The region of the bulbar reticular formation stimulation of which in the present experiments did not cause analgesia and did not affect thalamic unit activity corresponds to the magnocellular tegmental field (FTM) in Berman's nomenclature [3]. It was therefore decided to compare the effect of stimulation of CI and of other structures, during stimulation of which analgesia also develops. For this purpose, stimulating electrodes were implanted into DR (P = 0.2, L = 0, H = -0.5) of one of the animals. According to some workers [4, 5, 7, 9], stimulation of this nucleus in cats is accompanied by marked analgesia. In the present experiments the responses of the thalamic neurons to stimulation of DR were identical with changes in activity observed during stimulation of CI. If no changes took place during stimulation of CI, stimulation of DR also was ineffective.

The results thus indicate that changes in activity of some cells of the thalamic nuclei are observed during stimulation of CI, and that the predominant changes are inhibition of spontaneous and evoked activity.

## LITERATURE CITED

- 1. A. I. Basbaum, N. J. E. Marley, J. O'Keefe, et al., Pain, 3, 43 (1977).
- 2. J. E. Beall, R. F. Martin, A. E. Applebaum, et al., Brain Res., 114, 328 (1976).
- 3. A. N. Berman, The Brain Stem of the Cat; a Cytoarchitectonic Atlas with Stereotaxic Coordinates, Madison (1968).
- 4. G. Guilbaud, J. M. Besson, J. C. Liebeskind, et al., C. R. Acad. Sci. (Paris), 275, 1055 (1972).
- 5. G. Guilbaud, J. M. Besson, J. L. Oliveras, et al., Brain Res., 61, 417 (1973).
- 6. H. H. Jasper et al., A Stereotaxic Atlas of the Diencephalon of the Cat, Ottawa (1954).
- 7. J. C. Liebeskind, G. Guilbaud, J. M. Besson, et al., Brain Res., 50, 441 (1973).
- 8. D. J. Mayer, T. L. Wolfe, H. Akil, et al., Science, <u>174</u>, 1351 (1971).
- 9. J. L. Oliveras, J. M. Besson, G. Guilbaud, et al., Exp. Brain Res., 20, 32 (1974).
- 10. J. L. Oliveras, F. Redjemi, G. Guilbaud, et al., Pain, 1/2, 139 (1975).
- 11. D. V. Reynolds, Science, 164, 444 (1969).
- 12. R. T. Robertson and E. Rinvik, Brain Res., 51, 61 (1973).
- 13. M. Sasa, K. Munekiyo, and S. Takaori, Brain Res., 101, 199 (1975).
- 14. B. J. Sessle, R. Dubner, L. F. Greenwood, et al., Can. J. Physiol. Pharmacol., 54, 66 (1976).

# PATTERN OF SPREAD OF EXCITATION FROM THE VENTROMEDIAL HYPOTHALAMUS TO LIMBICO-RETICULAR BRAIN STRUCTURES

E. V. Koplik

UDC 612.826.4:612.826.2

The order of appearance of evoked potentials in different parts of the septum, amygdala, and reticular formation in response to gradually increasing stimulation of the ventromedial nucleus of the hypothalamus was studied. Excitation arising primarily in the ventromedial nuclei of the hypothalamus was shown to spread initially to structures of the septum and rostral reticular formation, and only later to the more caudal regions of the reticular formation and amygdala.

KEY WORDS: hypothalamus; limbico-reticular structures; evoked potentials.

In the modern view [2, 5-7], the so-called static emotional excitations are the neurophysiological basis of stable arterial hypertension. These excitations are formed by structures of the limbico-reticular complex, among which the central role is played by the hypothalamic region [1, 2, 8].

Laboratory of Emotions and Emotional Stresses, P. K. Anokhin Research Institute of Normal Physiology, Academy of Medical Sciences of the USSR, Moscow. (Presented by Academician of the Academy of Medical Sciences of the USSR S. S. Debov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 85, No. 4, pp. 390-392, April, 1978. Original article submitted July 29, 1977.

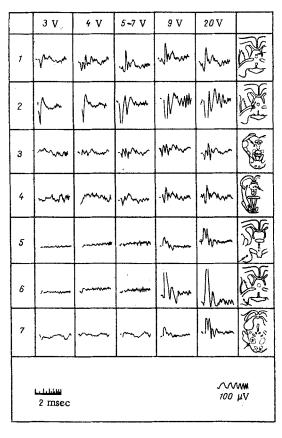


Fig. 1. EP in various brain structures during gradual increase in strength of stimulation of ventromedial hypothalamic nucleus.

1) Medial septum; 2) lateral septum; 3) rostral reticular formation; 4) middle reticular formation; 5) basomedial amygdala; 6) basolateral amygdala; 7) posterior reticular formation. Arrows indicate location of electrode tips. Remainder of explanation in text.

Anokhin [3] and Sudakov [6] postulated a "pacemaker" mechanism of formation of the basic biological motivations and emotions. According to their veiws the pacemaker point, which is located in the hypothalamus, consists of a group of selectively excited cortical elements and subcortical structures.

Meanwhile the order in which excitation arising primarily in the hypothalamus spreads to other brain structures has not yet been adequately studied. Data are available only on connections between different parts of the hypothalamus and the various limbico-reticular structures [4, 6, 9].

The investigation described below was accordingly carried out by the evoked potentials (EP) method to study of pattern of successive spread of excitation from the negative emotiogenic centers of the hypothalamus [2, 5, 8] to the limbico-reticular structures of the brain in waking rabbits.

### EXPERIMENTAL METHOD

Experiments were carried out on 15 adult unanesthetized rabbits. To record EP, electrodes made from insulated nichrome wire 0.3 mm in diameter were first inserted, in accordance with the coordinates of a stereotaxic atlas [10], into the ventromedial hypothalamic nuclei (VMH), septum, amygdala, and structures of the reticular formation.

Stimulation of the hypothalamic region in rabbits evoked a passive defensive response. EP were recorded by a monopolar method on the "Biofaz" four-channel cathode-ray oscilloscope. The reference electrode was implanted into the nasal part of the skull. VMH was stimulated with single square pulses, 0.2-0.5 msec in duration and from 1 to 25 V in intensity, from a "Biofaz" stimulator.

To determine the location of the electrode tip a direct current of 0.5 mA was passed through them for 30 sec. The site of coagulation was determined histologically in a series of frontal brain sections stained by Nissl's method.

### EXPERIMENTAL RESULTS

To discover in what order excitation arising primarily in the ventromedial hypothalamic nucleus spreads to the limbico-reticular brain structures, the voltage of the stimulating current was increased gradually. The voltage at which EP appeared in the structure tested was taken as the threshold.

During threshold stimulation of VMH (2.5-3 V) EP were recorded initially in the region of the septum. Responses to stimulation of VMH were recorded with the shortest latency (3.2  $\pm$  0.3 msec) in the medial septal nucleus. They consisted of a negative wave 200-280 mV in amplitude and 18-20 msec in duration, which was sometimes preceded by a very small (15-30 mV) positive wave (Fig. 1). EP in the lateral region of the septum in response to single stimulation of VMH took the form of a combined positive—negative wave with a latent period of  $7.5\pm0.3$  msec, an amplitude of up to 500 mV, and a duration of  $13\pm0.5$  msec for the positive phase and the latent period of  $16\pm0.8$  msec, an amplitude of up to 120 mV, and a duration of  $18\pm0.4$  msec for the negative phase (Fig. 1).

When the stimulating voltage was increased to 3-4 V, EP began to be recorded in the rostral portions of the reticular formation (cuneiform nucleus, central gray matter). In these regions the EP consisted of polyphasic waves with 3 or 4 components: an initial positive wave with a latent period of  $3\pm0.3$  msec, a duration of  $4\pm0.5$  msec, and an amplitude of 40-50 mV, followed immediately by a negative wave with an amplitude of 110-140 mV and a duration of 28-35 msec. As a rule, immediately after the primary negative wave, a secondary negative wave of the same amplitude and with a duration of 10-12 cm was recorded, separated from the primary wave by a small (40-50 mV, duration 3-4 msec) intermediate positive wave. Sometimes the two negative waves were joined together, thus increasing the duration of the negative wave to 50 msec (Fig. 1).

With an increase in the voltage of the stimulating current to 5-7 V EP were recorded in the middle part of the reticular formation (reticular nucleus). EP in this region of the reticular formation consisted of a positive-negative-negative wave in which the latent period of the positive component was  $6.5 \pm 0.5$  msec, its amplitude  $120 \pm 15$  mV, and its duration 6-8 msec, and the corresponding values for the negative components were  $10.3 \pm 3$  msec, up to 220 mV, and 6-8 msec, respectively (Fig. 1).

If the intensity of the stimulating current applied to VMH was increased to 9 V EP began to be recorded in the amygdala. The shape of the EP in the amygdala was largely dependent on the location of the recording electrode. In the basolateral nuclei short-latency EP (latent period  $8\pm0.3$  msec) were observed, with a latent period of  $8\pm0.3$  msec for the first negative or negative—negative wave with an amplitude of up to 500 mV and a duration of not more than 20 msec. EP were recorded from the basomedial region in the form of a simple negative wave, sometimes with a reduplicated peak, with a latent period of  $4.5\pm0.5$  msec, an amplitude of 120–150 mV, and a duration of 24 msec (Fig. 1).

An increase in the voltage of the stimulating currents to 20 V caused the appearance of EP in the posterior parts of the reticular formation. They usually consisted of 2 or 3 components, with a first negative wave with short latent periods (5-7 msec), a duration of 15-18 msec, and a reduplicated peak. These high-amplitude negative waves (250-200 mV) were accompanied by shallow positive (50-70 mV) and negative (30-40 mV) waves with a duration of not more than 16 msec (Fig. 1).

The results thus indicate that excitation arising primarily in the ventromedial hypothalamic nucleus spreads gradually to the limbico-reticular structures of the brain via oligo- and polysynaptic pathways. It spreads initially to structures of the septum and rostral reticular formation, and only later to the more caudal regions of the reticular formation and amygdala.

## LITERATURE CITED

- 1. P. K. Anokhin, Proceedings of the Fourth Session of the Academy of Medical Sciences of the USSR [in Russian], Moscow (1948), p. 34.
- 2. P. K. Anokhin, Great Medical Encyclopedia [in Russian], Vol. 35, Moscow (1964), p. 339.
- 3. P. K. Anokhin, The Biology and Neurophysiology of the Conditioned Reflex [in Russian], Moscow (1968).
- 4. G. P. Krachun, Zh. Évol. Biochim. Fiziol., No. 4, 276 (1968).
- 5. T. N. Sollertinskaya, Fiziol. Zh. SSSR, No. 7, 1050 (1972).
- 6. K. V. Sudakov, Patol. Fiziol., No. 1, 3 (1975).

- 7. S. Feldman and S. Robinson, J. Neurol. Sci., 1, 1 (1968).
- 8. J. Henry, P. Stephens, J. Axelrod, et al., Psychosom. Med., 33, 227 (1971).
- 9. P. MacLean, D. Ploog, and B. Robinson, Physiol. Rev., 40, Suppl. 4, 105 (1960).
- 10. G. Raisman, Exp. Brain Res., 7, 317 (1969).
- 11. C. Sawyer, J. Everett, and J. Green, J. Comp. Neurol., 101, 801 (1954).

EFFECT OF STIMULATION OF THE MEDIAL AND LATERAL ZONES
OF THE RESPIRATORY CENTER ON ELECTRICAL ACTIVITY OF
THE DIAPHRAGM, INTERCOSTAL MUSCLES, AND PHRENIC NEURONS

N. A. Gordievskaya, M. V. Sergievskii,\* and V. E. Yakunin

UDC 612.28+612.217

Experiments on cats showed that the nucleus of the tractus solitarius contains zones during stimulation of which electrical activity of the phrenic neurons and diaphragm is selectively stimulated or inhibited. Stimulation of inspiratory and expiratory zones of the nucleus ambiguus influences the electrical activity of the external intercostal muscles. During stimulation of the corresponding zones in the gigantocellular nucleus electrical activity is changed in both groups of inspiratory muscles simultaneously. It is postulated that the action of stimulation of the zones of the gigantocellular nucleus on both groups of inspiratory muscles is indirect in its mechanism, through neurons of the nucleus of the tractus solitarius and nucleus ambiguus.

KEY WORDS: respiratory center; phrenic neurons; diaphragm; intercostal muscles.

The respiratory center contains groups of neurons connected selectively with centers for the phrenic and intercostal nerves [1,5-6, 8, 10]. Without their connections with the respiratory center, the latter cannot maintain the rhythmic alternation of phases of the respiratory cycle [3, 4, 7, 10].

This paper gives the results of observations on responses of the phrenic neurons, diaphragm, and intercostal muscles to electrical stimulation of the nucleus of the tractus solitarius, nucleus ambiguus, and gigantocellular nucleus in order to compare the effects of such stimulation. The first two nuclei lie in the lateral zone and the third in the medial zone of the respiratory center.

### EXPERIMENTAL METHOD

Observations were made on 74 anesthetized (pentobarbital, 40 mg/kg, intraperitoneally) cats. The animals were fixed in a stereotaxic apparatus. The medulla and cervical part of the spinal cord were exposed from the dorsal aspect. Stimulation by square pulses (1-6 V, 5 msec, 100-200 Hz) was applied through bipolar electrodes (distance between them 150  $\mu$ ) inserted into the brain in accordance with coordinates of a stereotaxic atlas [12]. Action potentials of the respiratory muscles were recorded with bipolar electrodes. Spike discharges of the neurons were recorded by glass microelectrodes with a tip not more than  $8\mu$  in diameter, filled with 3 M KCl solution. Respiration was recorded by means of the MT-54 microthermistor, mounted in the tracheotomy tube.

#### EXPERIMENTAL RESULTS

Altogether 96 respiratory neurons were recorded in 4-6 cervical segments (70 inspiratory, 24 expiratory, 2 combined inspiratory—expiratory) at a depth of 3-5 mm and situated 1-1.4 mm from the midline. Probing of the nuclei at intervals of 0.5 mm in three planes revealed zones whose stimulation evoked activation or

<sup>\*</sup>Corresponding Member, Academy of Medical Sciences of the USSR.

Academy of Medical Sciences of the USSR Group, Kuibyshev Medical Institute. Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 85, No. 4, pp. 392-395, April, 1978. Original article submitted July 29, 1977.