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Based upon the accepted sensitivity of visual function, particularly the peripheral visual fields, to moderate changes in circulating oxygen subsequent to work at altitude and/or respiratory distress, studies were undertaken to determine the sight in the visual system of changes and the influence of blood factors upon these changes. In an animal model, controlled hypoxia, blood gas measures, and measures of electrical signals at various stages of the visual pathway were correlated. Findings were: ~~(1)~~ 1) there is a threshold

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effect for short term hypoxia where visual function is altered first between 10-12% inspired O_2^{π}. (2) Retinal action potentials are the most sensitive indicators of the onset of hypoxic visual loss with changes at the optic nerve and the visual cortex following. (3) Blood PaO_2^{π} is only partially correlated with the rate of visual loss and recovery, and (4) buffering of blood ph provides for protection from visual loss under hypoxic conditions which would otherwise produce functional deficits. Cumulative effects of hypoxia relating to visual function and the extent to which buffering can control visual functional losses requires additional research.

ABSTRACT

Based upon the accepted sensitivity of visual function, particularly the peripheral visual fields, to moderate changes in circulating oxygen subsequent to work at altitude and/or respiratory distress, studies were undertaken to determine the sight in the visual system of changes and the influence of blood factors upon these changes. In an animal model, controlled hypoxia, blood gas measures, and measures of electrical signals at various stages of the visual pathway were correlated. Findings were: (1) There is a threshold effect for short term hypoxia where visual function is altered first between 10-12% inspired O_2. (2) Retinal action potentials are the most sensitive indicator of the onset of hypoxic visual loss with changes at the optic nerve and the visual cortex following. (3) Blood PaO_2 is only partially correlated with the rate of visual loss and recovery. (4) Buffering of blood pH provides for protection from visual loss under hypoxic conditions which would otherwise produce functional deficits. Cumulative effects of hypoxia relating to visual function and the extent to which buffering can control visual functional losses requires additional research.

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FOREWORD

Numerous factors may contribute to respiratory stress; among these are pneumonia, changes in oxygen uptake efficiency of lung tissue, reduction of oxygen availability in closed quarters or in quarters with pollutants and by oxygen availability at altitudes above sea level. It has been established that reduced blood oxygen saturations are associated with functional changes in nervous-system mediated performance. The visual apparatus, including the eye, is central nervous (brain) in origin and is particularly sensitive to the effects of reduced arterial oxygen saturation. The military awareness of reduced efficiency under conditions of hypoxia is probably very old. However, organized examinations of the effects of oxygen deficit are easily traced to World War II, specifically for problems arising in visual function (1).

Basic science laboratories have produced a significant quantity of literature which relate changes in visual function, measured by objective techniques, to reduced oxygen intake (2, 3, 4). The vast majority of basic work has been done acutely in animals where respiration was interrupted or an artery was clamped for a period as a substitute for reduction in environmental oxygen. There is also a rich history of functional changes in humans which have been explored by psychophysical and clinical procedures (5, 6). Much of this literature is reviewed by VanLiere and Stickney (7) and in later publications by Kobrick (8) and Van den Bos (9). Early observations in aviators (1943) indicated that arterial O_2 saturations as high as 93% could produce subtle changes in normal visual

function. More recent psychophysical inquiries (8, 10, 11) conclude that exposure to hypoxic atmospheres above 13,000 feet produces changes in the size and shape of visual fields for colored test objects, increases reaction time to peripherally placed targets and causes some retinal vascular changes.

There are very few data dealing with the sensory and neural effect of controlled hypoxia. This report contains the results of our studies of acute anoxic hypoxia in the cat, where hypoxia is used as a model for the consequences of generalized respiratory stress originating from any cause. Our acute studies were designed to provide quantitative data for identifying those portions of the visual pathway which are foci of hypoxia sensitivity, the progress of hypoxia sequela with exposure time and recovery, and the relationship of these sequelae to blood gas measures.

Three series of experiments will be reported. The first will be our initial dark adapted studies, where we identified the nature of the hypoxic effect on the visual system, and established the range of inspired O_2 concentrations that were effective in producing visual dysfunction. The second series was conducted under a moderate level of light adaptation, and was a systematic study of the effect of four inspired O_2 concentrations (8, 10, 12, 14%) on visual system function. In addition, arterial blood samples were taken and pH, $PaCO_2$, PaO_2 values determined. The third series included data on attempts to ameliorate the effects of hypoxia with buffering (bicarbonate) and producing visual system dysfunction by inducing an acidosis without hypoxia to evaluate the effect of the acidosis alone.

Surgical Procedures

Chronic implantation of the cats was carried out at least two weeks prior to the experimental procedure. They were initially anesthetized with halothane, then an

intravenous dosage of nembutal, 40 mg/Kg, was administered and the halothane withdrawn. The cat was then placed in a standard sterotaxic apparatus. Stainless steel bipolar electrodes were implanted sterotaxically in the subcortical structures of interest (ON and/or LGN). The electrodes were lowered through burr holes in the skull. These electrodes had a diameter of .02 of an inch and were insulated except for up to 1 mm of the tip. The tips were mechanically sharpened and the individual electrode tips of each bipolar pair were separated by up to 3 mm. To insure proper electrode placement, the evoked response to photic stimulation was monitored during the actual implantation procedure. A length of the same insulated stainless steel wire with an uninsulated coil on the end was implanted on the pial surface of the visual CTX. A ground screw was placed in the skull above the frontal sinus. The ends of the subcortical and cortical electrodes were then soldered to an amphenol plug which was acrylicated on to the surface of the skull.

Method: Dark Adapted Studies

Subjects: A total of 38 cats were used in these experiments. They ranged from 2.3 to 4.4 Kg; 12 were males and 26 were females. Some were used more than once with a minimum of three weeks between experimental procedures.

Apparatus: Visual stimuli were diffuse white-light flashes produced by a Grass model PS-2 photo stimulator set at intensity 8. The output of the photo stimulator was reflected from a 24 inch diameter milk glass Ganzfeld. The cat was placed at the center of the Ganzfeld. Timing of the light flashes was electronically controlled.

The electroretinogram (ERG) was recorded using a corneal contact lens of the Burian-Allen type and an indifferent needle electrode placed on the supraorbital ridge. The corneal electrode was cushioned with 1% methyl cellulose. The electrode was placed on the

cornea after it had been anesthetized with 1-2 drops of 0.5% proparacine hydrochloride, and the pupil dilated with 2% cyclopentalate hydrochloride. The evoked response from the optic nerve (ON), lateral geniculate body (LGN) and visual cortex (CTX) were obtained by making connection with the chronically implanted electrodes through a connector on the cat's head. The four data channels were amplified with Tektronix type 122 amplifiers (bandpass 0.2 Hz-1 KHz) and fed into an averaging computer. Selected output channels could also be monitored on an oscilloscope and were sometimes recorded on FM tape. The EKG was monitored using needle electrodes.

Aftificial respiration was provided by a Harvard Model 670 positive pressure respirator set so that each respiratory cycle was 30% inspiration and 70% expiration. A positive expiratory end pressure (PEEP), 40-50 mm H_2O was utilized to minimize atelectasis. Expired CO_2 was monitored with a Beckman model LB-1 gas analyzer calibrated at 0 and 5%. Sampling rate for the gas analyzer was set at 200 ml/min. To obtain specified inspired O_2 concentrations, independent sources of medical grade oxygen and nitrogen were taped at specified rates using presision flow meters, mixed in a four liter expandable resivoir, and fed into the input port of the respirator. O_2 concentration was continuously monitored with a Biomarine Industries model OA-222 oxygen sensor placed between the respirator and the animal.

Infusion of the neuromuscular block was by an IV catheter in the femoral vein. Infusion rate was controlled by a Sage model 237-2 infusion pump. The mixture used to produce immobilization contained 3 mg Gallamine and 0.06 mg Tubocumine Chloride/ml, in 5% dextrose - normal saline carrier. Initial dose was 5 mg/Kg given in 1-2 minutes with that dose repeated during the first half hour. Infusion rate was then decreased to 4-5 mg/Kg/hr for the next 2-3 hours then slowly decreased afterward.

Procedure

At the beginning of each experimental session, the animal was pre-medicated with atropine (0.1 mg/kg, IM). The cat was then lightly anesthetized with halothane long enough to allow placement of an endotracheal tube and establishment of a patent IV infusion catheter. From then the animal was maintained under continuous IV infusion of Flaxedil (Gallamine) and artificially respirated. Respiration rate was set at the animals' normal spontaneous rate, and depth was adjusted to give an alveolar (expired) CO_2 value of 4%. Throughout the experiment, the animals' temperature was thermostatically controlled at 38°C. EKG, inspired O_2, and expired CO_2 were monitored and O_2 and CO_2 values held at specified levels. The animal was placed in a special molded head holder, attached to the recording equipment and aligned in front of the Ganzfeld stimulating field and dark adapted for at least 30 minutes. Through the session, the stimulus parameters were constant intensity, triplets of flashes repeated every 15 seconds. Each triplet consisted of an initial stressing flash followed 800 msec later by a second test flash, which was followed 100 msec later by a third test flash. Evoked response from the retina (ERG), optic nerve compound action potential (ON), lateral geniculate body action signal (LGN) and visual cortex action signal (CTX) were summed in an averaging computer. Output from the computer was by strip-chart recorder. Following dark adaptation, a series of responses were obtained to the standard stimulus (described above) at 21% inspired O_2. The animal was then placed under a specified inspired O_2 deficit (8%, 10%, 12% or 14% O_2) and responses to the standard stimulus condition periodically obtained. The animal was maintained under the hypoxic condition until cardiac and/or respiratory function was disrupted or disruption was imminent. Then the per cent inspired O_2 was returned to 21. Responses to the standard stimulus were again collected

periodically during recovery until prehypoxia baseline responding had been recovered. The infusion of Flaxedil was then stopped, the cat recovered and was returned to his home cage to be used again. The data from each of the recording sites were then hand scored and tabulated. To optimize the interpretation of the data across animals and recording sites, all results are expressed in terms of percentage of prehypoxia value. To convert the data into this form, the amplitude of, for example, the ERB b-wave to the first flash in the standard stimulus triplet was determined on at least six occasions while the animal was inspiring 21% O_2 and after dark adaptation was complete (i.e. when there was no systematic change in the response amplitude). The arithmetic mean of these six response amplitudes then served as the baseline against which succeeding response amplitudes obtained under hypoxic conditions were evaluated. This procedure was followed for each of the three responses to the standard stimulus triplet at each of the recording loci. To further enhance cross-animal or cross-site comparisons, all data are presented on a standard set of coordinates.

Results

Figures 1 and 2 present sample waveforms from three recording sites, retina (ERG and FRP), optic nerve (ON) and primary visual cortex (CTX) taken before, during and after a 95 minute exposure to a 10% O_2, hypoxic condition. The times (in minutes) from onset of hypoxia and recovery are shown along the left margin. The duration of each record is 1024 msec with the three stimulus flashes occuring at the times indicated below the ERG records in Fig. 1. Each waveform is the sum of four stimulus presentations. The fast retinal potential (FRP) is recorded at the cornea. It is the ERG signal passed through an active band-pass filter set to exclude frequencies below 50 Hz. These records show

that the effect of hypoxia is to reduce the amplitude of the waveforms at each recording site, that the original waveform amplitudes are recoverable, and that each of the waveforms are quantitatively scorable.

The data taken at each recording site are quantitatively displayed in Figures 3-6. Figure 3 presents the results for b-wave amplitude of the ERG when the animal was exposed to a condition of 10% inspired O_2 for a period of 95 minutes. (Data in Figures 1-6 were all recorded from the same preparation.) Inspection of Fig. 3 indicates that the amplitude of the b-wave elicited by the first flash (first b-wave) declines continuously following onset of hypoxic stress until the 50th minute of exposure, at which time it has been reduced to 10% of its original (pre-hypoxic) amplitude. Following termination of hypoxia this response does not regain its original amplitude until approximately two hours have elapsed. Following this, there is a suggestion of a period of hyper-excitability. The results for the second b-wave show an effect that is similar but more severe than that seen for the first b-wave.

The effect of hypoxia on the amplitude of the third b-wave is a pronounced result. Inspection of Fig. 3 discloses that onset of hypoxia results in an immediate diminution of this response to about 77% of its prehypoxia amplitude, but there is no further effect until the 50th minute of hypoxia. Further, this response has regained 58% of its prehypoxic amplitude by the fifth minute of recovery, and is fully recovered by the 35th minute into recovery - some 85 minutes before the other two b-waves are fully recovered.

Although still somewhat tentative, these results invite considerable speculation because of their apparent significance. Briefly, as described before and as will become apparent in the following data, the b-wave of the ERG response to the first two flashes

is the first response to decline with exposure to hypoxia and the last to recover following hypoxia. The source of the b-wave is thought to be the Muller cells, which are glia, not neurons. It thus appears that the b-wave per se does not reflect directly the information processing capability of the retina, rather it indicates the metabolic condition of the retina. Regardless, it is the most sensitive indicator of the onset of loss of function under hypoxia. The marked difference in the time course of change in the b-wave resulting from the third flash may be indicative of the relative shift toward central retinal function under hypoxia from a relative dominance by peripheral retinal function under normal O_2 conditions. This confirms previous literature, particularly the human psychophysical data of Kobrick. Lastly, the differential sensitivity of the first and second b-waves to hypoxia is an important finding. That the second b-wave is more susceptible to hypoxia is an important finding. That the second b-wave is more susceptible to hypoxic stress suggests that any requirement to process information combines with the hypoxic effect to further degrade the functioning of peripheral retina. Put another way, the retina's ability to recover from the stress imposed by the first flash is significantly impaired by hypoxia. This must have significant practical implications.

The Fast Retinal Potential (FRP) is obtained by actively filtering out all frequencies of the ERG below 50 Hz. The FRP thus is a measure of the high frequency activity of the retina as recorded from the cornea. Previous work with this signal has shown it to be photopic in spectral sensitivity in man (Adams and Dawson, 1971). The reason for using the FRP here is to try to get additional information about what is happening in the retina during hypoxia. The data in Fig. 4 present the results for this experiment on cat 1-L-6. Although these data are noisy, they suggest that the FRP is potentially a very

useful measure for evaluating effects of hypoxia. Comparison of Fig. 4 with Figures 3 and 5 (ERG and ON recorded simultaneously in this preparation) discloses a pattern of change for the FRP intermediate between the other two measures. This pattern, along with some changes in waveform suggest that the FRP may prove to be quite valuable.

The data presented in Fig. 5 describes the effects of hypoxia on the compound action potential of optic nerve (ON) as recorded by chronically implanted bipolar electrodes. The optic nerve is composed of the axons of the ganglion cells of the retina. Thus, this signal is a measure of the total information outflow of the retina.

The time course and magnitude of the effect of hypoxia on ON is quite different than that seen at the retina, as is the effect on the third response. The relationship between the first and second responses, in terms of relative susceptibility to stress, is, however, essentially the same as that seen at retina. Inspection of Fig. 5 shows that the amplitude of the first response is not effected until the 40th minute of hypoxia, following which there is continuous decline in the amplitude of this response until the end of hypoxia. The maximum effect on this response is seen at 80 minutes into hypoxia and represents a reduction to 45% of its original amplitude. By 10-15 minutes after termination of hypoxia, this response was fully recovered. Following this, there appears to be a period of hyper-responsiveness for this signal. Comparison of these results with those recorded simultaneously from retina (Fig. 3) is enlightening. By the 40th minute of hypoxia, the amplitude of the first b-wave had been reduced to 28% of its baseline amplitude. At that time, the amplitude of the first ON response was 110% of its original amplitude. In recovery, the first ON response was fully recovered by about the 100th minute of the experiment. At this time, the first b-wave had only recovered to 38% of its original

amplitude. This is, we believe, the most definitive documentation yet obtained that the generator of the b-wave is not in the mammalian neural chain, but rather that b-wave amplitude reflects a parallel or branched activity that does not directly reflect retinal outflow.

The relationship between the first and second ON responses is similar to that seen for those responses as recorded by the ERG. This substantiates and extends our contention that any requirement placed on the retina to process information potentiates or enhances the disruptive effect of hypoxic stress. That the second ON response is effected more by hypoxia than the first, indicates that actual information outflow capability of the retina is reduced in hypoxia for at least 900 msec following the first flash. The results for the third ON response (Fig. 5) give additional confirmation of the reduced information handling capability of the retina when both hypoxic and information processing stress is induced. The third ON response is effected earlier and more severely during hypoxia than either of the first two responses. This is in marked contrast to the results for the third b-wave when viewed in comparison to the first two responses, but when viewed in terms of time of onset, duration of maximum effect and rate of recovery, the third response at both retina and ON are quite similar. As peripheral retina is shut down during hypoxia, total retinal outflow would be expected to decline. Thus the third ON response data are entirely consistent with our interpretation of hypoxic effects at retina. The very rapid recovery of function of all three ON responses following termination of hypoxia is a phenomenon we shall see again further up the visual pathway.

The results for striate cortex (CTX) are presented in Fig. 6. In this animal the active electrode was an epidural platinum coil about 1 mm in diameter placed over the central

retinal representation in area seventeen. The reference electrode was placed in the frontal sinus. No third response was scored due to technical difficulties. Fig. 6 shows that there is no significant reduction in the amplitude of the first response until the 60th minute of hypoxia. At that time, the first b-wave of the ERG is at 10% of its original value, and the first response at ON is only 75% of its baseline amplitude.

In addition to the visual system data already presented, we also monitored EKG and expired CO_2. During the later stages of hypoxia in this preparation, we observed a moderate increase in cardiac rate (30-40 beats per minute). This returned to prehypoxic levels within 15-20 minutes after return to room air. During the first 60 minutes of hypoxia in this preparation, expired CO_2 remained constant at the preset value of 4%. Starting at about the 65th minute, there was a gradual increase in expired CO_2, until by the end of the hypoxic exposure, the animal appeared quite cyanotic and gave an expired CO_2 value of 9.5%. This value returned to normal by about the 15th minute of recovery. We have seen essentially the same cardiac and expired CO_2 relationships on all 8% and 10% inspired O_2 preparations.

In contrast to our findings of a precipitous decrease of neural function with an increase in cardiac rate and expired CO_2 under conditions of 8% and 10% inspired O_2, our findings for these measures under 12%-15% inspired O_2 show no discernible change for periods of exposure up to eight hours. We have, on occasion, had difficulty maintaining our neuro-muscular block preparation in excellent condition for long periods (6-8 hours) due to development of pulmonary edema and/or atelectasis (partial lung collapse). However, on at least three occasions, we have successfully maintained preparations at either 12% or 15% inspired O_2 for long periods (6-8 hours) with no complications or

equipment failures and have seen no progressive or systematic change in any neural, cardiac, or respiratory function we have monitored.

The second series of experiments was a systematic attempt to determine the extent of visual system dysfunction produced by each of four specified inspired O_2 levels (8, 10, 12, and 14 %).

The preparation is identical with the previously described neuro-muscular block preparation with the following additions. When the animal was anesthetized with halothane for placement of the endotracheal tube and IV catheter, the anesthetic was continued for an additionl 20-30 minutes to allow for cannulation of the femoral artery. The cut-down site and surrounding tissues were locally anesthetized with Lidocaine. The animal was then heparinized (1 mg/Kg, IV) to prevent clotting in the cannula and was placed on Flaxedil infusion as usual. The other difference in the preparation is that the animal was not dark adapted but maintained under a low photopic level of light adaptation so we could see to take the blood samples. Blood samples (0.3 ml) were taken every 10 minutes throughout the experiment. Samples were analyzed for PO_2, PCO_2, and pH with an IL model 117 blood gas analyzer.

Results from a representative experiment are shown in Fig 7. The data presented are the blood gas and ERG measures taken throughout the experiment. The top function (filled circles) shows PaO_2 values taken from the femoral artery at ten minute intervals before, during and after a 65 minute exposure to a 9% inspired O_2 hypoxic condition. For the first 90 minutes of the experiment, PaO_2 was maintained at 90-100 mm Hg. At the 90th minute, the inspired O_2 was reduced from 21% (room air) to 9% and maintained at this value until the 155th minute when it was returned to 21% and continued at that value

for the remainder of the experiment. Inspection of the figure shows that PaO_2 immediately dropped to 24 mm Hg following onset of hypoxia and slowly increased to a value of 36 mm Hg at the end of hypoxia. When inspired O_2 was returned to 21%, PaO_2 returned immediately to 85-95 mm and was maintained at that value through the remainder of the experiment.

The function just below the PaO_2 data is the results of $PaCO_2$ (open circles). In this experiment, as in most others, we observed only small changes in $PaCO_2$ throughout the session. We attach no particular significance to these changes.

The next lower function on Fig. 7 is of significance. The induced pH shifts resulting from hypoxia (filled triangle) were large and reliable. The data show that for the first 90 minutes of the experiment, we maintained the arterial pH at 7.32-7.35, which is normal for cat. Following onset of hypoxia, there was a slow but constant drop in pH throughout hypoxia and for 5-10 minutes following its termination. During recovery, the pH slowly returned to normal values. The acidosis induced during hypoxia is major in proportion. Marked acidosis was a consistent finding at all hypoxia levels below 12% inspired O_2.

The bottom function in Fig. 7 (open squares) shows the result for ERG b-wave amplitude. There is marked similarity between the ERG and pH functions. Both change progressively during hypoxia and recover slowly.

The data for this series of experiments are summarized in the left hand panel of Fig. 8. These data show that the lower the inspired O_2 concentration, the lower the PaO_2 during hypoxia (top function). In addition, the ERG and pH functions show that at 8% and 10% inspired O_2 concentration, progressive charges were produced (both during the session and across O_2 concentration), but at the 12% and 14% O_2 concentrations, no

significant changes were observed. It appears from the data that some form of "threshold" phenomenon occurs between 12% to 10% inspired O_2. The nature of the mechanism involved is not clear, since both PaO_2 and depth of acidosis (pH shift) are changing.

To begin to clarify what the relevant parameters are, we conducted the third series of experiments. These experiments are summarized in the 10% buffered "hypoxia" panel of Figure 8 and in Figure 9. There were investigations of three different parameters.

The first type of experiment involved producing a hypoxic stress with 10% inspired O_2, but during the hypoxic stress, infusing a buffer (bicarbonate) intraveneously to offset the developing acidosis and to maintain a constant pH. The results of these experiments are shown with open triangles in the right hand panel of Figure 8. The data show that we were able to control pH, that PaO_2 changed as in normal experiments and that the loss in ERG b-wave amplitude was considerably less than normally expected under a 10% hypoxic condition. Nevertheless, some loss of function was observed, so buffering, although offering some protection, is not the complete answer.

To determine whether a simple shift in pH, without an accompanying decrease in PaO_2 would effect loss of visual function, we conducted a second series of experiments where the animal was maintained throughout the experiment under 21% inspired O_2 but for a specified period of time, (approximately 70 minutes). A mild acid (ammonium chloride) was infused to produce a gradual pH shift as seen under the unbuffered 10% hypoxic condition. The results of these experiments are graphically depicted in the right hand panel of Figure 8 (filled squares). These data show that we were successful in producing a gradual but profound acidosis with no accompanying change in PaO_2. Further,

the decrease change in ERG for amplitude was moderate, but clear. There was no recovery period in these experiments, so no recovery of pH or ERG amplitude was expected (no buffer was injected to correct the acidosis).

A representative set of results from the last type of experiment we conducted are shown in Fig. 9. In this experiment, we produced first a respiratory alkalosis by successively (in steps) increasing the respiratory rate (minutes 45-155) thus coming back down in rate to normal (minutes 155-245). After recovery of baseline, we produced a metabolic alkalosis (minutes 285-360) by slowly infusing bicarbonate. We finished the experiment by injecting ammonium chloride to counteract the buffer (minutes 360-380). The data show that we successfully produced systematic changes in pH, with accompanying changes in PaO_2 and $PaCO_2$ respiratory alkalosis with both procedures, but produced a change in visual system function only under the metabolic alkalosis condition. Note particularly that the ERG b-wave amplitude increased under metabolic alkalosis and returned toward normal when acid was injected. There was no apparent change in cortical function (VER) under either condition. Further research on blood buffers is required to establish efficacy for counteracting visual loss in hypoxia.

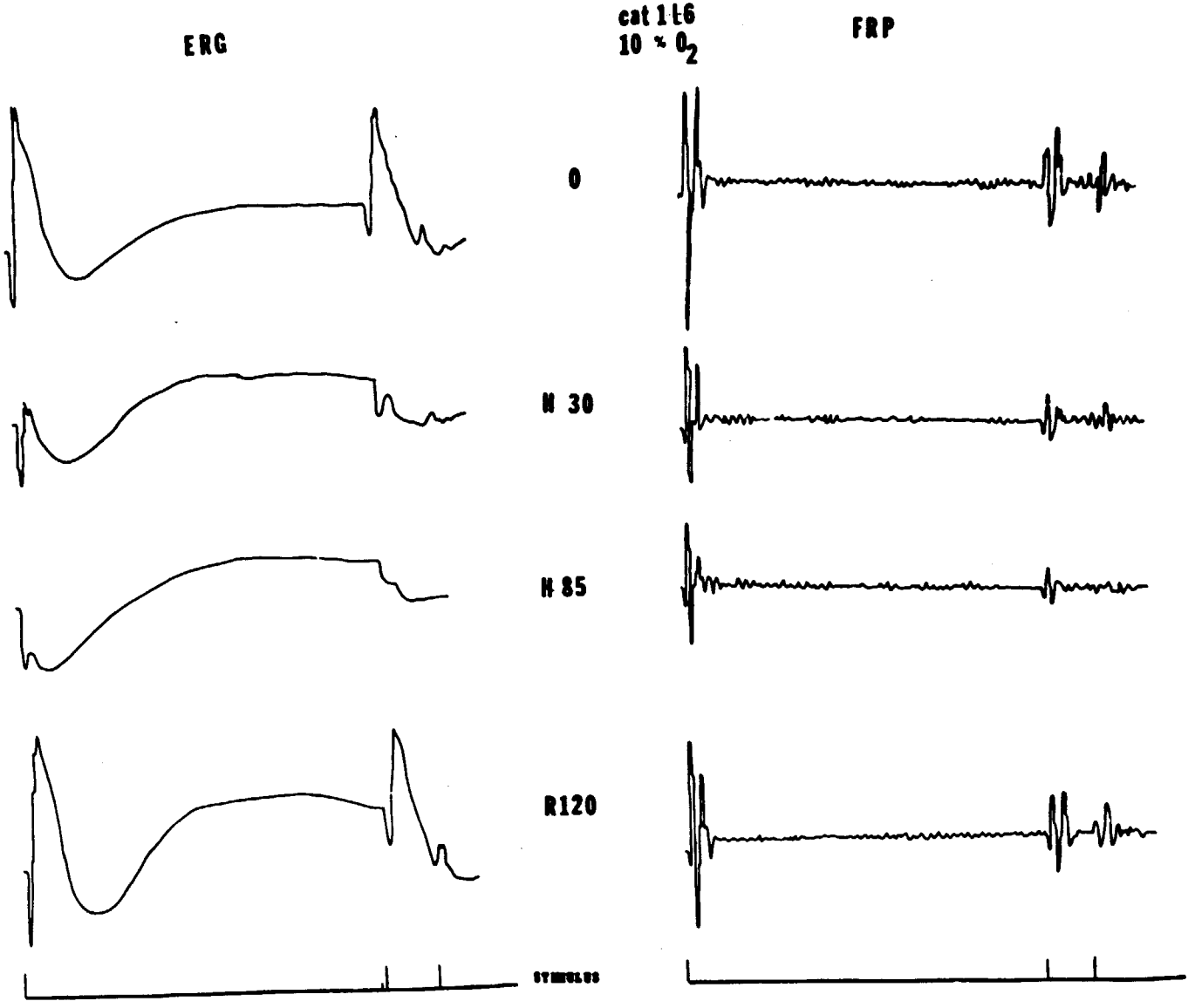

Fig. 1. Electroretinogram (ERG) and fast retinal potentials (FRP, see text) before, during, and following a reduction of inspired oxygen content from 21 to 10%. Stimuli were delivered in triplets, the initial stressing flash was followed 800 msec by a second flash and subsequently after 100 msec by a third flash. Time is indicated as 0 (before hypoxia) H30 and H85, minutes after onset of hypoxia; R120, after 120 of recovery. Amplitude of the ERG (upper left) is approximately 200mv.

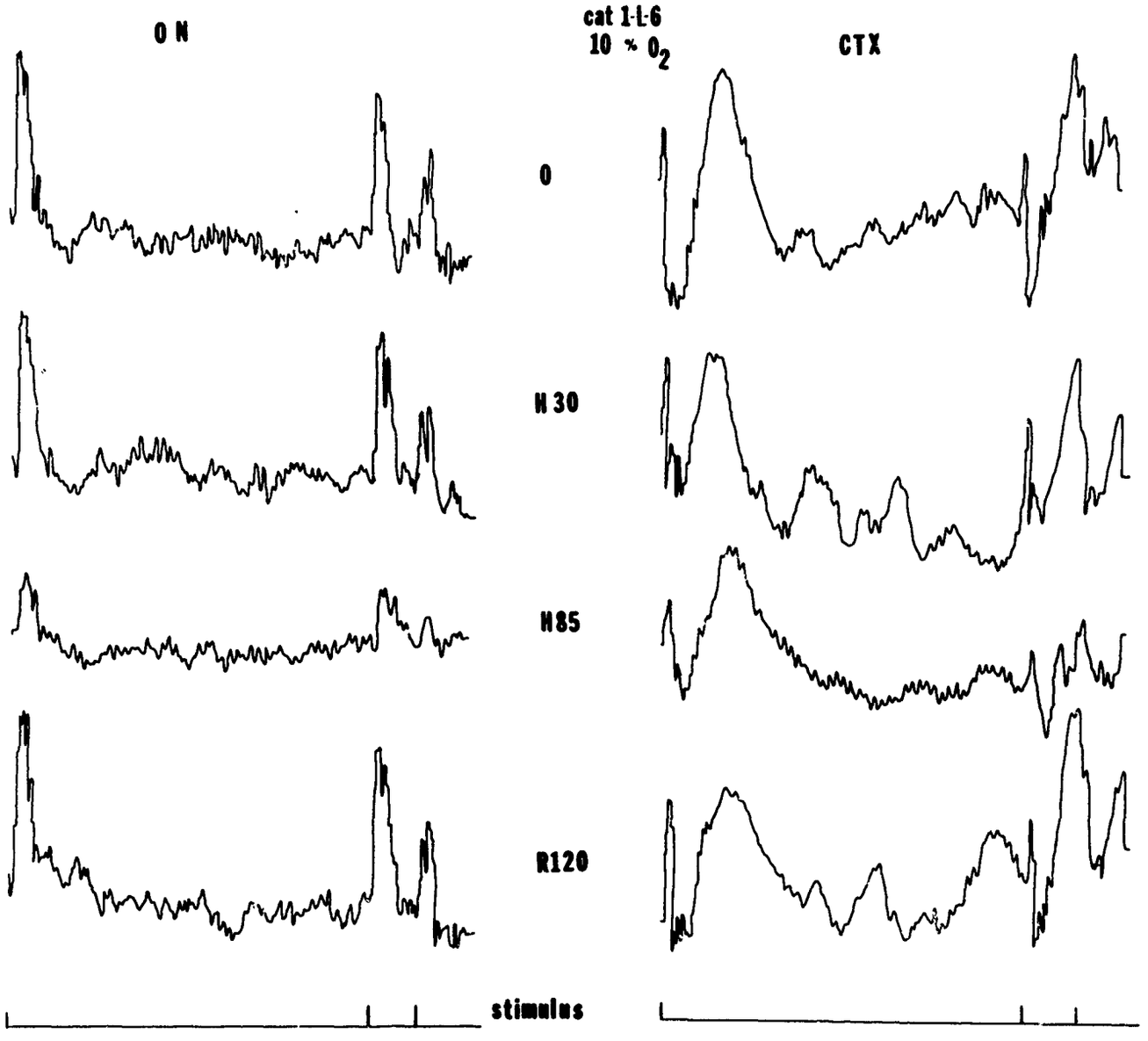

Fig. 2. Records of action potentials at the optic nerve and cortex before, during, and following hypoxia. Otherwise as Fig. 1.

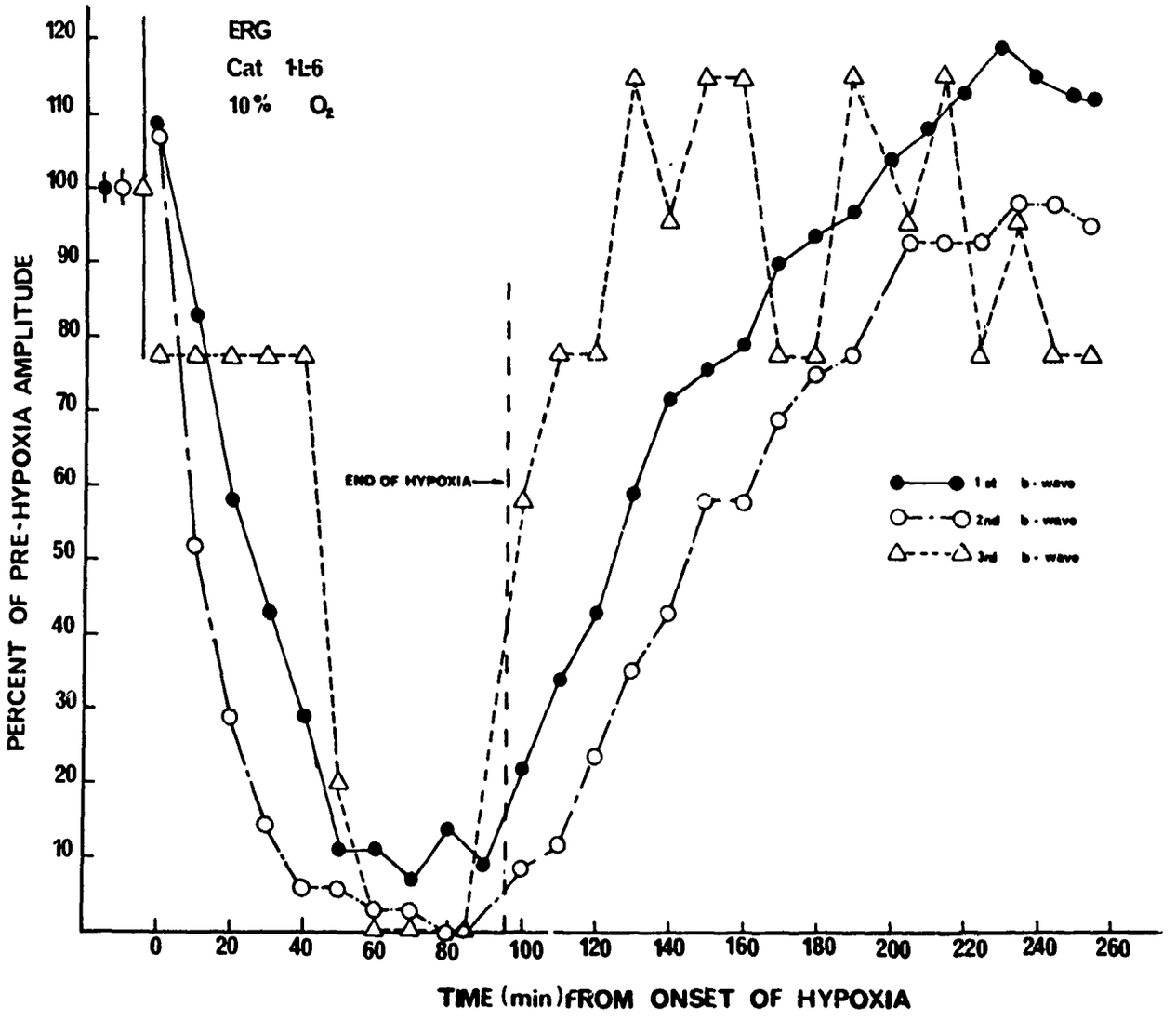

Fig. 3. Summary of retinal b-wave amplitudes of the stimulus triplet at times before and following hypoxia.

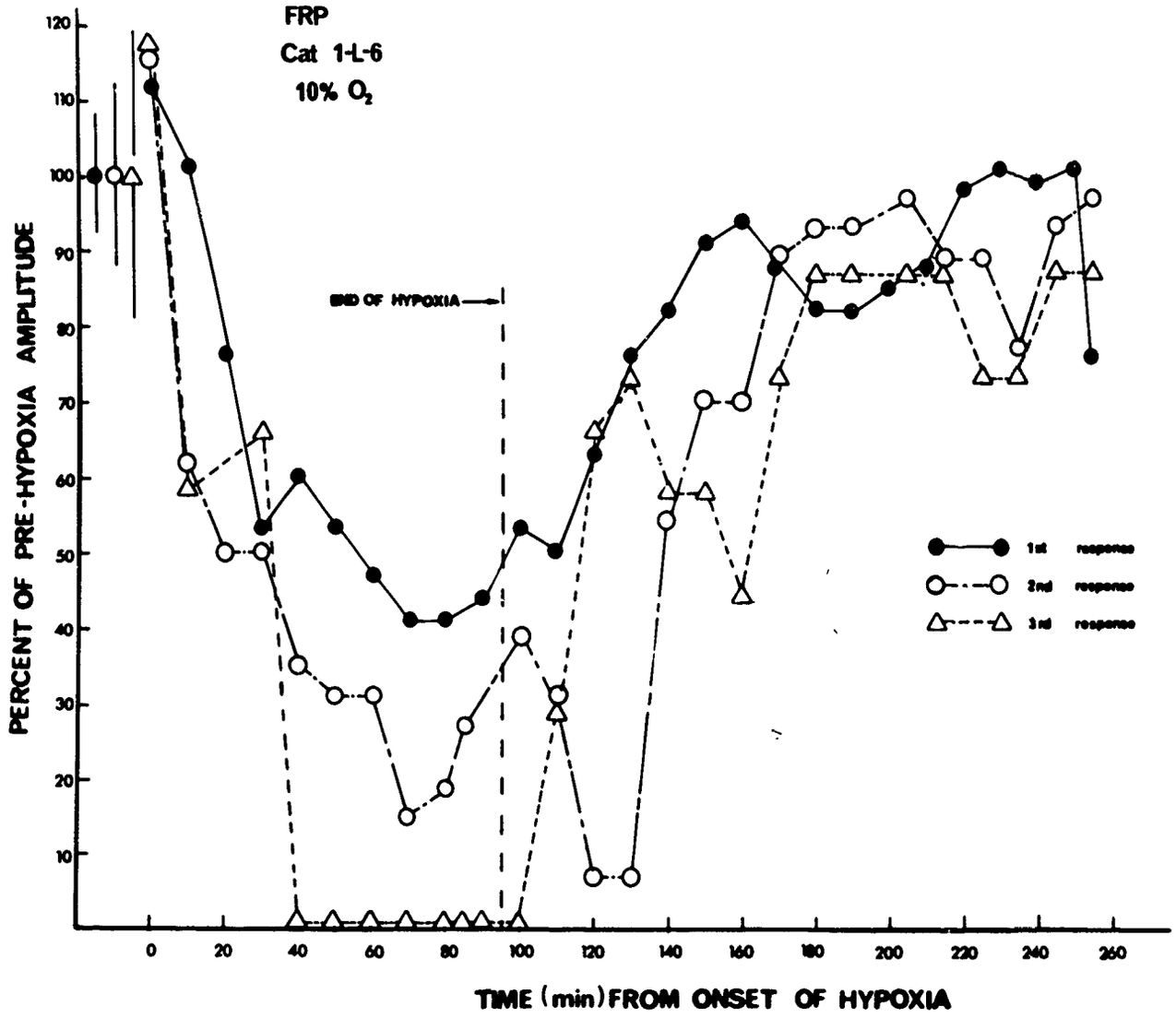

Fig. 4. Fast retinal potential (see text) alterations of response to flash triplet before, during, and after the onset of hypoxia (10% inspired O_2). Otherwise as Fig. 3.

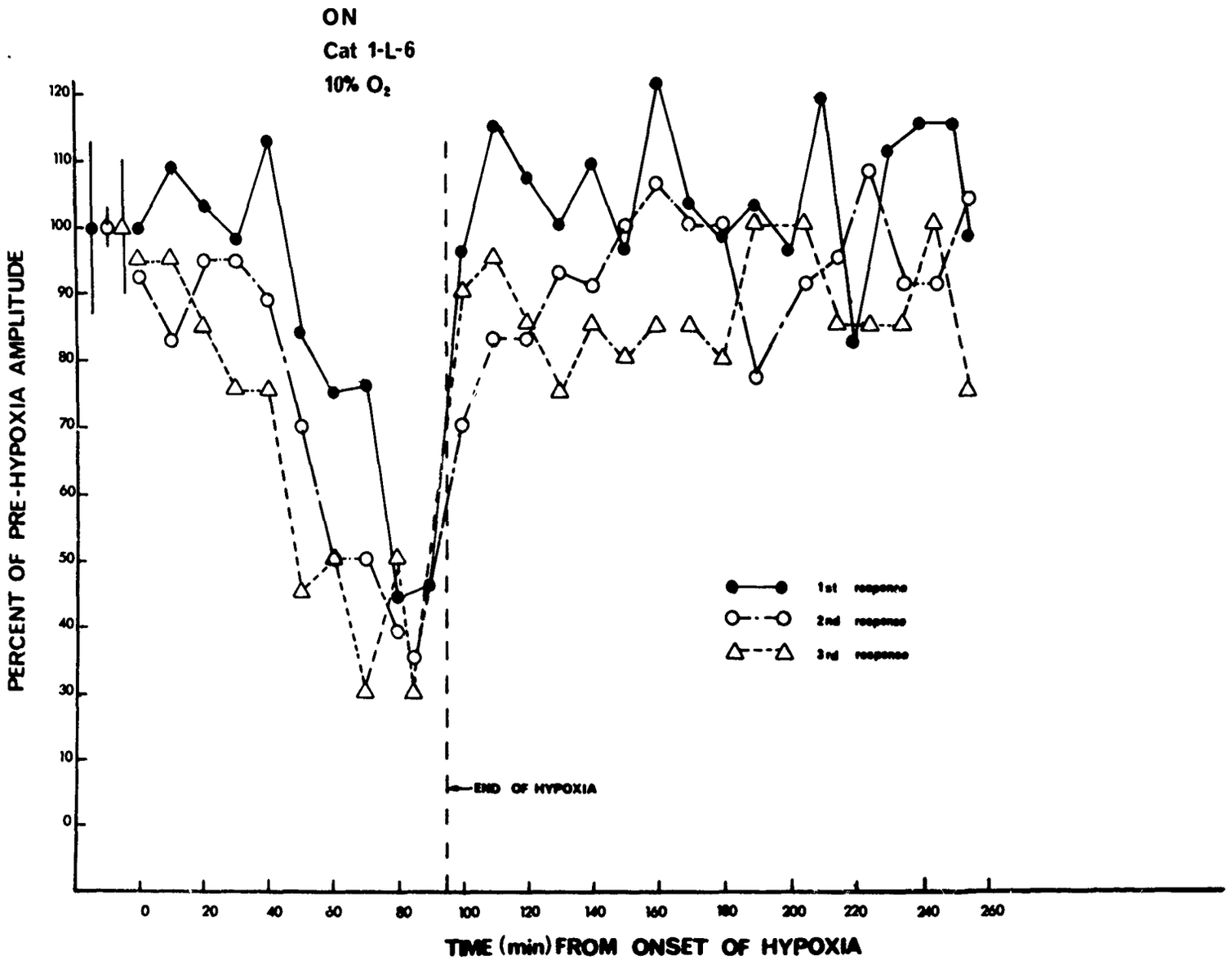

Fig. 5. Optic nerve compound response to flash triplet, before, during and following hypoxia (10% inspired O_2). Otherwise as Fig. 4.

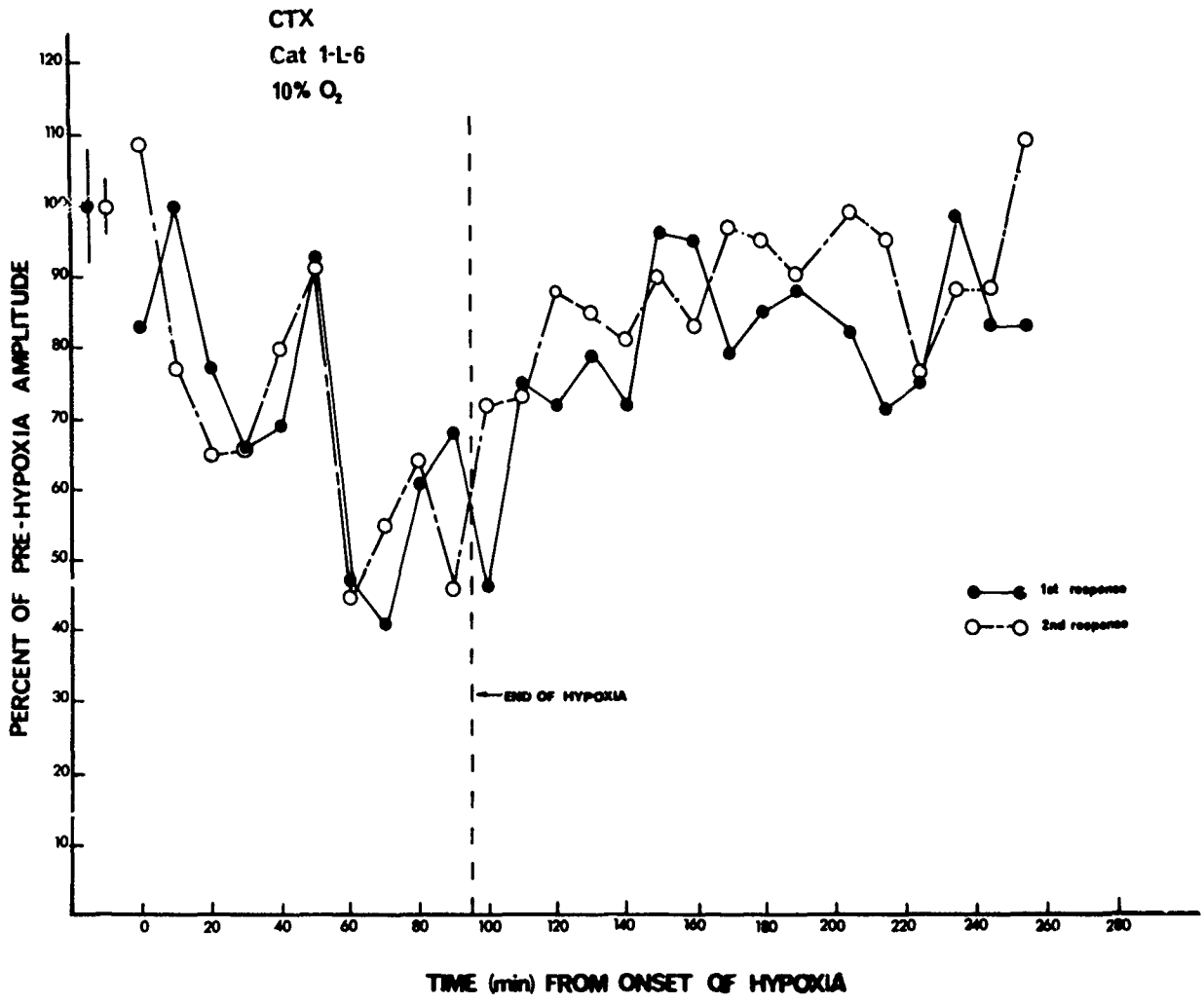

Fig. 6. Compound potential evoked at visual cortex by two components of the flash triplet before, during, and following the onset of hypoxia (10% inspired O_2) Otherwise as Fig. 5.

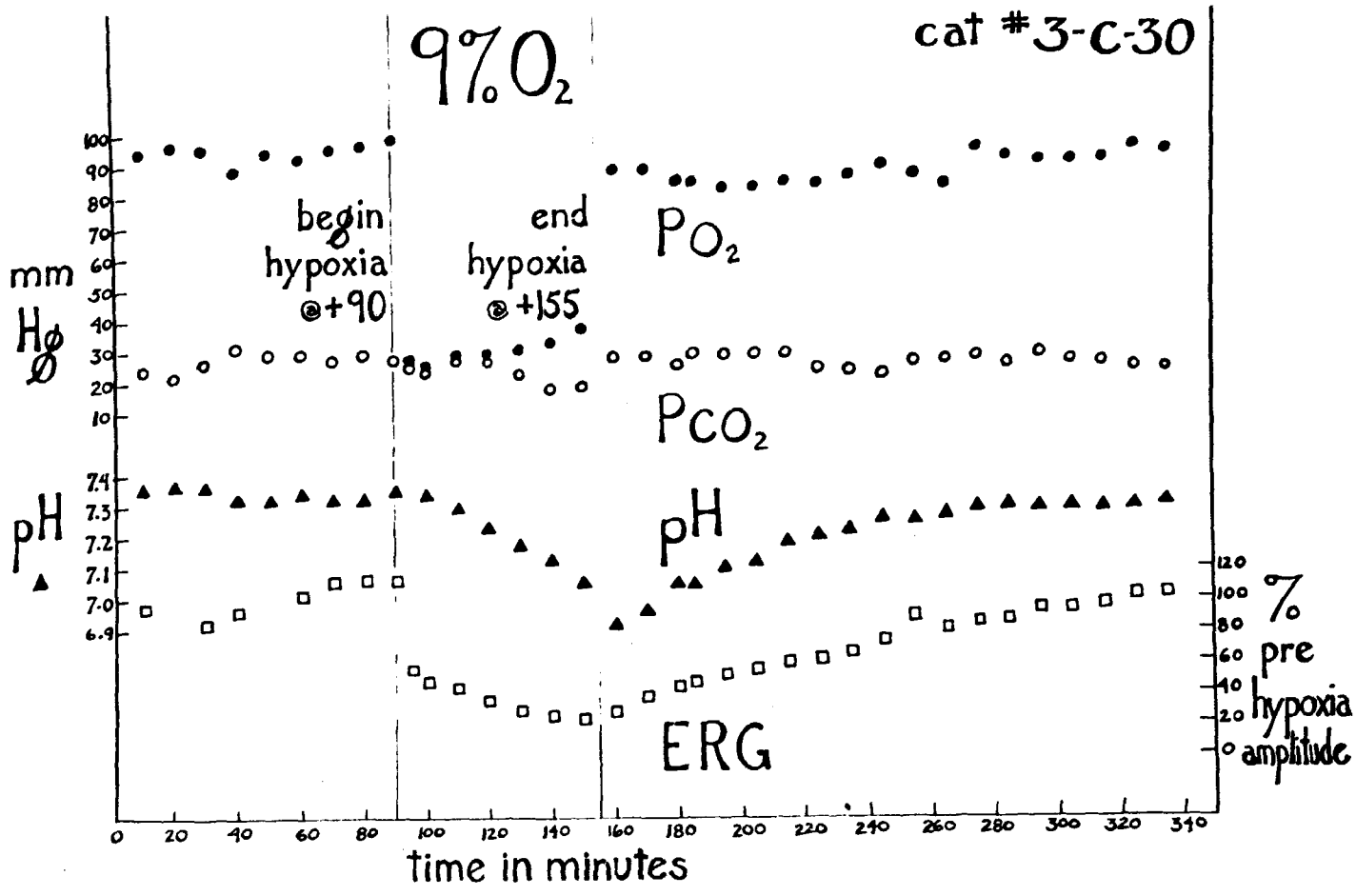

Fig. 7. Summary of blood gas measures and electroretinographic signal changes from a typical animal before, during, and during recovery from hypoxia (9% inspired O_2). Period of hypoxia began at 90 minutes and terminated at 155 minutes.

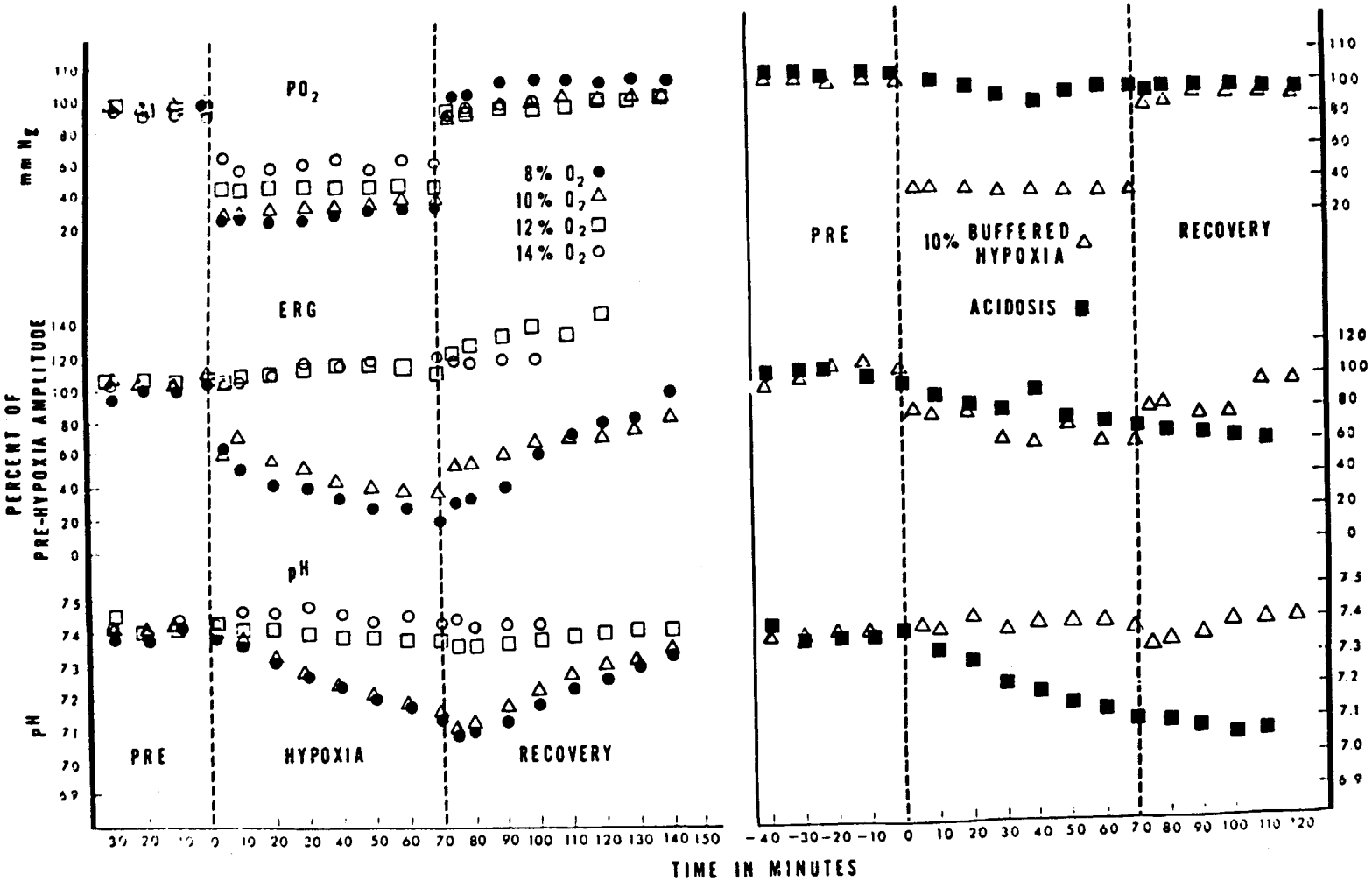

Fig . 8. (Left) Summary of retinal signal changes, PaO_2 and pH for controlled hypoxia exposures at 4 levels of inspired O_2. Results for these 3 variables are shown before, during, and following hypoxia. (Right) Measures of the same variables at left panel except hypoxic exposure was 10%. Experiment was repeated so that filled squares cover the same period as the experiments in panel to the left, but instead of induced hypoxia, acidosis of a circulatory nature was induced by IV infusion of a mild acid. The experiment was repeated again, but this time with 10% inspired O_2 and consequent hypoxia. pH was stabilized in this experiment by use of an intravenous bicarbonate buffer.

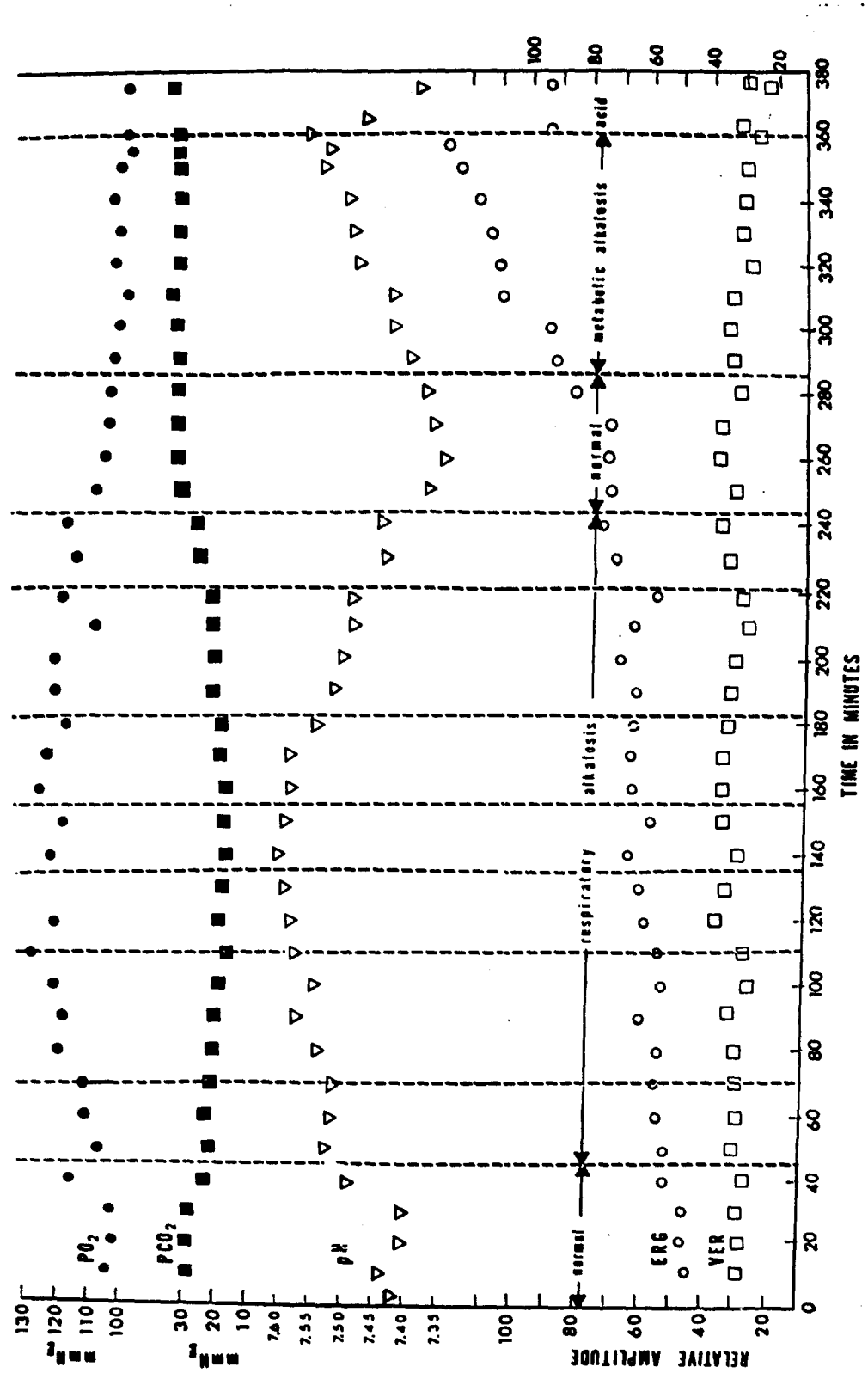

Fig. 9. Summary of experiments on induced alkalosis in the absence of hypoxia. Retinal and cortical signal changes are shown together with blood gas measures during respiratory alkalosis induced by increasing the rate of artificial ventilation. Subsequently, metabolic alkalosis was induced by infusing intravenous bicarbonate buffer. The metabolic alkalosis was terminated by the intravenous infusion of ammonium chloride.

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