EFFECT OF FLUOTHANE ON THE MESENCEPHALIC RETICULAR FORMATION AND CEREBRAL CORTEX

S. I. Plekhotkina

UDC 612.825+612.826.5]014.46:615.212.7

The effect of fluothane on evoked responses in the mesencephalic reticular formation, on the EEG desynchronization reaction during electrical stimulation of the reticular formation, and on transcallosal responses was studied in acute experiments on cats. Fluothane caused marked inhibition of evoked responses in the reticular formation. Although the EEG desynchronization reaction was depressed, this effect was much less marked than that on the evoked responses. The amplitude of the transcallosal responses was appreciably reduced with increasing depth of anesthesia.

Many investigations have been made of the effect of fluothane on the EEG and on other physiological indices in man [2, 9, 10, 15, 16].

The effect of fluothane on the functional state of the subcortical structures and cerebral cortex has been investigated experimentally to a far lesser degree. Kitahata [13] showd that recovery of excitability of the auditory cortex is depressed by an amount approximately proportional to the level of fluothane anesthesia. However, this investigation does not permit an unambiguous evaluation of the effect of fluothane on the cortex, because the recovery cycle largely reflects the functional state of subcortical structures also. The early disappearance of the evoked response in the reticular formation during fluothane anesthesia, described by Davis et al. [8], likewise does not fully explain changes in the activity of this structure, because disappearance of the evoked response in the reticular formation has been shown to be not invariably associated with its inhibition [5].

The object of the present investigation was to study the effect of fluothane on the functional state of the cerebral cortex and mesoencephalic reticular formation (RF).

The functional state of the cortex was assessed by means of the transcallosal response, because impulses evoking this response have been shown to be transmitted to the opposite hemisphere via the corpus callosum and to be independent of activity of subcortical structures [7]. The functional state of RF was assessed by two tests: by the evoked response in the RF to sensory (electrodermal) stimulation and by the appearance of an EEG desynchronization reaction during direct electrical stimulation of the RF.

EXPERIMENTAL METHOD

Experiments were carried out on 12 adult cats. Tracheotomy and venesection were performed under superficial ether anesthesia. Tubocurarine was injected and the animals transferred to artificial respiration. The head was fixed in a type ÉMIB stereotaxic apparatus; bilateral pneumothorax was formed under local anesthesia with 1% trimecaine, and the cisterna magna was opened. The rectal temperature was maintained throughout the experiment at 37-38°. After the dura had been opened the brain was irrigated with warm mineral oil. To record the transcallosal response, stainless steel stimulating electrodes

Laboratory of Anesthesiology and Resuscitation, and Laboratory of Physiology, A. V. Vishnevskii Institute of Surgery, Academy of Medical Sciences of the USSR, Moscow. (Presented by Academician of the Academy of Medical Sciences of the USSR A. A. Vishnevskii.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 70, No. 8, pp. 56-60, August, 1970. Original article submitted November 27, 1969.

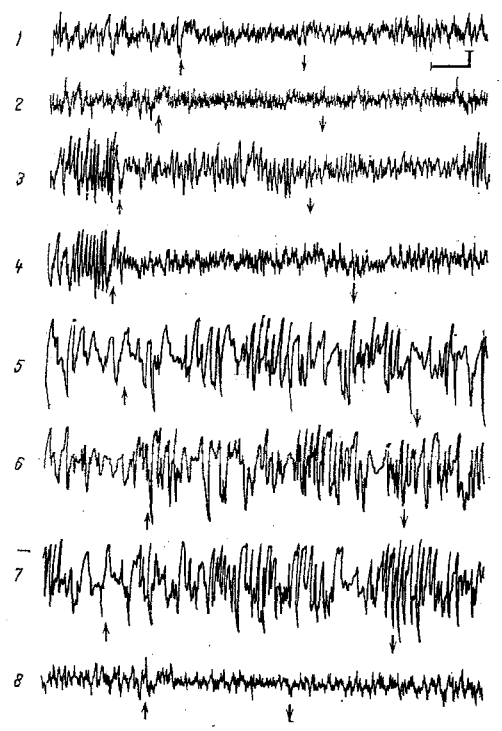

Fig. 1. Effect of inhalation of fluothane on EEG during electrical stimulation of reticular formation. 1) background, amplitude of stimulation 3 V; 2) background, amplitude of stimulation 4 V; 3) stage I_3 of anesthesia, amplitude of stimulation 3 V; 4) stage I_3 of anesthesia, amplitude of stimulation 4 V; 5) stage III_1 of anesthesia, amplitude of stimulation 4 V; 6) stage III_1 of anesthesia, amplitude of stimulation 5 V; 7) stage III_1 of anesthesia, amplitude of stimulation 6 V; 8) 30 min after end of inhalation of fluothane, amplitude of stimulation 3 V. Arrows indicate beginning and end of electrical stimulation; calibration of amplification 100 μV; time marker 1 sec.

mounted on a Plexiglas plate were placed in the middle part of the suprasylvian gyrus. The recording electrode, consisting of a silver wire, 0.5 mm in diameter, with a ball-pointed end, suspended on a thin spring, was placed symmetrically opposite to the stimulating electrodes in the contralateral hemisphere. The cortex was stimulated with single square pulses, 0.2-0.3 msec in duration. The amplitude of stimulation was 1, 2, and 3 times the threshold level. The electrode recording transcallosal responses was also used to record the EEG. A double electrode was inserted into the mesencephalic RF corresponding to the coordinates A +3, L3, H-I [12]. Desynchronization of the EEG was produced by electrical stimulation of RF (square pulses, 0.5 msec, 150 Hz). The threshold of onset of desynchronization, usually 2-4 V, was determined,and the amplitude of the stimulating pulses was equal to the threshold and 1, 2, and 3 V above it. Electrodermal stimulation of the forelimb was by means of single square pulses, 0.5 msec in duration, applied through needle electrodes. The voltage of the pulses used was 1, 2, and 4 times the threshold level. To record evoked responses from the RF, the stimulating electrode introduced into this structure was connected to the input of an amplifier. Recording electrodes were connected to the input of a "Galileo R32" 8-channel electroencephalograph. Responses were recorded from the screen of a type S1-18 CRO connected to the output of the electroencephalograph. Electrical stimulation was applied from a two-channel ÉSU-1 electronic stimulator. Fluothane was administered through a vaporizer manufactured at the "Krasnogvardeets" factory into the input of a type TsKB AMN SSSR artificial respiration apparatus for small laboratory animals. Inhalation of fluothane began not less than 3 h after the end of ether anesthesia.

EXPERIMENTAL RESULTS AND DISCUSSION

The EEG of waking cats immobilized with tubocurarine was dominated by β-rhythm with single θ- and δ-waves. Electrical stimulation of the RF at a frequency of 150 Hz evoked a desynchronization reaction on the EEG, and the higher the amplitude of the stimulating pulses, the more marked this reaction (Fig. 1:1, 2).

Inhalation of fluothane (0.25-0.5%) slowed the rhythm of the EEG and led to the appearance of high-amplitude α-like waves with a frequency of 8-12/sec, corresponding to stage I_3 of anesthesia [4, 11]. The threshold electrical stimulation RF at this stage evoked an ill-defined EEG-desynchronization reaction or had no effect, but with an increase in the strength of stimulation the desynchronization reaction became well marked (Fig. 1: 3,4). With deepening of anesthesia to stage III_1-III_3, high-amplitude (over 500 μV) θ- and δ-waves appeared on the EEG. In 83.4% of experiments electrical stimulation of RF, even at a strength much above threshold, evoked no appreciable changes in the EEG (Fig. 1: 5, 6, 7). Only in 16.6% of experiments did an increase in the amplitude of stimulation produce a clearly defined desynchronization reaction.

Evoked responses in the RF to electrodermal stimulation of waking animals consisted of a positive-negative or negative wave 60-90 μV in amplitude and about 20 msec in duration, with a latent period of the negative wave of about 15 msec. The amplitude of the responses was slightly increased with an increase in the strength of stimulation. The threshold of this response was usually 5-15 V. In stage I_3 of anesthesia the amplitude of the evoked responses fell sharply, while there was no response to threshold stimulation. Deepening of the anesthesia led to complete disappearance of evoked responses in the RF (Fig. 2).

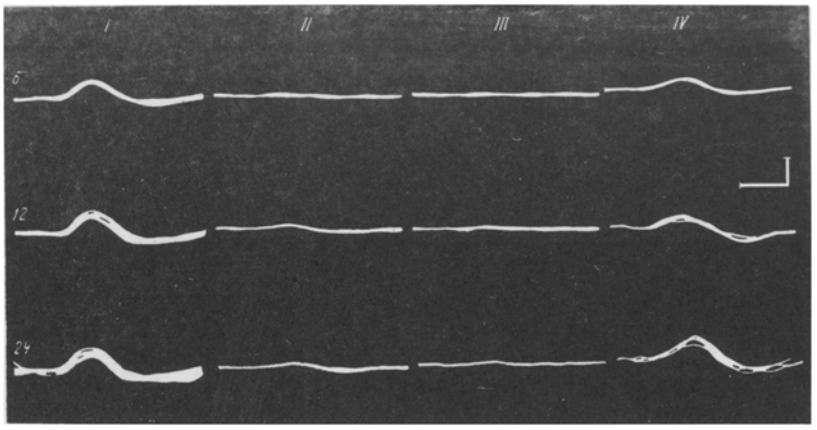

Fig. 2. Effect of inhalation of fluothane on evoked responses in mesencephalic reticular formation. I) background; II) stage I_3 of anesthesia; III) stage III_1 of anesthesia; IV) 30 min after end of inhalation of fluothane. Numbers on left show amplitude of stimulating pulse (in V); calibration of amplification 100 μV; time marker 20 msec. Positivity downward.

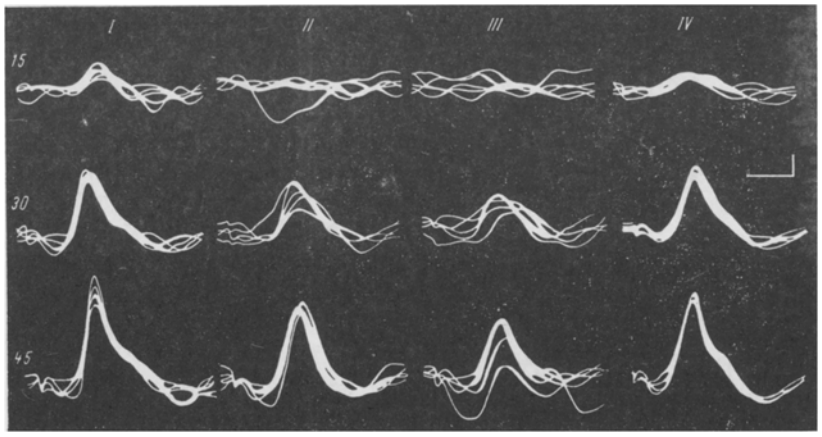

Fig. 3. Effect of inhalation of fluothane on transcallosal responses. Legend as in Fig. 2.

The transcallosal response in waking cats consisted of a positive-negative or negative wave with latent period of about 4 msec and amplitude 300-600 μV in response to stimulation of twice or three times the threshold level. In stage I_3 of anesthesia the amplitude of waves of the transcallosal response was slightly reduced, and a particularly marked decrease in amplitude was observed to threshold stimulation; sometimes the response to threshold stimulation disappeared completely. Deepening the anesthesia to stage III_1-III_3 led to a further decrease in amplitude of the response, but the amplitude to stimulation of twice and three times the threshold strength still continued (Fig. 3).

During fluothane anesthesia, marked depression of evoked responses in the RF developed. The EEG desynchronization reaction was depressed, although by a lesser degree than the evoked responses. In this way a discrepancy appeared in the evaluation of the functional state of the RF by two tests: evoked responses in the RF and the EEG desynchronization reaction in response to direct electrical stimulation of the RF. This discrepancy can be explained on the basis of Bradley's [5] findings, namely that chlorpromazine blocks synaptic structures of pathways into the RF while having no appreciable effect on the functional state of the activating system itself. On the basis of these findings it can be postulated that fluothane initially depresses synaptic structures on pathways into the RF, but with deepening of anesthesia it begins to depress the excitability of the reticular neurons. Evidence of this is given by the gradual increase in threshold of the EEG-desynchronization reaction, which persists even after disappearance of evoked responses in the RF.

The same differences in sensitivity of the evoked responses and EEG desynchronization reaction were found by the writer during an investigation of the action of ether and intranarcon [1].

Analysis of the transcallosal responses suggests that fluothane moderately depresses the cerebral cortex. It will be remembered that, besides afferent impulses passing along callosal fibers, this population of neurons receives a constant flow of afferent impulses from the thalamus [3] and structures of the brain stem [6, 14]. These afferent impulses, responsible for formation of the EEG, influence the amplitude of the transcallosal responses, although, as Fig. 3 shows, the scatter of amplitude of these responses is small in the waking animals just as after inhalation of fluothane. Consequently, interaction of the transcallosal responses with the background electrical activity has no significant effect on the amplitude. A change in the character of the flow of impulses to the cortex through the influence of various pharmacological agents can hardly exert an appreciable effect on the magnitude of these responses. For instance, an investigation by Darbinyan et al. [1] showed that if the bulbar RF is inhibited by barbiturates and the flow of afferent impulses to the cortex correspondingly reduced, the changes in the amplitude of the transcallosal responses is only very slight. Conversely, under ether anesthesia, which does not depress the RF, the amplitude falls sharply. These results suggest that the transcallosal response is a cortical phenomenon directly reflecting excitability of the cortical neurons.

It can be postulated that fluothane occupies an intermediate place between ether and the barbiturates in the strength of its action on the RF. The same remark can be applied to the effect of fluothane on the cortex, if it is remembered that ether strongly inhibited the cortex in stage I of anesthesia, while during barbiturate anesthesia no appreciable change in the transcallosal responses was observed even in stage III.

It can be postulated on the basis of these results that fluothane exerts a moderate inhibitory action both on the mesencephalic RF and on the cerebral cortex.

LITERATURE CITED

1. T. M. Darbinyan, V. B. Golovchinskii, and S. I. Plekhotkina, Khirurgiya, No. 1, 85 (1970).
2. A. Z. Manevich and R. A. Al'tshuler, Fluothane Anesthesia [in Russian], Moscow (1966).
3. P. Andersen and S. A. Andersson, Physiological Basis of the α Rhythm, New York (1968).
4. J. F. Artusio, J. Am. Med. Assn., 157, 33 (1955).
5. P. B. Bradley, in: The Reticular Formation of the Brain [Russian translation], Moscow (1962), p. 119.
6. F. Bremer, Res. Publ. Assn. Nerv. Ment. Dis., 36, 424 (1958).
7. H. T. Chang, J. Neurophysiol., 16, 117 (1953).
8. H. S. Davis, V. E. Quitmeyer, and W. E. Collins, Anaesthesia, 16, 32 (1961).
9. E. A. Gain and S. G. Paletz, Canad. Anaesth. Soc. J., 4, 289 (1957).
10. S. J. Galla, A. D. Olmedo, H. E. Kretchmer, et al., Anesthesiology, 23, 147 (1962).
11. A. R. Guedel, Inhalation Anesthesia, New York (1938).
12. H. H. Jasper and C. Ajmone-Marsan, A Stereotaxic Atlas of the Diencephalon of the Cat, Ottawa (1954).
13. L. M. Kitahata, Anesthesiology, 29, 523 (1968).
14. G. Moruzzi, Electroenceph. Clin. Neurophysiol., 16, 2 (1964).
15. J. Raventos, Brit. J. Pharmacol., 11, 394 (1956).
16. C. R. Stephen, G. Margolis, L. W. Fabian, et al., Anesthesiology, 19, 770 (1958).