ELECTROENCEPHALOGRAPHIC FREQUENCY SPECTRUM ANALYSIS DURING ETHER AND CYCLOPROPANE ANESTHESIA

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CHANGES in cortical activity during anesthesia have been described by a number of investigators (1–5). The descriptions are qualitative and note the change in frequency, wave form, and amplitude that occurred at various depths of anesthesia. Dawson and Walter pointed out the difficulty of interpreting electroencephalographic complexes visually and defining the frequencies that are summated to produce different complexes and at the same time appreciate the amplitude of each of these frequencies (6). In order to define more accurately the characteristic electroencephalographic pattern associated with the analgesic state of diethyl ether anesthesia we submitted this electroencephalographic pattern to frequency spectrum analysis (7). We were able to present a quantitative description of this pattern by using the Spencer Kennedy Laboratories filter. The purpose of this study is to extend these determinations to include the electroencephalographic changes noted with diethyl ether anesthesia and cyclopropane anesthesia, from emergence from very deep surgical anesthesia to analgesia using ether and from deep anesthesia to very light surgical anesthesia using cyclopropane.

METHOD

Observations were made on two healthy young (22 and 26 years) volunteers, one of whom received diethyl ether and the other cyclopropane as the sole anesthetic agent. The subjects were anesthetized to electroencephalographic level 6 and allowed to recover. Electroencephalographic recordings were made in a shielded room from frontocentral no. 25 needle-electrodes on a Mederaft Electroencephalograph Model D. Analysis of the electroencephalographic frequency spectrum was made by an Offner Electronics Frequency Analyzer Type 830 which was standardized with a Hewlitt Packard Audio Signal Generator Model no. 202B. The amplitude of the analyzer pen deflection was calibrated in microvolts at each frequency studied by feeding a known peak to peak sine wave signal into the electroencephalographic recorder and determining the relationship of signal strength to pen deflection. The electrocardiogram was recorded simultaneously on one

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TABLE 1

AMPLITUDE (IN MICROVOLTS) SUMMATED FOR 10 SECONDS AT FREQUENCIES FROM 1.5 TO 30 CYCLES PER SECOND DURING RECOVERY FROM ETHER ANESTHESIA

Time in Minutes After Discontinuance of Anesthesia	Frequency in Cycles Per Second																					
	1.5	2.0	2.5	3.0	3.5	4.0	5.0	6.0	7.1	8.4	9.7	11.0	12.2	13.5	14.0	15.0	16.0	18.0	20.0	22.0	24.0	27.0	30.0
16.5	51	30	21	30	51	84	120	87	108	81	99	75	54	60	48	78	87	90	87	93	174	135	81
15.0	201	150	87	78	96	114	144	138	207	117	102	78	87	66	93	96	78	90	123	99	156	132	69
13.5	72	48	33	42	48	69	81	81	129	51	69	51	51	51	45	54	66	81	81	84	114	93	57
12.0	84	72	48	48	90	84	111	156	135	81	81	69	48	48	54	69	81	63	90	81	99	66	45
10.5	66	48	30	54	51	87	78	108	165	57	66	48	39	39	30	45	81	75	60	54	90	63	45
9.0	150	108	120	138	174	213	204	210	150	108	135	81	51	45	51	54	81	72	66	57	66	54	39
7.5	216	198	180	156	207	213	189	195	123	93	123	72	39	45	51	48	51	57	39	30	51	45	33
6.0	219	213	210	213	210	216	207	177	126	108	114	36	27	21	15	18	21	27	21	15	21	21	24
4.5	213	216	210	210	210	216	204	144	111	81	78	30	21	18	15	18	18	15	12	12	18	18	18
3.0	222	213	204	207	210	213	195	132	93	81	72	21	18	12	12	12	12	12	9	6	9	9	12
1.5	219	216	189	189	195	189	132	84	66	54	51	15	9	6	3	6	6	6	6	3	9	9	15
0.0	210	195	180	195	198	192	135	87	60	60	51	12	12	9	0	9	9	15	9	12	12	18	24

channel of the electroencephalogragh recorder. Blood pressure was recorded at least every five minutes by sphygmomanometric technique. Premedication consisted of 0.6 mg. of atropine given intravenously 15 minutes prior to the start of anesthesia. After an awake pattern was obtained anesthesia was induced.

Ether.—Diethyl ether anesthesia was induced by a nitrous oxide-oxygen ether sequence. After the subject entered the stage of surgical anesthesia oral endotracheal intubation was performed. Lidocaine, 5 per cent, ointment was used on the cuffed endotracheal tube as a topical anesthetic. All nitrous oxide was eliminated from the breathing mixture. Anesthesia was continued using a Heidbrink closed circle-carbon dioxide absorber system until electroencephalographic level 6 was

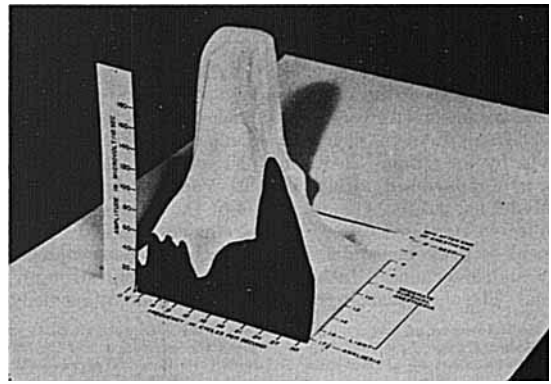

FIG. 1.

reached. The administration of ether was then discontinued, the expiration valve opened, and the oxygen flow was increased from 300 cc. to 2 liters per minute. This semiclosed system allowed the ether to be eliminated gradually. Continuous electroencephalographic recordings were started with simultaneous pattern analysis, using the frequency analyzer. Recordings were continued until the subject entered the stage of analgesia and responded to spoken voice.

The amplitude summated over 10 seconds at each frequency studied from 1.5 cycles per second to 30 cycles per second was calculated and tabulated at 30 second intervals from deep third stage anesthesia to analgesia (condensation of the data shown in table 1). From these data plots were made of amplitude versus frequency versus depth of anesthesia. From the plots of these variables a three dimensional model was constructed (fig. 1).

Cyclopropane.—Cyclopropane anesthesia was induced by a 50 percent oxygen and 50 percent cyclopropane mixture and continued using a Heidbrink closed circle-carbon dioxide absorber system with a face

TABLE 2

AMPLITUDE (IN MICROVOLTS) SUMMATED FOR 10 SECONDS AT FREQUENCIES FROM 1.5 TO 30 CYCLES PER SECOND DURING RECOVERY FROM CYCLOPROPANE ANESTHESIA

Depth of Anesthesia	Frequency in Cycles per Second																						
	1.5	2.0	2.5	3.0	3.5	4.0	5.0	6.0	7.1	8.2	9.2	10.2	11.2	12.4	13.5	14.2	15.0	16.0	18.0	20.0	22.0	24.0	27.0	30.0
1	108	93	51	45	39	74	103	100	120	66	74	96	74	52	42	49	30	33	42	21	19	18	16	21
2	177	180	157	165	156	168	127	100	60	25	37	18	19	14	18	27	12	16	21	10	9	6	5	7
3	204	207	203	201	169	198	172	119	87	48	42	33	21	20	30	30	12	16	21	12	11	9	6	7
4	202	204	193	195	186	204	157	119	72	48	34	28	15	13	10	18	12	13	18	8	8	3	5	6
5	207	206	203	141	162	166	93	64	45	24	19	15	6	3	3	6	3	6	9	6	7	6	6	7
6	207	209	199	150	141	120	97	66	39	24	19	15	5	3	3	2	0	3	5	2	2	0	0	3

mask until the subject entered electroencephalographic level 6. The administration of cyclopropane was then discontinued and the expiratory valve opened. The oxygen flow was increased from 300 cc. to 1 liter per minute and the continuous electroencephalogram was recorded simultaneously in association with analysis by the frequency analyzer. Recordings were made until the subject entered light surgical anesthesia.

The amplitude summated over 10 seconds at each frequency studied from 1.5 to 30 cycles per second was calculated and tabulated at six levels of anesthesia corresponding to the six levels of cyclopropane anesthesia described by Possati and others (4). From these data (table 2) a three dimensional representation was drawn (fig. 2).

RESULTS

The changes in amplitude of various frequencies with time after discontinuance of ether anesthesia were tabulated (condensed data

shown in table 1), and a picture of a three dimensional model of these data is shown in figure 1. In deep stages of ether anesthesia there is an abundant amount of 1–2 cycle per second activity. As anesthesia is lightened there is a decrease in the slow frequencies and an increase in the fast 24 cycle activity. If plots are made of frequency versus depth (time after discontinuance of ether) it can be seen from table 1 that the 24 cycle activity decreased directly with increasing depth of anesthesia. The 6 cycle activity when plotted forms a bell shaped curve. It reaches a maximum in moderately deep anesthesia and falls off in the light and deep stages. The 2 cycle activity forms a sigmoid shape plot. Its amplitude is low in light stages of anesthesia and rises to a maximum as anesthesia becomes deep. The solid representation of the amplitude variation of each frequency permits one to grasp the topography of these changes more easily.

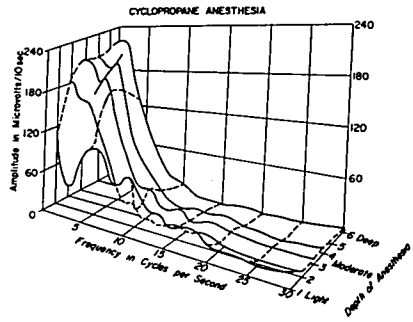

FIG. 2.

Table 2 indicates the changes in amplitude measured at various frequencies from 1.5 to 30 cycles per second during the recovery from cyclopropane anesthesia. A three dimensional representation of these data is shown in figure 2. This electroencephalographic pattern in deep cyclopropane anesthesia consists predominately of 2 cycle activity with little fast activity present. As anesthesia is lightened the amount of fast activity increases, but fast 24 cycle activity characteristic of light ether anesthesia is not noted. The topography of the electroencephalographic changes with varying depth of cyclopropane anesthesia is different from that seen with ether. It will be noted from table 2 that if the amplitude of the frequencies from 11.2 to 30 cycles is summated the energy represented tends to decrease with increasing depth of anesthesia.

No electrocardiographic disturbance or marked decrease in blood pressure was noted during these studies.

Discussion

The amplitude expressed in microvolts peak to peak as calculated from the plot produced simultaneously on the electroencephalographic record by the frequency analyzer is a representation of the continuous peak to peak sine wave signal that would produce the same pen deflections. Activity at a specific frequency in the electroencephalogram may vary from moment to moment so that the amplitudes expressed are the average value occurring during a 10 second interval.

The peak frequencies of the analyzer are accurate to $\pm .05$ cycles per second. The band pass is much narrower than that of the modified Spencer Kennedy Laboratories filter we used in determining the frequency spectrum of the analgesia pattern. The Offner Electronics Frequency analyzer with its narrower band pass allowed us to obtain higher resolution of the analgesic pattern. For this reason the 24 cycle peak is much sharper and higher than that found with the previous method of analysis. This fact was appreciated and predicted in a former paper (7).

It may be that the large slow waves observed in the electroencephalogram were not analyzed accurately since it is possible to overload the system and obscure changes that occur at larger voltages. When the amplitude approaches the maximum recorded by the analyzer as it did in the slower frequencies it would be best to recalibrate the analyzer to handle these greater amplitudes.

It is difficult to give absolute values to the axis labeled "Depth of Anesthesia." Possati and others (4) found a straight line correlation between the depth of cyclopropane anesthesia as determined by electroencephalographic classification and the arterial blood cyclopropane level. We have plotted the six patterns of cyclopropane anesthesia on the depth of anesthesia axis, and, based on the work of Possati, Faulconer, Bickford and Hunter (4), one might consider the arterial blood cyclopropane level to be increasing linearly from one through six. The depth of anesthesia axis on the ether anesthesia model is expressed in time from discontinuance of ether anesthesia. Desaturation of the body is a hyperbolic function. If blood anesthetic levels were available it would permit us to give the depth of anesthesia axis absolute units in these studies.

An attempt was made to keep pO_2 and pCO_2 within normal limits by assisting respiration when necessary. It has been shown that CO_2 and O_2 have marked effects on the electroencephalogram (10). In order to rule out interference from these factors it is necessary to do blood CO_2 and O_2 determinations. The patterns recorded during both these runs appeared to be similar to those seen regularly during cyclopropane or ether anesthesia. Therefore, we believe these analyses are of typical electroencephalographic changes produced by these anesthetics.

The analgesic pattern represented in this paper has small secondary peaks at 7.1 and 5 cycles per second. These peaks were not noted in our earlier analyses of the analgesic pattern (7). Whether they are significant or represent artifacts remains to be determined. It may be that the higher degree of resolution offered by this method of analysis permitted us to detect these secondary peaks.

Servo anesthesia offers an immediate practical application of the data presented here. It has been possible to control depth of anesthesia by use of servo control (8). All agents can now be screened as outlined in this study and the data analyzed so that the optimal frequency to be monitored can be selected. Hunter has discussed the pitfalls that the research worker can fall into when evaluating a system in which there are three variables (9). Contour surfaces or similar representation will help avoid some of these errors and aid in selection of optimum conditions.

We believe that the use of the electroencephalogram and frequency spectrum analysis in this way offers a new approach to the study of anesthetic agents. The differences in topography between cyclopropane and ether anesthesia probably attest to a different mode of action of these agents or a different site of action. Perhaps the day is not far off when certain peaks and troughs in the topography of the frequency spectrum analysis of an anesthetic agent will be related to specific sites of action or perhaps to specific enzyme systems influenced by the anesthetic agents.

Summary

Frequency spectrum analysis of electroencephalographic changes during diethyl ether and cyclopropane anesthesia has been performed by the use of an Offner Electronics Frequency analyzer. The data thus obtained has been presented in tabular and three dimensional representation. The difference in the topography of the electroencephalographic changes produced by ether and cyclopropane may indicate a different site or mode of action of these agents.

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