

Medullary Single Unit Activity: Response to Periodic Pressure Changes in the Carotid Sinus¹ (36766)

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(Introduced by D. Priola)

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The primary functional units of the baroreceptor reflex are the receptors, the central neuronal pathways and the peripheral effectors. In recent years attempts have been made to describe quantitatively the characteristics of the receptor mechanism (1, 2) the overall reflex (3-5) and a portion of the effector component (4). Studies of the central component have been concerned only with the localization of neurons within the reflex pathway (6-9). In addition these reports employed primarily the technique of electrically stimulating baroreceptor afferent fibers or have, to a limited extent, applied uncontrolled, nonrepetitive pressure pulses to the receptors (10).

There has been no work attempting to systematically relate changing pressure at the baroreceptors with central neuronal activity. This report presents some preliminary results obtained in a study designed to characterize the relationship between pressure changes in the carotid sinus and single cell activity in the classical integrative centers of the cat brain stem.

Methods. The carotid sinus baroreceptors of anesthetized cats (chloralose, 60 mg/kg or Dial² 0.6 ml/kg) were stimulated with a continuous pressure waveform generated by a pulsatile flow pump. The perfusion system was adapted from Levison, Barnett and Jackson (4) and allowed for continuous autoperfusion of the carotid sinus with pressure pulses of 50-75 mm Hg amplitude. The perfusion system, in brief, consisted of a roller pump whose speed and therefore sinus flow

and pressure was controlled by a low frequency oscillator. Blood from the common carotid artery was passed through the pump and back into the carotid artery caudal to the carotid sinus region. A variable resistance applied to a parallel venous shunt determined the mean pressure in the carotid sinus. In most experiments the pressure of only one sinus was controlled and the search for cells was made in the ipsilateral medulla. The pressure was set between 100 and 150 mm Hg. Baroreceptor regions not subjected to the controlled pressure were denervated by transecting the carotid sinus nerve on the opposite side and the vagus bilaterally. The dorsal surface of the brain stem was exposed and single cell activity was recorded extracellularly using etched tungsten microelectrodes with exposed tips of 4-8 μ . The electrodes were placed stereotaxically in the region of the obex for recording in the tractus solitarius and in other regions recently shown to be sites of baroreceptor integration (7, 9). When movement of the brain stem hindered recording unit activity the animal was paralyzed with Syncurine, given a bilateral pneumothorax and artificially ventilated. End-expired CO₂ was monitored with an infrared analyzer and maintained at 4-6%. A digital computer (PDP-12) was used to generate poststimulus time histograms for correlating the sinus pressure change with unit activity. Each histogram was constructed from the summation of the cell activity occurring over 5-10 consecutive pressure cycles. Depending on the cell firing frequency, histogram bin widths (storage time) were set at 100-300 msec.

Results and Comments. With the periodic pressure signal of approximately 30 sec in

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² Ciba Pharmaceutical Co., Summit, NJ.

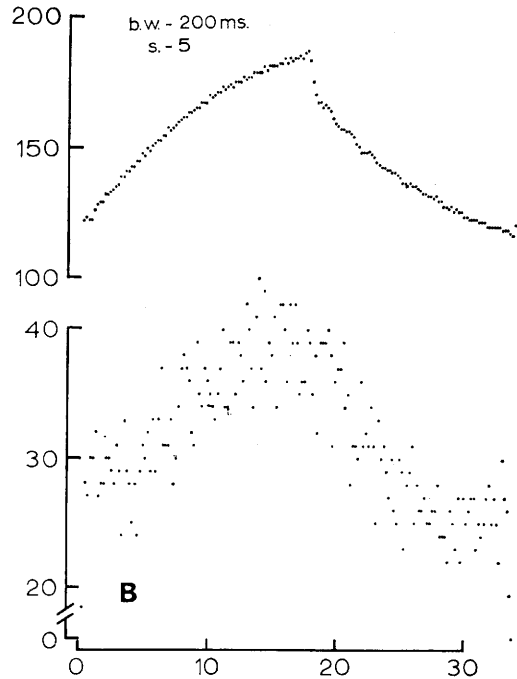
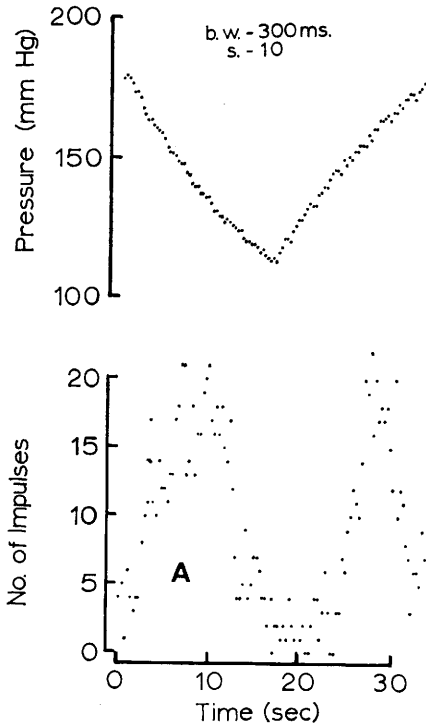
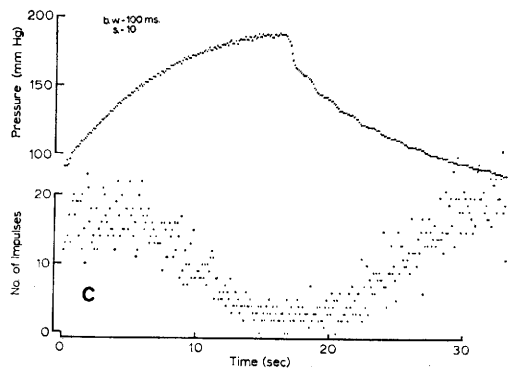


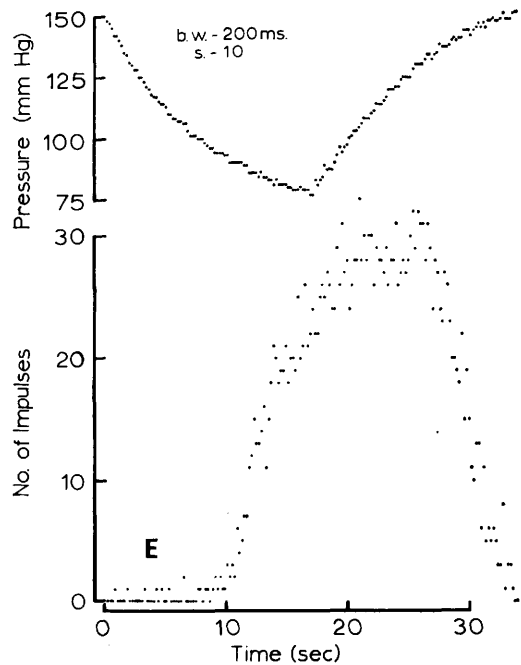
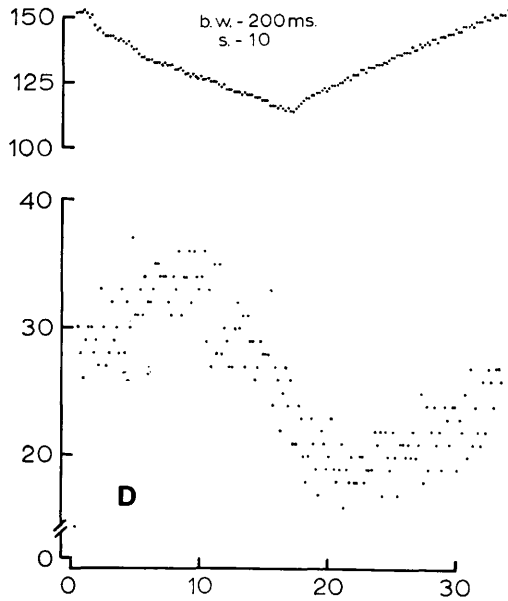
FIG. 1A-E. Representative poststimulus-time histograms for medullary cells responding to carotid sinus pressure changes. b.w. = bin width; s = number of pressure cycles used to construct the histogram.

duration employed in these initial studies two general classes of neural activity have been found. The first type consisted of cells which appeared to be independent of the direction of change and fire through a pressure range (Fig. 1A). These cells are sparsely represented in the medulla comprising only 2 of the 33 cells found in this study which respond to sinus pressure changes. There is no evidence that this type of behavior is a property of the sinus receptor since single fiber recordings from sinus nerve fibers show a maintained activity at high pressures (1). This pattern of activity (Fig. 1A) is most likely the result of a central integrative process, perhaps a central convergence of different activities similar to those shown in Fig. 1B and C.

The second group of cells was specifically directional-dependent, 20 cells increased their firing frequency as pressure was increased

(Fig. 1B) and 11 cells increased firing frequency as pressure was decreased (Fig. 1C). This group of cells, however, showed no consistent temporal relation between pressure and unit firing. For example, the maximal frequency of unit activity (Fig. 1B) or the minimum (Fig. 1C) may be coincident with the peak of the sinus pressure or there may be a time lag between peak pressure and maximum (or minimum) activity (Fig. 1D). The maximum time lag was 8 sec (Fig. 1D), which would be equivalent to a phase shift between pressure and unit firing of approx-





imately 90° . Changes in unit activity this far out of phase with sinus pressure is unexpected since it is much greater than the phase shift previously reported across the receptor (1, 2) and, in fact, is greater than the phase shift for the entire reflex arc (4). One possible explanation is that the periodic reflex changes in systemic pressure resulting from the periodic baroreceptor forcing is detected by other baroreceptors whose input to the brain stem controls the unit activity under study. This seems unlikely since input from the major baroreceptor areas has been eliminated in these experiments. An additional possibility is that the changes in unit activity may be related to changes in chemoreceptor stimulation during the pressure and flow variations occurring at the receptor region where pressure is being controlled. However, Biscoe, Bradley and Purves (11) report that chemoreceptor activity is independent of changes in flow and pressure in the range utilized for this study. Further description of the quantitative relationship between sinus pressure and unit activity should provide more information about the unexpected time lags.

The number of units found that correlated directly to the sinus pressure change (with or without a latency) was greater than cell activity inversely related to the pressure

change by approximately 2 to 1. This is not the result of a bias in the sampling as suggested by others (10) since the use of a periodic pressure waveform eliminates the necessity of a neuron being spontaneously active in order to be detected. Figure 1E illustrates a cell that is quiescent as pressure decreases but becomes active at a lower pressure. Most of the pressure waveforms used in this study lacked a constant rate of change of pressure throughout the cycle (Fig. 1E). As a consequence change in unit activity may be a function of the rate of change of pressure. For example, such a change may explain the onset of activity shown in Fig. 1E. The use of ramp pressure changes with various slopes in future experiments will clarify this point.

The location of cells influenced by sinus pressure changes in these experiments has not been limited to the classically defined tractus solitarius, but has been commonly found more ventral and lateral in the region between the paramedian reticular nucleus and nucleus ambiguus. This is in agreement with other work indicating that both monosynaptic and polysynaptic activity can be induced in this region by electrical stimulation of the

sinus nerve (6, 7, 10).

Summary. Medullary unit activity was recorded during application of a periodic pressure waveform to the carotid sinus of the cat. Poststimulus time histograms revealed twice as many cells showing increased activity to the pressure rise as those showing a decrease. Many cells showed surprisingly long latencies (up to 90° phase shift). In addition, two (of 33) cells increased activity through a pressure range independent of the direction of change. Cells were often found in the region between the paramedian reticular nucleus and the nucleus ambiguus as well as in the vicinity of tractus solitarius.

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