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## Cardiac sympathetic nerve activity during bradycardia induced by carotid chemoreceptor stimulation

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**Fisiologia.** — *Cardiac sympathetic nerve activity during bradycardia induced by carotid chemoreceptor stimulation* (*). Nota di PIER GIORGIO MONTAROLO, MAGDA PASSATORE e FEDERICO RASCHI, presentata (**) dal Corrisp. O. PINOTTI.

RIASSUNTO. — In animali a ventilazione controllata l'iniezione di NaCN attraverso l'arteria tiroidea provoca bradicardia, ipertensione ed aumento dell'attività nervosa respiratoria. In queste condizioni, le modificazioni del livello della pressione arteriosa sistemica mascherano l'effetto puro della stimolazione chemocettiva sul simpatico cardiaco. Per evitare che l'attività simpatica subisca modificazioni secondarie alla variazione dell'input barocettivo, è stato guidato artificialmente il battito cardiaco e mantenuta costante la pressione arteriosa sistemica. In queste condizioni la stimolazione dei chemocettori carotidei ha provocato in tutte le prove un netto aumento della scarica simpatica.

Questi dati dimostrano che la stimolazione dei chemocettori carotidei produce primariamente una generale, contemporanea attivazione dei centri bulbari, sia cardioeccitatori che cardioinibitori.

## INTRODUCTION

Carotid glomus chemoreceptor stimulation in thoracotomized or curarized and artificially ventilated animals enhances vagal cardioinhibitory and sympathetic vasomotor activity. The increase of cardiac vagal activity following such activation has been proved either by direct recording of the vagal efferent discharge to the heart [1, 2], or by comparing the effect of such stimulation on the heart rate before and after pharmacological block or section of the vagal supply [3–7]. A rise in vascular peripheral resistance due to sympathetic vasoconstrictor activation has been reported for all the major vascular districts [4, 7–11], although to a different extent.

As far as the response of the cardiac sympathetic nerve to carotid chemoreceptor stimulation is concerned, there is not much agreement in the literature. Here cardiac frequency can be used as an index of cardiac sympathetic output after section or chemical block of the vagus. Studies performed with this parameter have shown that the cardiac sympathetic exhibits either a decrease [4, 5, 12] or an increase [13] or no change [7]. Experiments carried out by direct recording of the cardiac sympathetic discharge also show the same contradictory results [14–16].

The behaviour of the cardiac sympathetic activity during the reflex bradycardia elicited by carotid glomus stimulation appears to be important not only in explaining the role played by the cardiac sympathetic efferents

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in this circumstance, but also as a matter of general interest. If, in fact, the cardioexcitatory and the cardioinhibitory centres behave in a reciprocal way, a decrease in the cardiac sympathetic activity should be expected. If, on the other hand, the cardiomotor and the vasomotor section of the sympathetic system behave as a unit, an increase in cardiac sympathetic discharge should occur.

Reinvestigation of this question seemed worthwhile. The cardiac sympathetic discharge was recorded while stimulating the carotid chemoreceptors in thoracotomized, artificially ventilated cats. At the end of each experiment, cardiocirculatory parameters were kept artificially constant to avoid secondary responses capable of interfering with the pure effect of chemoreceptor stimulation.

## Methods

The experiments were performed on 20 cats anaesthetized with urethane (250 mg/kg) and chloralose (30 mg/kg) given intravenously after the femoral vein had been cannulated under ether anaesthesia. These were thoracotomized along the midline and artificially ventilated. Tracheal $CO_2$ % was measured during the whole experiment by an infrared gas analyzer and ventilation adjusted to maintain the end-tidal $CO_2$ % at the control level.

Arterial blood pressure was measured using a variable inductance transducer connected to a catheter in the brachial artery.

Electric activity from the central cut ends of the inferior cardiac nerve and the phrenic nerve was recorded. Recordings were also taken from the peripheral cut end of the Hering nerve using the conventional " few fibres " technique. Monopolar or bipolar recordings were obtained with platinum electrodes connected through an RC-coupled amplifier to an oscilloscope or polygraph. These were then fed into an integrator.

When required, arterial blood pressure was kept constant by connecting the abdominal aorta (at the bifurcation) to a plastic tube leading to a reservoir containing buffered saline solution. The pressure in the reservoir was set at the same level as the mean blood pressure observed just before each trial. The heart was paced, when necessary, by electrical pulses at a suitable frequency, delivered through a couple of ring-shaped platinum electrodes fixed to the anterior wall of the right atrium. The carotid chemoreceptors were stimulated by a 50 μg/ml NaCN solution injected by an infusion pump through a cannulated thyroid artery.

## Results

The effects of carotid chemoreceptor stimulation on arterial blood pressure and on the efferent discharge of the cardiac sympathetic nerve were investigated in thoracotomized, artificially ventilated cats. The efferent discharge of the phrenic nerve was also recorded during each trial to make

sure that the NaCN solution injected through the thyroid artery really stimulated carotid chemoreceptors.

The injection of 0.2 ml NaCN solution usually enhanced phrenic nerve discharge and arterial blood pressure and decreased heart frequency. When an intense bradycardia developed, it counteracted the vasoconstrictory effect of chemoreceptor stimulation to such an extent that in some instances the

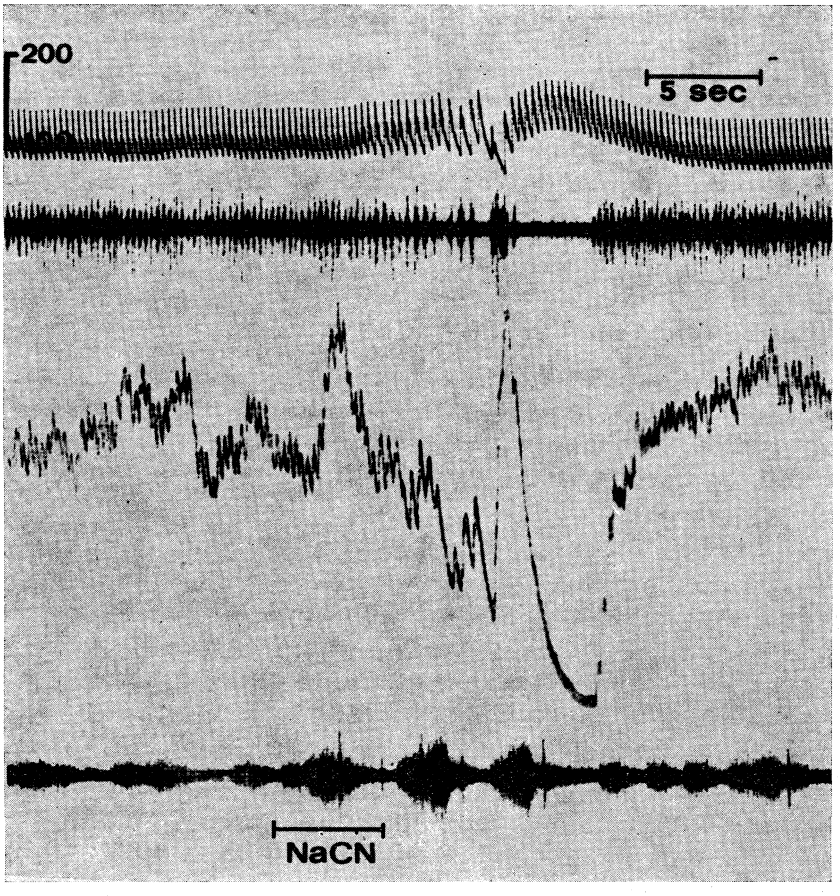


Fig. 1. – Effect of carotid chemoreceptor stimulation on cardiac sympathetic nerve discharge. Cat: urethane and chloralose anaesthesia, open chest, artificial ventilation. From top to bottom: blood pressure (calibration in mmHg), right cardiac sympathetic nerve activity, integrated discharge activity of the same nerve, phrenic activity. At the signal 0.2 ml of NaCN (50 μg/ml) were injected through the right thyroid artery.

level of arterial blood pressure did not change. Therefore the result of chemoreceptor stimulation on blood pressure differed from time to time depending on both the relative intensity and the duration of the bradycardic and vasoconstrictor effects.

Fig. 1 shows the typical effect of NaCN injection. Phrenic nerve activity increases, heart frequency decreases and blood pressure shows a complex

course, which is the resultant of the bradycardic and vasoconstrictor effects. The cardiac sympathetic discharge exhibits an abrupt increase, followed by a slow decrease synchronous with the rise in arterial blood pressure. A subsequent enhancement of sympathetic discharge occurs, together with a decrease in heart rate, to such an extent as to provoke a fall in the blood pressure. Eventually, since the bradycardic effect is now disappearing and the vasoconstrictor effect is still present, blood pressure increases and consequently the sympathetic discharge shows a complete inhibition phase.

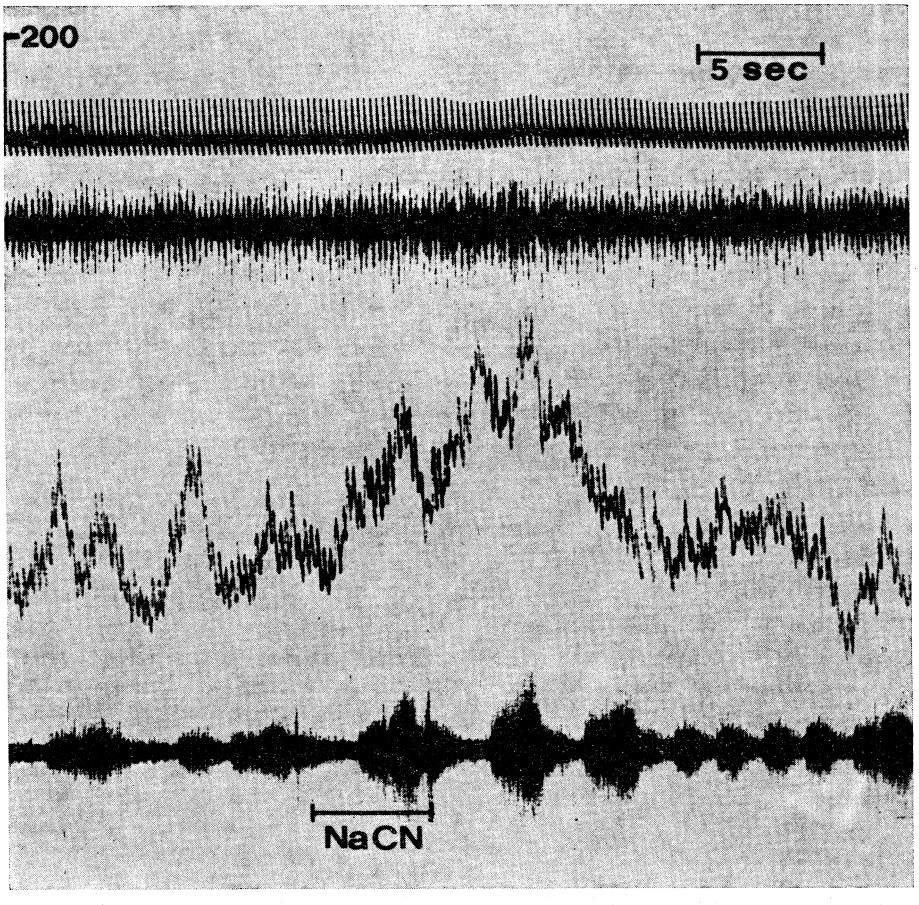


Fig. 2. - Effect of carotid chemoreceptor stimulation on cardiac sympathetic nerve discharge, blood pressure and heart frequency being kept artificially constant. Trial performed 5 minutes after fig. 1. Traces: same as in fig. 1.

Of course, in this kind of trial, sympathetic cardiac activity is dependent not only on chemoreceptor stimulation, but also on the modification of the baroreceptor afferents, due to fluctuations of arterial blood pressure level. To bring out the pure effect of chemoreceptor stimulation, in subsequent trials arterial blood pressure and heart frequency were kept constant (see methods). One of these trials is shown in fig. 2. The effectiveness of chemo-

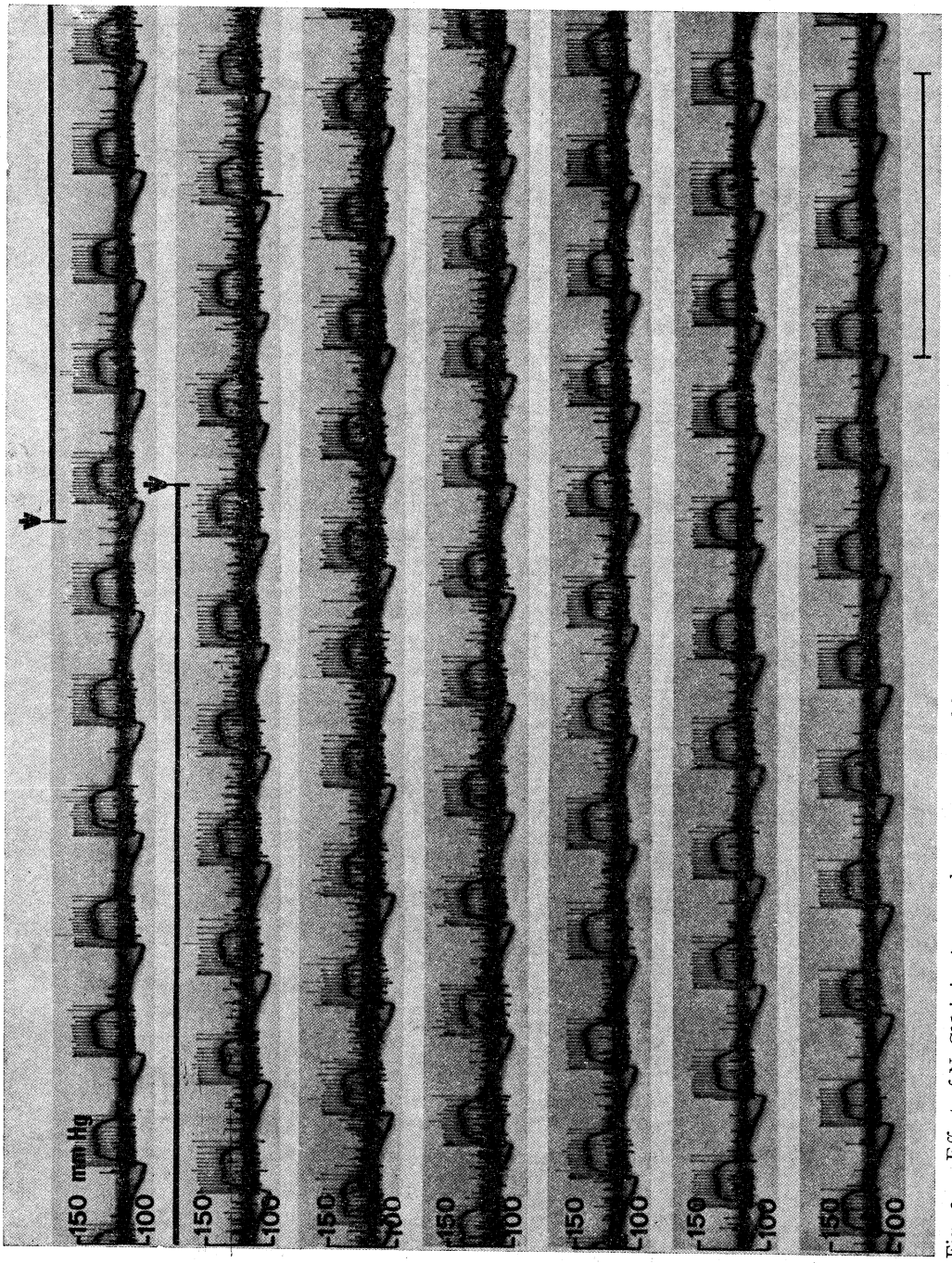


Fig. 3. – Effect of NaCN injection on chemoreceptor and baroreceptor activity of the Hering nerve. Cat: urethane and chloralose anaesthesia, open chest artificial ventilation. Continuous record: superimposed traces of blood pressure and electric activity of a preparation, made from the peripheral cut end of the right Hering nerve, containing a single baroreceptor fiber and few chemoreceptor ones. Between the arrow: NaCN injection (0,2 ml of a 50 μg/ml solution). Time: 1 second.

receptor stimulation was therefore proved by the increase in phrenic nerve discharge. In this condition of constant baroreceptor input, cardiac sympathetic discharge increased. This activation lasted approximately as long as the enhancement of the phrenic discharge.

At the end of each experiment, NaCN was again administered after cutting the Hering nerve. No effect on the cardiocirculatory and respiratory parameters was observed.

Another test was performed to make sure that NaCN did not modify the activity of carotid pressoreceptors either mechanically or by direct chemical action.

From the peripheral end of the Hering nerve, " few fibre " preparations were made, each containing a single baroreceptor unit and only a few chemoreceptor units. The NaCN injection provoked a great increase of chemoreceptor discharge, but on no occasion did it modify the pressoreceptor activity (fig. 3).

The results of the last two series of trials ruled out the possibility that the effects observed were due to the action of NaCN on the central nervous system or on other chemoreceptor areas or to modification of pressoreceptor discharge.

## Conclusions

Carotid chemoreceptor stimulation in thoracotomized artificially ventilated cats evokes the usual increase in phrenic discharge and enhancement of vasomotor sympathetic activity. A bradycardia lasting approximately as long as the increase in the phrenic discharge, and synchronous with it, was also observed. It is generally accepted [3–7] that such a decrease in heart frequency is mainly due to vagal activation.

In addition, in our experimental conditions, the cardiac sympathetic discharge exhibits an abrupt, short lasting increase followed by modifications that are synchronous and of opposite sign to those of the arterial blood pressure. We believe the first abrupt increase of the sympathetic discharge to be due to the pure effect of chemoreceptor stimulation; subsequently such an effect is hidden and counteracted by the pressoreceptor influence, every time there is a change in systemic arterial pressure.

The pure effect of carotid chemoreceptor stimulation on the cardiac sympathetic discharge has been made evident by keeping the arterial blood pressure and the heart frequency artificially constant. In these experimental conditions the cardiac sympathetic discharge shows a significant increase, lasting approximately the same time as the respiratory activation. Comparison of the results obtained in the two groups of trials shows that the phase of bradycardia observed in the first condition, and the increase in cardiac sympathetic discharge observed in the second, where both occurring with the same latency from the start of cyanide injection, and were synchronous with the increase of the phrenic discharge. This means that during carotid chemo-

receptor stimulation both the parasympathetic and the sympathetic supply to the heart can be activated at the same time.

These results account for the absence of a reciprocal effect exerted by the carotid chemoreceptor on the vagal and the sympathetic cardiac supply. They also prove that the vasomotor and the cardiomotor sections of the sympathetic system show a similar response to carotid chemoreceptor stimulation.

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