zinc[5] and calcospherulites[6] as quoted by Relkin[8] have been recognized. Quay[7] also stated that molybdenum, iodine, cobalt, aluminum, barium, chromium, titanium, silver, nickel, mercury, strontium and lead are worthy of analysis in the pineal organ. The results of the present analysis revealed that the pineal organ of the freshwater teleost, *M. vittatus* definitely contains chromium-nickel, chromium-phosphide, copper, aluminum-copper and zinc.

Histochemical studies suggest a variable presence of carbohydrates, proteins, lipids and mucoid substances in pineal organs from the same fish, containing many amino ($-NH_2$), carboxyl ($-COOH$), hydroxyl ($-OH$), phosphonyl ($-PO_3H_2$), sulfhydryl ($-SH$) and thiol groups[11]. As in most of the mammalian species it is possible that these histochemical fractions/ligands of neurosecretory activity within the fish pineal provide binding sites for these inorganic constituents. It is expected that the results of the present investigation will further induce pinealogists to elucidate the probable role of these elements in the metabolic fate of the pineal complex.

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Effects of carotid sinus nerve stimulation on respiratory sinus arrhythmia and respiratory blood pressure waves of the dog

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Summary. The effect on the amplitudes of RSA and RBPW of the time of the stimulus in the cardiac cycle, and also of continuous stimulation were studied. When the stimulus train was applied near peak systole the amplitudes of RSA and RBPW decreased. Stimulation in late systole increased both RSA and RBPW. Continuous stimulation did not exert any effects on RSA and RBPW.
Key words. Carotid sinus nerve stimulation (CSNS), R wave-triggered; respiratory sinus arrhythmia (RSA); respiratory blood pressure waves (RBPW); cardio-respiratory coordination.

The heart is under the continuous but changing influence of efferent sympathetic and parasympathetic activity[1]. In addition to various forms of peripheral and central mechanisms, this efferent activity is very efficiently influenced by baro- and chemoreceptors[2] as well as by respiratory rhythm[3,4]. The central interactions of these input into the 'common brain stem system'[5] affect sympathetic and parasympathetic activity usually in opposite directions. Consequences of such interaction are the respiratory cycle-related sensitivity of the baroreceptor reflex[4,6-8], the RSA[3,4,9,10] and the RBPW[3,8,11,12]. The effectiveness of the baroreceptor reflex is dependent on the position of the stimulus in the cardiac cycle, too[13,14]. Stimulation of the medullary pressor[15], the depressor[16] areas, the aortic depressor[17] and the carotid sinus nerve[18] produces a very pronounced effect on the efferent sympathetic activity in response to stimuli applied in the early systole.

The R wave-triggered CSNS during this cardiac phase causes the RBPW to vanish[19].

To date, however, no systematic studies have been carried out on RSA and RBPW responses with respect to stimulus position in the cardiac cycle. Therefore, we studied the influence of CSNS at various time intervals after the R wave of the ECG on the amplitudes of RSA and RBPW. It was the aim of this study to obtain new findings on interactions and interconnections between the respiratory and rapidly-reacting cardiovascular control systems.

Material and methods. Experiments were done on 13 adult spontaneously breathing dogs (11–34 kg) of either sex, anesthetized with ethyl urethane (375 mg/kg, i.m.) following premedication with morphine sulfate (15 mg/kg). Supplementary urethane was given by i.v. drip at a rate of 62.5 mg/kg/h. The carotid sinus nerves (CSN) were identified by recording their pulsatile nerve activity, and placed on bipolar platinum electrodes in a pool of mineral oil for stimulation.

The intact CSN was stimulated with short trains of impulses given at various times in the cardiac cycle. Each train consisted of five square-wave impulses inserted 0–210 ms after the R wave of the ECG. The impulse duration was 0.5–1 ms and the impulse spacing 25 ms. Identical parameters were used for continuous stimulation. The stimulating current was adjusted in such a way that the CSN depressor response would be 2 kPa (usually 0.1–3 mA). Current values and the impulse form were monitored on a cathode-ray oscilloscope. Breathing was enhanced only to a minor extent if at all, by the above stimulus parameters. Each stimulation series for the various delay settings lasted about 2 min and was followed by a recovery period of 2 min.

Polyethylene catheters were inserted into the femoral artery to record arterial pressure, and into the femoral vein for administration of drugs.

Arterial pressure, ECG and the beat-by-beat heart rate were recorded by means of a multichannel oscillographic recorder. The ECG potentials were used to operate a linear instantaneous rate meter, the function of which was to produce an output voltage whose amplitude was at all times inversely proportional to the time interval between the last two input impulses, i.e. proportional to the instantaneous rate (fig. 1). To evaluate the relative influence of the respiration on heart rate and blood pressure, the indexes $\triangle RSA = RSA_{st} - RSA_o$ and $\triangle RBPW = RBPW_{st} - RBPW_o$ (o = prior to, st = during stimulation) where $RSA = HR_{MAX} - HR_{MIN}$ and $RBPW = BP_{MAX} - BP_{MIN}$ (MAX = high, and MIN = low value during respiratory cycle), were calculated.

Statistical evaluation of the findings was made by use of the concordance coefficient (Kendall) with a given $p < 0.001$.

Results. The results presented here were obtained on dogs the mean heart rate of which was 60–80 beats/min and the respiration rate 6–16 cycles/min. The CSNS reduced the mean heart rate by 5–10 beats/min. The amplitudes of RSA and RBPW were 15.4±2.3 (SE) beats/min and 3.25±0.47 (SE) kPa, respectively. A record of a representative experiment is shown in figure 1. The respiratory heart rate variation (RSA_o) without CSNS is reflected by panel A. Stimuli applied 30 ms after the R wave caused the respiratory cycle-related variation (RSA_{st}) to vanish (panel B). When the delay was increased to 110 ms the HR modulation was again evident (panel C). The RSA was, after stimulation by 140 ms delayed trains, even greater when compared to the non-stimulated state (panel D). In panel E the stimulus was applied 210 ms after the R wave (left). A sudden decrease in delay time to 30 ms (arrowed) caused the RSA to disappear (panel E, right). The findings obtained for 11 dogs are summarized in figure 2. In agreement with the results shown in figure 1 it is seen that, when the stimulus train was applied close to the beginning of, or near, the peak systole, the RSA was diminished ($\triangle RSA < 0$) whereas application of the stimulus during late systole respiratory cycle-related variation caused the HR to rise ($\triangle RSA > 0$). The influence of CSNS on the RBPW was qualitatively equal to that seen on RSA (fig. 1F and fig. 2).

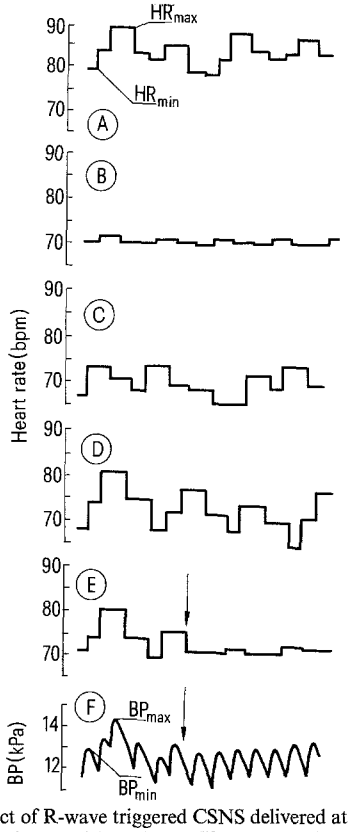

Figure 1. Effect of R-wave triggered CSNS delivered at different times in the cardiac cycle on RSA and RBPW. A: control; B–E: effect on the beat-by-beat HR occurring at the following delays from R wave of ECG: B, 30 ms; C, 110 ms; D, 140 ms; E, 210 ms (left) and 30 ms (right); F: arterial blood pressure BP (delays same as in panel E). Arrow indicates point of changes in delay. Records retouched.

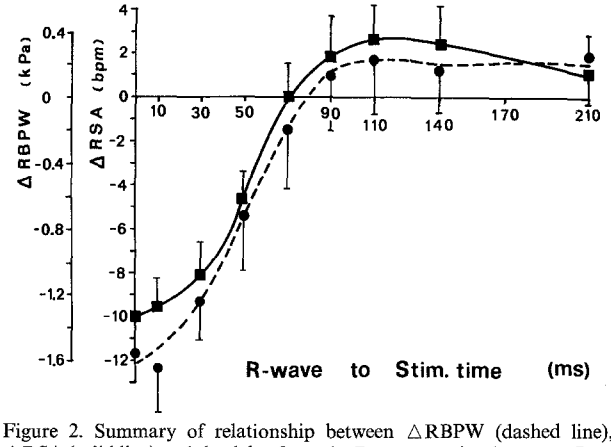

Figure 2. Summary of relationship between ΔRBPW (dashed line), ΔRSA (solid line) and the delay from the R-wave to stimulus onset. Bars show 1 SEM.

Continual stimulation diminished both the mean blood pressure and the mean heart rate. However, none of the experiments revealed any statistically significant influence on the amplitudes of RSA and RBPW.

Discussion. The heart is under the permanent influence of both sympathetic and parasympathetic activity[1]. This activity is powerfully governed by the afferent activity of the baroreceptors[1, 2, 20]. It should, therefore, be initially assumed that both parts of the autonomic nervous system would contribute to the occurrence of RSA. This assumption is favored by findings showing that both the sympathetic[8, 15, 21, 22] and parasympathetic[5, 6, 20, 23, 24] efferent activity exhibits a respiratory modulation. The parasympathetic (vagal) activity is inhibited during inspiration and the sympathetic activity is increased during this phase of respiration. It is reasonable to suggest that the RSA is substantially induced by the parasympathetic influence on the heart[3, 9, 10, 22]. Variations in peripheral resistance are an essential cause of the occurrence of RBPW[8, 12]. It is, therefore, reasonable to assume that a decrease in respiratory-related sympathetic activity would alter the RBPW in the same direction[11].

The sympathetic nervous discharge was inhibited in a pronounced way by a single stimulus delivered to a central baroreceptor pathway[16] and the aortic depressor nerve[17] during the early phases of the cardiac cycle. These findings can account for the decrease in amplitude of RBPW as induced by stimuli having a short delay after the R wave (figs 1, 2 and Bilgutay et al.[19]).

In the past, special investigations have been carried out into the relationship between RBPW and RSA. It was found that the RSA disappeared at almost the same time as did the RBPW and the cervical sympathetic activity vanished[11] (fig. 1).

To interpret the present results we have postulated a neuronal structure in the brain stem receiving afferents from presystolic active cardiac receptors and the carotid sinus nerve. Interneurones of this network are supposed to have a disfacilitating effect on the interaction between central inspiratory activity and the preganglionic sympathetic and parasympathetic brain stem neurones. CSNS during the early systole increases the activity of these interneurones and, consequently, the inhibition of inspiratory influence on the efferent sympathetic and parasympathetic activity. Therefore, we can observe a reduction or disappearance of RSA and RBPW as induced by CSNS during the early systole. Timing of inputs to the common brain stem system in the early systole is not very likely to occur with continual CSNS. Therefore, we noted a decrease in mean HR and RBPW, whereas little or not change in RSA and RBPW was observed.

This observation supports the suggestion that 1) the rhythmic fluctuations in blood pressure, heart rate, cervical sympathetic and parasympathetic cardiac activity have a common central origin and 2) the long-term and rhythmic short-term fluctuations may be initiated in different regions[5, 11, 17]

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The influence of hypertension upon the normal cardiovascular responses to hemorrhagic hypotension and shock[1]

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Summary. The data suggest that rats genetically inbred to be hypertensive (SHR) are less able to compensate for hemorrhage and shock than their normotensive controls (WKY). Two reasons for this genetic dysfunction are: 1) SHRs seem to depend more on innervated alpha 1 than noninnervated alpha 2 adrenoreceptors for vasoconstriction; and 2) the vascular smooth muscle hypertrophy noted in SHRs may interfere with effective vasoconstriction.
Key words. Hypertension; hypotension; vascular compensation; vascular decompensation; hemorrhage; shock.

The determination of the pretrauma cardiovascular state of patients admitted into a trauma unit is of paramount importance before rational diagnosis and therapy can be instituted. For example, a chronically hypertensive patient may well be in a state of cardiovascular shock even though his arterial pressure is within the normal range for a normotensive individual. If the physician is not aware of the preexisting hypertension, he may not know if his patient's normal cardiovascular compensatory response to trauma is compromised. This situation would be made even more complex if the patient were undergoing antihypertensive drug therapy which would also interfere with the normal mechanisms used by the body to return blood pressure to normal. The purpose of this study, therefore, was to examine the hypothesis that unmedicated spontaneously hypertensive rats (SHR), which have been shown to be an appropriate model for human hypertension[2], are less able to compensate for severe hemorrhage than genetically matched normotensive rats (WKY).

Methods. 10 rat pairs were evaluated in these studies. One of the rats in each pair was genetically inbred to be spontaneously hypertensive (SHR), while its control was a genetically matched normotensive Wistar Kyoto rat (WKY). The weight of the WKYs averaged 263 ± 14 g compared to 298 ± 14 g for the SHRs. All rats were acquired from the Charles River Breeding Laboratories Inc. of Wilmington, Massachusetts. Following anesthetic induction by i.p. administration of 35 mg/kg sodium pentobarbital[3], the right femoral vein and right carotid arteries were cannulated with PE 10 and PE 60 tubing respectively. Supplemental anesthesia and heparin sodium (10 mg/kg) were administered through the venous cannulae, while mean arterial pressure (MAP) and controlled hemorrhage were accomplished through the arterial cannulae. To insure an adequate airway a short (2 cm) PE 240 cannula was inserted into the trachea.

The following is a brief description of the hemorrhage protocol used in these studies. For a more detailed description including a diagram of the experimental apparatus, the reader is directed to a prior publication[4]. The arterial cannula of each rat in a pair (SHR and WKY) was connected to a T-tube. One arm of the T-tube was attached to a P23DB Statham pressure transducer, while the 2nd arm was afixed to the bottom of a calibrated 25-ml buret. The two burets, one for each rat in the pair, were connected by tubing and another T-tube in such a manner that a well controlled back pressure could be applied equally to the fluid surfaces in both burets. The back pressure exerted upon the fluid could be precisely controlled using a syringe and pressure regulating clamp[4]. The pressure on the surface of the fluid in the buret in contact with the SHR was then set at the inherent pressure of the WKY control, and the stopcock between the buret and SHR opened allowing blood to move into the buret (see fig.). Normally 3–5 min were required for the pressure in the SHR to fall to the WKY pressure. Once the MAPs were equalized, both buret pressures were set at 60 mm Hg for 15 min, then 30 mm Hg where they were maintained by carefully adjusting the syringe and pressure regulating clamp. The movement of blood from the rats into the burets represented a total body cardiovascular compensatory adjustment to the desired level of hypotension. The maximum blood volume removed divided by b.wt was consid-

	WKYs	SHRs
MAP (mm Hg)	123 ± 4	187 ± 3**
Comp. vol. (ml/kg)	32.1 ± 6	24.7 ± 1.4**
Comp. vol./p (ml·mm Hg/kg)	0.349 ± 0.02	0.154 ± 0.007**
Comp. time (min)	98 ± 6	77 ± 9*

MAP = mean arterial pressure. Comp. vol. = maximum shed blood volume at 30 mm Hg MAP. Comp. vol./p = maximum shed blood volume at 30 mm Hg at MAP normalized for pressure drop. Comp. time = time from onset of hemorrhage to maximum blood loss at 30 mm Hg MAP. Values are expressed as mean ± 1 SEM. * indicates statistical difference (WKYs vs SHRs) at $p < 0.05$; and ** indicates statistical difference at $p < 0.01$.