EFFECT OF GENERAL ANESTHETICS OF VARIOUS TYPES ON TRANSCALLOSAL RESPONSES IN THE ASSOCIATION AND SOMATOSENSORY AREAS OF THE CAT CORTEX

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The effect of ether, cyclopropane, halothane, methoxyflurane, thialbarbital, and propanidide on the amplitude of transcallosal responses recorded in the primary projection and association areas of the cortex was studied in acute experiments on cats. The most marked inhibitory effect on both waves of transcallosal responses was produced by ether, followed in order of diminishing effect by halothane and cyclopropane. Methoxyflurane and thialbarbital had no definite inhibitory effect on the amplitude of the responses and, on the contrary, an increase in their amplitude was more often observed; however, this increase was not always statistically significant. Propanidide caused a marked increase in the amplitude of both waves of transcallosal responses. The results suggest that general anesthetics differ in their action on the systems of interhemispheric connections of functionally different areas of the cortex.

Primary potentials evoked both by adequate and by electrical stimulation in specific cortical projection areas are known to undergo little change through the action of general anesthetics [1, 5, 10, 15, 17, 19-23, 26, 28]. The evoked potentials recorded in association areas, about whose relative sensitivity to general anesthetics there are differences of opinion [2, 9, 13, 14], have so far received comparatively little study. The transcallosal responses (TCR) provide a convenient test for comparing the sensitivity of cortical elements in different areas [8, 11, 18].

In the investigation described below the TCR were accordingly used as the criterion for comparing the sensitivity of cortical elements in functionally different areas (primary projection and association) to the action of several general anesthetics.

EXPERIMENTAL METHOD

Fifty adult cats were immobilized with tubocurarine and artificial respiration was applied by means of the type 661 Harvard Apparatus. After extensive bilateral trephining, stainless steel stimulating electrodes mounted on transparent plastic discs were applied to the middle part of the suprasylvian gyrus and to the posterior sigmoid gyrus. Platinum recording electrodes were arranged symmetrically to the stimulating electrodes in the opposite hemisphere.

The EEG was recorded by a Galileo R-32 electroencephalograph. TCRs were recorded from the screen of a VC-7 dual-beam oscilloscope by means of a PC-2A (Nihon Konden, Japan) camera. Electrical stimuli were generated by an MSE-40 (Nihon Konden, Japan) stimulator; square pulses with a duration of 0.2 msec were used. The effect of ether, cyclopropane, methoxyflurane, halothane, thialbarbital, and propanidide was investigated. The general inhalational anesthetics mixed with oxygen were introduced into the inlet of the artificial respiration apparatus, while noninhalational anesthetics were injected intravenously. In one experiment two or three general anesthetics were investigated in different orders. Fuller details of the method were described previously [12, 18].

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TABLE 1. Amplitude of Waves of Transcallosal Responses in Somatosensory Area I (top row of figures) and in the Association Area (bottom row of figures) on the Cat Cortex during Administration of General Anesthetics (in % of background value; M ± m)

General anesthetic		Stage I_3 of general anesthesia						Stage III_2 of general anesthesia					
		stimulation of thresh. intensity		stimulation of twice thresh. inten.		stimulation of three times thresh. inten.		stimulation of thresh. intensity		stimulation, twice thresh. intensity		stimulation of three times thresh. intensity	
		phase of response						phase of response					
		positive	negative	positive	negative	positive	negative	positive	negative	positive	negative	positive	negative
Ether		36±4	33±9	57±6	29±6	62±5	46±6	19±7	6±4	36±8	25±4	52±5	33±9
		59±7	63±7	65±4	65±5	70±6	71±4	30±7	34±6	44±5	43±5	56±7	49±5
	P_1	>0,99	>0,99	>0,99	>0,99	>0,99	>0,99	>0,99	>0,99	>0,99	>0,99	>0,99	>0,99
	P_2	>0,99	>0,99	>0,99	>0,99	>0,99	>0,99	>0,99	>0,99	>0,99	>0,99	>0,99	>0,99
	P	0,98	0,98	<0,9	>0,99	<0,99	>0,99	<0,9	>0,99	<0,9	>0,99	<0,9	0,9
Cyclopropane		70±30	47±25	110±17	48±16	108±13	65±17	39±16	17±10	77±4	36±10	88±9	42±8
		109±10	101±11	121±9	97±6	114±5	90±7	86±9	72±8	101±7	64±5	96±6	69±5
	P_1	<0,9	>0,99	<0,9	>0,99	<0,9	>0,99	>0,99	>0,99	>0,99	>0,99	<0,9	>0,99
	P_2	<0,9	<0,9	0,96	<0,9	0,99	<0,9	0,9	>0,99	<0,9	>0,99	<0,9	>0,99
	P	<0,9	0,93	<0,9	0,98	<0,9	<0,9	0,98	>0,99	>0,99	0,99	<0,9	>0,99
Methoxyflurane		77±13	107±20	109±12	117±16	105±8	129±10	146±19	124±17	118±20	162±12	110±13	148±11
		124±19	118±14	105±15	109±15	89±8	112±10	96±4	116±12	98±8	118±8	93±8	94±5
	P_1	<0,9	<0,9	<0,9	<0,9	<0,9	0,97	0,92	<0,9	<0,9	>0,99	<0,9	>0,99
	P_2	<0,9	<0,9	<0,9	<0,9	<0,9	<0,9	<0,9	<0,9	<0,9	<0,9	<0,9	<0,9
	P	0,96	<0,9	<0,9	<0,9	<0,9	<0,9	0,95	<0,9	<0,9	>0,99	<0,9	>0,99

Table 1 (continued)

General anesthetic		Stage I_3 of general anesthesia						Stage III_2 of general anesthesia					
		stimulation of thresh. intensity		stimulation of twice thresh. inten.		stimulation of three times thresh. inten.		stimulation of thresh. intensity		stimulation, twice thresh. intensity		stimulation of three times thresh. intensity	
		phase of response						phase of response					
		positive	negative	positive	negative	positive	negative	positive	negative	positive	negative	positive	negative
Halothane		94±20	31±20	74±8	50±11	74±8	60±18	56±17	17±17	35±11	21±8	43±8	38±9
		67±9	91±8	109±7	91±10	105±8	77±6	52±8	77±11	76±7	71±7	91±10	77±6
	P_1	<0,9	>0,99	>0,99	>0,99	>0,99	>0,99	>0,99	>0,99	>0,99	>0,99	>0,99	>0,99
	P_2	>0,99	<0,9	<0,9	<0,9	<0,9	>0,99	0,99	>0,99	>0,99	>0,99	<0,9	>0,99
	P	<0,9	>0,99	>0,99	>0,99	0,98	<0,9	<0,9	>0,99	>0,99	>0,99	>0,99	>0,99
Propanidide		146±15	209±21	122±10	123±13	128±16	124±13	144±17	189±35	145±18	207±35	159±33	190±36
		125±9	157±11	138±8	128±6	134±9	129±5	119±8	137±10	140±10	139±9	156±14	140±5
	P_1	>0,99	>0,99	0,96	0,9	0,9	0,9	>0,98	>0,99	>0,99	>0,99	0,92	0,96
	P_2	>0,98	>0,99	>0,99	>0,99	>0,99	>0,99	0,96	>0,99	>0,99	>0,99	>0,99	>0,99
	P	0,91	0,95	<0,9	<0,9	<0,9	<0,9	<0,9	<0,9	<0,9	0,92	<0,9	<20,9
Thialbarbital		115±18	164±13	127±17	147±16	118±17	120±12	130±10	147±11	154±18	124±12	124±14	137±8
		96±10	149±19	125±9	126±16	111±7	101±10	110±10	132±15	123±12	122±15	108±9	108±9
	P_1	<0,9	>0,99	<0,9	>0,99	<0,9	<0,9	>0,99	>0,99	>0,99	0,96	0,9	>0,99
	P_2	<0,9	>0,99	0,98	0,99	<0,9	<0,9	<0,9	0,95	0,9	<0,9	<0,9	<0,9
	P	<0,9	<0,9	<0,9	<0,9	0,9	<0,9	<0,9	<0,9	<0,9	<0,9	<0,9	>0,99

Legend: P_1) significance of differences between mean amplitudes of response waves in waking and anesthetized animal in somatosensory cortical area I; P_2) the same in cortical association area; P) significance of differences between mean amplitudes of response waves in somatosensory area I and association area of cortex during exposure to the anesthetics tested.

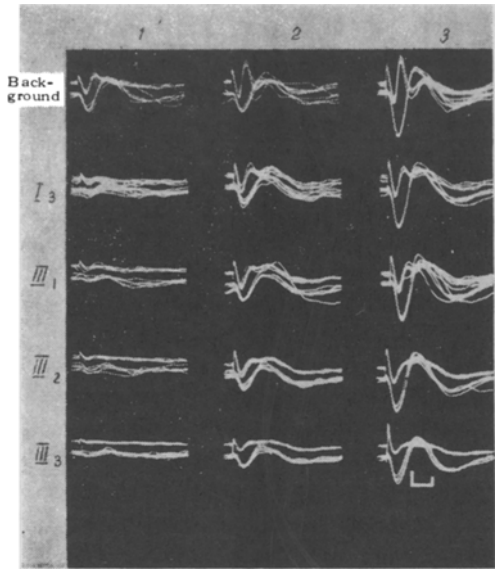

Fig. 1. Effect of ether on transcallosal responses in somatosensory area I (above) and association area (below) of cortex: 1) responses to stimulation of threshold intensity; 2) to stimulation of twice the threshold; and 3) of three times the threshold intensity. Stages of general anesthesia shown on the left. Time marker 20 msec, calibration 100 μV. Positivity downward.

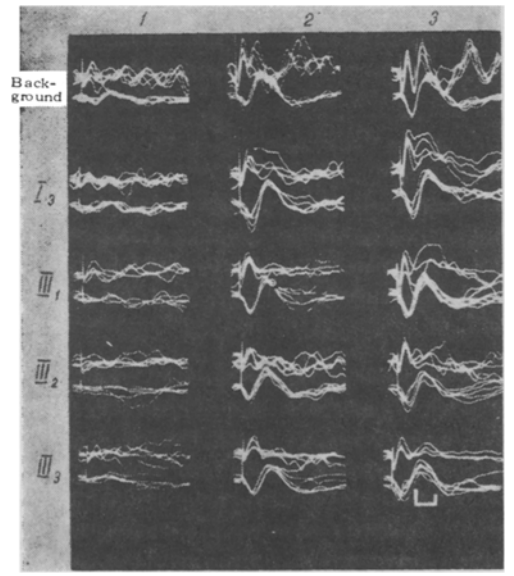

Fig. 2. Effect of cyclopropane on transcallosal responses in somatosensory area I (above) and association area (below) of the cortex. Legend as in Fig. 1.

EXPERIMENTAL RESULTS AND DISCUSSION

Changes in the amplitude of the TCR during administration of the tested anesthetics are given in Table 1. Ether had the strongest inhibitory effect on both TCR waves (Fig. 1). Next in order of diminishing effect were halothane and cyclopropane (Fig. 2). In stage I_3 of cyclopropane anesthesia an increase in amplitude of the positive TCR wave was sometimes seen. Methoxyflurane and thialbarbital had no definite inhibitory action on the amplitude of the TCR but, on the contrary, an increase in the amplitude of the responses was more frequently observed although this increase was not always statistically significant. Propanidide caused a marked increase in the amplitude of both waves of the TCR (Fig. 3).

The appreciably higher sensitivity of the neuronal populations of somatosensory area I than those of the association cortex to the action of all general anesthetics tested is an interesting fact (Table 1).

It is unlikely, however, that the marked differences in sensitivity to the action of the substances tested actually reflect differences in the morphological organization of the interhemispheric connections between two cortical areas although these differences were manifested in the different form of the responses. Since the integral TCR reflect excitability of the neuron bodies (beneath the stimulating electrodes) and the amplitudes of the postsynaptic potentials (under the recording electrode), the changes in integral excitability detected in different areas in response to stimulation of equal intensity (expressed in thresholds) are presumably largely dependent on the changes in parameters of the neuron membranes caused by the general anesthetics rather than on morphological differences between the two cortical areas. For that reason the results obtained by comparing responses of functionally different zones of the cortex confirm the existence of a definite selectivity of action of the general anesthetics on membranes of different types of neurons.

The decrease in amplitude of the TCR during the action of certain general anesthetics can be explained as follows. Biophysical analysis of the distribution of currents in biological structures [3] suggests that during electrical stimulation of the cortex the probability of excitation of an element is proportional to its size. For that reason the bodies of cortical neurons are excited chiefly, and not their axons, and a mainly orthodromic volley is directed into the opposite hemisphere, where it causes the generation of postsynaptic potentials in the zone of recording; antidromic activation of neurons in the zone of recording as a result of stimulation of their axons in the opposite hemisphere probably plays a much less important role in the genesis of TCR. In response to stronger electrical stimulation (2-3 thresholds) comparatively moderate changes in the critical depolarization level of the stimulated neurons, developing as a result of the action of the general anesthetics, were probably not significant and an afferent volley of com-

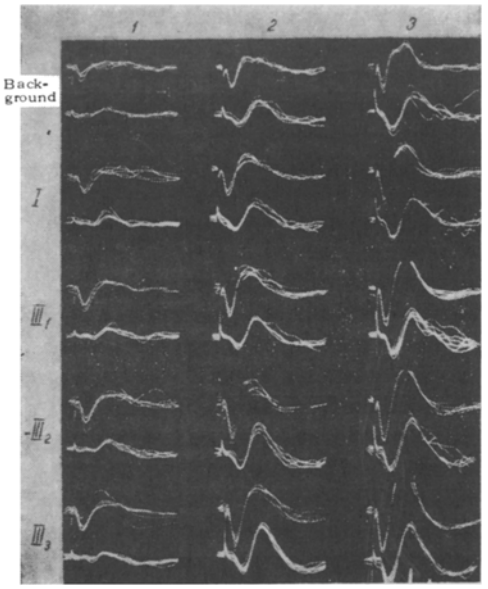

Fig. 3. Effect of propanidide on transcallosal responses in somatosensory area I (above) and in association area (below) of cortex. Legend as in Fig. 1.

paratively steady intensity was directed into the opposite hemisphere. It therefore seems likely that the decrease in amplitude of the TCR during the action of general anesthetics takes place mainly on account of the inhibitory effect of these substances on the synaptic transmission of excitation.

The causes of the increase in amplitude of the TCR during the action of pentobarbital [8, 11] and also of thialbarbital, propanidide, and methoxyflurane observed in the present experiments, should also be analyzed. This increase cannot be explained by changes in the passive properties of the cerebral cortex [6]. It is also known that recurrent inhibition in the cortex is intensified to a varied degree under the influence of general anesthetics [16, 27]. The increase in amplitude of the TCR can therefore hardly be explained by weakening of intracortical inhibitory influences. Since it was the barbiturates and propanidide which induce the strongest inhibition of ascending reticular influences [18, 23] this suggests that the increase in amplitude of the TCR during the action of these substances is connected to a certain extent with the removal of inhibitory influences from the cortex. During the action of methoxyflurane, however, inhibition of the reticular formation is less marked [7] but, nevertheless, under general methoxyflurane anesthesia a significant increase in amplitude of the TCR develops in somatosensory area I, and if the stimulation is strong it appears as early as in stage I_3. Consequently, the increase in amplitude of cortical electrical activity cannot be explained in every case by the removal of inhibitory reticular influences. The most important factor is an increase in the amplitude of the TCR as a result of elevation of the critical level of depolarization, as described in several investigations [15, 24]. This elevation results in a decrease in the limitation of amplitude of the evoked postsynaptic potentials by the depolarization level at which the spike arises, and this is exhibited more clearly in response to stimulation of considerable strength. The slow waves recorded from the surface of the cortex presumably reflect only postsynaptic potentials and not spike discharges of cortical neurons [4, 25]. There is no evidence in the literature of the strengthening of excitation during the action of general anesthetics. It can therefore be concluded that the increase in amplitude of TCR reflects an increase in the critical level of depolarization of cortical neurons during the action of propanidide, thialbarbital, and methoxyflurane; under these circumstances the mechanism of synaptic transmission is evidently changed less. These mechanisms can equally give rise to the increase in amplitude of the evoked potentials and also of spontaneous electrical waves in the cortex (EEG) during general anesthesia described by many writers.

The results of this investigation suggest that definite differences exist between the action of general anesthetics on systems of interhemispheric connections between functionally different areas of the cerebral cortex.

LITERATURE CITED

1. Ya. A. Al'tman and A. M. Maruseva, Fiziol. Zh. SSSR, No. 11, 1345 (1960).
2. A. S. Batuev, Fiziol. Zh. SSSR, No. 6, 659 (1968).
3. K. Yu. Bogdanov, Author's Abstract of Candidate's Dissertation, Moscow (1972).
4. K. Yu. Bogdanov and V. B. Golovchinskii, Biofizika, No. 3, 536 (1969).
5. V. A. Gmyrya-Novi, Fiziol. Zh. SSSR, No. 5, 538 (1965).
6. V. B. Golovchinskii, K. Yu. Bogdanov, and É. D. Rapoport, Neirofiziologiya, 3, 260 (1971).
7. T. M. Darbinyan, V. B. Golovchinskii, and S. I. Plekhotkina, Vestn. Akad. Med. Nauk SSSR, No. 8, 3 (1972).
8. V. V. Zakusov and R. U. Ostrovskaya, Byull. Éksperim. Biol. i Med., No. 11, 85 (1967).
9. N. V. Kazakov, Fiziol. Zh. SSSR, No. 9, 1070 (1969).
10. É. M. Nabil', Fiziol. Zh. SSSR, No. 5, 472 (1966).
11. R. U. Ostrovskaya, Byull. Éksperim. Biol. i Med., No. 8, 65 (1969).

12. S. I. Plekhotkina, Byull. Éksperim. Biol. i Med., No. 8, 58 (1971).
13. A. G. Polyakov, Byull. Éksperim. Biol. i Med., No. 9, 13 (1966).
14. A. S. Timchenko, Soobshch. Akad. Nauk Gruz. SSR, 59, No. 1, 161 (1970).
15. I. A. Shevelev, The Dynamics of the Visual Sensory Signal [in Russian], Moscow (1971).
16. P. Andersen and S. A. Andersson, Physiological Basis of the Alpha Rhythm, New York (1968).
17. M. A. B. Brazier, J. Anaesth., 33, 194 (1961).
18. T. M. Darbinjan, V. B. Golovchinskii (Golovchinsky), and S. I. Plekhotkina, Anesthesiology, 34, 219 (1971).
19. H. S. Davis, W. F. Collins, C. T. Randt, et al., Anesthesiology, 18, 634 (1957).
20. H. S. Davis, W. H. Dillon, W. F. Collins, et al., Anesthesiology, 19, 441 (1958).
21. A. Forbes, Am. J. Physiol., 113, 43 (1935).
22. A. Forbes and B. R. Morison, J. Neurophysiol., 2, 112 (1939).
23. J. D. French, M. Verzeano, and H. W. Magoun, Arch. Neurol. Psychiat. (Chicago), 69, 519 (1953).
24. J. M. Fuster, O. D. Creutzfeldt, and M. Straschill, Z. vergl. Physiol., 49, 605 (1965).
25. D. R. Humphrey, Electroenceph. Clin. Neurophysiol., 25, 421 (1968).
26. N. Y. Kiang, J. H. Meame, and L. F. Clark, Science, 133, 1927 (1961).
27. L. M. Kitahata, Anesthesiology, 29, 523 (1968).
28. W. H. Marshall, C. N. Woolsey, and P. Bard, J. Neurophysiol., 4, 1 (1941).