tioned in the introduction above. The recorded mean integrated potential for flapping flight was approximately 500 mV, against about 90 mV for gliding flight of the unloaded bird. Bearing in mind that gliding flight primarily involves isometric contraction (the energy turnover in isometric contraction is less than in isotonic contraction[6]) and that during flapping flight the pectoral muscles are only activated during the down beat, the magnitude of the potentials are in accord with the measured oxygen consumption for these 2 types of flight.

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## Intravital measurement of arteriolar pressure and tangential wall stress in normotensive and spontaneously hypertensive rats (established hypertension)

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*Summary.* Under intravital conditions, intravascular pressures of mesenteric resistance vessels were measured in normotensive (NR, mean blood pressure 92 mm Hg) and spontaneously hypertensive rats (SHR, 161 mm Hg) being elevated over all by about 75%; the tangential wall stress ($\sigma = p \cdot r/h$; p represents the intravascular pressure and r/h the ratio of internal radius to wall thickness) was found to be increased by 120–140% in SHR.

The tangential (circumferential) wall stress as a basic haemodynamic parameter[2] was recently determined in cat mesentery vascular bed by direct measurement of intravascular pressures[3,4]. For normotensive control rats (NR) and spontaneously hypertensive animals (SHR), intravital pressure measurements have been performed in the microvasculature of the cremasteric muscle[5]. These measurements could technically be done only in young animals, and therefore the SHR studied were prehypertensive and their blood pressure was only slightly elevated (116 mm Hg). By using the mesentery microvascular bed, measurements in older SHR suffering from established hypertension (161 mm Hg) could be performed[6]. The studies presented attempt to answer the question whether intravascular pressures in the smallest precapillary arterioles would be reduced to a normal level, perhaps for the sake of protecting the capillary bed. It was of further interest to study the effect of pressure elevation, 'rarification of resistance vessels'[6] and wall hypertrophy[7] on the tangential wall stress in precapillary arterioles of spontaneously hypertensive rats.

*Materials and methods.* The experiments were performed in 16–20-week-old sex-matched Kyoto-Wistar rats of the Okamoto-Aoki strain. The SHR had an average b.wt of 209±10 g and a systemic blood pressure measured in the carotid artery of 161±4 mm Hg, the NR reached 225±7 g and 92±9 mm Hg, respectively. The animals were anaesthetized with chloralose-urethane (10 or 50 mg/ml 0.9% NaCl/100 g b.wt). The mesentery preparation was suffused with modified Tyrode's solution containing 1% dextran[8]. Using dextran in the suffusing solution, we could not see any anaphylactoid response in the rat microcirculation like vasodilatation, elevation of red cell velocity or formation of oedema, which is reported for intravascular application of dextran[9].

The preparation was allowed to stabilize for about 30 min after surgery. The tissue was transilluminated by a 150 W Halogen light source and simultaneously displayed on a video monitor and on video tape. Inside vessel diameters were measured on line by the video-angiometer[10] or by using a ruler (optico-electronic magnification × 1100). Using intravital microscopic techniques, the in vivo determination of the real outer diameters of microvessels is actually difficult or impossible. Therefore, the muscular media layer of the arterial wall[11] was taken, representing the most relevant structure of the vessel wall, especially of the hypertrophic wall in hypertensive animals[7].

Pressures in microvessels were measured by using a modified servo-null system after Wiederhielm. We used micropipets with an outer tip diameter of 0.3–3.0 µm. Besides microscopic observation, the criterion for a successful measurement of intravascular pressures was a corresponding systolic-diastolic amplitude of microvascular and systemic pressures. Results obtained under an unsteady level of blood pressure were discarded. The arterioles to be measured were classified according to their branching order: the precapillary arterioles (A 4) were fed by terminal arterioles (A 3), which arose from large arterioles (A 2).

*Results and discussion.* Figure 1 shows averaged data of diameters and pressures in microvessels. The mean values of systemic pressure for NR was 92 mm Hg and for SHR 161 mm Hg representing a difference of 75%. The mean arteriolar pressure (i.e. in A 4, A 3 and A 2 together) ranged from 34 mm Hg in NR to 55 mm Hg in SHR, being a difference of 61%. This confirms the findings of pressure distribution in the cat mesentery microvascular bed, where a correlation between systemic and microvascular pressures in arterioles below 60 µm inner diameter could not be found[12]. Compared with the data obtained in prehypertensive SHR[5], our measurements, performed in SHR during the established phase of hypertension, showed pressures even twice as high. The mean blood pressure of the NR, however, differed only by 3% under the same anaesthesia. Consequently, hypertension in its established phase led to a distinct elevation of the precapillary pressures. Referring to this, the observation of a decreased number of precapillary arterioles in SHR should be taken into account, which is shown for prehypertensive SHR[13] as well as for SHR with established hypertension[14]. Measuring tangential wall stress in these particular arterioles further confirms this aspect.

As the table shows, tangential wall stress is increased in both, NR and SHR, for vessels with increasing branching order. This agrees with values of cat mesenteric arterioles (with larger diameters as corresponding rat vessels), where an optimum range of $1\text{-}1.5\times10^5$ dyn/cm$^2$ is reported[4]. Our in vivo findings in these resistance vessels are not consistent with values computed for the isolated rat tail artery. We should therefore, like to underline the authors' remark that 'the tail artery of the rat is a conduit artery rather than a resistance vessel'[15], which might explain the differences seen.

For calculating our data, we used the equation $\sigma = p \cdot r/h$, where p is the intravascular pressure and r/h represents the ratio of internal radius to wall thickness. In SHR in comparison to NR, the intravascular pressure is elevated (A 2+17%, A 3+122%, A 4+84%) as the internal radius is (A 2+13%, A 3+35%, A 4+13%); wall thickness, however, is only increased in terminal arterioles (A 2−33%, A 3+30%, A 4−18%). The cause for the elevated wall stress in A 2 and A 4 of SHR can be seen partly in a pressure elevation, partly in a reduction of wall thickness; the high wall stress in SHR in terminal arterioles, however, is mainly caused by the elevated pressure; internal radius and wall thickness are both increased to about the same value. The high wall stress found in A 3 can be explained with the observation that precapillary pressure is mainly brought down in microvessels of this type[12,16].

Our findings as well as those of others using microcirculatory measuring techniques[5,11,13,15], are not consistant with the hypothesis that a thickened media of small arterioles in SHR encroaches upon the lumen of the precapillary vessels, which would protect the capillary level from arterial pressure rise in SHR[17]. From our results, we expect that in SHR flow resistance is mainly raised more upstream, i.e. in vessels with an inner diameter of more than 30 µm, for which an increase of wall thickness encroaching upon the vessel lumen is tendentially shown by in vitro experiments[18].

The elevated pressure in real precapillary vessels (about 20 mm Hg), however, can obviously be tolerated by the spontaneous hypertensive organism. This had also been shown for prehypertensive SHR. Their intravascular pressures are increased compared to NR in comparable precapillary vessels (+43%) as in capillaries (+16%) without the formation of oedema etc.[5]. Therefore it seems not to be necessary to postulate a higher pressure reduction in the microvasculature for protection of the capillary system. As a consequence of both, elevated intravascular pressure and tangential wall stress in the microcirculation, one should take into account our findings of an over-all elevated lymph flow rate of SHR measured in the intestinal main lymph duct (SHR:9.4 µl/min vs NR:5.8 µl/min)[19], which might suggest a higher microcirculatory filtration rate in SHR.

In cat mesentery, pressures in different capillaries fed by the same arteriole ranged from 41 to 20 mm Hg indicating that 'pressure-related phenomena in the microcirculation' depend on the 'anatomical and physical features characteristic of individual tissues'[12]. Our intravital investigations referring to vessel dimensions led to the same conclusion for rats. Fig. 2 shows that tangential wall stress differs distinctly in vessels with the same inside diameter: for a diameter of 20 µm wall stress ranges from 1.4 to $3.6\times10^5$ dyn/cm$^2$.

The following 2 examples may further outline the variability of wall stress values depending on certain haemodynamic conditions: Tangential wall stress, measured in an A 4 near the branching point of A 3 (⌀10.0 µm), reached a value of $1.36\times10^5$ dyn/cm$^2$; further downstream near the subsequent vessel branch (⌀ 8.7 µm), a stress value was measured of only $0.80\times10^5$ dyn/cm$^2$.

As a 2nd example, the data obtained in a thorough-fare channel is presented: The arteriolar side showed an inner diameter of 19.3 µm with $\sigma = 0.78\times10^5$ dyn/cm$^2$, as compared to its venular side ⌀ = 10 µm with $\sigma = 0.54\times10^5$ dyn/cm$^2$. Naturally, wall stress as a function of intravascular

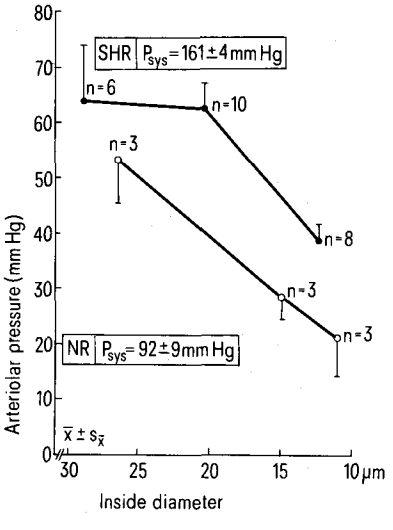


Fig. 1. Comparison of precapillary pressures related to inside vessel diameters in normotensive (NR) and spontaneously hypertensive rats (SHR). The arteriolar pressures, measured in SHR are significantly increased as compared to NR. Reading from left to right, the points and triangles represent values of large arterioles (A 2), terminal arterioles (A 3) and precapillary arterioles (A 4). The corresponding arteriolar diameters are smaller in NR than in SHR. $P_{sys}$ = systemic mean blood pressure.

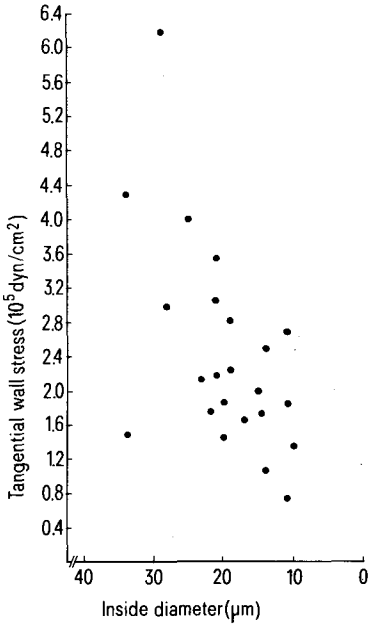


Fig. 2. Tangential wall stress of individual arterioles with different inside diameters in SHR. The computed correlation coefficient ranges to 0.58 indicating a weak correlation between these 2 parameters. It also points to the variability of intravascular pressure and vessel wall thickness.

pressure is elevated in old SHR (41 weeks old) with high systemic pressure (172 mm Hg) as compared to younger ones given in the table: the wall stress was increased to about 32% in A3 of the old animals (⌀ 17.7±0.2 µm, $\sigma = 2.98 \pm 0.14 \times 10^5$ dyn/cm$^2$).

Obviously, the elevated precapillary pressure and the increased tangential wall stress in hypertensive animals indicate an insufficiently increased flow resistance in series; in addition, the elevation of the flow resistance in spontaneous hypertension is also caused by an increased parallel resistance[20]. The findings of a decrease in the number of resistance vessels (rarification) in spontaneous hypertension[13,14] could furthermore favour our conclusion.

Intravitally measured tangential wall stress in arterioles of different branching order in normotensive (NR) and spontaneously hypertensive rats (SHR)

| | A2 | A3 | A4 |
|---|---|---|---|
| NR | 1.66±0.43 | 0.94±0.05 | 0.76±0.27 |
| SHR | 3.80±0.78 | 2.26±0.21 | 1.69±0.21 |
| Δ% | +129% | +140% | +122% |

The data are given as mean values ± SEM (× 10$^5$ dyn/cm$^2$); the percent differences are added.

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## Action of glutamic acid and of some glutamate analogues on the molluscan central neurones

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*Sumary.* The effects of L-glutamic acid and of some glutamate analogues have been studied on the central nervous system of the snail *Heobania vermiculata*, using conventional electrophysiological techniques. The glutamate H-response had the mean equilibrium value of −(57±4) mV and was associated with a $Cl^-$ conductance change. The D-response to glutamate application showed an involvement of sodium ions. Aspartate was agonist of glutamate action and displayed similar equilibrium value of the H-response, whereas quisqualate H-response was 'non-invertible'.

L-glutamic acid is probably an excitatory transmitter in the mammalian central nervous system[2], and in crustaceans[3] and insects[4] it is suggested as chemical transmitter at many excitatory neuromuscular junctions. In molluscs, L-glutamic acid was found to evoke depolarizing and hyperpolarizing potentials in the nerve cells[5-7]. The present report is a study of some characteristics of glutamate receptors on ganglion cells in the land snail *Heobania vermiculata* (Helicidae).

*Methods.* The experiments were carried out in the left parietal, visceral and right parietal ganglia. The techniques have been described previously[8]. Intracellular records were obtained from giant nerve cells of ganglion dorsal surface with microelectrodes filled with $K^+$-acetate 1.5 M; Snail-Ringer: NaCl, 75 mM; KCl, 5 mM; MgCl, 15 mM; $CaCl_2$, 10 mM; Tris/HCl, 5 mM; pH, 7.8.

Glutamate and its analogues (D-glutamate, L-aspartate, L-α-Kainate, DL-homocysteate, N-methyl-DL-aspartate, L-quisqualate), were applied locally to a given cell by iontophoresis from a single micropipette filled with a concentrated solution of Na-glutamate or Na-glutamate analogue (0.2 M, pH 7.3).

*Results and discussion.* A depolarizing or hyperpolarizing potential was observed when glutamate ions were applied iontophoretically to the soma membrane of some nerve cells. A weaker response to glutamate was observed if the glutamate pulse was repeated a few sec later, presumably because of receptor desensitization. The latency, onset and time course of the glutamate response potential were variable, even when the glutamate was applied to different regions of the same cell. This variability may be due to the interposition of non-neural elements between the probe and the active membrane, or to non-uniform sensitivity to glutamate over the cell body surface. In addition it was not rare to observe a biphasic response to glutamate application.

The mean value of the equilibrium potential (±SD) for the H-response (hyperpolarizing potential), determined by introducing a 2nd electrode in 5 different somata, was (57±4) mV. The H-response to glutamate had reversed 6–8 min after $Cl^-$-free saline ($Cl^-$ substituted by the impermeant sulphate anion) entered the bath.

Over a period of 40–60 min, the new 'depolarizing' H-response declined in amplitude and disappeared completely. Reapplication of normal saline to preparation caused the reappearance of the H-response. No significative varia-