Sensitivity and Behavior of Muscle Spindles to Systemic Arterial Hypoxia[1] (34377)

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(Introduced by R. C. Little)
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Current information suggests that muscle-spindle afferents may respond to acute asphyxiation with a variety of discharge patterns. These include: (A) complete cessation of activity (1), (B) immediate cessation of activity followed, after a variable time interval, by a series of high-frequency discharges (2, 3), or (C) very little effect (4). The study reported here was carried out to determine the range of arterial O_2 tensions over which primary spindle afferents can remain functional for a prescribed time period, and to observe the discharge behavior of spindles during a constant degree of arterial hypoxia when changes in other blood parameters are minimized.

Methods. Sixteen adult cats weighing from 2.2 to 3.6 kg anesthesized with pentobarbital (30 mg/kg ip) were used. The lungs were ventilated mechanically throughout the experiment. The sural nerve and all nerves to muscles in the left hind limb were sectioned except those to the gastrocnemius and soleus which were carefully isolated. All exposed nerves were kept submerged in warm (38°) paraffin oil. The animal was immobilized in a frame and the left foot and knee were clamped to immobilize the lower leg. The calcaneous was sectioned and a braided silk ligature was secured to the Achilles tendon with the opposite end tied to a strain-gauge transducer. The dura was sectioned dorsally in a retracted position to expose the cord. The ventral roots of L_6 to S_2 were sectioned.

Spindle afferents from the gastrocnemius-soleus muscles were isolated from L_7 or S_1 dorsal roots whch had been sectioned adjacent to the spinal cord. These filaments were placed on platinum wire electrodes which were attached to preamplifiers (Grass P511) with the output displayed on a 5-trace oscilloscope (Tektronix 565). An audiomonitor was in parallel.

Single afferent units were identified by a series of action potentials of equal configuration occurring in response to stretching of the triceps surae muscles. Group Ia afferents were identified by a conduction velocity above 72 m/sec (5) and by the temporary cessation of discharge during the twitch of the extrafusal muscle. Tendon organ afferents were identified by a similar conduction velocity and by an increase discharge during an extrafusal twitch. The animal was given 1 mg curare (Tubocurarine Chloride, Squibb) over a 2-min period after the isolation and classification of muscle afferents via a cannulated brachial vein. The intake on the respiratory pump was attached to a breathing bag into which flowed a gas mixture of 97% oxygen and 3% carbon dioxide. The respiratory system was closed and the animal respired at a rate of approximatey 18/ min at 50 cc/stroke.

The triceps surae muscle was stretched a distance of 8 mm at a velocity of 17 mm/sec at 90-sec intervals and maintained for 6 sec. Prestretch tension on the muscle was adjusted to approximately 25 g with the peak stretch tension rising to 150 g and declining to approximately 100 g. These tensions remained constant throughout the experiment. Stretching was initiated at least 10 min before control frequencies were measured.

After 30–45 min on the high O_2 mixture, control discharge frequencies were recorded

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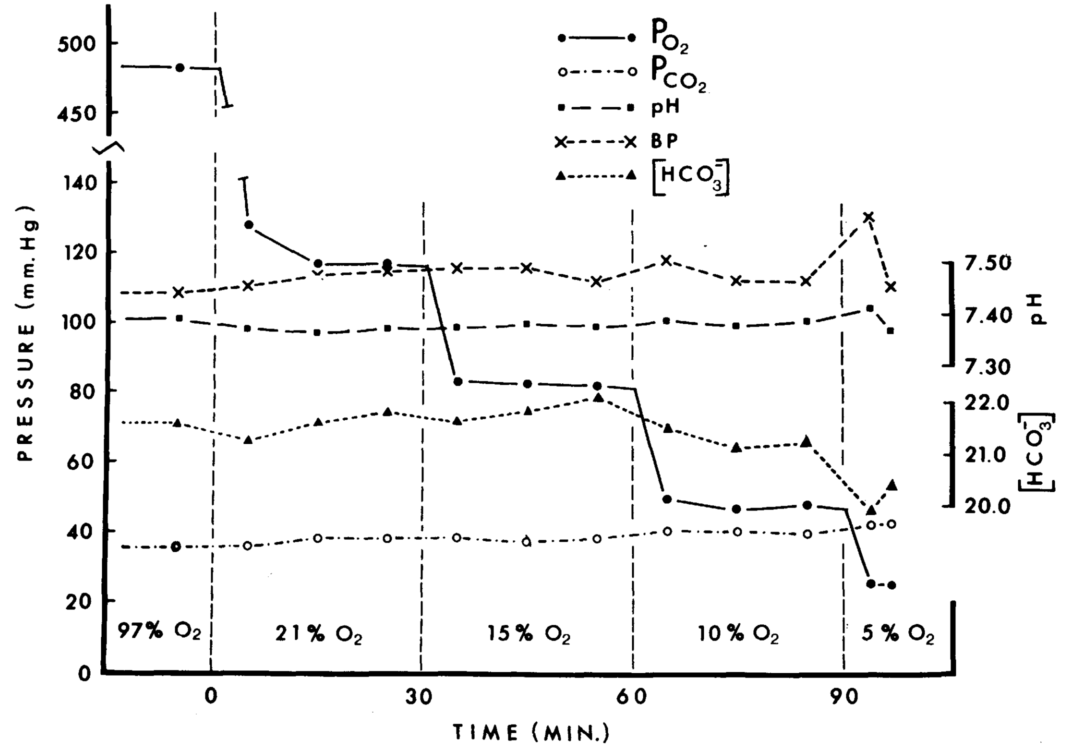

FIG. 1. Mean blood pressure (BP), carbon dioxide (PCO_2) values during periods when oxygen tension (PO_2) was lowered. Left ordinate represents pressure in mm Hg. Standard bicarbonate [HCO_3^-] and pH are displayed on right ordinates. Data from 11 cats.

in 11 cats. This oxygen level was used to insure an adequate oxygen supply to all spindles. Arterial oxygen was then lowered in steps at 30-min intervals by switching the breathing bag to tanks containing 21, 15, 10, and 5% oxygen. All gas mixtures contained 3% carbon dioxide with the balance nitrogen.

Arterial blood samples were withdrawn from the right femoral artery 5 and 15 min before and after every change of gas mixture. The pH, pCO_2, pO_2, and standard bicarbonate were immediately determined on each 0.7-ml sample. The pCO_2 was maintained relatively constant by means of small adjustments in respiratory rate. The pH was maintained between 7.3 and 7.5 by adjusting an intravenous infusion of 5% sodium bicarbonate. If the pH exceeded these limits or if carotid blood pressure declined below 80 mm Hg, the data were recorded but excluded in the final analysis.

Results. Oxygen levels were lowered in steps so that afferent activity could be assessed at known, steady PaO_2 levels. The mean levels of arterial blood pressure, PaO_2, pCO_2, pH, and standard bicarbonate for each of the oxygen levels utilized is shown in Fig. 1. The changes in the mean discharge frequency of the spindle afferents as PaO_2 levels were lowered are plotted in Fig. 2. The mean frequency of all components of the spindle discharge to stretch increased slightly as the PaO_2 was lowered from 480 to the normal level of 126 mm Hg (21% O_2). This increase continued throughout the initial 30-min period as the PaO_2 declined from 126 to 115 mm Hg. Reductions of the PaO_2 to 80 mm Hg (15% O_2) had virtually no immediate effect on spindle frequency, whereas slight increases in mean frequency occurred 15 and 25 min later. However, when analyzed by a test of *t* on a basis of a frequency change and compared to the frequency change for a similar period in animals maintained at nor-

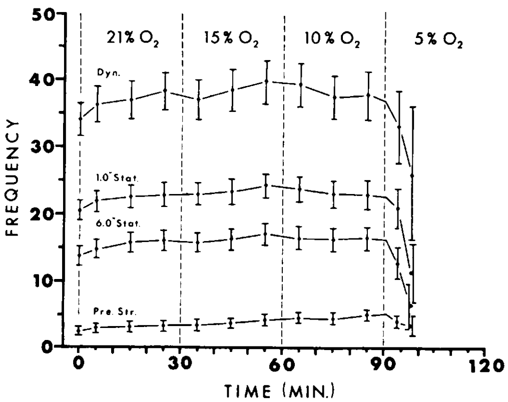

FIG. 2. Mean frequencies of primary spindle afferents during the arterial oxygen changes depicted in Fig. 1. Squares represent the dynamic component of the stretch-induced afferent discharge of primary spindles. Triangles and open circles represent, respectively, the first and sixth second of the static component of the discharge. Closed circles represent afferent activity immediately before stretch induction. Vertical bars represent standard error. Ordinate represents mean frequency (imp/sec).

mal PaO_2 levels for 120 min (Fig. 3), the increase was not statistically significant ($p=0.1$). No afferent showed precipitous frequency changes during this PaO_2 level nor were there any spontaneous high-frequency discharges.

Reduction of the PaO_2 to 48 mm Hg (10% O_2) for 5 min caused the abolition of afferent activity of three spindles. After 15 min exposure to this PaO_2, one additional afferent failed to respond and after 25 min exposure, activity in three more afferents was abolished. The remaining 41 afferents continued to respond at frequencies similar to those observed during exposure to a PaO_2 of 80 mm Hg. No high-frequency discharge from afferents known to be from gastrocnemius-soleus spindles were observed during this period. However, at this PaO_2 high-frequency discharges were observed from other afferents but their origin and receptor type could not be unequivocally identified since they usually failed to respond until the PaO_2 had reached a low level.

The 5% O_2 gas mixture produced a mean PaO_2 of 23 mm Hg. At this level of PaO_2 the static component of 14 of 33 spindle afferents was abolished. The remaining 19 afferents showed little change from the previous PaO_2 level of 48 mm Hg. After 7 min exposure to a PaO_2 of 23 mm Hg, 8 of 13 spindles showed an abolition of the static component discharges. Depression of the static components preceded that of the dynamic, thus causing a larger standard error for this component (Fig. 2). Data from many afferents were rejected because of excessive pH or blood pressure changes. It is of interest, however, that the discharge rate in these afferents rapidly decreased and they did not show a high-frequency discharge within the 20-min observation period. In two cats, all the blood parameters remained constant for periods beyond those shown in Figs. 1 and 2. In these cats, a gradual slowing of frequency and finally abolition of activity with no subsequent responses during the observation period occurred in the seven afferents studied. In a separate group of three cats the PaO_2 was reduced from 480 mm Hg and maintained at 120 mm Hg with all other blood parameters the same as in Fig. 1. Fifteen primary spindle afferents recorded from

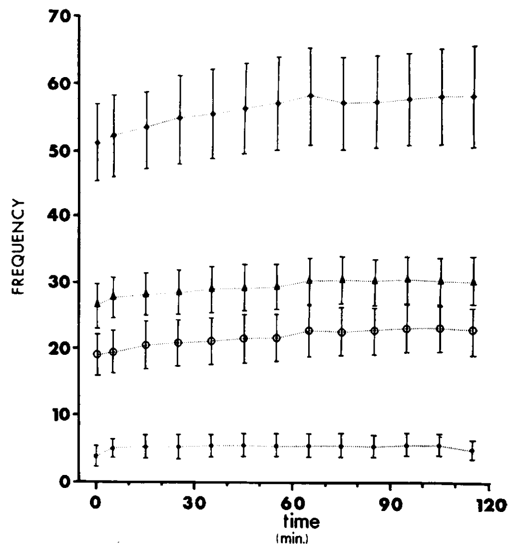

FIG. 3. Mean frequencies of primary spindle afferents when arterial oxygen tension was lowered from 480 mm Hg and maintained at 120 mm Hg for 120 min (three cats). Symbols are same as in Fig. 2. Vertical bars represent standard error. Ordinate represents frequency in impulses per second.

these cats showed a gradual increase in frequency during the 120- min observation period, (Fig. 3) showing that the extended recording time *per se* was not the cause of the depressed activity.

Discussion. Exposure to reduced oxygen tensions resulted in an increase in the discharge frequencies of muscle-spindle afferents above the frequencies recorded during exposure to high PaO_2 levels for the first 60 to 90 min of exposure. The greater portion of this increase is probably not the result of oxygen changes since similar changes were observed in 15 spindles from three cats in which the PaO_2 was maintained at approximately 120 mm Hg for 120 min (Fig. 3). It was formerly believed that the increase observed in both cases was the result of changing PaO_2 levels from high to approximately normal. Two additional cats were maintained at 490 mm Hg after a control observation at a PaO_2 of 120 mm Hg. The same gradual increase in afferent activity as those shown in Fig. 3, occurred in 10 spindle afferents recorded from these animals.

These data on spindle-afferent frequency in the present report shows that most primary spindles are only slightly affected by reductions of oxygen tension to as much 40–50% of normal for 25 min. This finding was unexpected since others have shown that occlusion of the blood supply or stoppage of respiration, (1–3) produces reductions of afferent activity in about 2 min. Assuming that the PaO_2 and muscle blood flow were approximately normal in these experiments (1–3), the degree of hypoxia produced through oxygen depletion would be slight in this period because the expected oxygen consumption of resting skeletal muscle is only 0.3–0.5 ml/min/100 g (6). This estimation suggests that spindle-afferent activity can be changed with only slight degrees of asphyxia and/or hypoxia. Our data do not support this conclusion.

The usual behavior of the afferents studied in this investigation to increasing degrees of hypoxia was an initial slowing of the discharge frequency and final cessation of activity. High-frequency discharges did not occur after the initial depression in afferents known to be from spindles in the gastrocnemius-soleus muscles even though it was predicted from other reports (2, 3) and has been observed in this laboratory after pentobarbital euthanasia. This response was not observed even when the arterial pH and pressure declined below acceptable levels. The lack of this discharge behavior indicates that hypoxia *per se* exerts only a depressing effect on spindle ending, whereas the changes in the spindle environment resulting from asphyxiation appear to instigate various degrees of hyperexcitibility.

The slight increase in activity observed at a PaO_2 of 80 mm Hg is not considered to be of significance. It was not observed after 5 min at PaO_2 and if it represented the slight hyperexcitability shown in a previous report (2), then considerable depression would be expected to occur in many afferents upon further reduction in the PaO_2, a situation which did not occur.

Undoubtedly other factors, such as catecholamine release, had some influence on spindle-afferent behavior as PaO_2 levels were lowered. Normally, catecholamines have a stimulating effect on spindle afferents although vasoconstriction is believed to be the indirect cause of subsequent depressions. However, spindle discharge behavior in these experiments generally bore little if any resemblance to those observed after doses of epinephrine (1, 2, 4).

Summary. The effects of systemic arterial hypoxia on the afferent discharge of muscle spindles has been studied. In 48 primary spindle afferents, reductions of arterial oxygen tensions to approximately 80 mm Hg had no effect. Reduction of O_2 tensions to approximately 45 mm Hg had no depressing effect in 41 of 48 spindle afferents whereas oxygen tensions of approximately 23 mm Hg abolished activity in all spindle afferents. High-frequency discharge from primary afferents known to be gastrocnemius-soleus spindles were not observed at the oxygen levels used.

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