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INHIBITORY INFLUENCES ON PRIMARY AND SECONDARY CORTICAL PHOTIC POTENTIALS ORIGINATING IN THE LOWER BRAIN STEM

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In a recent communication (Palestini, Lifschitz & Armengol, 1959), a study of the habituation of primary and secondary cortical photic potentials in cats which had been subjected to a mid-pontine pre-trigeminal transection was reported. E.e.g. recordings of these evoked potentials after the transection showed a definite lengthening of the period of time in which the primary cortical photic potentials would attain habituation. This lengthening was even more striking in the secondary cortical photic potentials, since normally they reach habituation in a very short time.

To explain these results it was suggested (Palestini & Lifschitz, 1959) that an inhibitory influence, arising in structures situated below the level of the lesion, was being exerted. The present paper presents results, obtained in preparations with a mid-pontine pre-trigeminal section, on the changes of the photically evoked cortical potentials, which give additional support to this hypothesis.

METHODS

Fifty cats were used in these experiments. After anaesthesia with sodium pentobarbitone, extradural monopolar stainless-steel electrodes were implanted on the suprasylvian gyrus, on the gyrus lateralis and gyrus lateralis anterior.

Control recordings were taken from these animals, non-anaesthetized, at least 5 days after implantation. The light stimulus in all experiments consisted of flashes at a rate of one per second from a Grass PS 1 photic stimulator. To ensure relatively constant stimulation of the retina the light source was always held at the same distance from the eyes, the animal was slung in a hammock and head excursions were restrained by an aluminium cone. All cats were dark-adapted at the beginning of each experiment and their pupils dilated with homatropine. Satisfactory isolation from outside sounds was achieved in all experiments. As a further means of ensuring a constant stimulus to the retina, the nictitating membranes were removed and the facial nerves were divided in some animals.

Both monopolar (with an indifferent electrode on the frontal sinus) and bipolar electrodes were used and the electrical changes were recorded by a Grass e.e.g. machine on paper or photographed from an oscilloscope trace. In the latter method successive cortical responses were superimposed on the same picture.

After securing control recordings of approximately one hour's duration daily, on at least 3 consecutive days, a pre-trigeminal transection, either mid- or rostropontine, was made under ether anaesthesia according to the procedure described by Batini, Moruzzi, Palestini, Rossi & Zanchetti (1959). The plane of the section is shown in Fig. 1. Recording was re-started 6–12 hr after the operation under the same conditions as for normal preparations and repeated daily for as long as they remained in good condition, usually not longer than 4 days. After the last recording the animals were killed and examined for cerebral oedema and any other abnormality.

In order to check the level and completeness of the brain-stem section the brains were fixed in 20% formalin, cut in the horizontal plane and stained by the Nissl and Weil techniques.

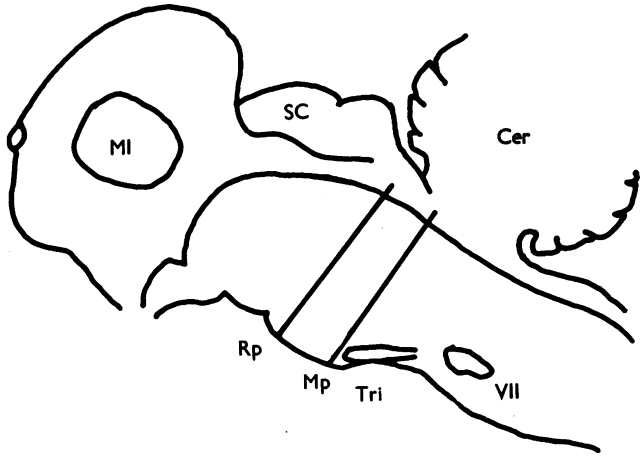

Fig. 1. Diagram of a longitudinal section of the brain stem of the cat, showing the position of the transections in relation to the pons and trigeminal nerve roots. Rp, rostropontine transection; Mp, mid-pontine transection; Cer, cerebellum; MI, massa intermedia; SC, superior colliculus; Tri, roots of trigeminal nerve; VII, roots of facial nerve.

RESULTS

Changes in the secondary cortical photic responses after pre-trigeminal transection

In normal cats a brief flash stimulus elicits the so called secondary photic response from the suprasylvian and anterior lateral gyri. Buser & Borenstein (1959) have shown that it differs distinctly from the primary responses recorded from the visual cortical area. In the normal awake cat the secondary response is of small amplitude and negative potential, with longer duration than that of the primary response. Its latency, about 20 msec, is variable and hence very difficult to measure in pictures of superimposed records (Fig. 2). To observe this secondary response more clearly it is necessary to start recording from the beginning of repetitive stimulation, and to superimpose several responses on the film, because at a stimulation rate of one flash per second the amplitude of the

secondary response decreases rapidly and is soon masked by spontaneous cortical activity.

After a pre-trigeminal mid-pontine brain-stem section, several changes are apparent in this secondary photic response:

(1) The amplitude increases, frequently reaching double that of normal cats, so that it stands out clearly against the typical desynchronized cortical activity of the mid-pontine pre-trigeminal preparation (Fig. 2).

(2) The latency remains constant at about 20 msec.

(3) In some cases the negative potential is preceded by a positive phase, so that the secondary response resembles that observed by Buser & Borenstein (1959) on cats anaesthetized with chloralose. In our experiments, however, the background cortical activity remained desynchronized.

(4) The amplitude of the secondary response decreases only after continued repetitive stimulation for several hours (Palestini *et al.* 1959).

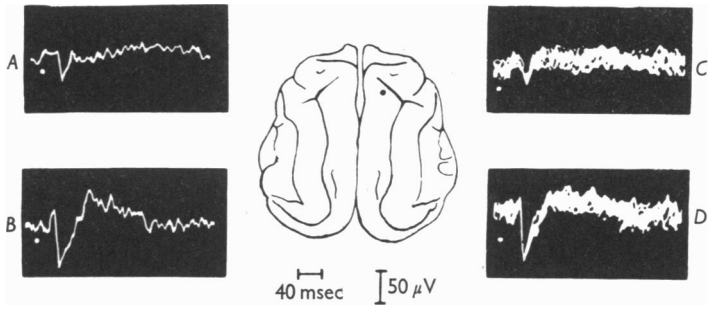

Fig. 2. Potentiation of the secondary photic cortical potential after mid-pontine pre-trigeminal transection; oscilloscope recording. The dot in the diagram of the cortex shows the position of the monopolar recording electrode. *A–B*: single response (*A*) before and (*B*) after the transection. *C–D*: superimposed records showing the same changes (*C*) before and (*D*) after transection. Dots mark the stimulus artifact. Upward deflexion positive.

Two of these effects, the slow decrease in amplitude and the potentiation of the secondary response, appear also in cats with a rostropontine lesion, who usually show a synchronized cortical activity (Fig. 3).

Changes in the primary cortical photic responses after pre-trigeminal transection

The primary cortical photic potentials recorded at the gyrus lateralis in cats have been described by many investigators (Albe-Fessard, 1957). The typical response has five components. The first deflexion in our records had a mean latency of about 12 msec, and all five components were not always clearly visible. While there was some variability in the amplitude

of the different components this was minimized by photographic superimposed traces, and such records when measured for amplitude, as was done by Schoolman & Evart (1959), formed a more reliable basis for comparison.

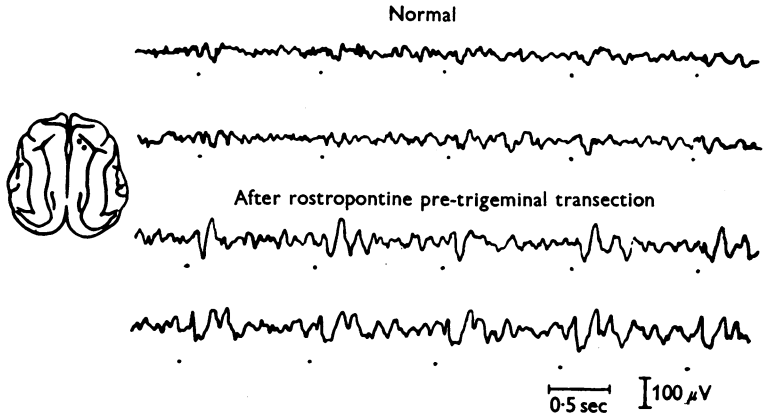

Fig. 3. E.e.g. showing synchronized background activity and potentiation of the secondary photic cortical potential after rostropontine pre-trigeminal transection. Dots on diagram at left indicate the position of the bipolar electrodes. Dots below records indicate the light stimulus.

A pre-trigeminal mid-pontine lesion produced changes in the primary cortical photic potentials (Figs. 4 and 5). A consistent increase in the amplitude of positive waves 3 and 4 and negative wave 5 was observed. Positive wave 1 remained almost unchanged.

After a rostropontine lesion this primary response showed a marked potentiation, though interference from large synchronous waves made its appearance sometimes irregular (Fig. 6). In a few instances after pre-trigeminal section the primary response showed a marked potentiation, even when the secondary response remained unchanged.

In order to check the possibility of interference from factors such as closure of the eyelids and/or the nictitating membrane, and pupillary changes, all the experiments of the foregoing type were performed in a few cats whose nictitating membranes had been removed, whose pupils had been dilated with homatropine and whose eyelids had been paralysed by nerve section. The results from these cats were the same as those described above.

DISCUSSION

The fact that the results described above are obtained consistently from a few hours after transection up to the end of the survival period (about 4 days in our experiments) makes it rather improbable that the potentiation

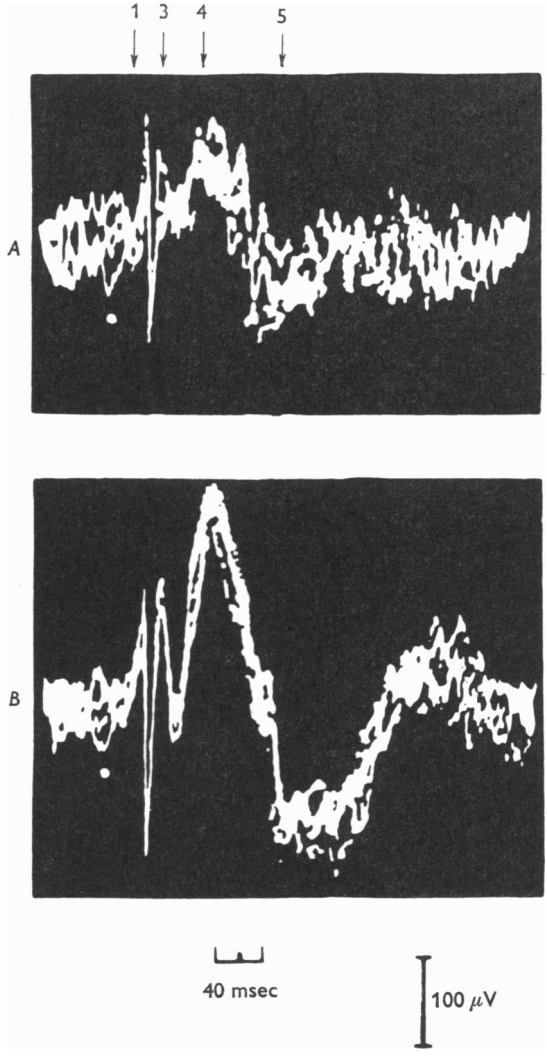

Fig. 4. Oscilloscope records from primary visual area to show potentiation of the primary photic cortical potential after mid-pontine pre-trigeminal transection. Deflexions numbered according to the nomenclature of Schoolman & Evart (1959). *A*: superimposed tracings of evoked potentials before the transection. *B*: superimposed tracings of evoked potentials after transection. Monopolar recording. Upward deflexion positive. Dots mark the position of the stimulus artifact.

of the cortical photic potentials, both primary and secondary, is attributable to an irritative stimulation from structures above the level of lesion. In the experimental situation described here such a stimulation would probably affect all the rostral nervous structures, especially the cortex, and would gradually decrease and finally vanish. Furthermore, such an irritative action might be expected to affect all the components of the primary cortical photic response equally, but in these experiments the

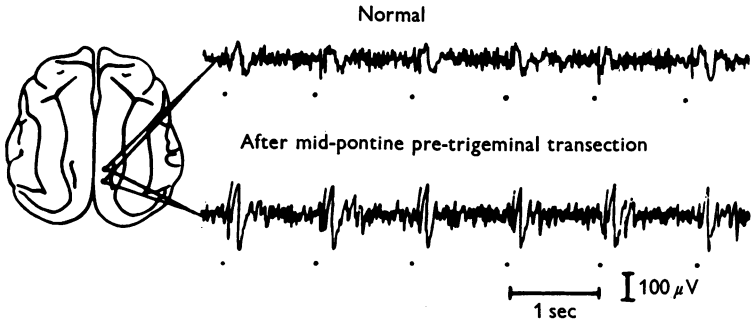

Fig. 5. E.e.g. showing desynchronized background activity and potentiation of the primary photic cortical potential after mid-pontine pre-trigeminal transection. Bipolar recording. Dots below records indicate the light stimulus.

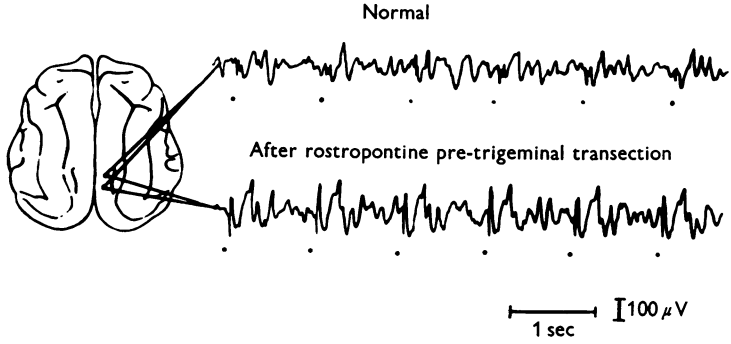

Fig. 6. E.e.g. showing synchronized background activity and potentiation of the primary photic cortical potentials after rostropontine pre-trigeminal transection. Bipolar recording. Dots below records indicate the light stimulus.

first component remained practically unchanged after the transection. If the irritative effect appeared only at the cortical level, both primary and secondary responses would be equally affected. However, it has been pointed out that in several cases there was a potentiation of primary responses while secondary responses remained unchanged. Furthermore, Palestini, Armengol, Mendoza & Lifschitz (unpublished results) have recently seen cats with a semi-pre-trigeminal transection that present

potentiation of the primary cortical photic response ipsilaterally only to the semisection of the brain stem, an observation obviously inconsistent with the irritative hypothesis.

Mid-pontine transection and secondary cortical photic potentials

Since Derbyshire, Rempel, Forbes & Lambert (1936) and Forbes & Morison (1939) first described a cortical response of long latency, elicited by an electrical stimulus applied to the sciatic nerve of a deeply anaesthetized cat, and Dempsey, Morison & Morison (1941), Dempsey & Morison (1942*a*, *b*) and Morison & Dempsey (1942) showed it to be conveyed in a secondary pathway, many papers have been published on investigations into this non-primary sensory response, and they have been reviewed recently by Buser (1957).

Such features as the distribution on the cortex, latencies and wave shapes suggest a relation between the secondary cortical photic potentials described in this paper and those recently studied by Buser & Borenstein (1959). Yet certain differences are apparent. According to Buser & Borenstein secondary responses in association areas from a curarized, non-anaesthetized cat depend on the background activity, the maximum irradiation of these potentials being obtained when there is a medium level of vigilance. Our observations on non-curarized, non-anaesthetized cats confirm their results but with the difference that the secondary responses are potentiated, following either a mid-pontine pre-trigeminal lesion, with its desynchronized e.e.g. pattern, or a rostropontine pre-trigeminal lesion, when the e.e.g. pattern is synchronized. These results suggest that although there is normally a correlation between the amplitude of secondary photic potentials and e.e.g. pattern, it is not a causal one, i.e. the potentiation described here is not due to the presence of low voltage fast activity.

The fact that potentiation appears only after transection of the brain stem leads to the assumption that the transection eliminates ascending tonic inhibiting influences from below the level of the lesion and possibly also leads to an increased action of facilitatory connexions from above the lesion level. This assumption is supported by the observations of Bremer & Stoupel (1959) which show that stimulation of the mesencephalic reticular formation facilitates the secondary response, although this effect was obtained only by concurrent electrical stimulation of the optic pathway.

In brief, we assume that inhibitory influences originate caudally to the lesion and act directly or indirectly upon the secondary cortical photic potentials recorded from the suprasylvian gyrus and from the anterior lateral gyrus.

Mid-pontine pre-trigeminal preparation and primary cortical photic potentials

The origin of the different components of the primary response evoked in the visual area has been studied by many investigators, but is still a controversial subject. It is, however, generally accepted that the first wave reflects the activity of the optic radiation and waves 3, 4 and 5 have an intracortical origin (Albe-Fessard, 1957). As to the second component, Bishop & Clare (1952, 1953) think it shows post-synaptic activity of Golgi II neurones. Bremer & Stoupel (1956) suggest it comes from presynaptic intracortical activity, and Malis & Kruger (1956) think it could originate in a second group of afferent fibres in the optic radiation. This paper, though not dealing specifically with this problem, seems to support the idea that waves 1 and 2 have a different origin from the others, as both remain unchanged after brain-stem transection.

We are inclined to attribute the potentiation of primary cortical photic potentials to a suppression of inhibitory influences coming from structures below the lesion level and to the enhanced facilitating action of the mesencephalic reticular formation. In support of this view some papers that describe the influence of the reticular formation upon evoked cortical potentials can be mentioned. While some authors have described a decrease in the amplitude of evoked cortical potentials during electrical stimulation of the mesencephalic reticular formation (Hernández-Peón, Scherrer & Velasco, 1956), the more recent work of Bremer & Stoupel (1959), Dumont & Dell (1960) and Steriade & Demetrescu (1960) has demonstrated an enhancement of this response under similar conditions when they are evoked by electrical shocks applied to the sensory pathways. The facilitation described by both Dumont & Dell (1960) and Bremer & Stoupel (1959) in their papers affects the same components of the primary cortical responses as are found potentiated after a pre-trigeminal lesion.

These results support the idea, already enunciated (Palestini *et al.* 1959), that there is no correlation between the facilitatory action of the cortical photic evoked potentials and the synchronizing-desynchronizing mechanisms, since the facilitating effect is observed both in the mid-pontine pre-trigeminal preparation (desynchronized e.e.g.) and the rostropontine pre-trigeminal preparation (synchronized e.e.g.). Dumont & Dell (1960) have also described a similar dissociation.

Published results and some inferences from the work described here suggest the probable pathways and the site of action of the inhibitory influence normally acting upon the secondary and primary cortical photic evoked potentials. Three probabilities are worth further consideration:
(*a*) The inhibitory influence arising below the lesion level might act

through a depression of the activity of the facilitatory mesencephalic reticular formation.

(*b*) The inhibitory influence might act directly on the cortical neurones themselves. The present experiments seem to point towards this mechanism, since the post-transection potentiation affects predominantly waves 3, 4 and 5 of the primary cortical photic response, which are generally considered to be of intracortical origin (Albe-Fessard, 1957).

(*c*) Another probability is an effect on the diffusely projecting thalamic nuclei, either directly or indirectly through the mesencephalic reticular formation. This probability is given considerable weight by virtue of the fact that long ascending axons originating both in the medulla and mesencephalic reticular formation (Brodal & Rossi, 1955) have been described and the facilitatory effect that these nuclei exert on the visual cortex is well known (Jasper & Ajmone-Marsan, 1952).

SUMMARY

1. Changes of the primary and secondary cortical photic potentials were studied in non-anaesthetized cats after mid-pontine and rostropontine total transections.

2. Both kinds of evoked potentials showed a clear potentiation after the mid-pontine pre-trigeminal transection. Positive deflexions 3 and 4 and negative deflexion 5 of the primary cortical photic potential were especially enhanced.

3. The rostropontine transection showed the same potentiation.

4. It is postulated that this potentiation would be due to the elimination of tonic inhibitory influences arising caudally to the lesion and probably also to the releasing of facilitatory activity in structures above it.

5. The lack of correlation between the mechanisms responsible for the e.e.g. pattern and the amplitude of the cortical photic evoked potentials is discussed.

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