, OR, and Lc at 10/sec may be related to that of the B potential in GL as well as the similar activity of the B' potential in Pul and CS, too. The B and C potential activities of Lc were somewhat peculiar because of the dominance of the activity at about 5/sec. The activities of the A and A' potentials in CS, which showed approximately a monotonous declination, were in agreement with the A and A' potentials in the previous findings in the anesthetized state. As a whole, it is evident that (i) characteristic activity changes were shown in each of the specific and nonspecific subcortical structures, (ii) activities in the cortical areas were reflected by those of the two subcortical systems, and (iii) there may be a peculiar activity change in the limbic system.

2. *Repetitive electrical stimulation of GL and RF.* In the above findings, the cortical activities were divided into specific and nonspecific activity changes on the basis of similarity in the frequencies of augmentations. Whether this similarity is really of GL and RF origin or not was confirmed by the behavior of the activities in response to GL and RF stimulations.

Markedly augmenting responses were elicited by electrical stimulation of GL (FIG. 9X). The average evoked responses in OR, Vc, RF and Lc elicited by stimulation of various frequencies are shown in FIG. 9Y. The wave forms of the responses to 1/sec stimulation and the amplitudes of the response components are indicated as I_0 , I, I', II, III and IV potentials in FIG. 10. The amplitude-frequency diagrams of each of these components in various sites derived from averaging four cases in OR and Lc, and three cases in Vc and RF under the same experimental conditions were presented in FIG. 11. Maximal responses of short latency were brought out respectively in OR (I) and Vc (I_0) at about 5.5 and 5-5.5/sec stimulation and a 7/sec and 5.5-7/sec stimulation in II and I. Augmentation at similar frequencies was observed in the I and I' potentials of RF and the I and III of Lc though a few peaks responses of the IV potential in OR and Lc and II in Vc, the slow component, occurred by 3.5/sec stimulation.

FIG. 9. An example of repetitive electrical GL stimulation. X: Ink records at 1/sec GL stimulation. Except in Mc and ERG, marked responses were observed in every site, even in Lc. Y: A series of average responses to GL stimulations of various frequencies.

FIG. 10. Average responses in various sites to single GL stimulation. Amplitudes indicated as I_0 , I , I' , II , III and IV components were measured in the same fashion as in the case of flash stimulation.

FIG. 11. Summarized amplitude-frequency relation in response to GL stimulation. Early potentials in the specific structures were augmented at 4 to 7-8/sec and late slow components were enhanced at 3-3.5/sec.

appeared additionally in these sites. In addition to these augmentations, other augmented activities were exhibited in RF and Lc at 3-3.5/sec, which seemed to occur also in Vc and OR slightly. The III potential in OR and Lc, I' in Vc and II in RF showed a maximum peak at about 5/sec, except for a peak at 3.5/sec in OR and peaks at 7-8/sec in OR, Vc and Lc. Markedly enhanced

FIG. 12. A case of low frequency repetitive RF stimulation (1-15/sec). X: Ink record at 1/sec RF stimulation. Pulse-like responses appeared in all tracings but a remarkable slow component was not observed as compared with GL stimulation. Y: Averaged responses in various recording sites to RF stimulation.

FIG. 13. Averaged wave forms of the responses to single RF stimulation. Amplitudes of I, I', II, II' and III components were measured in the same way as in the case of flash or GL stimulations.

FIG. 14. Summarized amplitude-frequency diagrams to low frequency repetitive RF stimulation (1-15/sec). I, I', II, II' and III: The wave components as shown in FIG. 13. Contrary to GL stimulation, peaks showing augmentation of responses did not appear at 4 to 7-8/sec but rather at less than 5/sec, although late components such as III were slightly similar with those of GL stimulation.

On the contrary, the response patterns in RF stimulation differed considerably from those in GL stimulation. An example of the records is shown in FIG. 12X, where no remarkable slow responses are recognized although there are spike-like potentials. In FIG. 12Y, the average response time-patterns obtained by the ATAC-401 are depicted. Their wave forms and the amplitudes of the wave components are indicated as I, I', II, II' and III potentials in FIG. 13. In their amplitude-frequency diagrams (FIG. 14), no prominent activities of I and I' potentials at 5 to 7/sec such as seen in GL stimulation were observed, but the activities at frequencies lower than 5/sec were strengthened in every recording site. Even in the long-lasting III and II' potentials of OR and Vc, this tendency persisted, though 5 or 5.5/sec activities were strengthened slightly. However, the small II potential preceded by the primary upward and downward deflections in GL responded more greatly at 5.5-6/sec than at the above lower frequencies.

These confirm the fact that augmentations at such relatively higher frequencies as 5 to 7-8/sec are associated chiefly with the specific activity, while those at lower frequencies of less than about 5/sec depend mainly upon the non-specific activity. However, the augmenting responses may also be included in the lower frequency activities as shown in the latest potentials in GL stimulation.

DISCUSSION

As shown at the beginning in the peak latency, it seems strange that impulses from the retina reach to RF faster than GL, and that the A potential of RF was very similar to that of CS in its wave form, latency and amplitude. It may be possible, therefore, that the response recorded from RF may not be the response of RF itself but rather be due to current leakage from CS. However, VON GUDDEN (1881) and GILLILAN (1941) have demonstrated fibers running from the optic tract to a number of midbrain nuclei in rabbits. The potential with a shorter latency than that of the GL response may be elicited through this tract. In spite of the similarity in the potential itself, the activity of the potential A of RF in relation to the flash frequency was markedly different from that of CS (see FIG. 3 and 8). Hence the possibility of leakage from CS can be denied.

It is well known that the evoked potential is affected by anesthesia. In general, when anesthesia is not so deep, the transmission of impulses to the brain through the primary sensory pathway is not disturbed (FRENCH et al., 1953; BRAZIER, 1954) though reduction is recognized in the amplitude of the potential (ARDUINI and ARDUINI, 1954). However, there have been paradoxical findings on the components which follow the primary response. Cortical evoked responses with medium latency (12-30 msec) produced by stimulation of the

sensory nerve or reticular structure have been observed only in the unanesthetized state (MORUZZI and MAGOUN, 1949; STARZL and MAGOUN, 1951) and all components except for the primary response provoked by sensory stimulation are reduced or disappear during anesthesia (ARDUINI and ARDUINI, 1954). On the other hand, the "secondary discharge" of FORBES and MORISON (1939) is augmented by barbiturate anesthesia. In order to define the components of the evoked potentials observed in this paper, some average responses obtained during the anesthetic state and those obtained during the unanesthetized state by the same method are shown in FIG. 15 for comparison. Each of the A and

FIG. 15. Comparison of average response time-patterns under anesthetized (ane.) and unanesthetized states (unane.). These average responses to a single flash (indicated by arrow) were obtained by averaging ten responses. Calibration is the same in each recording site under both anesthetized and unanesthetized states (50 μ V). For details see text.

B potentials under anesthesia correspond respectively to those in the unanesthetized state. The B' potential of RF under anesthesia is distinct, whereas it is not so clear in the unanesthetized state. In this figure, the most conspicuous differences are seen in the evoked potentials in the visual cortex. Though the A potentials in both states are very similar in their configurations, the B potential was shifted tremendously to the positive side much prolonged under anesthesia, showing that it coincides with the "secondary discharge" mentioned above. Contrarily, the C potential attenuated to be practically obscured under anesthesia. The potential may correspond to the "secondary potential" of FUSTER and DOCTER (1962). In GL, the B potential increased in size by anesthesia, while the C potential was reduced considerably. The peak latencies of both were prolonged. In RF, the amplitude of the A potential was decreased slightly here, demonstrating that the evoked responses in RF are reduced or

disappear in the anesthetized state (ARDUINI and ARDUINI, 1954).

In the previous paper (MIMURA and SATO, 1965), it was found that amplitudes of the slow components of the cortical potential of the rabbit evoked by repetitive flash stimulation were augmented at about 3 and 5/sec while those of the b-wave of ERG were monotonously declined with increasing flash frequency. Such augmentations at definite frequencies as verified by peaks in the frequency response curve indicate that the periodic activity is more predominant at these frequencies than others (SATO et al., 1961). Therefore, it seems reasonable to assume that such cyclic activity changes take place within the central nervous system while not in the retina. Furthermore, it was found that in both the anesthetized and unanesthetized states the cyclic activity originates at least in part from the subcortical specific and nonspecific systems, although some differences were recognized as will be discussed later. Under anesthetized condition, in view of the augmentation of the responses in the cortex to repetitive flash stimulation and repetitive GL or RF stimulation, the cyclic activities appeared at 5-6/sec is attributed to GL, the specific system, and those at 4/sec to RF, the nonspecific system. On the other hand in the unanesthetized situation, the most characteristic periodic activities were seen at 1 and 4.5-6/sec in the peaks of the A potentials in GL and OR, and at about 2-3.5/sec in the peaks of the C potentials in GL, OR and visual cortex. The latter peak of the A potential was ascertained by the activities of the early two components in GL stimulation and the peak of C potential by the late two potentials so that these activity behaviors of A and C potentials are associated respectively with those of the specific afferents as well as under anesthesia. The activity at the relatively higher frequency of 4.5-6/sec, which is attributable to the specific system only, may correspond to BISHOP's cyclic excitability change (1933) or the excitability cycle within the specific structure in other studies (CHANG, 1950, 1951; GASTAUT et al., 1951). On the other hand, the activities in RF in response to flash stimulation was characterized by moderate trough at 6/sec in the A potential and the vast augmentations in the B potential at frequencies lower than about 5/sec as well as the inactive patterns at lower frequency in the C potential in RF as compared with the C potential in the specific structures (GL, OR). Such activity patterns at lower frequency in the A and B potentials were confirmed also by the I, I', II' and III potentials in response to RF stimulation. Every component at each recording site demonstrated the acceleration of peaks at less than 5/sec. Consequently, it would not be unreasonable to assume that the activity pattern of RF might be conspicuous at frequencies lower than 5/sec. In the unanesthetized state, however, a characteristic periodic activity was not demonstrated, because the activity patterns did not appear as one or two conspicuous peaks but as a group of several small peaks of nearly the same height both in repetitive flash and electrical stimulation. The activity patterns of the B and B' poten-

tials in GL, OR and Vc were too complicated to attempt classification as simply as in the case of the anesthetized state. However, in part, B and B' potentials appear to show a mixture or summation of A potential activities in both the GL and RF. These activity changes in GL and RF show characteristic patterns for the specific and non-specific systems respectively and the property of the activity patterns of the cortex exhibit a mixture of patterns of both specific and non-specific systems. Many authors have demonstrated interactions between the specific and non-specific afferent systems at the cortical level. Some of them (JASPER and AJMONE-MARSAN, 1952; BREMER and STOUPPEL, 1959; NARIKASHVILI and MONIAVA, 1959; LANDAU et al., 1961) demonstrated facilitations, whereas a few investigators observed occlusions in the primary evoked sensory potentials. Though no direct interactions were observed in these experiments, the amplitude-frequency diagrams produced by repetitive electrical stimulation to GL and RF showed that the cortical activity had properties characteristic to the two subcortical afferent systems. Furthermore, these characteristic activities in the specific and nonspecific systems may be attributable to the augmenting and recruiting-like responses respectively. If so, there must be an interaction between these two responses. Interactions between recruiting and augmenting phenomena were first denied by DEMPSEY and MORISON (1942), but were observed later by PARMA and ZANCHETTI (1956) and BROOKHART et al. (1957). However, the same authors postulated the fundamental differences between the augmenting and recruiting responses (DEMPSEY and MORISON, 1942; HANBERY and JASPER, 1953; BROOKHART and ZANCHETTI, 1956). On the other hand, BISHOP et al. (1961) did not think that these differences were very fundamental. KLEE and OFFENLOCH (1964) described the postsynaptic potentials accompanying the augmenting response as consisting of a primary response and a response of recruiting character. Such a combined nature of the responses is supported by the cyclic activities at the relatively lower frequency of about 1-2/sec which originate from both the specific and nonspecific activities as verified here.

The A and B' potentials of Pul did not indicate any characteristic pattern, but the activities of B and C were very similar to those of A and C of the specific structures, respectively. Therefore, it may be possible to consider the activity patterns of Pul, the specific elaborative or association nucleus, to be closely related with the specific activity. The A potential activities in Lc very resemble any other activity patterns but demonstrated unique features. This may suggest that they are related to the rhinencephalic synchronizing mechanism (GANGLOFF and MONNIER, 1956) or a pace maker activity of the septum (GREEN and ARDUINI, 1954; MAYER and STUMPF, 1958; BRÜCKE et al., 1959; BRUGGE, 1965) that are independent from the above mentioned periodic activity systems. Further research on the relation between the cyclic activity changes and spontaneous "theta" rhythm of the rabbit will be dis-

cussed in detail in a paper to follow (MIMURA et al., 1965, 1967b).

In comparison of the activity behaviors in the unanesthetized state with those under anesthesia, the similarities between both states were divided into the following three groups: highly similar, different in part and not similar. The first group contains the A and A' potential of CS in flash stimulation and the I' and II potentials of Vc in GL stimulation. The second group consists of the A potential of GL, Vc and RF, the B potential of Vc and RF in flash stimulation and the I potential of Vc in GL stimulation. All other potentials, i.e. the B potentials of GL due to flash; the I, I' and II potential of RF in GL stimulation; the I and II' potentials of Vc and the I, I' and II potentials of GL in RF stimulation, belong to the third group. Because of agreement with the fact that barbiturate anesthesia has more intense depressive effects on the reticular system than other structures (FRENCH et al., 1953; BRAZIER, 1954; ARDUINI and ARDUINI, 1954), the above classification suggests that the activities associated with the specific afferent impulses were resistant to anesthetics, whereas the deeper the components are related with RF, the more the activities are affected by anesthetics. Though points on the activity curves were scattered more widely in the anesthetized experiment (1/sec) than in the unanesthetized state (0.5/sec), the latter curves were more complicated than the former. In the B potential of Vc, there appeared three peaks on the amplitude-frequency diagram. The intermediate peak at 4.5/sec corresponds to that at 4/sec in the anesthetized state, and the two peaks at 3.5 and 7/sec had been newly produced. Judging from the anesthetized effect, this B potential was defined as the "secondary discharge" as shown before. Although the "secondary discharge" is augmented under anesthesia, this potential as shown here in the unanesthetized state showed new activities depending upon the stimulating frequency. This paradoxical phenomenon can be explained by the following speculations. The "secondary discharge" had been investigated on the somatosensory response. However, the evoked potential of cat and monkey by brief flash stimulus has a very complicated form in the unanesthetized state as recently demonstrated (HIROTA, 1964; HUGHES, 1964; STEINBERG, 1965). Further, the response in rabbits also has a complicated form such as in cat and monkey (IWASE et al., 1965; MIMURA et al., 1967a). Therefore, the B potential may not be the response of the same nature as the "secondary discharge" of FORBES and MORISON. In addition, MORISON suggested two afferent pathways from the brain stem for the cortical evoked responses with medium latency. One of them is an extrathalamic route and the other runs forward through the subthalamic structure and thalamus (personal communication with FRENCH, FRENCH, 1960). He pointed out that the "secondary discharge" may be due to the former. If this is so, it may be possible to speculate that the newly revealed activities of the B potential in the unanesthetized state are caused

via this latter route which is depressed during anesthesia. Also such reasoning may explain the cause for the new peaks produced in the I potential activity of Vc by RF stimulation in which no peaks were observed under anesthesia.

SUMMARY

The activity patterns (response amplitude-frequency diagram) of ten anesthetized and eleven unanesthetized rabbits brain evoked by repetitive flash stimulation of varying frequencies (1-15/sec) were observed with respect to the stimulating frequency in the lateral geniculate body (GL), optic radiation* (OR), midbrain reticular formation (RF), Pulvinar* (Pul), superior colliculus (CS) and visual (Vc) and limbic cortex* (Lc), wherein those in the starred sites were observed under unanesthetized situation only.

The activities in each of the specific and nonspecific structures presented characteristic patterns and in Lc, too. In GL and OR, the initial potential with short duration (A potential) was augmented at 4.5-6/sec flash stimulation and the slow component (C potential) was enhanced at 2-3.5/sec which suggests cyclic activity changes at these frequencies. On the contrary, it was demonstrated that the activities of RF were characterized by 1 and 4/sec under anesthetized state and by vast augmentation at less than 5/sec under unanesthetized state, though no conspicuous cyclic property. In the Lc, an independent cyclic property from the above specific systems was observed. These observations were confirmed by the repetitive electrical stimulation to GL or RF, suggesting that the augmenting and recruiting-like responses play a rôle at least in part.

The activity patterns associated mainly with the specific activity were not affected by anesthetic condition, while the activities or the potential components related closely with RF were most affected by anesthesia.

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