

AUTONOMIC RESPONSES TO VESTIBULAR STIMULATION

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13. ABSTRACT Decerebrate, paralyzed cats were used to determine some autonomic effects of vestibular stimulation and to establish through which peripheral links this vestibulofugal activity was transmitted. Vestibular stimulation increased both rate and depth of respiration, as demonstrated by phrenic and recurrent laryngeal nerve recording, and a marked elevation in blood pressure accompanied this effect. When the strength of stimulation was reduced and the evoked respiratory effect weak or questionable, the systemic blood pressure declined. Vestibular stimulation elicited strong responses from the neck vagus nerve, but this vestibulo-vagal activity was found to be conducted exclusively in the recurrent laryngeal nerve and not in the vagus nerve proper. Only the sympathetic portion of the autonomic system responded to vestibular stimulation, thus providing vestibular impulses a channel for reaching different effector organs. The responses obtained from the neck sympathetic nerve were analyzed and their characteristics described.		

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THE PROBLEM

A rather comprehensive picture of the functional organization of the neuronal circuitries involved in vestibular activation of the somatic system has now been developed. Information about vestibular influence on the autonomic system has been mostly obtained indirectly from the responses of the effector organs such as the cardiovascular system, the digestive tract, pupils, sweat and salivary glands, et cetera, but few recordings of vestibulofugal impulse traffic have been made directly from either autonomic centers or peripheral nerves.

FINDINGS

In decerebrate, paralyzed cats, vestibular stimulation resulted in increased rate and depth of respiration and marked elevation of blood pressure. When the stimulation strength was reduced and the evoked respiratory effect weak or questionable, the blood pressure declined. Vestibular stimulation elicited strong responses from the neck vagus nerve, but this vestibulo-vagal activity was found to be conducted exclusively in the recurrent laryngeal nerve and not in the vagus nerve proper. Only the sympathetic portion of the autonomic system responded to vestibular stimulation, thus providing the only channel for vestibular impulses to reach autonomic effector organs.

*The animals used in this study were handled in accordance with "Principles of Laboratory Animal Care" established by the Committee on the Guide for Laboratory Animal Resources, National Academy of Sciences-National Research Council.

The findings in this report are not to be construed as an official Department of the Army position, unless so designated by other authorized documents.

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INTRODUCTION

It is generally accepted that vestibular stimulation evokes a variety of somato-visceral effects throughout the body. A rapidly growing number of studies have been devoted to vestibular activation of the somatic system, as displayed by recordings within the neuraxis or from different motor outputs, and a rather comprehensive picture of the functional organization of the neuronal circuitries involved has developed (18). Information about vestibular influence upon the autonomic system has been obtained mainly by recording the responses of the effector organs, i.e., the physiological manifestations. Some of these responses, however, do not always lend themselves readily to quantitative estimations, and, in addition, it is difficult to differentiate between a true primary response and a homeostatic counteraction. It is well known that vestibular stimulation may elicit responses from the vasomotor system, digestive tract, pupils, sweat and salivary glands, et cetera, but few recordings of vestibulofugal impulse traffic have been obtained from either autonomic centers or peripheral nerves. Obviously, vestibular afferents must be linked to these systems but to what extent and by which connections remains an open question.

The widespread effects on sympathetic outflow evoked by impulses of labyrinthine origin have been demonstrated by Megirian and co-workers. They recorded from the splanchnic nerve (26), abdominal sympathetic chain, and cardiac sympathetic nerves (9). Vestibulo-vagal activity, elicited by electrical stimulation of the peripheral branches of the vestibular nerve and recorded from the cervical vagus nerve in the cat, has been studied (2, 9, 16, 17). This kind of recording from the vago-accessory complex of nerve fibers showed that the evoked reflex responses changed in amplitude with the respiratory cycle. The spontaneous rhythmic discharge, occurring in volleys during both inspiration and expiration, is conducted over the superior laryngeal (5) and the recurrent laryngeal nerves (4, 6, 14, 22, 23, 28).

The number of factors which can affect respiration is so great that virtually the entire organism can be said to contribute something to the control of respiration. For example, it is well known that neurons of the respiratory center are influenced by impulses transmitted over collaterals of the major ascending afferent tracts and entering divisions of the cranial nerves. In the present study, a further analysis has been carried out of the effect of vestibular stimulation upon: (a) the respiratory activity, as reflected by recordings from the motor fibers of the recurrent laryngeal and phrenic nerves; (b) the vagal outflow, as manifested by recordings from the efferent fibers of the chest vagus nerve beyond the point of emergence of the recurrent laryngeal nerve; and (c) the activity of the neck sympathetic nerve.

PROCEDURE

The experiments were performed on cats decerebrated by electrocoagulation of the tegmentum at the stereotaxic level A2.5. They were paralyzed by an initial dose of 6 mg/kg body weight of gallamine triethiodide, kept fully immobilized by smaller, iterative doses during the extent of the experiment, and maintained on artificial

respiration. The peripheral vestibular nerve branches were exposed in the vestibule of the left side and equipped with stimulating electrodes according to the technique previously described (3). The electrodes, two enamelled silver wires (0.13-mm diameter) with Ag-AgCl tips, were firmly attached to the bony edge of the opened bulla with dental cement. Square wave pulses of 0.3-msec duration and of different intensities were delivered at frequencies varying between 0.5 and 30 pulses per second.

The branch of the fourth spinal nerve supplying the phrenic nerve (PN) was exposed and sectioned in the neck without opening the thorax, and the spontaneous and evoked activity was recorded from the central end (Figure 1*). The vagal efferent activity, as specified in the Results, was recorded from three levels of the central end: (a) the neck vagus nerve (NV); (b) the chest vagus nerve just beyond the point where the recurrent laryngeal nerve turns rostrally, designated as the upper chest vagus nerve (UCV); and (c) dorsal or ventral vagal bundles just above the diaphragm, defined as the lower chest vagus nerve (LCV). The efferent activity of the recurrent laryngeal nerve (RLN) as well as that of the neck sympathetic nerve (NS) was recorded from the central end in the neck. The nerves were placed across bipolar Ag-AgCl electrodes, protected by pools of warm mineral oil, and, after adequate amplification, the activity was displayed on a polygraph and/or an oscilloscope. In some experiments the phrenic nerve firing was integrated by means of a Grass Integrator. Throughout the experiments the rectal temperature was monitored with a thermistor probe and maintained at 39°C ($\pm 0.2^\circ\text{C}$) with a relay circuit controlling radiant heat. The arterial blood pressure was recorded with a strain gauge from the femoral artery. The alveolar CO₂ tension was estimated with an infrared CO₂ analyzer (Capnograph) according to a technique previously described (36). Other procedures, relevant to the evaluation of the results, are considered in the appropriate sections of this paper.

RESULTS

EFFECT OF GALLAMINE ON RESPIRATION

To prevent the violent, compensatory movements evoked by each vestibular shock stimulation, the cats had to be paralyzed, and gallamine triethiodide was selected because of its supposedly weak central effect (12). It soon became obvious, however, that this drug somehow affected respiration. A decerebrate cat breathes smoothly at a rate of 20 to 25/min. In Figure 2A are depicted, from above, the integrated (PNI) and direct (PN) phrenic nerve discharges, the respired CO₂ concentration, and the arterial blood pressure (BP) of such a preparation. The respiratory rate was about 25/min, and the peak value of the alveolar CO₂ was 4.3 per cent which is equivalent to an alveolar tension of 32.0 mm Hg. In Figure 2B the thorax had been opened and the animal was artificially ventilated in a way that reflected the spontaneous respiration as closely as possible, i.e., a pump rate of 22/min and an alveolar CO₂ concentration of 4.2 per cent. The rate of the integrated phrenic nerve discharge was synchronous with the pump

* All illustrations appear at the end of the text.

rate, indicating that the respiratory center was triggered by the pump action through the Hering-Breuer reflex. After an initial intravenous injection of gallamine, however, the phrenic nerve discharge (11/min) became clearly dissociated from the pump action (Figure 2C), suggesting a suppression or elimination of the Hering-Breuer reflex similar to that following bilateral vagotomy.

Further evidence that gallamine exerts a central effect upon respiration is presented in Figure 3. The well-known respiratory arrest elicited by central stimulation of the sectioned vagus nerve (Figure 3A) was changed into a moderate decline in respiratory rate following gallamine administration, as shown in both the neck vagus and phrenic nerve recordings (Figure 3B). It is also evident that the vagal rhythmic efferent discharge followed faithfully that of the phrenic nerve but became more pronounced after the injection. The fall in blood pressure during vagal afferent stimulation appeared to be the same before as after the drug administration, indicating that the depressor reflex was not affected. The vagal afferent discharge, reflecting the activation of pulmonary stretch receptors, was always synchronous with the pump action, even after gallamine injection.

EFFECT OF VESTIBULAR STIMULATION UPON RESPIRATION AND BLOOD PRESSURE

Single shock stimulation evoked weak or questionable responses from the phrenic nerve and had no visible effect upon respiration. Higher frequency vestibular stimulation increased respiration, implying excitatory connections between the vestibular system and inspiratory center as reflected by recordings from the final motoneurons. Thus, only when the rate of motor pool barrage was increased did clear-cut vestibulo-phrenic responses become recordable, demonstrating that considerable temporal summation of subliminal stimuli was necessary to make the motoneurons discharge. Repetitive stimulation may be considered a better means of delineating neuronal connections and, in a sense, more physiological since persistent bombardment is a more normal process in the central nervous system. The influence upon the phrenic nerve firing of applying 10 pulses per second (pps) vestibular stimulation of submaximal strength, as judged by the phrenic nerve effect, is shown in Figure 4A. The rhythmic discharge increased in amplitude and rate as displayed particularly by the integrated recording (PNI). Since a direct relationship has been shown to exist between the amplitude of the integrated phrenic nerve firing and the depth of respiration (35), it can be stated that vestibular stimulation increases respiration, both depth and rate. When submaximal vestibular stimulation was applied at 30 pps, a similar but weaker effect was observed (Figure 4B). In Figure 4C the frequency of vestibular stimulation was again 10 pps but the strength was increased to supramaximal value. Following a delay, phrenic nerve responses of gradually increasing amplitude were evoked by each vestibular shock stimulus. The rhythmic phrenic nerve discharge then appeared in the form of "gasps" which were particularly conspicuous in the integrated recording. The gasping rate was about 60/min during the initial period of stimulation but declined rapidly during the latter part, approaching the prestimulatory respiratory rate of 15/min.

In addition to the marked effect of temporal summation upon the vestibulo-phrenic responses, there were great variations in amplitude of the responses, depending upon their occurrence during the respiratory cycle; the largest responses appeared mainly during the inspiratory phase (Figures 4, 6, and 7).

Vestibular stimulation elicited either depression or elevation of blood pressure after a latency of one second or less, and the direction of change correlated with the respiratory effect. Stimulation that evoked a clear-cut increase in phrenic nerve firing also elicited a rise in blood pressure (Figures 4A, C; 6A, B; 7B, C), and since the animals were paralyzed, this was not simply secondary to the respiratory effect. In some experiments pulse pressure widened but pulse rate was not altered. The blood pressure fell only when the respiratory effect was absent or weak due to a reduced strength of vestibular stimulation (Figures 4B and 7A). Thus, the effect of vestibular stimulation on blood pressure was variable, depending to some extent upon the parameters used. In cats anesthetized with chloralose, vestibular stimulation always resulted in a fall of blood pressure, confirming the previous observations by Gernandt and Schmitterlöw (19).

VAGAL MOTONEURON RESPONSE TO VESTIBULAR STIMULATION

Rhythmic spontaneous discharges were recorded from the central end of the neck vagus nerve. When these were correlated with the phrenic efferent firing, two distinct phases were seen: an inspiratory phase, synchronous with the phrenic discharge; and an expiratory phase, consisting of some high-amplitude firing immediately following the cessation of the phrenic nerve activity (Figure 5). This rhythmic firing suggested that the activity was conducted along the fibers of the recurrent laryngeal nerve. It must be taken into account that section of the neck vagus nerve for the recording may give rise to the well-known prolongation of inspiratory activity but the general pattern of discharge may not be significantly altered.

In the following comparisons between the vagal and the phrenic nerve responses to vestibular stimulations, the evoked potentials recorded from the neck vagus trunk must be considered to represent only those of the recurrent laryngeal nerve (RLN) as it will be shown that the vestibulo-vagal activity is conducted exclusively in its RLN component. Recordings from the neck vagus trunk and the phrenic nerve during ipsilateral vestibular nerve stimulation of an intensity submaximal for the phrenic nerve response are depicted in Figure 6. The alveolar CO₂ concentration was maintained at a level of 5.1 to 5.5 per cent, equivalent to a tension of 38.0 to 41.0 mm Hg (Figure 6A). Stimulation at a frequency of 10 pps evoked clear responses from the neck vagus nerve, but their amplitude declined rhythmically in synchrony with the spontaneous inspiratory firing. In contrast, the phrenic nerve responses became more pronounced during this phase. In Figure 6B, the alveolar CO₂ concentration was lowered and maintained at 3.4 per cent, equivalent to 25.3 mm Hg, and at this level the phrenic nerve discharge was barely visible, but during 5-pps vestibular stimulation it increased slightly in size because of the added drive upon the respiratory center. The neck vagus nerve still responded to

each shock stimulus but now the amplitude fluctuations were less pronounced, indicating that the degree of suppression of vagal responses is directly related to the amplitude of the RLN rhythmic firing.

In contrast to the phrenic nerve response which did not occur without temporal summation, the vagal response appeared immediately, as is demonstrated in Figure 7A. The initial frequency of vestibular stimulation was 1 pps which evoked a vagal discharge to each stimulus. No phrenic response was observed, but the spontaneous rhythmic firing seemed to be suppressed during the stimulation. Toward the end of the record, the frequency of stimulation was suddenly changed from 1 to 5 pps. The vestibulo-vagal volley of impulses still appeared in response to each stimulus, but during the course of the prolonged period of stimulation the amplitude of this evoked activity gradually declined and disappeared. The phrenic response, however, first appeared after several seconds of stimulation then rapidly reached full amplitude. When the rate of vestibular stimulation was increased to 10 pps, the vagal discharge still appeared immediately in response to each stimulus while there was a delay before the phrenic response occurred and gradually reached final amplitude (Figure 7B). At that moment the vestibulo-vagal responses started to become smaller and irregular in size. When 20-pps stimulation was applied, the phrenic nerve recordings showed a slight delay in appearance of the responses which grew promptly to maximal amplitude and rapidly declined (Figure 7C).

In order to determine how much of the response evoked by vestibular stimulation was carried in the fibers of the recurrent laryngeal nerve as compared to the vagus nerve proper, the recording electrodes were placed more peripherally; one pair on the upper chest vagus nerve (UCV) and the other on the recurrent laryngeal nerve (RLN, Figure 1). As shown in Figure 8A, the UCV recording still displayed some low-amplitude rhythmic firing in synchrony with that of the RLN but not at the same rate as the artificial respiration. Since the spontaneous discharge of the RLN is synchronous with that of the phrenic nerve, it can be concluded that the UCV contains some fibers showing respiration-synchronous discharge. When vestibular stimulation was applied at various frequencies, evoked responses were recorded from the RLN but never from the UCV. Thus, the predominantly ipsilateral evoked activity obtained from the neck vagus trunk in response to vestibular stimulation must be conducted exclusively in its RLN component, as demonstrated in Figure 8A to G. In A, the frequency of vestibular stimulation was one shock every other second, and the responses from the RLN varied in amplitude according to when they occurred in the respiratory cycle. These fluctuations are also depicted in the oscilloscope recordings of Figure 8, B to G.

To determine the distribution of the respiration-synchronous fibers in the vagus nerve proper, one pair of electrodes was placed on the lower chest vagus nerve (LCV) while the other pair remained on the RLN. As depicted in Figure 9, neither rhythmic firing nor evoked potential was recorded from the LCV. Thus, the respiration-synchronous fibers must all be contained in the vagal nerve branches which innervate the thoracic viscera and not the abdominal viscera.

SYMPATHETIC RESPONSE TO VESTIBULAR STIMULATION

Spontaneous rhythmic discharge, in synchrony with the phrenic nerve firing, was consistently observed in the neck sympathetic nerve (NS). In Figure 10, the duration of the discharge was approximately the same as that of the phrenic nerve but preceded it by about 0.5 sec. Vestibular stimulation at 1 and 5 pps elicited clear responses from the NS. With 1-pps vestibular stimulation there was a 15-mm Hg fall of systolic pressure (Figure 10A), and during 5-pps vestibular stimulation there was a minute increase in systolic pressure in addition to the blood pressure fluctuations in synchrony with the artificial ventilation (Figure 10B). At the peak of the blood pressure wave there was a corresponding decline in amplitude of the evoked responses. This became particularly clear during 10-pps vestibular stimulation (Figure 11). Before stimulation the systolic pressure was 110 mm Hg, and after about 1.5 sec of stimulation it reached a value of 125 mm Hg, with a corresponding decline of the sympathetic nerve response. When the systolic pressure reached 175 mm Hg, the evoked response disappeared completely but even during its absence the blood pressure continued to rise. When the blood pressure reached its peak, the spontaneous rhythmic discharge was also depressed. Despite the continuation of the vestibular stimulation, the blood pressure gradually declined, and the spontaneous discharge reappeared.

In the oscilloscope records, the NS response to 1-pps vestibular stimulation showed wide variations in configuration and had a latency of about 30 msec and a duration of 50 to 60 msec (Figure 12A). When the frequency of stimulation increased to 5 pps, the responses displayed cyclic variations from short latencies and long durations to long latencies and short durations (Figure 12B), probably reflecting changes in the excitability of the sympathetic system as a result of blood pressure fluctuations.

The phrenic nerve response appeared after a latency of 10 msec and lasted approximately 5 msec (Figure 12A and B). It was succeeded by a period of suppression of more than 50 msec, during which hardly any spontaneous activity could be noticed.

DISCUSSION

The first aspect requiring comment concerns the relationship between the normal animal and the experimental preparation in which gallamine has been injected. It is apparent that gallamine elicits two types of central effects upon the respiratory system: (a) an increase in amplitude of the spontaneous, rhythmic discharge recorded from the recurrent laryngeal nerve; and (b) a suppression of the inhibitory action of the Hering-Breuer reflex. The first finding seems to be in accordance with most previous ones demonstrating that this drug, which passes the blood brain barrier (15), increases the central nervous system excitability (24, 30, 31). The increase in amplitude of the RLN firing and the weaker inhibitory effect by the Hering-Breuer reflex, however, favor the hypothesis that gallamine suppresses central inhibition; thus, the supposedly excitatory action of the drug may be explained as a release phenomenon. This interpretation also agrees with the observation of DeJong et al. (12) that gallamine does not give rise to

any perceivable changes in the segmental monosynaptic and polysynaptic reflex responses in animals in which, at the outset, tonic inhibition has been eliminated by section of the cord and dorsal roots.

In accordance with previous findings (10, 11, 27, 32), vestibular stimulation in the present study clearly increased respiration, both rate and depth, as demonstrated by phrenic and recurrent laryngeal recordings. In addition, as vestibular activation was strengthened, large amplitude, rhythmic discharges of a frequency as high as 60/min arose. Since the animals were paralyzed, it is uncertain whether these gasp-like inspirations represent true gasping, coughing, or even retching. Borison (7) observed similar respiratory responses to electrical stimulation of the dorsolateral region of the myelencephalon, which includes the vestibular nuclei, in decerebrate cats and described them as coughing, sneezing, and retching.

It has been shown that vestibular stimulation leads to a gross activation of the bulbar reticular formation (20, 21) where inspiratory and expiratory neurons are intermingled (13, 29). Although specific, well-defined neuronal connections between the vestibular system and respiratory motoneurons have not been demonstrated, there are reasons to believe that vestibular impulses reach the cells of the reticular formation and via this intercalated system exert their influence upon the respiratory center, where a continuous stream of impulses is converted into a rhythmic discharge which is then transmitted to the respiratory motoneurons. Spontaneous rhythmic firing, in synchrony with the phrenic discharge, was observed in the neck vagus nerve, the recurrent laryngeal nerve, and the upper chest vagus nerve immediately beyond the point of the emergence of the recurrent laryngeal nerve, but not in the lower chest vagus nerve. Eyzaguirre and Taylor (14) described this kind of firing from the recurrent laryngeal nerve only, but this discrepancy is easily explained by difference in anesthesia. The upper chest vagal rhythmic discharge appeared consistently in all our decerebrate preparations.

The amplitude of the evoked discharges transmitted from the vestibular input to the respiratory motoneuron output fluctuates with the respiratory cycle, but the reflection of this depends upon the peripheral nerve employed for recording. If the appearance and amplitude of the vestibulo-phrenic response are used as indicators, then the excitability of the internuncial systems, respiratory center and motor pools, seems greater during inspiration and lower during expiration. If, however, the excitability is judged by the size of the evoked discharge obtained from the recurrent laryngeal nerve, then the findings are the opposite, i.e., decreased responsiveness during inspiration and increased excitability during expiration and expiratory pause. In addition to this functional dissimilarity, the results show that the neuronal circuitry for transmitting vestibular impulses to the phrenic motor pool is different from that of the recurrent laryngeal nerve. The response obtained from the phrenic nerve to 1-pps stimulation is small or questionable, and only upon repetitive stimulation is there a gradual, profound increase in amplitude of successive responses until a maximum is reached. The evoked discharge recorded from the recurrent laryngeal nerve, however, appears at a frequency of 0.5-pps vestibular stimulation and is of maximal amplitude from the beginning.

The effect of vestibular stimulation upon blood pressure is variable (34). Spiegel and Démetriades (33) demonstrated that not only caloric and galvanic stimulation but also rotational stimulation of the labyrinth elicited a fall of blood pressure. Hemingway (25) reported that, among subjects nonsusceptible or susceptible to motion sickness, the usual response to a swing test was a fall in systolic pressure; but in a group of highly susceptible individuals who vomited during the stimulation, the majority exhibited a rise in pressure. In the present experiments, the effect upon the blood pressure depended upon the strength of vestibular stimulation. Thus, weak stimulation, that barely influences respiration, usually elicits a fall of blood pressure while strong stimulation, producing clear-cut respiratory responses, always gives rise to an increased pressure.

The only effect of vestibular stimulation upon the autonomic system is exerted on the sympathetic portion, as reflected by recordings from the neck sympathetic nerve. Spontaneous rhythmic firing in this nerve and in synchrony with the phrenic nerve discharge was consistently observed, with the former activity leading the latter by about 0.5 sec. This is similar to the respiration-synchronous firing recorded from the greater splanchnic nerve (1). The rhythmicity in this nerve is generated in two ways: (a) indirectly, by the influence exerted upon the vasomotor center by the blood pressure fluctuations resulting from mechanical movements of the chest during spontaneous or artificial respiration; and (b) directly, by the respiratory center influence on the vasomotor center (37).

The neck sympathetic nerve discharge clearly follows vestibular stimulation of varying frequencies, i. e., similar to the responses recorded from the recurrent laryngeal nerve. The blood pressure rise accompanying these evoked sympathetic responses indicates that vestibular stimulation elicits a general increase in systemic sympathetic firing, not limited to the neck sympathetic nerve (9, 26). An additional support for this assumption is the continuing rise in blood pressure even after the disappearance of the evoked responses, which suggests a delayed action of released sympathomimetic amines. Moreover, the intimate relationship between blood pressure and the appearance of evoked sympathetic responses to vestibular stimulation is shown by the suppression of the evoked and spontaneous sympathetic firing caused by a rise in blood pressure. This may be due to a feedback mechanism mediated by the depressor reflex which, as stated, is not influenced by the gallamine injection.

While an analysis of the characteristics of the activity evoked by vestibular stimulation and transmitted in different motor and autonomic nerves has been our concern, brief reference to the significance of the findings in regard to motion sickness may be made. Despite voluminous literature on the subject and the current plethora of hypotheses, few experimental facts are available for explaining the appearance of the composite manifestations (38).

In order to bring out the full syndrome of motion sickness--nausea, visceral changes, retching, and vomiting--the influx of vestibular impulses must continue for some length of time. The present experiments have demonstrated that the effect of temporal summation upon the phrenic motoneurons is quite different from that on the vagal motoneurons

and sympathetic system. The visceral effects have been looked upon as a result of increased firing in the autonomic efferent fibers. It has now been shown, however, that the response to vestibular stimulation recorded from the neck vagus nerve is conducted exclusively in the fibers of the recurrent laryngeal nerve; no responses were ever obtained from the upper and lower chest vagus nerves. Thus, part of the vagal nuclear complex is undoubtedly invaded by vestibular impulses, but only the motor and not the parasympathetic component reflects this activity. The early findings that many of the symptoms of motion sickness could be induced by injecting acetylcholine or anticholinesterase suggested that the parasympathetic system was one of the channels through which vestibular impulses were funneled (8, 38). Only on such indirect evidence or on a misinterpretation of experimental facts (16) has the parasympathetic portion of the autonomic system been given an important role in the development of motion sickness. This leaves the sympathetic connections as the only autonomic link between the vestibular system and different effector organs; and gastric atonia, cessation of peristalsis, pallor, cold sweating, salivation, and rise in blood pressure, all common symptoms of motion sickness, probably have their genesis in the strong responses of the sympathetic system to vestibular stimulation. The ultimate, more drastic display of motion sickness, retching and vomiting, is a purely somatic act.

REFERENCES

1. Adrian, E. D., Bronk, D. W., and Phillips, G., Discharges in mammalian sympathetic nerves. J. Physiol., 74:115-133, 1932.
2. Akert, K., and Gernandt, B. E., Neurophysiological study of vestibular and limbic influences upon vagal outflow. EEG. Clin. Neurophysiol., 14:383-398, 1962.
3. Andersson, S., and Gernandt, B. E., Cortical projection of vestibular nerve in cat. Acta otolaryng., Stockh., Suppl. 116, 10-18, 1954.
4. Andrew, B. L., The respiratory displacement of the larynx: A study of the innervation of accessory respiratory muscles. J. Physiol., 130:474-487, 1955.
5. Andrew, B. L., A functional analysis of the myelinated fibres of the superior laryngeal nerve of the rat. J. Physiol., 133:420-432, 1956.
6. Bianconi, R., and Raschi, F., Respiratory control of motoneurons of the recurrent laryngeal nerve and hypocapnic apnoea. Arch. Ital. Biol., 102:56-73, 1964.
7. Borison, H. L., Electrical stimulation of the neural mechanism regulating spasmodic respiratory acts in the cat. Am. J. Physiol., 154:55-62, 1948.
8. Chinn, H. I., and Smith, P. K., Motion sickness. Pharmacol. Rev., 7:33-82, 1955.
9. Cobbold, A. F., Megirian, D., and Sherrey, J. H., Vestibular evoked activity in autonomic motor outflows. Arch. Ital. Biol., 106:113-123, 1968.
10. Colehour, J. K., and Graybiel, A., Biochemical changes occurring with adaptation to accelerative forces during rotation. Aerospace Med., 37:1205-1207, 1966.
11. Crampton, G. H., Studies of motion sickness: XVII. Physiological changes accompanying sickness in man. J. appl. Physiol., 7:501-507, 1955.
12. DeJong, R. H., Robles, R., and Morikawa, K. I., Gallamine (Flaxedil) and synaptic transmission in the spinal cord. Science, 160:768-769, 1968.
13. Dirken, M. N. J., and Woldring, S., Unit activity in bulbar respiratory center. J. Neurophysiol., 14:211-226, 1951.
14. Eyzaguirre, C., and Taylor, J. R., Respiratory discharge of some vagal motoneurons. J. Neurophysiol., 26:61-78, 1963.

15. Galindo, A., Krnjević, K., and Schwartz, S., Patterns of firing in cuneate neurones and some effects of Flaxedil. Exptl. Brain Res., 5:87-101, 1968.
16. Gernandt, B. E., A comparison between autonomic and somatic motor outflow to vestibular stimulation. Confin. neurol., 24:140-157, 1964.
17. Gernandt, B. E., Somatic and autonomic motor outflow to vestibular stimulation. In: Fields, W. S., and Alford, B. R. (Eds.), Neurological Aspects of Auditory and Vestibular Disorders. Springfield, Illinois: Charles C Thomas, 1964. Pp 194-211.
18. Gernandt, B. E., Vestibular influence upon spinal reflex activity. In: de Reuck, A. V. S., and Knight, J. (Eds.), Myotatic, Kinesthetic and Vestibular Mechanisms. London: Churchill, 1967. Pp 170-183.
19. Gernandt, B. E., and Schmitterlöw, C. G., Some observations concerning the mode of action of the antihistaminic drug "Lergigan" (N(α-methyl-β-dimethylaminoethyl) phenothiazine hydrochloride) in motion sickness. Brit. J. Pharmacol., 8:181-186, 1953.
20. Gernandt, B. E., and Thulin, C. A., Vestibular connections of the brain stem. Am. J. Physiol., 171:121-127, 1952.
21. Gernandt, B. E., Irunyi, M., and Livingston, R. B., Vestibular influences on spinal mechanisms. Exptl. Neurol., 1:248-273, 1959.
22. Green, J. H., and Neil, E., The respiratory function of the laryngeal muscles. J. Physiol., 129:134-141, 1955.
23. Guth, L., Soutter, L., Frank, K., Campell, J. B., and Lloyd, J. B., Diaphragmatic function following anastomosis of recurrent laryngeal and phrenic nerves. Exptl. Neurol., 2:251-260, 1960.
24. Halpern, L. M., and Black, R. G., Flaxedil (gallamine triethiodide): Evidence for a central action. Science, 155:1685-1687, 1967.
25. Hemingway, A., Cardiovascular changes in motion sickness. J. Aviat. Med., 16:417-421, 1945.
26. Megirian, D., and Manning, J. W., Input-output relations of the vestibular system. Arch. Ital. Biol., 105:15-30, 1967.
27. Pozerski, E., Appareil pour l'étude de l'influence des oscillations rythmiques sur les animaux de laboratoire. Compt. rend. Soc. de Biol., 85:702-704, 1921.

28. Rijlant, P., L'étude des activités des centres nerveux par la exploration oscillographique de leurs voies efférentes. I. Centre phrenique et centres moteurs non autonomes du pneumogastrique. Arch. Int. Physiol., 44:351-386, 1937.
29. Salmoiraghi, G. C., and Burns, B. D., Localization and patterns of discharge of respiratory neurones in brain-stem of cat. J. Neurophysiol., 23:2-13, 1960.
30. Salmoiraghi, G. C., and Steiner, F. A., Acetylcholine sensitivity of cat's medullary neurons. J. Neurophysiol., 26:581-597, 1963.
31. Schwartz, S., Galindo, A., and Krnjević, K., Flaxedil and cuneate neurons. Federation Proc., 26:492, 1967.
32. Spiegel, E. A., Respiratory reactions upon vertical movements. Am. J. Physiol., 117:349-354, 1936.
33. Spiegel, E. A., and Démetriades, Th. D., Beiträge zum Studium des Vegetativen Nervensystems. III. Mitteilung der Einfluss des Vestibularapparatus auf das Gefässsystem. Pflüg. Arch. ges. Physiol., 196:185-199, 1922.
34. Spiegel, E. A., and Sommer, I., Vestibular mechanisms. In: Glasser, O. (Ed.), Medical Physics. Chicago, Illinois: The Year Book Publisher, Inc., 1944. Pp 1638-1653.
35. Tang, P. C., Brain stem control of respiratory depth and rate in the cat. Resp. Physiol., 3:349-366, 1967.
36. Tang, P. C., Environmental factors affecting the performance of infrared CO₂ analyzer and the estimation of alveolar CO₂ tension. NAMI-1034. Pensacola, Fla.:Naval Aerospace Medical Institute and U. S. Army Aeromedical Research Unit, 1968.
37. Tang, P. C., Maire, F. W., and Amassian, V. E., Respiratory influence on the vasomotor center. Am. J. Physiol., 191:218-224, 1957.
38. Tyler, D. B., and Bard, P., Motion sickness. Physiol. Rev., 29:311-369, 1949.

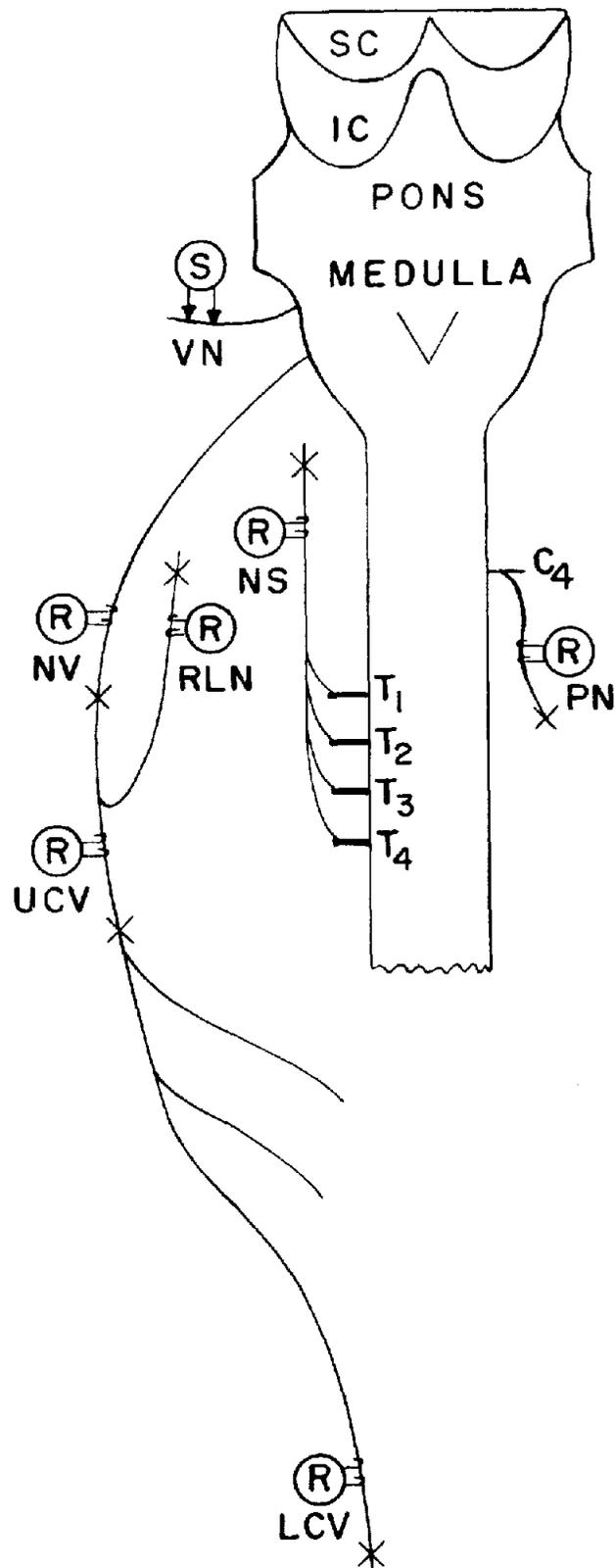


Figure 1. Diagram of sites of stimulation (S), recording (R), and neurotomy (X). Stimulation applied to peripheral branches of vestibular nerve (VN) and recordings made from phrenic (PN), neck sympathetic (NS), recurrent laryngeal (RLN), neck vagus (NV), upper chest vagus (UCV), and lower chest vagus (LCV) nerves. SC, superior, and IC, inferior colliculus; C₄ and T₁-T₄, fourth cervical and first four thoracic spinal nerves, respectively.

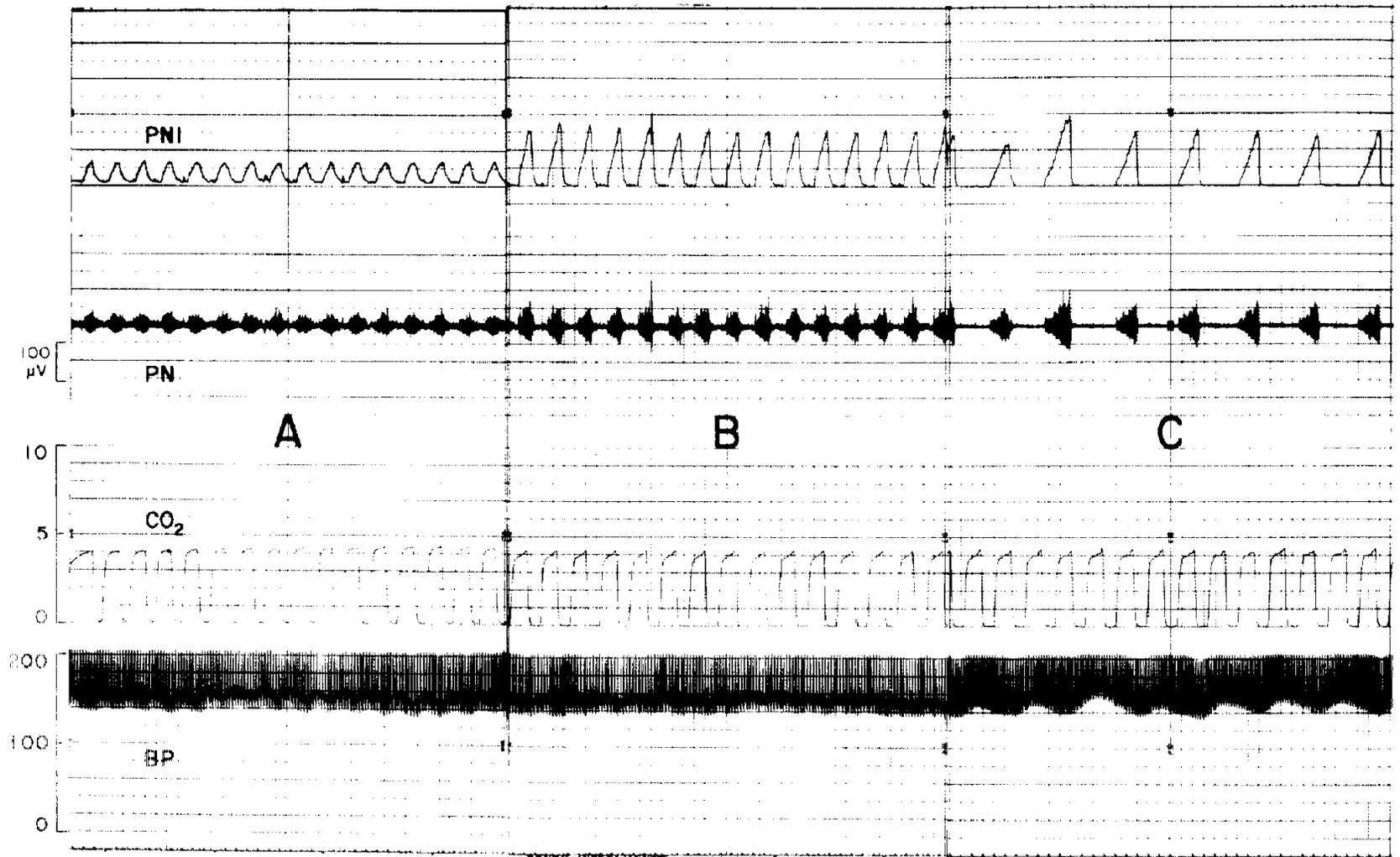


Figure 2. Decerebrate cat breathing spontaneously (A), with open thorax, artificially ventilated (B), and after intravenous injection of gallamine (C). Recordings of integrated (PNI) and direct (PN) phrenic nerve discharges, respired carbon dioxide concentration (CO₂) in per cent, and arterial blood pressure (BP). Phrenic nerve discharge reflects rate of respiratory center activity while CO₂ curve shows rate of mechanical respiration (rise corresponds to expiration, fall to inspiration). Synchrony between phrenic firing and CO₂ rise in A and B is lost in C. CO₂ tension 32.0 mm Hg in A and C and 31.3 mm Hg in B. Time marks on bottom line at 1-sec intervals.

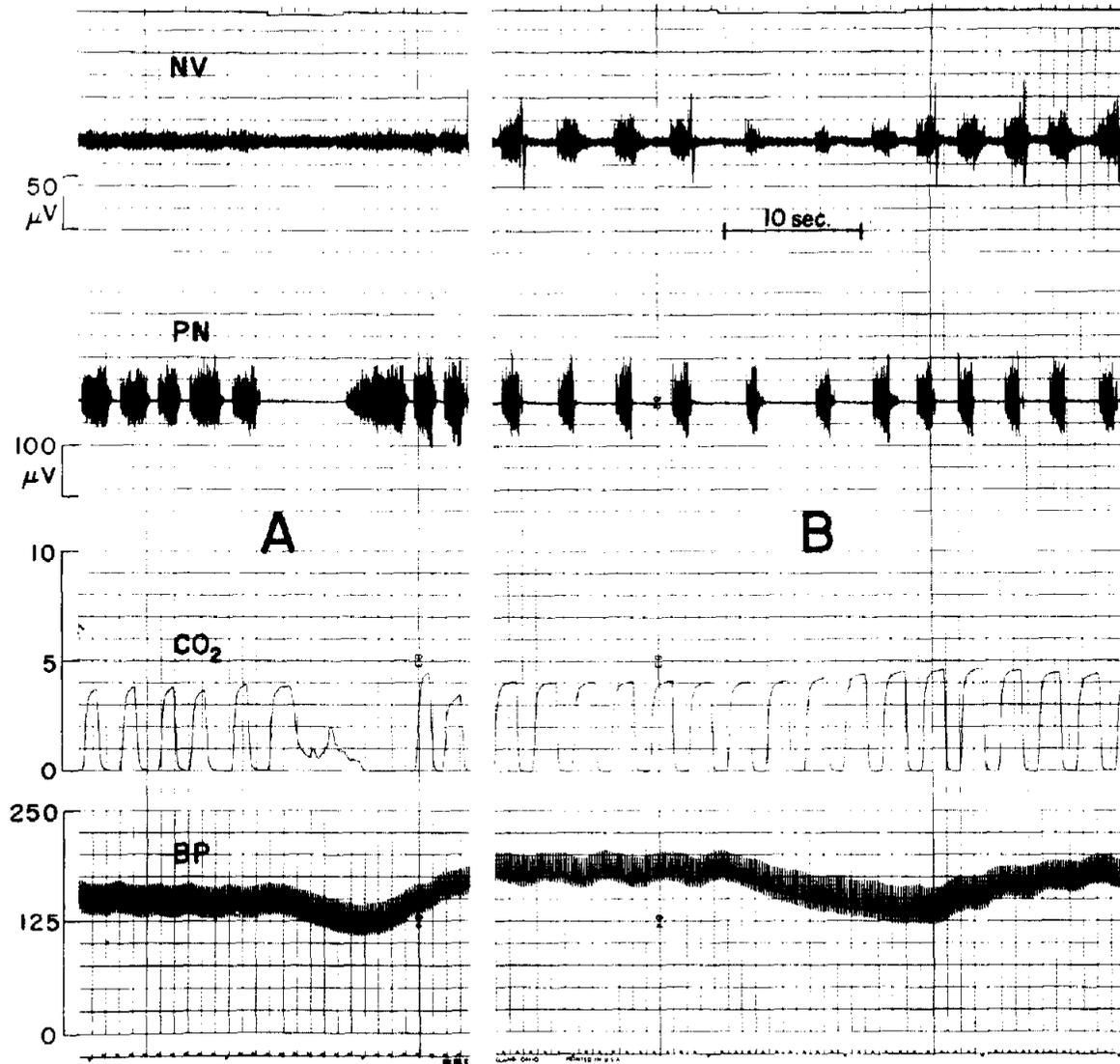


Figure 3. Decerebrate cat, before (A) and after (B) intravenous injection of gallamine. Recordings of neck vagal (NV) and phrenic (PN) efferent activities, respired carbon dioxide concentration (CO₂) in per cent, and arterial blood pressure (BP). Periods of contralateral afferent vagal stimulation marked on top line; time marks on bottom line at 1-sec intervals. Alveolar CO₂ tension 28.2 mm Hg in A and 30.5 mm Hg in B.

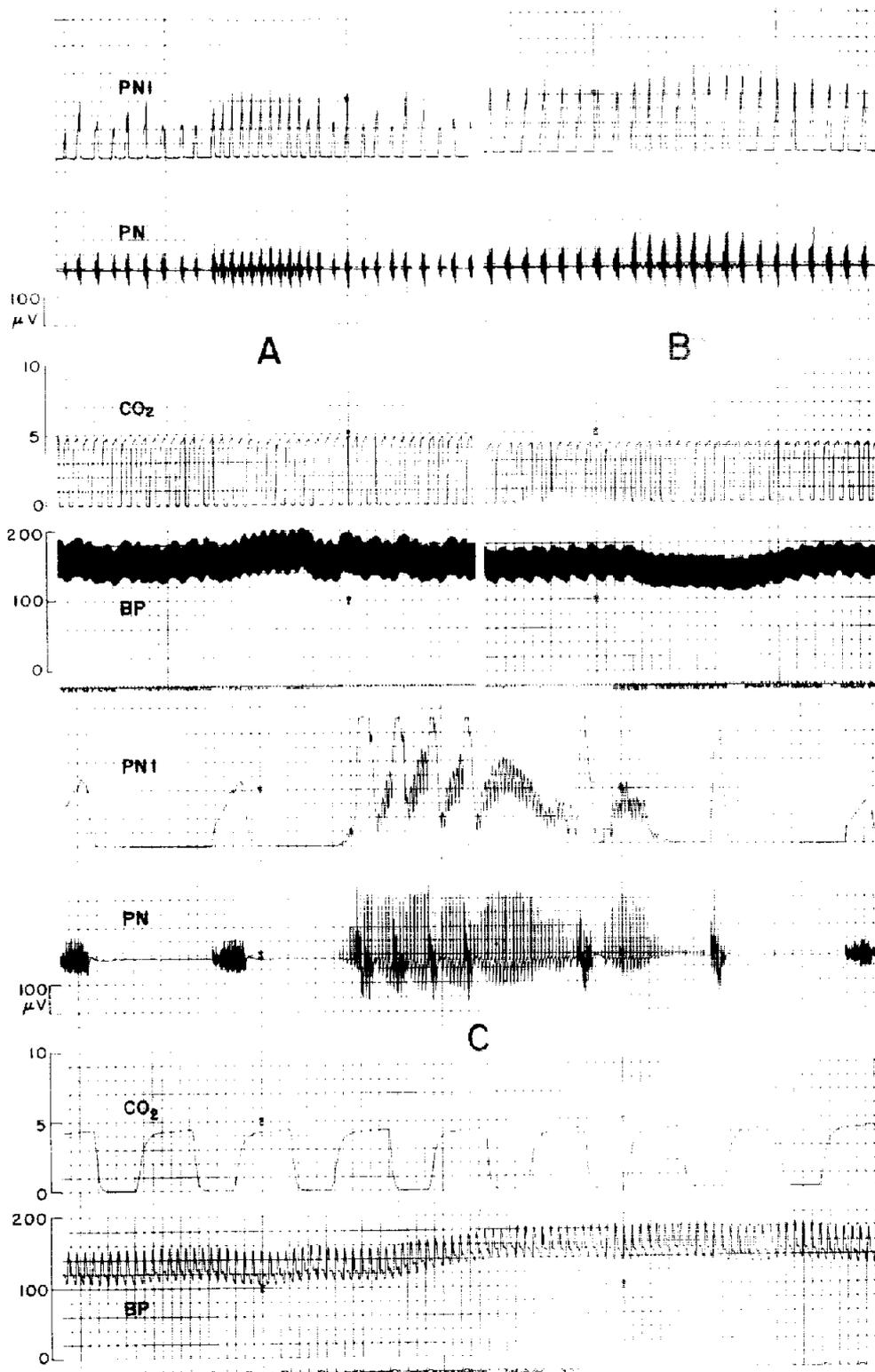


Figure 4. Decerebrate cat, paralyzed and artificially ventilated. Recordings of integrated (PNI) and direct (PN) phrenic nerve discharges, respired carbon dioxide concentration (CO_2) in per cent, and arterial blood pressure (BP). Periods of vestibular stimulation indicated on top line; time marks on bottom line at 1-sec intervals. Vestibular stimulation, submaximal for phrenic response, at 10 (A) and 30 (B) pulses per sec. Supramaximal stimulation at 10 pps (C) gave rise to 60/min gasping type of respiration. Alveolar CO_2 tension 35.8 mm Hg in A, 32.3 mm Hg in B, and 33.0 mm Hg in C.

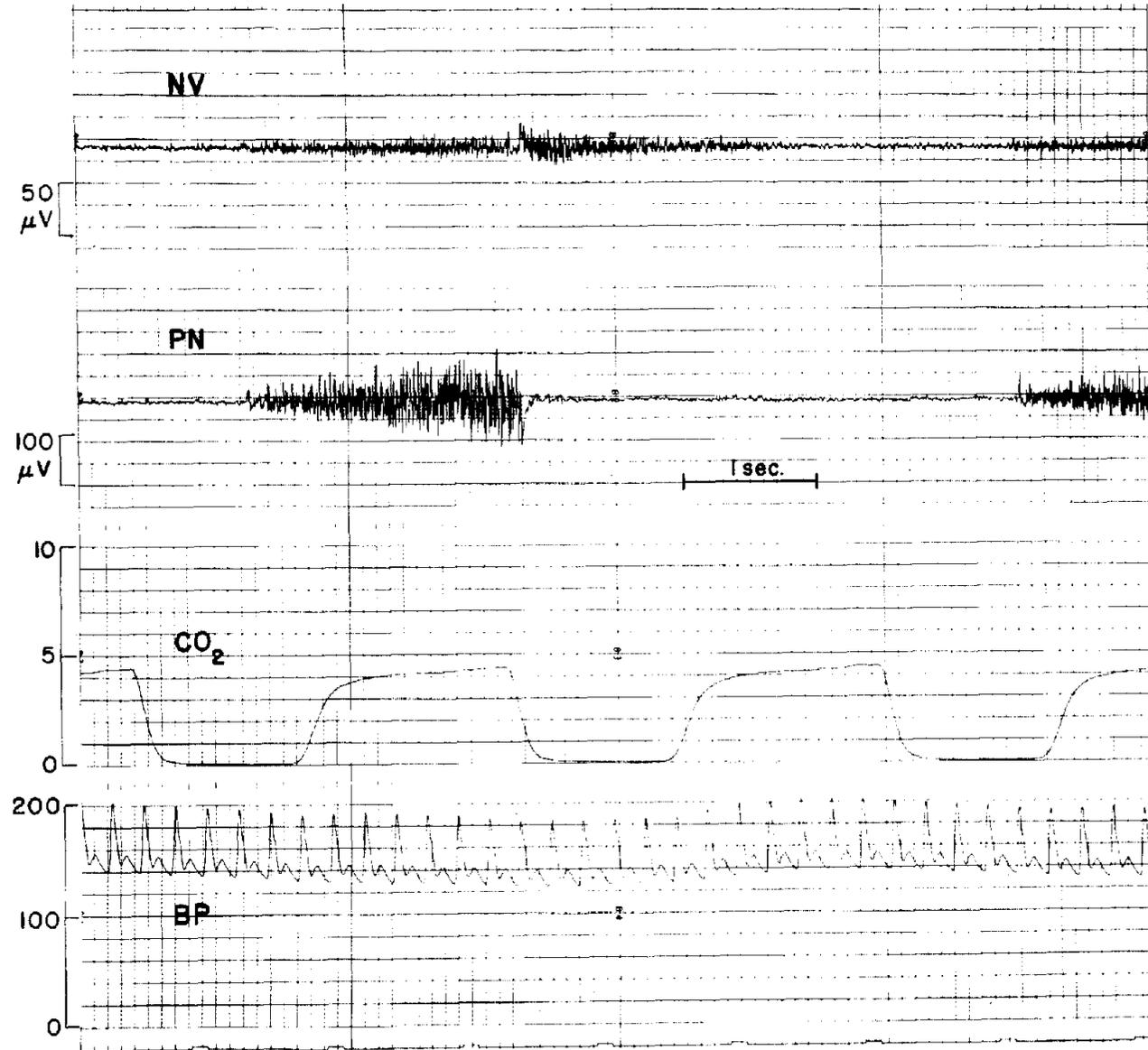


Figure 5. Decerebrate cat, paralyzed and artificially ventilated. Recordings of neck vagus (NV) inspiratory and expiratory, and phrenic nerve (PN) inspiratory discharges, respired carbon dioxide concentration (CO₂) in per cent, and arterial blood pressure (BP). Alveolar CO₂ tension 32.7 mm Hg. Time marks on bottom line at 1-sec intervals.

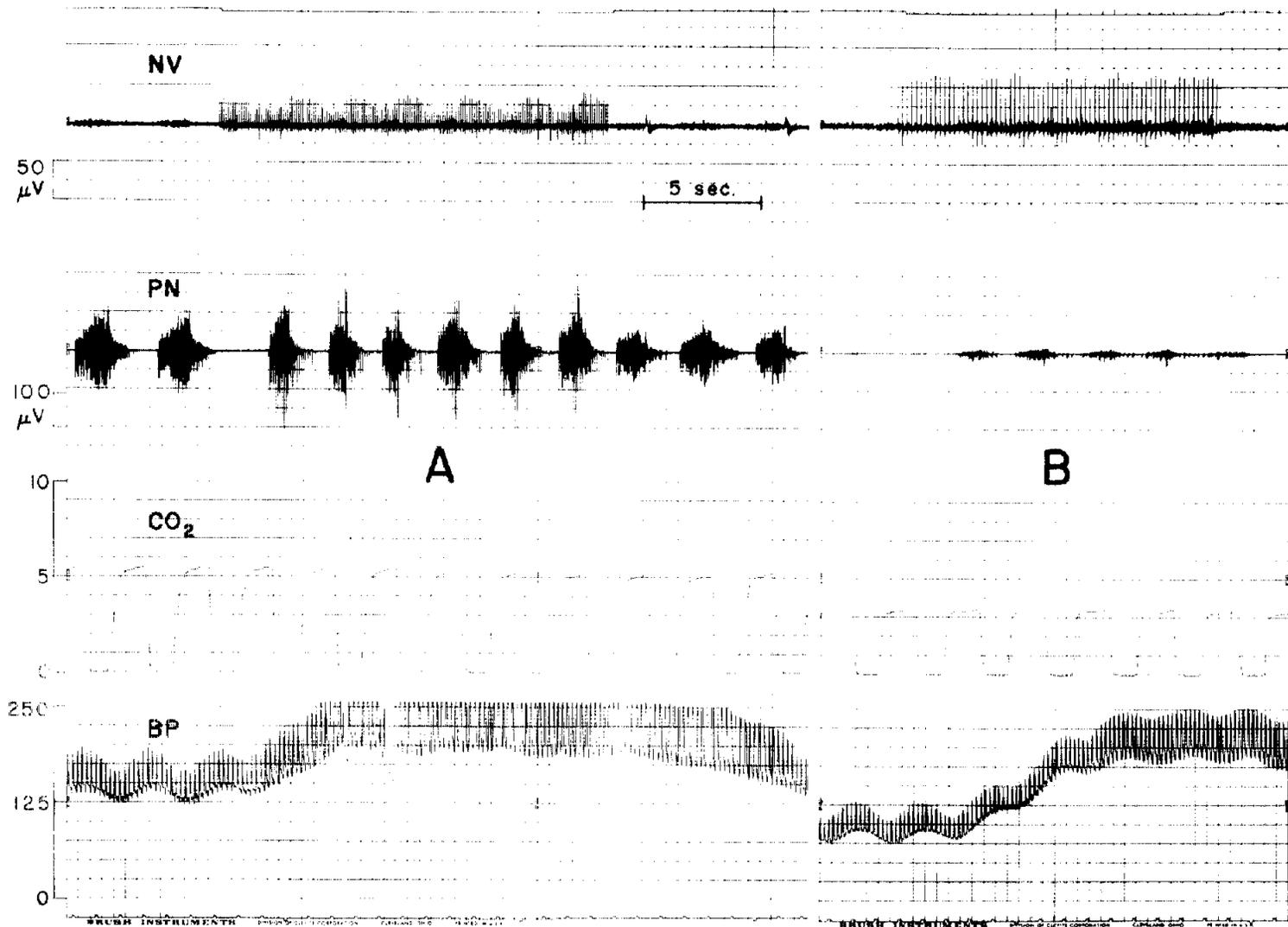


Figure 6. Decerebrate cat, paralyzed and artificially ventilated. Periods of submaximal vestibular stimulation at 10 pps (A) and 5 pps (B) indicated on top line; and time marks on bottom line at 1-sec intervals. Recordings of neck vagus (VN) and phrenic nerve (PN) discharges, respired carbon dioxide concentration (CO_2) in per cent, and arterial blood pressure (BP). Alveolar CO_2 tension 39.5 mm Hg in A and 25.3 mm Hg in B.



Figure 7. Decerebrate cat, paralyzed and artificially ventilated. Periods of vestibular stimulation, at a frequency of 1 pps changing abruptly to 5 pps in A, 10 pps in B, and 20 pps in C, indicated on top line; and time marks on bottom line at 1-sec intervals. Recordings of neck vagus (NV) and phrenic nerve (PN) discharges, respired carbon dioxide concentration (CO₂) in per cent, and arterial blood pressure (BP). The alveolar CO₂ tension 32.7 mm Hg in A, 27.5 mm Hg in B, and 32.0 mm Hg in C.

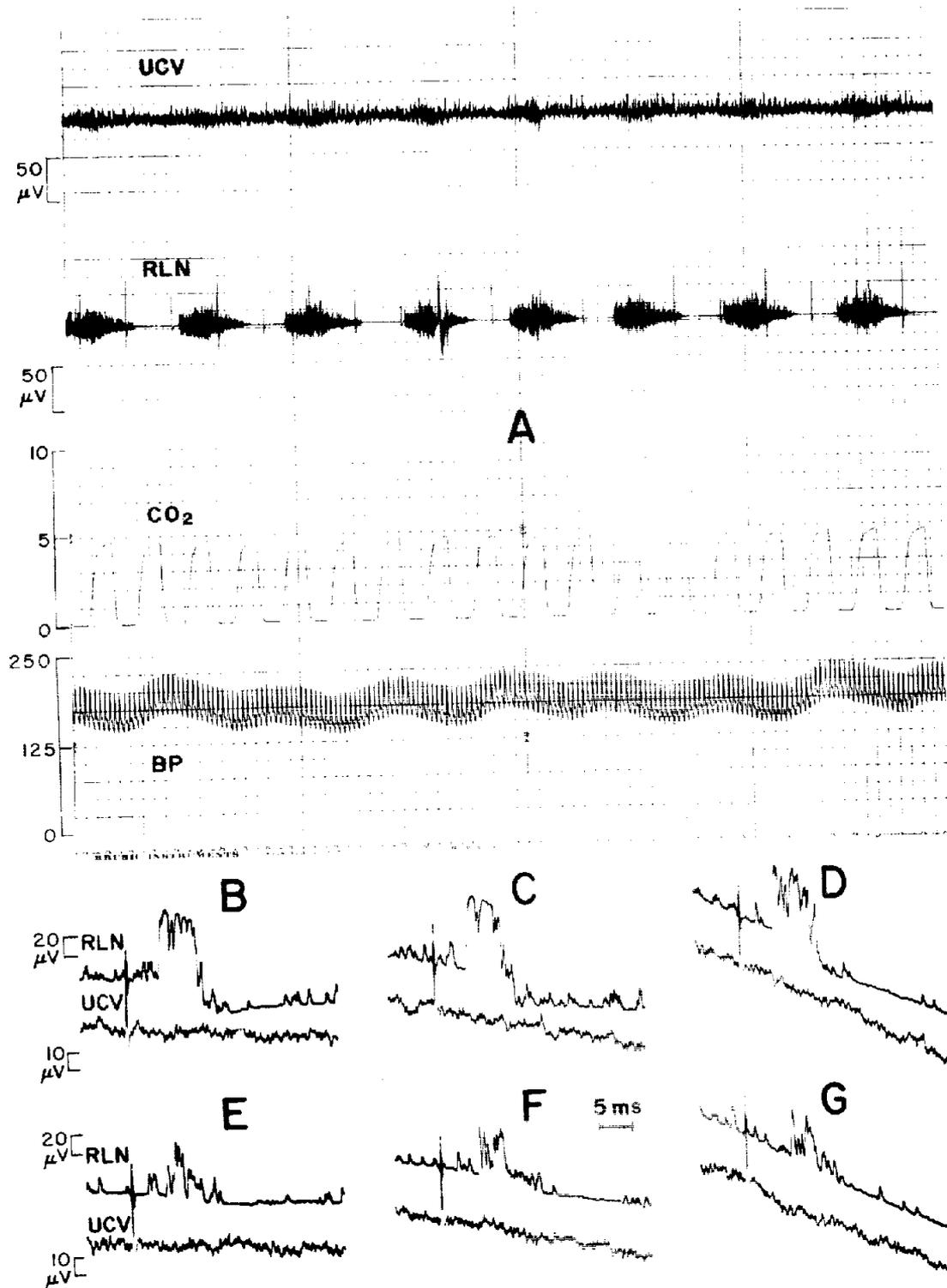


Figure 8. Decerebrate cat, paralyzed and artificially ventilated. In A, recordings of upper chest vagus (UCV) and recurrent laryngeal nerve (RLN) discharges during vestibular stimulation at a frequency of 0.5 pps, respired carbon dioxide concentration (CO₂) in per cent, and arterial blood pressure (BP). Notice responses to vestibular stimulation only from RLN. Alveolar CO₂ tension 30.2 mm Hg. Time marks on bottom line at 1-sec intervals. In B to G, oscilloscope recordings of maximal and minimal responses from RLN: 1 pps (B, E); 5 pps (C, F); and 10 pps (D, G) vestibular stimulation. Notice absence of responses from UCV.

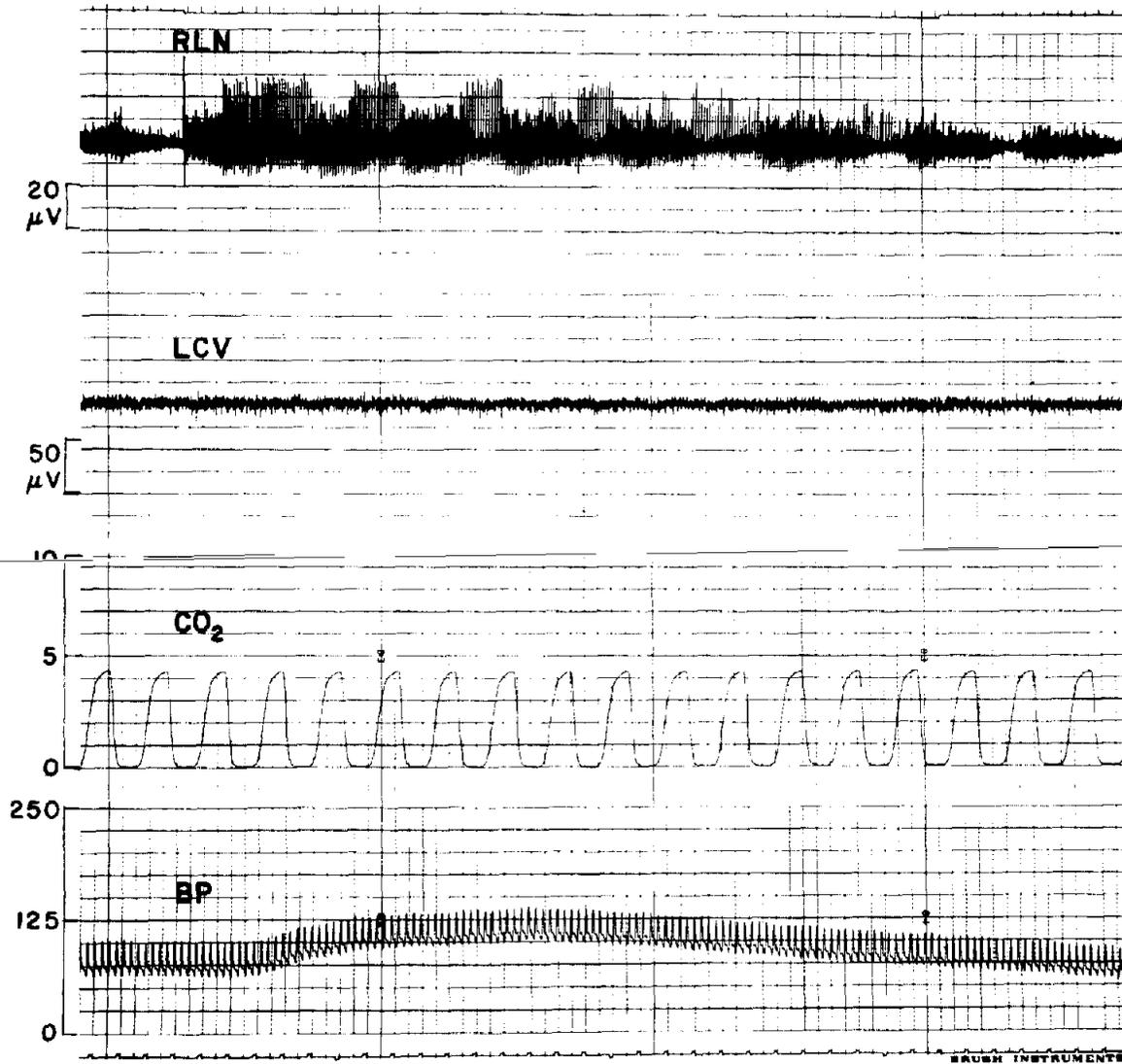


Figure 9. Decerebrate cat, paralyzed and artificially ventilated. Recordings of recurrent laryngeal (RLN) and lower chest vagus (LCV) nerve discharge, respired carbon dioxide concentration (CO_2) in per cent, and arterial blood pressure (BP). Period of vestibular stimulation at 10 pps indicated on top line; time marks on bottom line at 1-sec intervals. Notice the absence of LCV spontaneous rhythmic firing and activity evoked by vestibular stimulation. Alveolar CO_2 tension 32.0 mm Hg.

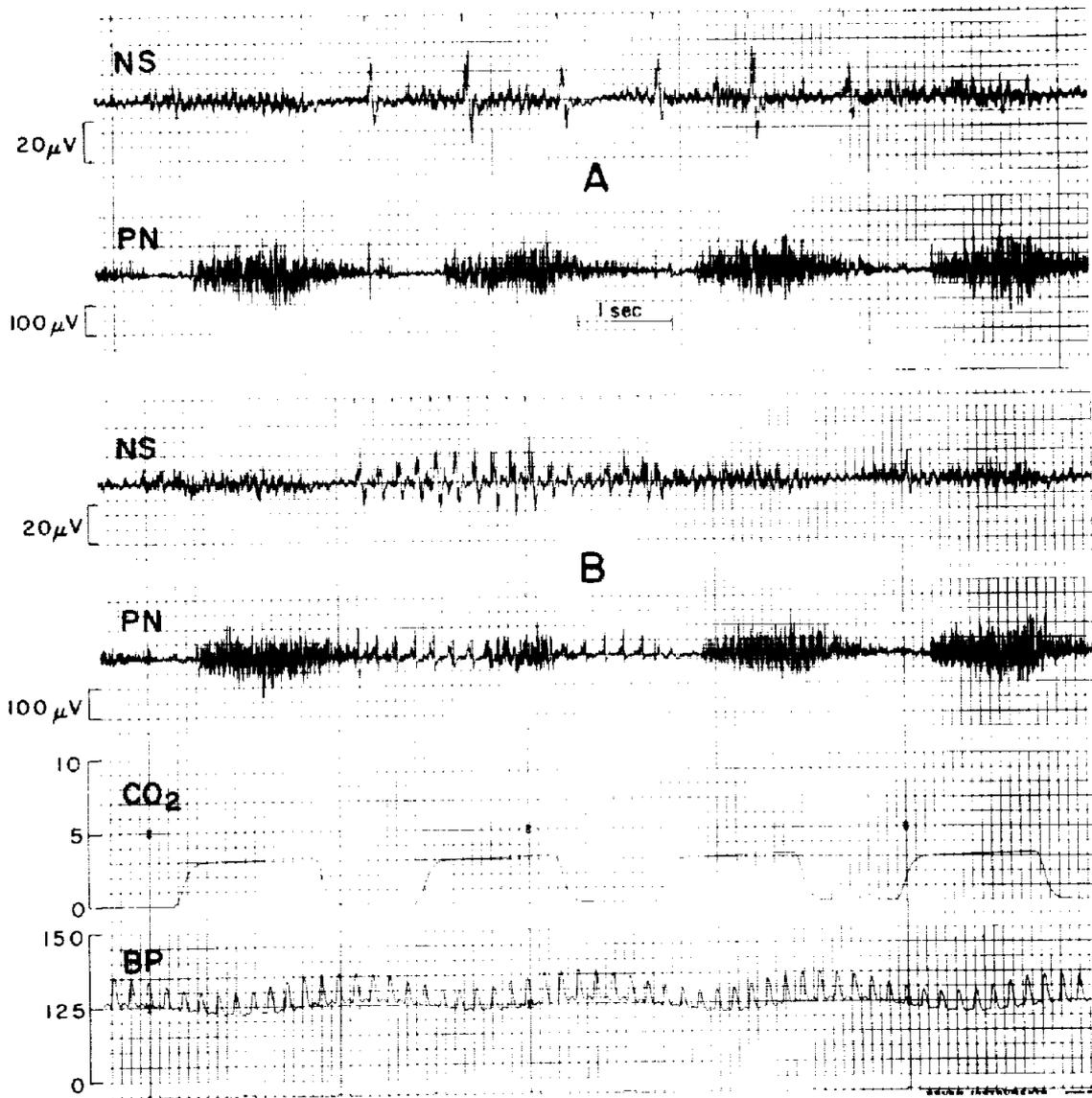


Figure 10. Decerebrate cat, paralyzed and artificially ventilated. Recordings of responses from neck sympathetic (NS) and phrenic (PN) nerves to vestibular stimulation at 1 ppm in A and at 5 ppm in B. In B are also shown respired carbon dioxide (CO_2) in per cent and arterial blood pressure (BP). Notice reduction in amplitude of NS responses in relation to blood pressure peaks in B. Alveolar CO_2 tension 24.7 mm Hg.

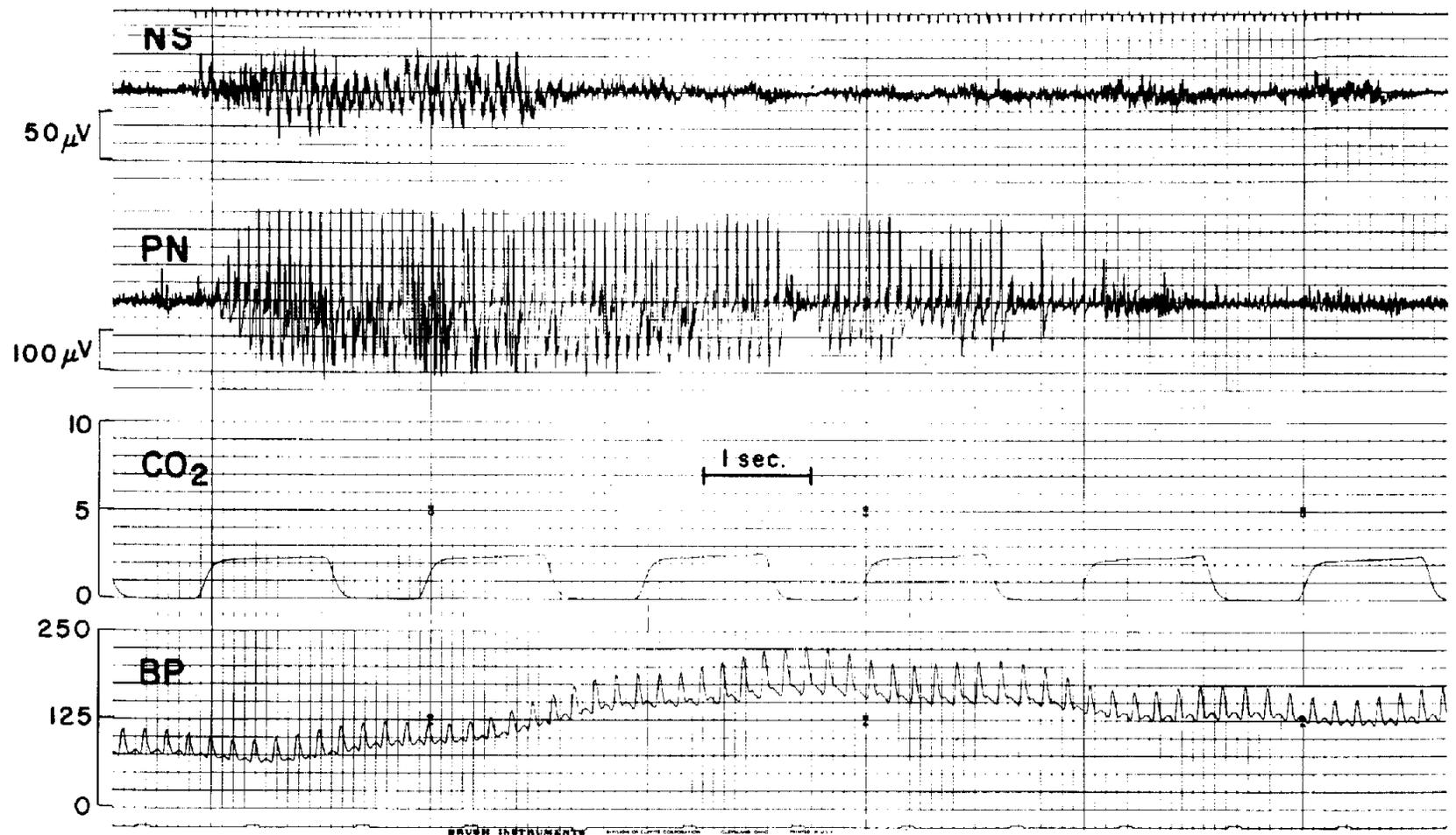


Figure 11. Decerebrate cat, paralyzed and artificially ventilated. Recordings of neck sympathetic (NS) and phrenic nerve (PN) responses to vestibular 10-pps stimulation as marked by the down-strokes on top line, respired carbon dioxide (CO_2) in per cent, and arterial blood pressure (BP). Notice reduction in amplitude and disappearance of NS evoked responses as well as the spontaneous rhythmic discharge during gradually increasing blood pressure. Alveolar CO_2 tension 18.8 mm Hg.

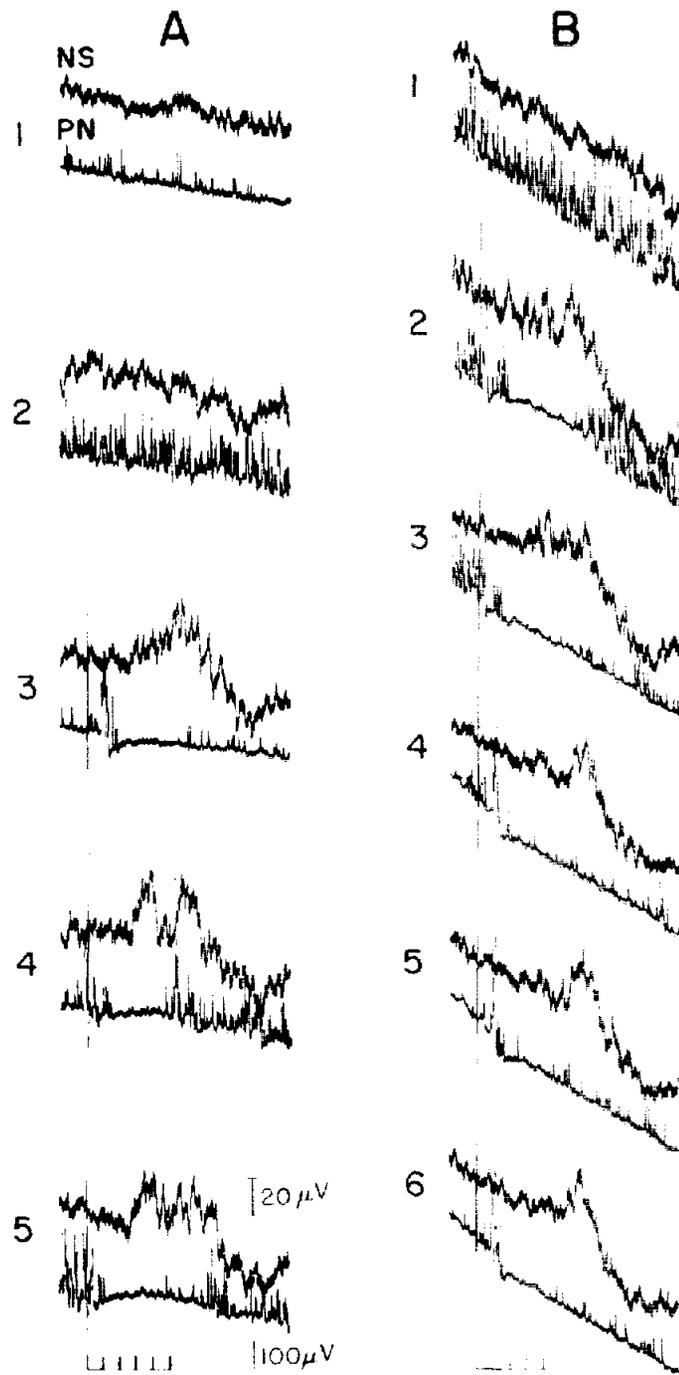


Figure 12. Decerebrate cat, paralyzed and artificially ventilated. Recordings from neck sympathetic (upper beam) and phrenic (lower beam) nerves during an inactive period (A1) and during a period of rhythmic discharge (A2). The variability in configuration of sympathetic responses to single shock vestibular stimulation is shown in A3 to A5. Spontaneous firing is depicted in B1, and consecutive responses to 5-pps vestibular stimulation are displayed in B2 to B6. Time scale at 10-msec intervals.