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Slow Potential Changes Evoked in Nucleus Medialis Dorsalis of the Thalamus by Stimulation of the Amygdaloid Nuclear Complex *

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Slow potential changes in the nucleus medialis dorsalis, resulting from stimulation of the amygdaloid nuclear complex, have been recorded with bipolar electrodes in chloralosed cats. The sequence of potential changes was made up of three phases of activity which reached their peaks at 10-15, 40-50 and 100-130 msec after the stimulus artefact. The distribution of these phases of activity was analyzed. Phase I had its optimum amplitude in the caudal half of the medial third of the nucleus. Phase II showed a wider distribution, being the predominant component in the dorsal half of the middle third. Phase III did not show any specific localization. The effects of repetitive stimulation and the recovery cycle of excitability are described. Results are consistent with the suggestion that phase I is due to activity generated through a direct pathway between the amygdala and nucleus medialis dorsalis. Phases II and III represent activity elicited through multisynaptic pathways.

This research was undertaken in order to obtain information concerned with the functional characteristics of the amygdalothalamic connections. NAUTA (10, 11) emphasized the importance of these connections as a component of a wider neural organization which involves the amygdala, the n. medialis dorsalis of the thalamus and the orbitofrontal cortex. This author confirmed and extended previous findings by Fox (4) establishing the existence of a massive amygdaloid projection to the magnocellular division of the n. medialis dorsalis of the thalamus in the monkey. Morphological studies carried out in the cat did not produced concordant evidence for a direct amygdalo-thalamic pathway. While HALL (7) did not observe degenerated fibres to the n. medialis dorsalis after producing lesions in the nuclei basalis and lateralis VALVERDE (15) traced degenerated fibres from the anterior amygdaloid area and rostral parts of the n. ba-

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salis to the caudomedial region of this thalamic nucleus.

A systematic study of the distribution and properties of the activity elicited in the n. medialis dorsalis after stimulation of the amygdaloid nuclear complex has not yet been made. The available data were obtained from experiments in the cat and are contradictory. While KAADA (8) confirmed Fox's data through the neuronographic method GLOOR (5) did not obtain any response in this nucleus after stimulation of the amygdala. SAGER *et al.* (14) and NIEMER *et al.* (12) repported evoked responses with latencies (7-10 msec) which pointed out the possibility of the existence of direct connections between these two structures. Finally the shortest latency of the unitary neuronal responses recorded by ENCABO *et al.* (1) do not support the monosynaptic nature of the amygdalo-thalamic pathway.

The present paper is concerned with the analysis of the slow potential changes elicited in different areas of the n. medialis dorsalis when the amygdaloid nuclei are activated, paying special attention to their distribution, recovery cycle and response to repetitive stimulation. The results of experiments dealing with the analysis of the unitary neuronal responses will be published elsewhere (3).

Materials and Methods

Experiments were performed on 17 cats anesthetized with chloralose (70-80 mg/kg). The trachea and saphenus vein were cannulated and the head of the animal was fixed in a standard stereotaxic apparatus. After completion of the surgical procedure and before recording the animals were immobilized with gallamine triethiodide (Flaxedil) and artificially ventilated with a positive pressure pump. Rectal temperature was monitored and kept between 37 and 38° C. The n. medialis dorsalis of the thalamus was reached by means of stereotactically oriented electrodes. The exploring probe consisted of an 125 microns insulated stainless steel wire introduced into a 0.5 mm insulated steel needle, the tip separation being 0.5 to 0.8 mm. The area between stereotaxic coordinates A 8-10.5, L 0.5-2.5 and H 5-1 was explored systematically in a vertical direction at 0.5 mm steps. Two to four penetrations were made in each experiment. At the end of the last track a small current was passed through the electrode tip to allow for a better histological control. The electrical activity was amplified by a Tektronix 122 and displayed on an oscilloscope for photography. Recording was usually bipolar between both tips of the electrode. Positivity of the inner tip resulted in a downward deflexion. The amygdaloid nuclei were stimulated through concentric bipolar electrodes delivering rectangular pulses of 0.2 to 1 msec duration and with frequencies between 0.5 and 10/sec. Three electrodes were placed in the amygdala with a minimum interelectrode distance of 2.5 mm. The electrode placement which evoked more prominent responses was used throughout the experiment to map out the electrical activity generated in the n. *medialis dorsalis.* At the end of the experiment the brain was perfused with saline and 10 % formalin. Frontal or sagital sections were mounted and stained for histological control of the position of the electrodes.

Results

The potential changes. When a series of records was taken at various depths in frontal or sagital planes of the n. medialis dorsalis and the amygdala stimulated a characteristic pattern of potential change was obtained. Fig. 1 illustrates the results of such an experiment in which two vertical descents were made in a sagital plane at 1 mm from the midline at the antero-posterior positions indicated by the lines A and B at the schema shown at the left. The stimulating electrode was praced in

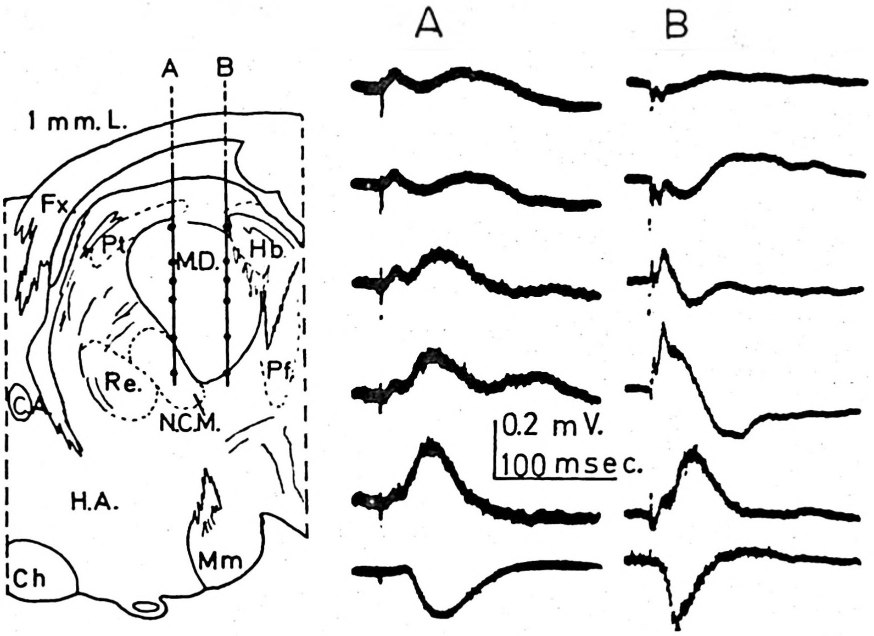

Fig. 1. *Pattern of distribution of phases of nucleus medialis dorsalis potential to amygdala stimulation*

Two series of records obtained along tracks A and B in the same sagital plane at 1 mm from the midline. Filled circles indicate position of the electrode tip for each record. Responses to single rectangular pulses (1.0 msec duration, supramaximal intensity, frequency 0.5/sec) to the anterior third of the nucleus basalis of the amygdala.

the anterior third of the n. basalis of the amygdala. The potential sequence as seen in the fourth record of column A is made up of three phases of activity which reach their peaks at 12, 40 and 125 msec after the stimulus artefact. Taking together the data from all the experiments the variation of the time to the peak for each phase of activity ranges from 10 to 15, 40 to 50 and 100 to 130 msec respectively. As we are using the bipolar leading arrangement these phases of activity represent the successive components of the potential gradient developed between both tips of the concentric electrode. The phases showed a characteristic distribution and had their maximum amplitudes and reversals in polarity at different depths within the nucleus. In Fig. 1 can be seen that phase I reverses its polarity between the second and third records shown in column B whereas phase II changes the polarity at a more ventral level, between the two last records in both series. The amplitude of both phases changes as the electrode moved deeper into the nucleus, the optimum amplitude for phase I being reached in the fourth record of column B and in the fifth one for phase II in both columns. Phase III had its maximum in the fourth record of column A. It seems then that phases I and II show certain differences in the level of both their maximum amplitudes and polarity reversals, phase I being more prominent at more caudal levels.

A similar phenomenom could be observed when the exploring electrode was moved from a medial to a more lateral position. Fig. 2 shows the results of an experiment in which two descents were made. The records obtained in the more medial position are illustrated in column A

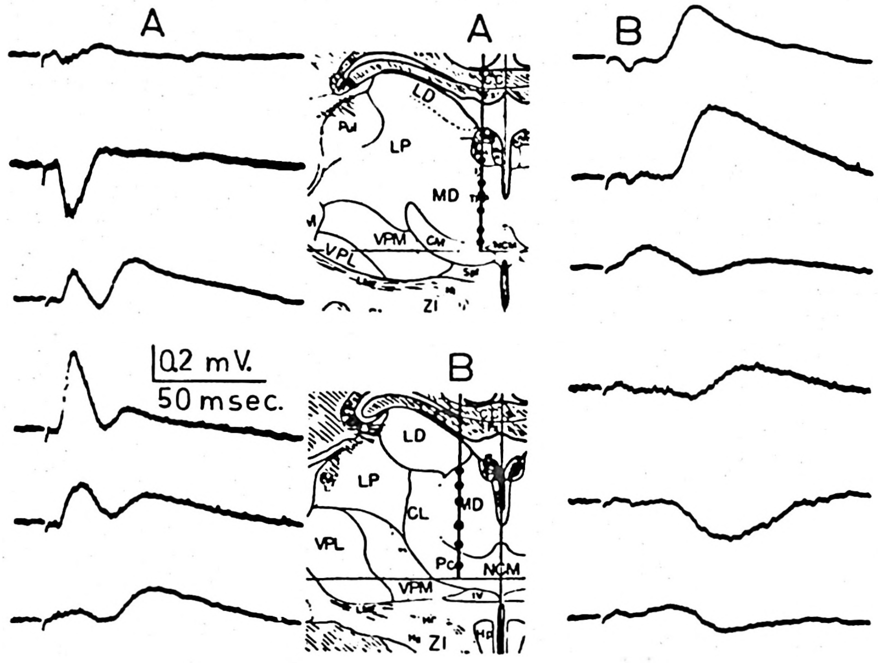

Fig. 2. *Pattern of distribution of phases I and II of nucleus medialis dorsalis potential to amygdala stimulation.*
Two series of records obtained from caudal and rostral levels at different degree of laterality. Stereotaxic coordinates: track A (A 8, L. 1) and track B (A 9, L 1.8). Filled circles indicate position of the electrode tip. Stimulation of the limiting region between the anterior amygdaloid area and the nucleus basalis with pulses of 0.5 msec duration, supramaximal strength and frequenzy 1/sec.

and those from the more lateral in column B. The placements of the electrode tip for each record are indicated by the filled circles along the lines A and B at the respective schema shown in the central part of the figure. The anteroposterior coordinate was 8 for A and 9 for B. The stimulating electrode was placed at the limiting region of the anterior amygdaloid area and the n. basalis of the amygdala. It can be seen that phase I is the most prominent feature in the series of records obtained along track A whereas phase II is more conspicuous in those obtained along track B. Again phase I had its polarity reversal between the second and third trace and showed its maximum amplitude in the fourth record of the column A. Phase II is almost the only recorded deflexion in column B and shows its polarity reversal at a more ventral region than phase I. At this level of laterality the optimum amplitude of phase II was developed in a more dorsal region than when the exploring electrode was in a more medial position. It should also be emphasized that no polarity reversal appeared for phase II in the more medial track. In this experiment phase III could not be elicited; this late component of the potential sequence was not so constant as phases I and II, being present in only five experiments and without showing any specific localization.

A total of 51 stimulating electrodes were implanted in 17 experiments within the amygdaloid nuclear complex: 19 in the n. basalis, 18 in the n. lateralis, 6 in the

n. centralis and 8 in the anterior amygdaloid area. Phases I and II were always evoked when stimulating the n. basalis or the anterior amygdaloid area. Stimulation of the n. lateralis elicited both phases in 7 out of 18 placements in this nucleus and only phase II in the remaining 11; when both phases were evoked phase II always had a larger amplitude than phase I. Activation of the n. centralis only evoked phase II in two experiments. In the five experiments in which phase III was evoked the stimulated nuclei were either the n. basalis or the n. lateralis. The largest amplitude of the whole potential change sequence was obtained when stimulating the anterior portion of the n. basalis.

Effect of repetitive stimulation. The three phases of activity were affected in different ways by repetitive stimulation. Fig. 3 illustrates the effect of stimulating with various frequencies (figures at the left) on the amplitude of the potential sequence elicited in the n. medialis dorsalis by stimulation of the n. basalis. All records were obtained with a supramaximal strength of stimulation. The first two records are single traces; in the third record there are two and in the fourth one there are five superimposed traces as the bursts of stimuli, repeated every three seconds, had a duration of half a second. Each record is the fifth of the series for a given frequency. At 0.5/sec the three phases of activity were present. At 2/sec phase III was completely suppressed and phase II greatly reduced. At 5/sec only phase I was present. Finally a frequency of 10/sec reduced to a 70 % the amplitude of phase I. These results point out the oligosynaptic nature of the pathway responsible for the elicitation of phase I and the propagation through more synapsis of the incoming activity which evoked phases II and III.

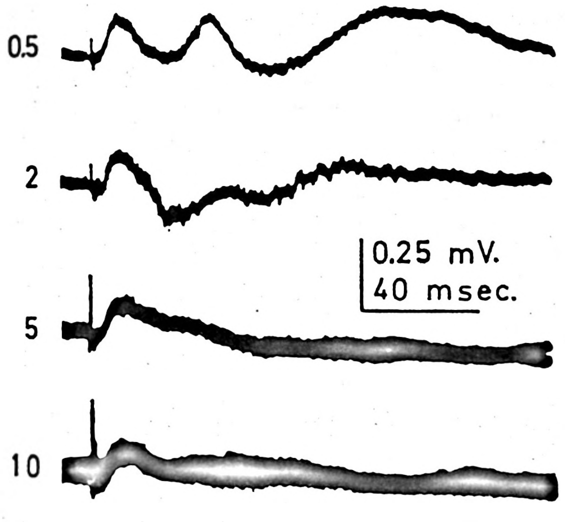

Fig. 3. *Effect of repetitive stimulation on the phases of activity.*
Series of records from the inner third of the nucleus medialis dorsalis. Figures ar the left indicate frequenzy of stimulation. Rectangular pulses of 0.5 msec duration and supramaximal intensity delivered to the nucleus basalis.

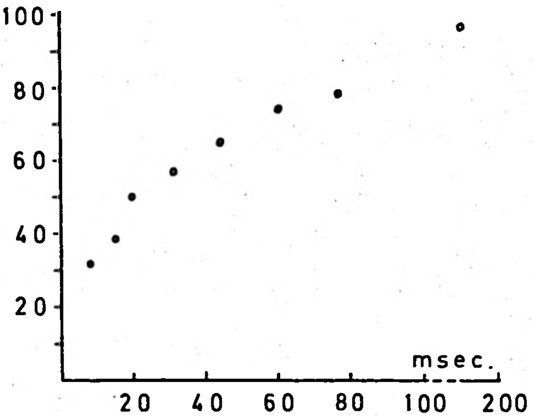

Fig. 4. *Recovery cycle of excitability of phase I.*
Ordinate plots the amplitude of the test response as a percentage of the amplitude of the conditioning one. Abscissa, intervals.

Recovery cycle of excitability. In order to gather more data on the temporal capabilities of the system under study the recovery cycle for phase I was studied. Fig. 4 shows the results obtained in four experiments. The ordinate plots the amplitude of the second response as a percentage of the amplitude of the conditioning one at the intervals shown on the abscisa. At 8 msec interval the second response reached some 33 % and at 20 msec the 50 % of the amplitude of the first response. This means a large degree of responsiveness after a previous activation. The recovery of excitability of phase II is much slower since intervals from 50 to 60 msecs were needed for the second response to appear after the conditioning one. These results are consistent with those obtained when stimulating repetitively at various frequencies.

Discussion

Present data demonstrate that a sequence of potential changes consisting of three phases of activity can be elicited in the nucleus medialis dorsalis when certain regions of the amygdala are stimulated. Phase I was the most prominent feature all over the medial third of the nucleus, particularly in its caudal half, just in front of the habenular nuclei. Phase II had a wider distribution, being the more characteristic potential in the middle third. Finally phases I and II had their reversals in polarity at different depths, the one for phase I being always more dorsal than that for phase II.

When a bipolar leading arrangement is used as in this series of experiments, the recorded potential changes have the meaning of a potential gradient produced between both tips of the electrode (13). It appears from the results that changes both in slope and direction of the gradient have been shown for each phase of activity when the exploring electrode was moved along the nucleus medialis dorsalis in a dorsoventral direction. This is an strong indication that the phases of activity are being generated at or close to the region from which we are recording, in another words, that the electrical activity has a local origin.

An attempt will now be made to correlate these results with the existent morphological knowledge. Two types of pathways, direct and indirect, have been repported to connect the amygdaloid complex to the nucleus medialis dorsalis of the thalamus. The direct pathway was described by Fox (4) and NAUTA (9, 10, 11) in the monkey and by VALVERDE (15) in the cat. As our experiments were carried out in the cat we will mainly be concerned with anatomical data obtained from this animal. Lesions which produced terminal degeneration in the n. medialis dorsalis were placed by VALVERDE in the anterior amygdaloid area and rostral part of the n. basalis. The degenerated fibres enter the n. ventralis anterior of the thalamus and join the inferior thalamic peduncle at the level of the n. ventralis medialis to end in the posteromedial part of the n. medialis dorsalis. The fine fibres described by GUILLERY (6) do also terminate in the medial part of this nucleus but the site of origin was not precisely localized, although GUILLERY indicated that these fine fibres might well correspond to the amygdaloid projection. On the other side NAUTA (10) repported that a fibre degeneration, comparable to his findings in the monkey, was produced in the cat by lesions in the preoptic region and the substantia innominata (2), both structures receiving numerous fibres from the amygdala. However as GUILLERY pointed out the degeneration produced by lesions which lie close to the midline and rostral to the anterior commisure showed that there is an additional projection to the n. medialis dorsalis from the medial septal nucleus and the diagonal band, structures which also receive projections from the amygdala. This indirect projection is distributed in the medial three quarters of the n. medialis dorsalis.

The topographical distribution of the phase I corresponds very closely to the region in which the direct pathway have been shown to terminate, the medioposterior part of the n. medialis dorsalis. The response of this phase of activity to repetitive stimulation and its recovery cycle of excitability lend support to the suggestion that afferents from the amygdala which evoke phase I have their first synapse in the caudomedial region of the n. medialis dorsalis. Phase II showed a wider distribution, which is in agreement with morphological data. The indirect amygdalo-thalanic pathway seems of to end in the medial three-quarters of the n. medialis dorsalis. The suppression of phase II with frequencies of stimulation of 5/sec and its recovery of excitability are consistent with the presence of one or two synapses in the pathway from the amygdala to the n. medialis dorsalis.

Our results confirm and extend previous findings. The latencies of the responses described by SAGER *et al.* (14) and by NIEMER *et al.* (12) were slightly longer (10 and 7 msec. respectively) than the latency of the phase I described here. In records such as those illustrated in figure 2 A, this latency is of the order of 5 to 6 msec. The responses recorded by these authors were obtained in the inner part of the n. medialis dorsalis. Finally they also stimulated the n. basalis of the amygdala. None of these authors explored in a systematic way the n. medialis dorsalis. This may be the reason why they did not record potential changes with a longer latency in this thalamic structure.

Resumen

En gatos anestesiados con cloralosa se han registrado los cambios de potencial lento evocados en el núcleo dorsomedial del tálamo por la estimulación del complejo nuclear amigdalino. En la secuencia de cambios de potencial generados se distinguen tres fases de actividad que alcanzan su punta a los 10-15, 40-50 y 100-130 mseg, respectivamente después del artefacto del estímulo. Se analizó la distribución de estas fases de actividad. La amplitud óptima de la fase I se registró en la mitad caudal del tercio interno del núcleo. La fase II presentó una distribución más amplia, siendo el componente predominante en la mitad dorsal del tercio medio del dorsomedial. Finalmente, la fase III no mostró localización específica, siendo el más inconstante de los tres componentes. Se describen los efectos de la estimulación repetida con diversas frecuencias y los ciclos de excitabilidad. Los resultados obtenidos apoyan la conclusión que la fase I es debida a la actividad generada a través de una vía directa entre la amigdala el núcleo dorsomedial. Las fases II y III representan actividad evocada a través de vías multisinápticas.

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