Electroencephalogram in Hypothermic Circulatory Arrest

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Electroencephalographic observations were performed during hypothermic circulatory arrest at various temperature levels. Changes in cortico- and subcortico-grams recorded from 28 ether-anesthetized mongrel dogs were divided into three stages. The termination of arrest within the 1st and the 2nd stages resulted in a complete recovery; whereas that at the 3rd stage resulted in no recovery.

This criterion was satisfactorily applied to 20 patients operated on cardiotomy under hypothermic circulatory arrest. Though EEG (scalp) was used, a characteristic pattern appearing exclusively at the beginning period of the 1st and the 2nd stages led to a precise estimation of the length of the 2nd stage proportionally to the length of the 1st stage from the experimental experiences. The safety time limit of circulatory arrest, by the end of the 2nd stage, was 25 to 30 minutes at body temperature of 28°C.

A series of experimental study on hypothermic circulatory arrest to aid open heart surgery had been performed in 1956 at University of Nagoya, and the conclusion was that the circulation could be interrupted for 15 minutes at body temperature of 28°C without any sequela on the circulatory system postoperatively. In June 1957 a 13-year-old girl with atrial septal defect was first operated on primary closure of the defect with the aid of hypothermic circulatory arrest successfully. Thereafter, 46 cases of atrial septal defect, 41 cases of ventricular septal defect and 3 cases of the tetralogy of Fallot had been operated on by the end of 1962 using this technic, and the duration of circulatory arrest had been prolonged up to 25 minutes at body temperature of 28°C in some cases.

The further conclusion from another series of experiment carried on parallelly to the clinical experiences of this technic was as follows: (1) Deep ether anesthesia was best for hypothermic circulatory arrest comparing barbiturate or light ether anesthesia, and (2) combination of surface rewarming and intrathoracic rewarming, a kind of core rewarming by the warm saline circulating through the chest cavity, was superior to surface rewarming alone.

An additional animal experiment to investigate the influence of hypothermic circulatory arrest on the brain clarified that histochemical and enzymological changes appearing in the brain tissue after 30 minutes of circulatory arrest at 28°C was reversible; that is, the safety time limit of circulatory arrest to the brain was 30 minutes at body temperature of 28°C.

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On the other hand, many investigators have reported that EEG became isoelectric during hypothermic circulatory arrest. However, EEG changes, if notable, seem to be the best indicator for clinical use to estimate the safety time limit of circulatory arrest.

The present investigation was undertaken to reevaluate EEG changes during hypothermic circulatory arrest if EEG would be a parameter to manage the patients under hypothermic circulatory arrest.

**Methods**

Twenty-eight adult mongrel dogs were used. A 0.015 mg/kg of body weight of atropine sulfate was administrated intramuscularly as premedication. After the trachea being intubated with the minimal intravenous dose of Isozol, sodium 5-allyl-5-(1-methyl butyl)-2-thiobarbiturate, the animal was anesthetized using ether in pure oxygen. The inhaled ether concentration was increased gradually from 4 to 10 per cent by means of non-rebreathing method until the 3rd plane of the 3rd stage was obtained.

Animals were then, cooled down by blanket cooling to a desired temperature level where circulatory arrest was projected. During cooling no shivering was seen in deeply anesthetized animals.

Circulatory arrest was obtained by means of occlusion of both venae cavae with tapes surrounding them under thoracotomy through the 5th intercostal spaces and transverse sternotomy. After occlusion was released, animals were rewarmed by intrathoracic rewarming first until blood pressure became stable, when blanket rewarming was combined. When the heart remained in arrest or developed ventricular fibrillation, resuscitation was performed with cardiac massage after nor-epinephrine being injected into the left ventricular cavity. Countershock of 130 volt for 0.1 second was applied, if necessary. When body temperature exceeded 30°C, intrathoracic rewarming was discontinued, and the chest was closed. For the further rewarming, blanket rewarming alone was utilized.

A pair of 4-needle-electrodes, newly devised, was so fixed symmetrically that cortico- and subcortico-grams were recorded throughout the experimental course, or, in some cases, for one week postoperatively.

The location of the electrodes was confirmed histologically at autopsy. Rectal temperature was selected as the index of the body temperature. Since surface cooling and rewarming was mainly used and the distribution of temperature to the whole body was relatively even, rectal temperature was very similar to brain temperature, as has been proved in preliminary experiments.

**Results**

By the time when the 3rd plane of the 3rd stage of anesthesia was obtained, no slow waves were observed but a gradual decrease in the amplitude in corticogram. Subcorticogram maintained fast waves and showed slight changes, if any. During cooling no changes were seen in corticogram except for some decrease in the frequency below 30°C. In subcorticogram some increase in the amplitude by 30°C, with a peak at 33°C, and some decrease in the frequency below 30°C were observed. No slow waves or suppression were noted in both cortico- and subcortico-grams.

As soon as circulatory arrest was obtained at normothermia, the electrical activity of the brain showed a transient high voltage initially followed by a progressive diminution, and almost disappeared at one minute of occlusion time. The precolosion pattern, however, reappeared at 3 minute of occlusion time and remained up to 7 minute of occlusion time when the electrical activity became diminished again (Fig. 2).

When the circulation was occluded at 32°C, EEG decreased its amplitude after showing a transient initial high voltage, then began to increase again at 5 minute of occlusion time. Contrary to normothermic arrest, the decrease in the subcortical activity at 15 minute of occlusion time was followed by that in the cortical activity at 20 minute of occlusion time. At 30 minute of occlusion time both cortico- and subcortico-grams showed the low amplitude together with various types of burst (Fig. 2).

In circulatory arrest at 28°C the transient initial high voltage was not so significant, and the decrease in the frequency and the amplitude continued gradually up to 8 to 10 minute of occlusion time. From 10 to 12 minute until 30 minute of occlusion time the frequency and the amplitude increased again. After 35 minute of occlusion time the electrical activity became irregular to show slow waves; however, the electrogenesis did not disappear up to 60 minute of occlusion time (Figs. 1 and 2).

In circulatory arrest at 23°C aforementioned
changes appeared more slowly and mildly: the transient initial high amplitude being slight, the amplitude decreasing up to 15 minute of occlusion time followed by a gradual increase, and the subcortical rhythm becoming irregular at 45 minute of occlusion time (Fig. 2).

In circulatory arrest at 20° C these changes progressed much more slowly and mildly; no

Fig. 1. Cortico- and subcorticograms during circulatory arrest at 25°C for 35 minutes.
  C-G: Coticogram
  SC-G: Subcorticogram

Fig. 2. Schematic presentation of changes in the frequency and the amplitude during circulatory arrest at normothermia and body temperature of 32, 28-26, 25-23 and 20°C.
  C-G: Coticogram  SC-G: Subcorticogram

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Transient initial high amplitude being observed, the amplitude decreasing up to 20 minute of occlusion time followed by a gradual increase, and the subcortical rhythm becoming irregular at 60 minute of occlusion time (Fig. 2).

At whatever temperature level the circulation was interrupted, EEG never disappeared, but did change along the following three stages; though the lower the temperature, the less the characteristic changes.

The first stage, where the brain activity decreased to disappear seemingly both in the frequency and the amplitude. In the initial period of this stage a transient increase in the amplitude was seen.

The second stage, where the brain activity having disappeared seemingly at the end of the 1st stage recovered to show the preocclusion pattern, and then diminished again. At the end of this stage the subcortical activity increased temporarily, and then became low earlier than the cortical activity did.

The third stage, where EEG showed a marked degree of the low amplitude and the irregular pattern modified by various types of burst and the high frequency, higher than that at the end of the 2nd stage (Fig. 2).

When circulatory arrest was terminated at the 1st stage, EEG restored the preocclusion pattern immediately, and showed a quick recovery parallelly to body temperature (Fig. 3-1). When the circulation was reestablished at

In the upper column i.r.: Intrathoracic rewarming, b.r.: Blanket rewarming, ●—●: Esophageal temperature, ×—×: Rectal temperature
In the lower column cps: cycle per second, μV: microvolt
●—●: Frequency from corticogram
×—×: Amplitude from corticogram
●—●: Frequency from subcorticogram
×—×: Amplitude from subcorticogram

Fig. 3. EEG changes during rewarming after circulatory arrest at 28°C for (1) 5–10 minutes, the 1st stage arrest, (2) 10–30 minutes, the 2nd stage arrest, and (3) 30–45 minutes, the 3rd stage, arrest.
the 2nd stage, recovery of the brain activity was behind that of temperature (Fig. 3-2). When circulatory arrest was reestablished at the 3rd stage, no recovery of the frequency was observed. The amplitude, also, kept becoming lower to show no tendency of recovery after a long term follow-up (Fig. 3-3).

**Comment**

The reason why the brain activity during hypothermic circulatory arrest could have been obtained in this series of experiment, contrary to other reporters, is as follows:

1. EEG was recorded with a pair of needles-electrodes placed directly into the brain. These electrodes could pick up a very weak brain activity which may not be recorded on EEG (scalp).
2. Animals were anesthetized with ether exclusively, and a minimal dose of barbiturate was administrated only at intubation. Thus, the depressing effect of barbiturate on the brain activity was excluded.

It is natural that the brain activity is influenced by the hemodynamic condition and the depth of anesthesia at any time. However, as far as the post-occlusion hemodynamic condition recovers satisfactorily and the depth of anesthesia stays constant at the proper level throughout the hypothermic period, the recovery of EEG after the termination of arrest depends chiefly upon how long arrest has been maintained, as seen above.

The safety time limit of circulatory arrest reported by many investigators would be divided into 2 groups; one is relatively short, and the other relatively long. The former covers the 1st stage of our criterion and the latter the 1st and the 2nd stages. The average duration of the 1st and the 2nd stages in circulatory arrest at 28°C are 10 and 20 minu-

![Fig. 4. Changes in various parameters during hypothermic procedures.](image-url)

S. M. 11-year-old boy; Known to have cardiac murmur since at the age of one year and 2 months. Had a tendency to catch cold easily.

Complained of exertional palpitation and shortness of breath. EKG showed right bundle branch block. Chest X-ray showed increased pulmonary vascularity and prominent pulmonary arteries. Cardiac catheterization revealed oxygen step-up of 2.80 vol. % at the atrial level. Diagnosis of atrial septal defect was established.

The chest was entered through 5th interspaces and transverse sternotomy. Cardiectomy was performed with the aid of circulatory arrest of 7 minutes under hypothermia of 26.5°C, and atrial septal defect foramen secundum type, 5 cm in length, was closed primary with running suture. Recovery from anesthesia was excellent and postoperative course was uneventful. He was discharged from hospital on the postoperative 22nd day.


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The safety time limit of circulatory arrest at 28°C reported previously by us to be 30 minutes revealed to include the 1st and the 2nd stages of this criterion; and, as far as arrest is terminated by the end of the 2nd stage, the animal recovers completely without any postoperative sequela.

**Clinical Observations**

Of 91 patients operated on open heart surgery during circulatory arrest under hypothermia, 20 were subjected to this observation. Three death, not related to hypothermic arrest, were encountered; the mortality rate being 15 per cent. Clinically, EEG (scalp) was utilized in bipolar fashion.

A 0.5 mg of atropine sulfate and a 10 mg of morphine chloride for adults were administrated subcutaneously one hour prior to intubation.

Otherwise the technic for hypothermic circulatory arrest was essentially same as in the experiment.

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Fig. 5. Changes in EEG (scalp) during hypothermic procedure; the same patient as seen in Fig. 4.

During EEG (scalp) showed slow waves dominant for a short period; however, it restored the α-activity soon by the inhaled ether concentration being reduced. At 25 second of occlusion time EEG (scalp) became isoelectric. After the occlusion was released, the base line began to move at 7 minutes, and it appeared slow waves superimposed with the α-activity at 39 minutes. Thereafter, EEG (scalp) recovered parallelly to rectal temperature. The postoperative course was uneventful and no abnormal pattern was seen.

During blanket cooling the inhaled ether concentration was so adjusted that the best EEG pattern at the preoclusion period, the $\alpha$-activity, was maintained, and, as far as the depth of anesthesia was kept at this level no shiverering occurred during cooling. Any suppression in the brain activity was controlled by decreasing the concentration of ether.

According as body temperature came down, as shown in Fig. 4, the inhaled ether concentration was decreased stepwise from 10 to 5 per cent. In the clinical cases circulatory arrest was usually obtained at 26 to 28°C of rectal temperature.

During arrest the transient initial high voltage at the 1st stage and the reappearance of waves at the beginning period of the 2nd stage were recorded on EEG (scalp) for 35 and 10 second, in average, respectively. Otherwise no EEG (scalp) was observed. As soon as the circulation was reestablished, EEG (scalp) recovered the amplitude; and, the duration of time between the reestablishment of the circulation and the reappearance of EEG (scalp) was one to 7 minutes (average 3 minutes and 35 seconds), when the circulation was reestablished at the 1st stage.

During circulatory arrest and the beginning of the post-occlusion period, until EEG (scalp) restored the $\alpha$-activity, no ether was given.

A 2 to 3 per cent of the inhaled ether concentration was enough to keep the $\alpha$-activity on EEG (scalp) during rewarming. Nitrous oxide would be substituted to ether at the time.

Thereafter, EEG (scalp) recovered parallelly to the body temperature, i.e., the same pattern of EEG (scalp) appeared at the same level of temperature during cooling once and during rewarming again. On the other hand, when the circulation was reestablished at the 2nd stage, recovery of EEG (scalp) was much behind that of temperature (Figs. 5 and 6).

**Comment**

The condition of hypothermic anesthetized patient depends greatly upon what kind of anesthesia is used and how deep the patient is anesthetized. During hypothermia the classical eye sign at anesthesia is not always dependable and blood pressure itself is not reliable in some occasions. Employing EEG (scalp) as a parameter, therefore, the anesthesia level under such circumstances would more easily and reasonably be adjusted and kept constant with one of the advanced anesthesia apparatuses, by which any desirable concentration of ether is provided.

EEG (scalp) was substituted to cortico- and subcorticograms in the clinical cases. This substitution might introduce some disadvantages. In some instances the brain activity which may be recorded on corticogram can not be noted on EEG (scalp) because of the electrodes being placed far from the brain. However, once the beginning of the 2nd stage is noted, as described above, the end of this stage, by which time the circulatory arrest should be released to obtain a complete recovery, can be estimated by correlation to the length of the 1st stage according to the experimental experience. For example, the ratio of the length of the 1st stage to the second is 1:2 during hypothermia, as seen in Fig. 2.

When the period of circulatory arrest will be utilized thoroughly and safely, the restoration of an effective cardiac output immediately after the release of arrest is mandatory in addition to an accurate estimation of the end of the 2nd stage. Coronary perfusion during circulatory arrest and intrathoracic rewarming methods would meet to this purpose well10.

A 2 to 3 per cent of the inhaled ether concentration is enough to keep the best EEG pattern of the $\alpha$-activity during rewarming. This means to save much of ether during, and, consequently, not only to minimize the com-

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**Fig. 6.** Recovery in the frequency during rewarming and postoperative period.
plication of the ether anesthesia but also to accelerate recovery from anesthesia.

When circulatory arrest is released at the 1st stage and EEG (scalp) restores the precocclusion pattern of the α-activity, another arrest may safely be repeated as long as the end of the 2nd stage, if necessary.

By the repetition of an arrest in this fashion, the more complicated intracardiac procedures would be subjected to this technic.

SUMMARY

1. EEG changes during hypothermia were studied experimentally using cortico- and subcorti cogngrams and clinically using EEG (scalp).

2. The best EEG pattern of the α-activity was maintained by adjusting the inhaled ether concentration throughout the hypothermic period.

3. EEG never disappeared during experimental circulatory arrest, and its changes were divided into three stages according to their patterns.

When arrest was terminated at the 1st stage, recovery was prompt and complete. When arrest was terminated at the 2nd stage, recovery was complete but delayed. When the arrest was terminated at the 3rd stage, no recovery was obtained.

4. Clinically, the characteristic EEG pattern appearing exclusively at the beginning period of the 1st and the 2nd stages led to a precise estimation of the length of the 2nd stage proportionally to the length of the 1st stage from the experimental experience. The duration of time by the end of the 2nd stage, the safety time limit of circulatory arrest, was 25 to 30 minutes at 28°C.

REFERENCES


