STUDIES ON NITROUS OXIDE, MEPERIDINE AND LEVALLORPHAN WITH UNIPOLAR ELECTROENCEPHALOGRAPHY

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During the course of other studies on meperidine-supplemented nitrous oxide anesthesia it became desirable to be able to quantitate the depth of depression of the patients under anesthesia. There are reports of electroencephalographic changes seen during nitrous oxide (1), but none were found describing the electroencephalogram during anesthesia with nitrous oxide using meperidine as a supplement. We undertook, therefore, to investigate the electroencephalogram of surgical patients during this form of anesthesia.

The fronto-occipital bipolar derivation of the electroencephalogram, as used in defining the electroencephalographic levels of ether anesthesia (2), was used initially. Fortuitously, a second channel of the recorder was set to record a unipolar vertex lead measured against an indifferent electrode attached to the ear lobe. The rather striking differences in these two leads led to the investigation reported here.

Method

Patients scheduled for routine surgery were anesthetized electively with nitrous oxide and meperidine. Electroencephalographic recordings were made during the anesthetization and subsequent surgery of 14 subjects. A bipolar fronto-occipital lead was recorded on one channel of a Grass model IIID recorder, and a unipolar vertex derivation with indifferent electrode attached to the ear lobe was recorded on another channel. The subjects were not premedicated. Some were given up to 300 mg. of meperidine intravenously in several intermittent injections, prior to induction with nitrous oxide. Other subjects were given nitrous oxide for five to ten minutes, after which intermittent injections of meperidine were given intravenously. The nitrous oxide was administered in a 70 per cent delivered concentration with oxygen. In some cases a nonrebreathing system was used, and total flow of nitrous oxide and oxygen adjusted to the minute volume of the subject.

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In other cases a semiclosed carbon dioxide absorption system was used, and the total flow of gases was regulated at 5 liters per minute. The delivered concentration of nitrous oxide was in all cases metered at 70 per cent of the total flow from the anesthetic apparatus.

In some cases it was deemed advisable to ventilate the subjects artificially by manual compression of the rebreathing bag. All subjects were maintained in a state of adequate ventilation as determined by clinical observation of pulse, blood pressure, capillary bed color, rebreathing bag and chest movement, and general appearance.

Levallorphan tartrate was administered as a 1 mg. intravenous injection to 5 patients as the operative procedure approached termination. The indication for its administration was a respiratory rate of less than 8 per minute.

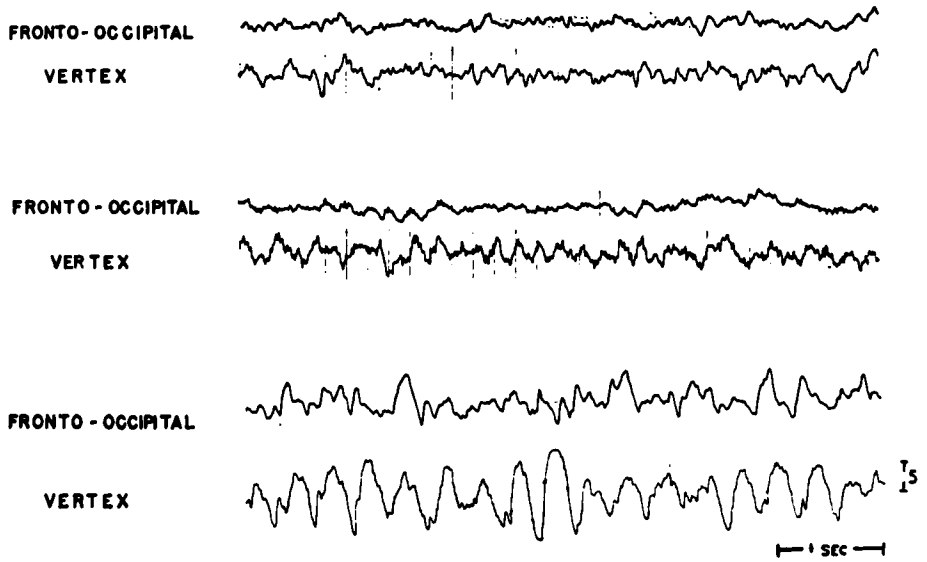

FIG. 1. Simultaneous fronto-occipital and vertex leads from different subjects at different levels of depression.

RESULTS

The unipolar vertex lead of the electroencephalogram consistently gave higher voltages and more readily interpretable changes during nitrous oxide-meperidine anesthesia than did the bipolar fronto-occipital lead. Figure 1 shows, in different subjects, the simultaneous recordings of these two leads. Close examination of the frequencies appearing in the fronto-occipital lead will show them to be similar to those recorded from the vertex. The legibility of the vertex lead, however, is much better.

The sequence of changes produced by adding intravenous meperidine during nitrous oxide anesthesia appeared consistently. Admin-

istration of meperidine to a patient under nitrous oxide anesthesia was followed by a breaking up of the regular 5 to 7 cycles per second activity seen with nitrous oxide alone. With initial injections of meperidine, an irregular mixture of many frequencies, ranging from 5 to 30 cycles per second, was produced. As more meperidine was administered the faster frequencies gradually became less prominent and tended to disappear. Concomitantly, with the reduction in the faster activity there was a progressive slowing of the theta activity and introduction of frequencies in the delta range. Frequencies as slow as 1 cycle per second

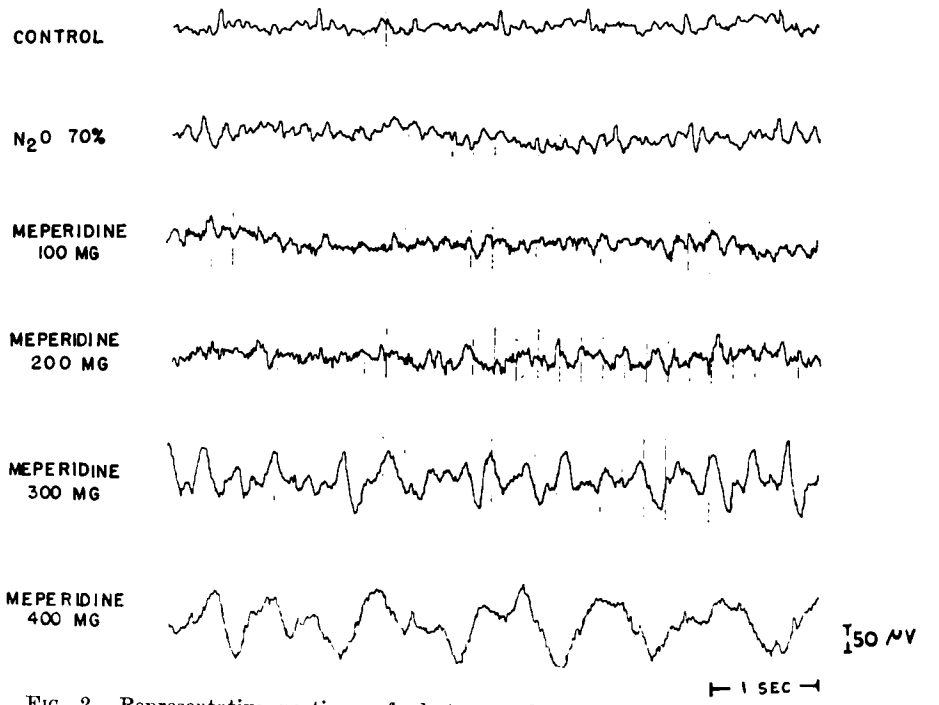

FIG. 2. Representative portions of electroencephalographic tracing of vertex-ear lobe lead from one subject showing typical changes with addition of meperidine. Total quantity of meperidine administered was 400 mg.

were seen after doses of meperidine in the range of 0.5 Gm. The slowing was gradual, and no sudden changes in either frequency or voltage were observed as the subject was depressed with additional meperidine. Figure 2 presents representative portions of the vertex-ear lobe electroencephalographic lead recorded during nitrous oxide-meperidine anesthesia, and illustrates the slowing of the frequencies with addition of meperidine. These tracings were obtained by purposely inducing the subject with nitrous oxide and adding intravenous meperidine. At least five minutes elapsed between each dose of meperidine.

Meperidine administered prior to induction with nitrous oxide altered somewhat the sequential relationships of the electroencephalo-

graphic frequencies. The gradual slowing described for figure 2 was not apparent. When the meperidine was given prior to the nitrous oxide, there was, instead of the progressive slowing, a relatively sudden appearance of slow theta or delta frequencies after the nitrous oxide was started. The resultant slow frequency appeared to be related to the amount of meperidine previously given. Larger amounts of meperidine were associated with slower frequencies than were smaller amounts of meperidine.

Surgery could be performed satisfactorily with electroencephalographic activity comparable to the lighter levels of figure 2. It was not necessary at any time for the basic frequency to be below 3 cycles per second to maintain satisfactory surgical anesthesia.

Administration of levallorphan to patients anesthetized with nitrous oxide and meperidine was followed regularly by a slowing of the electroencephalographic frequency. A typical tracing before and after intravenous administration of 1 mg. of levallorphan is shown in figure 3.

FIG. 3. Representative segments of tracing of anesthetized subject before and after administration of 1 mg. levallorphan.

The slowing was observed to appear in one to three minutes and persisted for only about one minute. Concomitantly, with or before the appearance of the slower frequency the subject's respiratory rate increased.

DISCUSSION

Since the original definition by Courtin, Bickford, and Faulconer (2) of the electroencephalographic levels of ether anesthesia, most anesthesiologists have confined their observations on the electroencephalogram to the bipolar fronto-occipital lead used by Courtin. An exception is the report by Morris, Knott, and Pittinger (3) on electroencephalographic studies during xenon anesthesia, in which an ear lobe-vertex lead was recorded.

The observations reported in this communication would suggest that anesthesiologists should be attentive to electrode placement. It appears that during anesthesia, as in awake states, the position of the recording electrodes determines the resulting electroencephalogram. It follows, therefore, that in order to monitor anesthetic depth by use of a sequence of electroencephalographic changes one should be especially careful to place the electrodes in the positions originally used in defining that sequence.

Since the potentials recorded by the electroencephalograph depend upon the potential fields at the surface of the head, the fact that electrode placement may be critical should not be any surprise to experienced workers in this field. We would like to point out the further possibility, based on our unpublished observations, that the distribution of potential fields at the surface may be different for different anesthetic agents. This in turn may provide a method for determining site of action of various agents. In all probability, the most adequate interpretation of the electroencephalogram during anesthesia will depend upon multi-channel recording, and will further depend upon a continuing experimental attitude, rather than the early acceptance of what might be premature "standards." It seems fairly certain that by limiting recording to only one channel there will be a sharp decrease in the information available to the anesthesiologist and the electroencephalographer. In instances where a servosystem is proposed for control of depth of anesthesia, it is possible that some electrode placements may be more adequate than others for providing data to the system.

It is interesting to note that the progressive slowing of frequency observed during xenon anesthesia (3) was also observed during nitrous oxide-meperidine anesthesia. The frequencies became slower with the nitrous oxide-meperidine sequence than with xenon alone, but the similarity of the progressive slowing is striking.

No burst suppression was observed with nitrous oxide- meperidine in either lead. Perhaps had the administration of meperidine been continued further, this phenomenon would have appeared. However, such a depth of depression would not appear to be needed during clinical anesthesia.

The observations on administration of levallorphan are consistent with the report (4) that the antagonist is in its own right a depressant. Further systematic investigation of the electroencephalographic changes after administration of this drug would appear indicated.

The electroencephalographic changes reported here with nitrous oxide and meperidine are quite unlike those seen with nitrous oxide alone (1). This might suggest a complementing interaction of the two drugs in their effects on the nervous system. Normative data for nitrous oxide alone would not, therefore, be adequate for nitrous oxide and meperidine. This observation lends support to the contention of Pittinger and associates (5) that "the use of the electroencephalogram as an indicator of depth of anesthesia must be done empirically, and scales must be changed as agents are varied."

Summary

Simultaneous vertex-ear lobe and fronto-occipital electroencephalographic leads were recorded during nitrous oxide-meperidine anesthesia. Differences found in these two leads are reported. It is sug-

gested that further investigation of multiple electroencephalographic leads during anesthesia appears indicated.

A gradual slowing of the electroencephalographic frequency was recorded as subjects were given additional doses of meperidine during nitrous oxide anesthesia.

Slowing of the electroencephalographic frequencies subsequent to administration of levallorphan during nitrous oxide-meperidine anesthesia is reported.

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