within the ranges which have been used hitherto[5,7]. The calculations depend on current estimates of the free metal ion concentrations in plasma. Such estimates can be obtained for the transition metal ions from a knowledge of the dissociation constants of the predominant metal protein complexes in the biofluid. The value for calcium can be measured directly using ion sensitive electrodes. The excellent agreement between the theoretical and practical values for this metal ion reflects this. On the other hand, the greatest uncertainty is associated with magnesium because neither the free ion concentration in plasma nor the relevant metal binding constants are well characterized.

These findings imply that the noxious effect of TPN on trace element metabolism can be minimized by a suitable choice of fluid composition, and suggest that transition metal supplements can be calculated to suit the particular mixture being administered.

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Cardiac hypertrophy accelerated by left cervical sympathectomy in spontaneously hypertensive rats[1]

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Summary. Cardiac hypertrophy in spontaneously hypertensive rats was accelerated by denervation of the left cervical sympathetic ganglia. Supersensitivity due to denervation may also exist in cardiac muscles.

Cardiac hypertrophy is usually the consequence of an increased circulatory resistance. Myogenic and neurogenic factors may participate in cardiac hypertrophy. With regard to the neurogenic factor, it is a relevant question how the nervous control of heart muscle may influence cardiac hypertrophy. In 1939, Cannon[3] reviewed a law of denervation. According to this review, a supersensitivity to chemical and physical stimuli is developed in the denervated muscles. The present experiments were performed to elucidate whether cardiac hypertrophy was accelerated by denervation.

Male spontaneously hypertensive rats (SHR) from the Okamoto strain, kept in our laboratory for more than 25 generations, were used for these experiments. 10 male SHR, weighing 210–300 g, were used at the age of 3.5 months, and 11 male age-matched Wistar-Kyoto (WKR), weighing 225–280 g, were employed at the age of 3.5 months. In 6 of the SHRs and 6 of the WKRs, the left superior and middle cervical ganglia including the sympathetic trunk were removed under ether anesthesia. Other SHRs and WKRs as control groups underwent sham operations. 8 weeks after denervation, the heart was removed under ether anesthesia. The tissue was immediately fixed by the vascular perfusion method for electron microscopic examination, using cold 2.5% glutaraldehyde buffered with 2% paraformaldehyde at a pH of 7.4. Some pieces of the tissue were refixed with 10% formalin for light microscopic examination. Electrocardiograms and blood pressure were measured every 2 weeks.

Although blood pressure in the non-denervated SHR was significantly elevated, an appreciable elevation of blood pressure was not seen in the denervated SHR and both groups of WKR. 8 weeks after denervation the electrocardiogram was markedly changed: A leftward deviation of the electrical axis was observed in all denervated SHR and 3 of the denervated WKR. The leftward deviation was not necessarily related to the elevation of blood pressure. The QRS duration in lead II became wide only in the denervated SHR ($p < 0.02$). The PQ interval was prolonged in denervated groups of SHR and WKR, an effect which was statistically significant ($p < 0.01$). The amplitude of the QRS wave in $R_I + S_{III}$ and R_{aVL} decreased 8 weeks after the

Cell diameters at various portions of left and right ventricles

	Left ventricle Anterior	Lateral	Posterior	Septum	Right ventricle
Spontaneously hypertensive rats (SHR)					
Denervation	12.58±2.46* (n:80)	13.02±2.72* (n:80)	12.83±2.22** (n:80)	12.28±2.08* (n:80)	9.61±2.35 (n:80)
Sham-operated	11.75±2.21 (n:60)	12.06±2.25 (n:60)	11.77±2.13 (n:60)	11.49±1.85 (n:60)	9.50±1.70 (n:60)
Wistar-Kyoto rat (WKR)					
Denervation	9.79±1.90 (n:90)	10.26±1.81 (n:90)	10.15±1.66 (n:90)	9.93±1.85 (n:90)	9.10±1.70 (n:90)
Sham-operated	9.52±2.00 (n:60)	9.74±2.10 (n:60)	9.99±1.91 (n:59)	9.53±1.53 (n:60)	8.78±1.62 (n:60)

The values are mean±SD (μm); * $p < 0.05$ by t-test; ** $p < 0.005$ by t-test.

operation in all groups. The amplitude of the summation of S waves in the right precordial lead and R waves in the left precordial lead increased significantly in all denervated SHR ($p < 0.05$). In contrast, a decreased amplitude was seen in the same summation in the control groups. The ratio of heart weight to b.wt in SHR was larger than that in WKR. However, there were no significant differences between the denervated and the non-denervated groups in SHR and WKR.

Histologically, the cell diameters in the anterior, lateral and posterior portions of the left ventricle, and also in septum and right ventricle were measured at the cross position of the nuclei. The diameters of all portions of left ventricle and septum in the denervated SHR were significantly larger than those in the non-denervated SHR (table). Electron microscopic findings showed a decrease in glycogen storage, swelling of mitochondria, disruption of cristae and edematous changes in the myocardial cells. These results suggest that cardiac hypertrophy in SHR is enhanced by denervation of the heart despite the lack of elevation of blood pressure. The mechanism by which cardiac hypertrophy is increased after denervation is not clear. However, a report says that the left stellate ganglectomy may lead to a reduction in free lysosomal enzyme activity, implying a possible reduction in protein degradation in the cell[4]. In conclusion, our data supply evidence that cardiac hypertrophy in SHR may be accelerated by left cervical sympathetic denervation.

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Effect of adrenalectomy on sound-induced seizure susceptibility and intensity in genetically susceptible rats

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Summary. Neither seizure susceptibility nor intensity was altered by sham-operation or by adrenalectomy in adult rats that are genetically susceptible to sound-induced seizures. Thus, sound-induced seizures in genetically susceptible rats are analogous to those in genetically susceptible mice to the extent that removal of the adrenal glands does not alter established seizure characteristics in either species.

There are several mouse and rat models which exhibit characteristic seizures in response to loud sounds. These audiogenic seizures have been found to occur in mice following acoustic priming or ethanol withdrawal, and in several strains of mice that have a genetically determined predisposition to this type of seizure[1-3]. There is also a strain of rats which has a genetically determined sound-induced seizure susceptibility. This rat model has generally been called the audiogenic seizure (AGS) susceptible rat. More recently, however, we have come to realize that this designation is too restrictive and these animals might more appropriately be called epilepsy-prone rats.

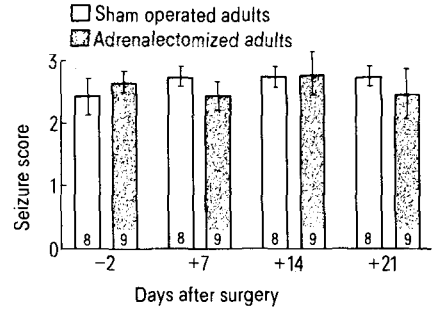
Adrenalectomy, inhibition of glucocorticoid synthesis or administration of a glucocorticoid receptor antagonist prevents the development of audiogenic seizures induced by acoustic priming or by ethanol withdrawal in mice[1-3]. Neither adrenalectomy[4] nor inhibition of glucocorticoid synthesis[1] alters susceptibility to audiogenic seizure in genetically susceptible mice. There are a number of similarities and a number of differences between rats and mice that are genetically susceptible to sound-induced seizures[5]. Therefore, experiments were carried out to determine the effect of adrenalectomy on seizure susceptibility and intensity in the epilepsy-prone rats with a genetically determined predisposition to sound-induced seizures.

Methods. Adult male and female rats from the Shreveport Veterans Administration Medical Center Colony of Sprague-Dawley derived epilepsy-prone rats were employed in this experiment. Since not all animals in this colony are susceptible to sound-induced seizures, each animal was tested 4 separate times to assure susceptibility to sound-induced seizures. The acoustic stimulus was administered to individual rats in a cylindrical metal chamber approximately 40 cm in diameter and 50 cm in height. A sound level of approximately 115 dB relative to 2×10^4 dyne/cm^2 was generated by 2 Edwards bells ringing simultaneously. The sound stimulus was initiated within 15 sec after each animal was placed into the chamber. Seizure intensity was assessed through use of the audiogenic response score (ARS) rating scale (0–9, where each higher number represents a greater seizure intensity) which has been described previously[6].

Seizure incidence

	Days after surgery			
	−2*	+7	+14	+21
Sham-operated	8/8	8/8	8/8	8/8
Adrenalectomized	9/9	9/9	9/9	9/9

* Minus 2 indicates 2 days before surgery.



Seizure intensity (mean ± SEM) in sham-operated and adrenalectomized rats. -2 indicates 2 days before surgery. The numbers inside the bar graphs indicate the number of animals. There were no statistically significant differences.