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Left Ventricular Hypertrophy is Prevalent in Sprague–Dawley Rats

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Unrecognized cardiovascular abnormalities may confound the interpretation of research data collected using rats. However, although SPF rat colonies are screened for microbes and kept under standardized environmental conditions, their cardiovascular status is largely unknown. We recently performed surgery on anesthetized 80-d-old Sprague–Dawley rats and observed a high mortality that could not be attributed to the procedures or preceding treatments. Upon necropsy, cardiomyopathy was readily apparent in a substantial proportion of these rats. To further evaluate the nature of this condition, we evaluated the histology and morphology of hearts from both Sprague–Dawley and Lewis rats. Compared with Lewis rats, Sprague–Dawley rats had greater left ventricular wall thickness and larger cardiomyocyte cell size. Severe left ventricle hypertrophy was present in 38% of young adult Sprague–Dawley rats. These findings may have implications for research models that use Sprague–Dawley rats.

Abbreviations: CO, cardiac output; CSA, cross-sectional area; HDAC3, histone deacetylase 3; LVH, left ventricle hypertrophy; MCAO, middle cerebral artery occlusion.

Variability in the health of laboratory rats can confound the interpretation of experimental data. The use of research animals maintained under SPF conditions helps to reduce variation in animal health by standardizing environmental conditions and eliminating exposure to pathogens, but these goals cannot be achieved without adherence to stringent quality assurance procedures.[29] Quality assurance involves routine screening for microbial contamination and monitoring of environmental parameters. In contrast, specific indices of cardiovascular health still go unmonitored in colonies of laboratory animals. For example, a recent concern is that health-related problems secondary to obesity in rats may invalidate research results.[5,12]

Sprague–Dawley rats are widely used for biomedical research. Our laboratory developed an experimental protocol to examine the vulnerability of adult Sprague–Dawley rats to middle cerebral artery occlusion (MCAO) after specific neonatal treatments. Multiple animals died during anesthesia or MCAO surgery; death was often preceded by prolonged gasping. However, these deaths were not readily attributable to procedural errors. Necropsies of these rats revealed cardiomyopathy. We speculated that the combination of cardiomyopathy, anesthesia, and cerebral ischemia was lethal. To better characterize the cardiomyopathy, we performed histologic and morphologic measurements on hearts taken from both Sprague–Dawley and Lewis strain rats. In this report, we describe prevalent left ventricular hypertrophy (LVH) in Sprague–Dawley rats.

Materials and Methods

Animals. All experimental protocols were approved by the Animal Care and Use Committee at the University of Washington, and following the recommendations set forth in the *Guide for the Care and Use of Laboratory Animals*[8] and complied with the *Animal Welfare Act*[1] and the US Public Health Service Policy on the Humane Care and Use of Laboratory Animals.[17] Time-mated Sprague–Dawley rats (n = 104) purchased from Harlan (San Diego, CA) and Charles River (Holister, CA and Portage, MI) or Lewis rats (n = 63) purchased from Charles River (Holister, CA and Portage, MI) in 2009 were shipped to arrive 1 wk prior to term gestation to ensure that all animals were raised in the local vivarium under SPF conditions and screened for fur mites, pinworms, *Mycoplasma pulmonis*, pneumonia virus of mice, rat parvoviruses, Sendai virus, and sialodacryoadenitis virus. The animals were housed with a 12:12-h light:dark cycle. Rats were fed a commercial diet (PicoLab Rodent Diet 20 5053, LabDiet, Brentwood, MO; 20% protein, 5% fat, 4.7% crude fiber, 3.07 kcal/g, 210 ppm iron) ad libitum. Rats were weaned and separated by sex on postnatal day 24.

Neonatal treatments. Neonatal rats were treated from postnatal days 3 to 7 in 1 of 4 experimental conditions designed to evaluate effects of maternal separation (daily from 0800 until 1600 h), combined with daily subcutaneous injections of saline or morphine sulphate (2 mg/kg) as described in detail in a prior report.[13] Dam-reared controls and untreated controls were included. After neonatal treatments, the rats were raised in the vivarium under standard conditions.

Anesthesia and surgery. Adult rats were anesthetized by using inhaled 3% isoflurane in 30% oxygen and underwent surgery for MCAO on postnatal day 80 (± 3 d). After induction of sedation with isoflurane, 0.25% bupivacaine hydrochloride (1 mg/kg ID; Bupivacaine, Hospira, Lake Forest, IL) was given, a midline neck incision was made, and the right carotid, external carotid, and pterygopallantine arteries were isolated and ligated with silk sutures. A prepared 4.0 monofilament was inserted into the internal carotid artery to obstruct the MCA and induce cerebral ischemia.

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The initial surgical procedure lasted for 15 to 30 min. Two hours after induction of ischemia, the rats again were anesthetized for 5 min while the monofilament was withdrawn from the MCA and the incision stapled. The rat was returned to the home cage. Deaths were considered to be early if they occurred during the procedure or within 24 h after return to the rat's home cage.

Necropsy. At 48 h after the MCAO procedure, all surviving rats were euthanized by phenobarbital–phenytoin overdose (1 mL/kg IP, Euthasol, Delmarva Laboratories, Midlothian, VA) followed by decapitation. Immediately after euthanasia (or as soon as possible when early death occurred), midsternal thoracotomy was performed, and the abdomen of each rat was opened with a medial incision. The heart, thoracic aorta, and kidneys were removed and immediately immersion fixed in 4% phosphate-buffered formalin for at least 48 h. The cardiac ventricles were cut in coronal sections of approximately 3 mm thickness at the midventricular short-axis level and embedded in paraffin. Hearts were sectioned parallel to the short axis, and 5-µm slices were mounted on slides.

Histology. *Imaging*. Histologic staining was performed and photomicrographs were captured (BX41 microscope [Olympus, Center Valley, PA] connected to a Microfire camera [Olympus]). Calibrated measurements were made from the digital images by using image analysis software (AnalySis, Olympus). Multiple measurements were taken and averaged together to produce a single measurement for each animal. All scorers were blinded to strain and treatments.

Heart morphology. To quantify gross morphology and cardiac wall thickness, images of hearts stained with hematoxylin and eosin were examined. For gross morphology, multiple measurements (12 per heart) were made from the inner endocardium to outer epicardium of the right ventricle, left ventricular free wall, and interventricular septum. Because concentric thickening narrows the left ventricle and reduces end-diastolic volumes and cardiac function, we also measured left ventricular chamber areas and cross-sectional areas (CSA). Trabeculae were excluded in the measurements.

Thoracic aortas. Vessels were cut proximally just below the aortic arch and distally above the diaphragm. Aorta tissues from adult Sprague–Dawley and Lewis rats were paraffin-embedded, and 5-µm sections were stained with hematoxylin and eosin. For the purpose of this study, we used the term 'lesion' for any thickened intimal area seen microscopically. Aorta wall thickness (internal elastic lamina minus outer edge of the tunica media) was determined as the mean of 4 measurements per aorta cross section.

Kidneys. Renal dysplasia may lead to chronic hypertension which, in turn, could be associated with LVH. To assess for histopathologic kidney abnormalities, 5-µm kidney sections were stained with hematoxylin and eosin.

Collagen content. To determine collagen content, heart cross-section slides from random animals of each group were pretreated with picric acid and stained with Sirius red (Polysciences, Warrington, PA). Digital images were collected by using a 20× objective, and collagen-positive areas were quantified in a total of 8 fields from 4 predefined regions of the left ventricular free wall. Measurements were spaced equally from the subendocardium to the subepicardium. The collagen-containing area was expressed as a proportion of the total myocardial cross-sectional area.

Hypertrophy. Sirius red-stained slides were used to quantify cardiomyocyte CSA as an index of hypertrophy. By using a 40× objective, digital images were taken from the subendocardium to the subepicardium of the anterior and posterior interventricular septum and left ventricular free wall, and the CSA of individual cardiomyocytes were quantified by tracing the boundaries of each cell on each image. For cell sizes, CSA were outlined from an average of 278 cardiomyocytes per rat (range, 125 to 461 measurements per rat).

Hyperplasia. To assess developmental proliferation of cardiomyocytes, histone deacetylase 3 (HDAC3) immunolabeling was performed on Sprague–Dawley hearts taken on postnatal days 5, 7, and 21 and on a subset of adult hearts. Slide-mounted paraffin-embedded tissues were dewaxed (Histoclear, Electron Microscopy Sciences, Hatfield, PA; 3 times for 5 min each), rehydrated through repeated serial-alcohol rinses (100%, 95%, 70%, 0% twice each for 5 min), boiled for 5 min in 10 mM sodium citrate buffer (pH 6.0), cooled, rinsed in 10 mM PBS, incubated in PBS containing 5% normal goat serum (60 min), incubated against rabbit monoclonal antiHDAC3 antibody (1:250, 18 h at 4 °C; catalog no. 04-230, Millipore, Billerica, MA), and detected with a goat antirabbit biotin-conjugated secondary antibody (1:150, 60 min; catalog no. BA-1000, Vector Laboratories, Burlingame, CA) and avidin–peroxidase (Vectastain Elite, Vector Laboratories) before being dehydrated through graded alcohols and coverslipped. Myocyte-specific overexpression of HDAC3 has been associated with increased cardiomyocyte hyperplasia without hypertrophy.[24]

Statistics. ANOVA and Dunnett post hoc tests, Student *t* tests, and nonparametric comparisons (Fisher exact and χ^2 tests) were made when appropriate by using SPSS software (SPSS, Chicago, IL). Parametric data are expressed as mean values and may include SEM. An α criterion of P less than 0.05 was used with 2-tailed testing.

Results

Neonatal treatments were not associated with differences in any measure, and rats from all treatment groups were combined for comparisons between rat strains. Overall, postMCAO mortality rates were not significantly different between Sprague–Dawley and Lewis rats, with unexplained deaths evident in 21.2% (22 of 104) of Sprague–Dawley compared with 15.8% (10 of 63) of Lewis rats. Early deaths (deaths occurring during anesthesia or within 24 h postMCAO) occurred in 16.6% (8 of 48) of Sprague–Dawley male compared with 12.5% (7 of 56) of Sprague–Dawley female rats and in 14.3% (5 of 35) of Lewis male versus 14.3% (4 of 28) of Lewis female rats. Therefore, we found no strain differences in overall mortality after MCAO or sex differences in early mortality. In addition, Sprague–Dawley rats purchased from Harlan did not differ from those obtained from Charles River for any parameter.

On gross examination, the majority of Sprague–Dawley rats that died during or shortly after MCAO had solid, stiff hearts and sometimes hemorrhagic lungs. Many Sprague–Dawley rats that survived MCAO also had palpably solid, stiff hearts. Overall, Lewis rat hearts were more pliable and soft and, unlike Sprague–Dawley hearts, would spontaneously collapse and flatten when placed in a dish after removal. Figure 1 displays 2 gross specimens from Sprague–Dawley rats to compare a hypertrophic heart with a normal heart.

Left ventricular free wall thickness was greater in Sprague–Dawley than Lewis rats (Table 1). In addition, the average left ventricular chamber area (left ventricular chamber area/entire left ventricular area × 100%) was smaller in Sprague–Dawley rats

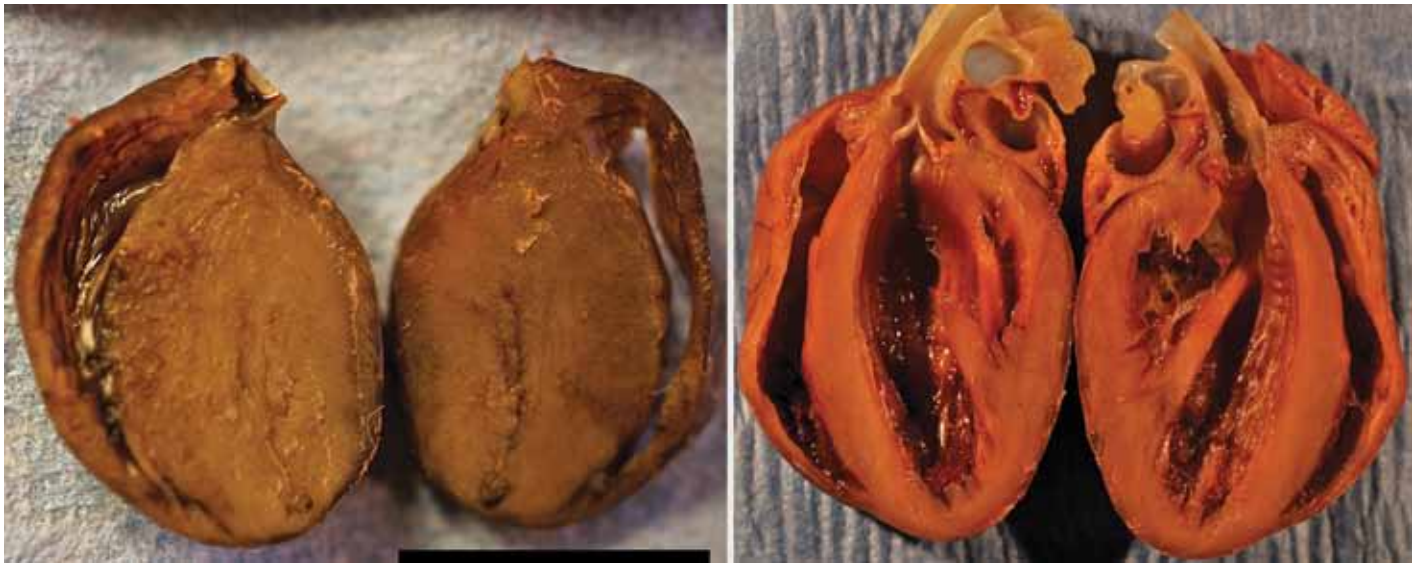

Figure 1. A hypertrophic heart (left) and normal heart (right) from Sprague–Dawley rats. The image on the left is a heart taken from a Sprague–Dawley rat that died prematurely during exposure to anesthesia and shows concentric left ventricular wall thickening and a severely narrowed left ventricular chamber. Bar, 10 mm.

Table 1. Heart wall thickness and chamber area (mean ± SEM) in adult rats

	Sprague–Dawley (n = 104)	Lewis (n = 63)
Interventricular septum (mm)	2.39 ± 0.05	2.19 ± 0.05[a]
Left ventricle (mm)	2.67 ± 0.05	2.38 ± 0.04[b]
Right ventricle (mm)	0.79 ± 0.03	0.82 ± 0.02
Chamber area (% of left ventricle)	13 ± 0.01	16 ± 0.01[a]
% of hearts with chamber area ≤ 10% of left ventricle	38	13[b]

[a]$P < 0.01$ compared with value for Sprague–Dawley rats
[b]$P < 0.001$ compared with value for Sprague–Dawley rats

compared with Lewis rats (Figure 2). To assess the prevalence of severe left ventricular chamber narrowing, we calculated the proportion of left ventricular chamber areas that were 10% or less of the total left ventricular area (Table 1). We found that 38% of Sprague–Dawley and 13% of Lewis rats showed severe narrowing of the left ventricular chamber. A box–whiskers plot (Figure 3) shows that the distribution of left ventricular free wall thickness measurements for Sprague–Dawley rats is skewed and contains 9 high outliers. By comparison, measurements for the Lewis rats are more normally distributed.

Data separated according to the proximity of mortality to MCAO surgery (Table 2) show that unexplained early death of Sprague–Dawley rats after MCAO was associated with severely decreased left ventricular chamber area. Death within 24 h after MCAO was associated with increased left ventricular wall thickness, reduced chamber area, and a corresponding increased prevalence of severe chamber narrowing. These associations were not evident for Lewis rats.

For Sprague–Dawley only, sex-associated differences in left ventricular free wall thicknesses and chamber areas for male (n = 48) and female (n = 56) rats were compared. Although mean left ventricular wall thickness measures were slightly greater in male rats than female rats (2.79 ± 0.08 compared with 2.57 ± 0.07 mm, $P < 0.05$), the mean chamber area percentages (12.4% compared with 13.3%) and prevalence of severe chamber narrowing (35.4% compared with 39.3%) were equivalent between sexes.

Cardiomyocyte mean CSA measurements were increased in Sprague–Dawley compared with Lewis rat hearts (471 ± 31 μm^2 compared with 309 ± 16 μm^2, $P < 0.001$). This finding indicates that hypertrophy is present in Sprague–Dawley rat hearts. The proportion of Sirius red staining was negligible in both Sprague–Dawley and Lewis rat hearts (1.8% ± 0.3% compared with 2.2% ± 0.2%), indicating that cardiac collagen content was not different.

To evaluate whether hyperplasia was present, immunostaining for HDAC3 was performed on rat hearts collected at several postnatal ages. Developmental HDAC3 immunolabeling was highest at postnatal day 5, declining on postnatal day 7, and absent by postnatal day 21 (Figure 4). Correspondingly, HDAC3 immunolabeling was not detected in any of the adult rat hearts (not shown). These data demonstrate that prolonged expression of HDAC3 was not evident, so hyperplasia is not indicated.

Analysis of age and weight data showed that Sprague–Dawley rats were significantly larger than Lewis rats on postnatal day 80. Although the respective mean ages for Sprague–Dawley and Lewis rats at time of MCAO (80 compared with 77 d) did not differ, Sprague–Dawley rats were significantly heavier than Lewis rats (male rats, 362 ± 7 g compared with 296 ± 3 g; female rats, 238 ± 3 g compared with 190 ± 3.7 g; $P < 0.001$ for both comparisons).

In addition to hearts, kidney and aorta tissues were examined. Histopathologic examination of stained sections of kidney appeared normal, with no indications of chronic progressive nephropathy, such as basophilic tubules, thickened basement membranes, hyaline cast formation, glomerulosclerosis, and interstitial fibrosis. Mean aorta wall thickness differed for Sprague–

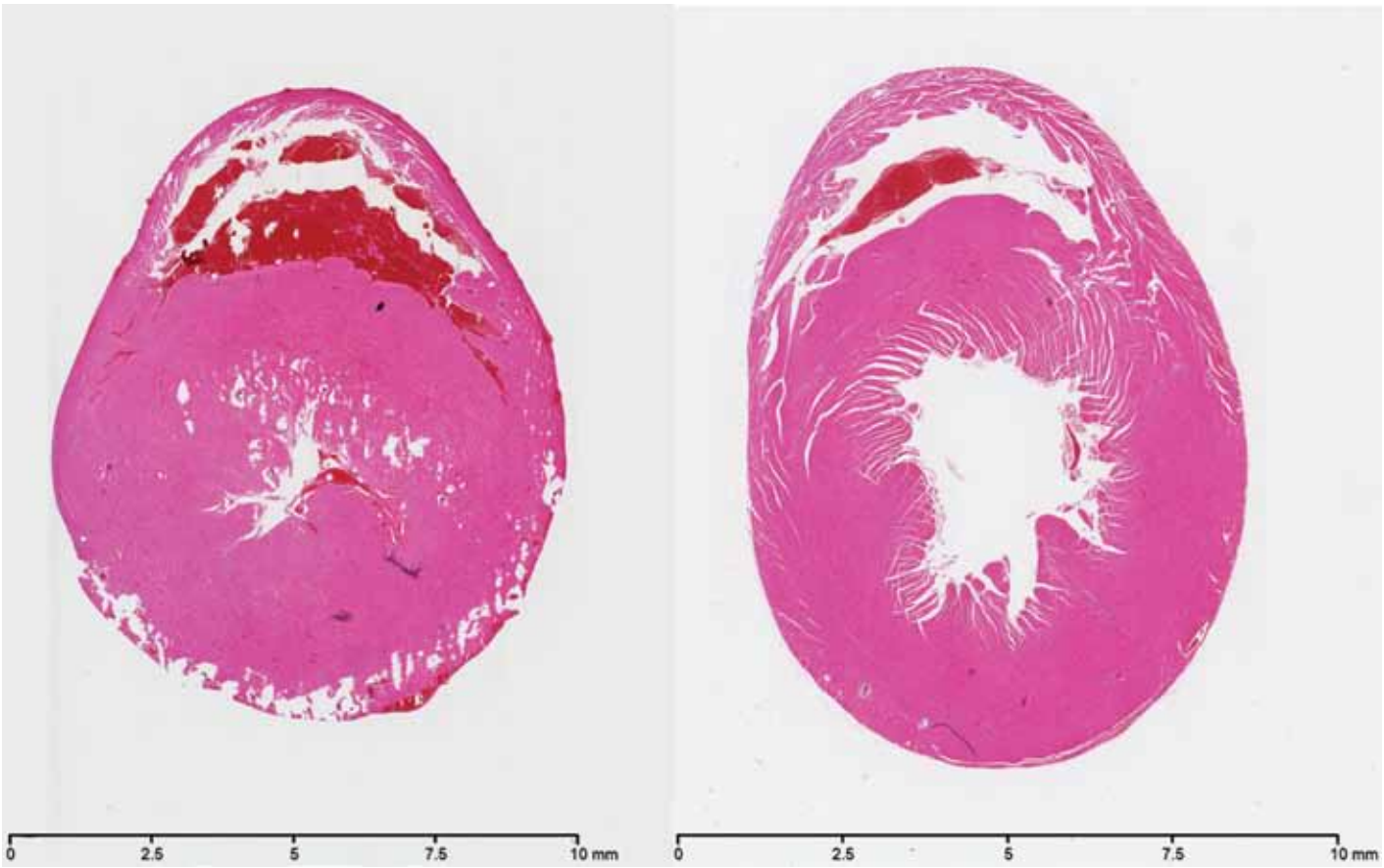

Figure 2. Digital microscans of hearts in cross-section taken at midventricle along the short axis from Sprague–Dawley (left) and Lewis (right) rats. These images illustrate the amount of left ventricular free wall thickening and chamber narrowing in Sprague–Dawley rats compared with Lewis rats. Hematoxylin and eosin stain; bar, 10 mm.

Dawley compared with Lewis rats (103 ± 3 µm versus 183 ± 5 µm, $P < 0.001$). No other aortic wall lesions were noted.

Discussion

Left ventricular wall thickness was increased, the corresponding left ventricular chamber area was decreased, and individual cardiomyocytes were larger in hearts from Sprague–Dawley rats compared with Lewis rats. During normal rat postnatal cardiac development, there is a transition from cardiomyocyte proliferation to cell growth and differentiation that occurs from postnatal day 6 to 14.[2,23] Consistent with this pattern, we found HDAC3, a marker of early cardiomyocyte proliferation,[24] was expressed in cardiomyocytes on postnatal day 5 and 7 but not on postnatal day 21 or in adult rats. Therefore, the observed increased left ventricular wall thickening appears to be secondary to cardiomyocyte hypertrophy and not due to hyperplasia. To our knowledge, these data are novel and indicate that spontaneous LVH is prevalent in 38% of young adult Sprague–Dawley rats.

This study was not based on an a priori hypothesis about cardiac hypertrophy and, therefore, this report is intended to be primarily descriptive. We only investigated Sprague–Dawley rat hearts to understand why a substantial proportion of rats were unexpectedly gasping and dying soon after MCAO surgery. The MCAO procedure was performed as part of a separate project intended to examine neonatal treatment effects on adult brain injury.

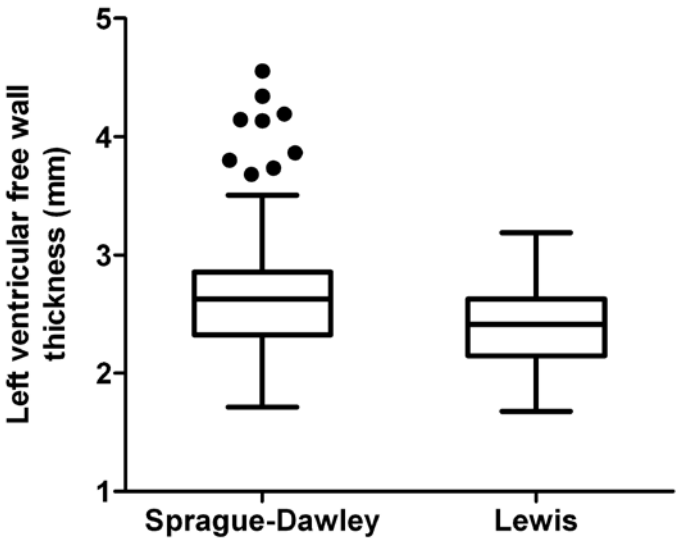

Figure 3. Boxplot showing the distribution of left ventricular free wall thickness measurements from Sprague–Dawley and Lewis rats. Statistical comparisons of these data are presented in Table 1. The median (heavy line), 25% quartiles (box), range (whiskers), and outliers more than 1.5 interquartile range units from the 75% quartile (filled circles) are shown.

Table 2. Mortality, thickness of left ventricular free wall, and chamber areas (mean ± SEM) for Sprague–Dawley and Lewis rats

	Sprague–Dawley (n = 104)				Lewis (n = 63)			
	% (n) of rats that died	Left ventricle (mm)	Chamber area (% of left ventricle)	% with chamber area ≤10%	% (n) of rats that died	Left ventricle (mm)	Chamber area (% of left ventricle)	% with chamber area ≤10%
Died at or before 24 h	14.4 (15)	3.46 ± 0.19	7.4 ± 1.3	80.0	14.3 (9)	2.43 ± 0.05	15 ± 1.3	11.1
Died after 24 h	6.7 (7)	2.64 ± 0.22[b]	16 ± 3.8[a]	14.3[a]	1.6 (1)	2.16	13.6	0
Euthanized at 48 h	78.9 (82)	2.53 ± 0.04[b]	13.6 ± 0.7[b]	31.7[b]	84.1 (53)	2.38 ± 0.05	15.6 ± 0.8	13.2

Left ventricular free wall thickness and chamber area were evaluated by ANOVA followed by Dunnett tests, and prevalence of severe chamber narrowing (% chamber area ≤ 10%) was evaluated by nonparametric comparisons. Measurements from rats that died early (< 24 h) after surgery were compared within strain (compared with rats that died after 24 h and at 48 h). The strain × time ANOVA was not significant and did not permit any within-strain comparisons for Lewis rats. Between-strain comparisons are in Table 1.

[a]$P < 0.01$ compared with value for rats that died early

[b]$P < 0.001$ compared with value for rats that died early

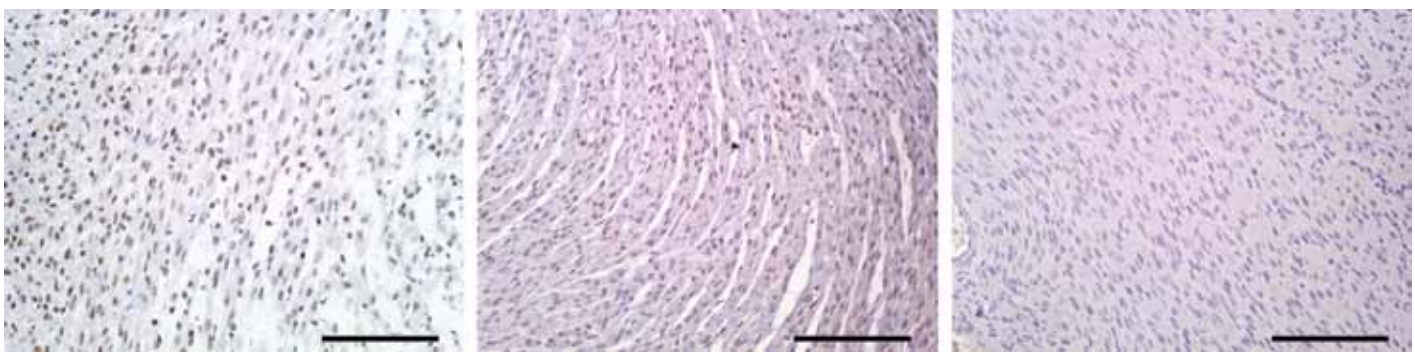

Figure 4. HDAC3 immunolabeling (brown) to detect proliferation of cardiomyocytes in developing rat hearts collected on postnatal days 5 (left), 7 (center), and 21 (right). The declining pattern of expression with increasing age is normal; therefore, prolonged proliferation of cardiomyocytes, characteristic of cardiac hyperplasia, is not evident. Immunostaining followed by hematoxylin counterstain (blue); magnification, ×40; bar, 100 µm.

We discovered LVH in 38% of Sprague–Dawley rats, regardless of treatment group. The high prevalence of LVH in Sprague–Dawley rats prompted us to shift to Lewis rats, a strain commonly used in MCAO research. Subsequent analysis revealed that although overall postsurgical mortality was similar between strains, 80% of the Sprague–Dawley rats that died early had LVH.

The basis for similar postsurgical mortality in Lewis and Sprague–Dawley rats is unclear. Because MCAO can cause stroke, the mortality for both strains may be due to the effects of MCAO on cerebral perfusion. Nevertheless, the discovery that hearts were different between the 2 strains raised concern and prompted investigation to understand this cardiac phenotype. We compared several measurements of heart parameters between the 2 strains to document this phenomenon. We expected that because all hearts were excised and then immersion-fixed, gross measurements would include minor variation based on the contractile state of each heart at death. We preface the remainder of this discussion by acknowledging that the entire analysis is post hoc and, therefore, speculative.

We speculate that rats with LVH may have limited tolerance for anesthesia and surgery compared with rats with normal cardiac morphology. LVH reduces both end-diastolic filling volume and stroke volume. Cardiac output (CO) is determined by heart rate and stroke volume according to the formula CO = stroke volume × heart rate. The decrease in stroke volume due to LVH will decrease CO unless heart rate increases to compensate. Given that anesthesia may decrease both heart rate and respiratory rate, rats with LVH may suffer a prolonged decrease in CO after anesthesia. The combination of reduced CO and cerebral hypoxia–ischemia could be lethal to a rat with LVH. Follow-up studies evaluating oxygen saturations during and after anesthesia or incorporating echocardiographic measures of CO[20] could confirm whether LVH is associated with prolonged hypoxia and reduced CO after anesthesia.

Reduced stroke volume due to LVH also might explain differences in aortic thickness between strains. The tunica media, which constitutes a large part of the arterial wall, is the principal determinant of the vessel's mechanical properties.[28] Aorta tunica media thickness was lower in Sprague–Dawley compared with Lewis rats despite greater left ventricular wall thickness. This difference may be related to reduced physiologic circumferential aorta wall stress[27] produced by lower CO in Sprague–Dawley rats with LVH compared with Lewis rats without LVH. We did not assess the viscoelastic properties of purified aortic elastic fiber rings to assess for mechanical property differences between Sprague–Dawley and Lewis aortas.

Aged rats can exhibit cardiac abnormalities. For example, spontaneous cardiomyopathy is a common age-related finding in outbred normotensive Sprague–Dawley rats, particularly males, manifesting as myocardial degeneration and necrosis, mononuclear cell infiltration, and replacement fibrosis.[10]Aging is also associated with myocyte hypertrophy in Sprague–Dawley rats.[25] Although cardiomyopathy can be expected in Sprague–Dawley rats at 1 to 2 y of age, the rats we examined were younger than 3

mo, yet they displayed spontaneous LVH. We speculate that LVH is present earlier than expected in Sprague–Dawley rats. Considering that hypertrophic cardiomyopathy has familial origins in humans,[22,26] it is reasonable to postulate that a genetic phenotype predisposing precocious LVH may be present in colonies of commercial Sprague–Dawley rats.[15]

In addition, hypertension is associated with cardiac hypertrophy and heart failure in rat models. Approximately 30% of spontaneously hypertensive rats develop cardiac hypertrophy,[21] with right ventricular enlargement or myocardial fibrosis and heart failure seen in aged specimens.[3,4] Therefore, the population of Sprague–Dawley rats may be becoming more hypertensive, and rats may be developing an adaptive cardiac hypertrophy to normalize wall stress in response to the enhanced load.[21] A limitation of our study is that we did not perform blood pressure measurements on our rats. Researchers using Sprague–Dawley rats may find it beneficial to screen rats to assess cardiac function (for example, electrocardiography or echocardiography) prior to using them for study. In addition, monitoring of blood pressure by commercial vendors as a measure of colony health would be useful.

We examined kidney histology to see whether hypertensive nephropathy may have contributed to development of LVH in Sprague–Dawley rats. Chronic progressive nephropathy is a common, age-related renal disease affecting all conventional strains of rat used in safety evaluation studies, and in particular, the Sprague–Dawley strain.[6,7] Renovascular hypertension rat models, such as the 1-clip, 2-kidney Goldblatt hypertension model,[14] demonstrate increased concentric cardiac mass with LV wall thickening associated with increased fibrosis. In our Sprague–Dawley rats, stained kidney sections appeared normal and left ventricular fibrosis was absent. Therefore there was no indication that chronic progressive nephropathy was a factor contributing to LVH.

Chronic anemia from deficient dietary intake of iron and copper produces an unbalanced load on the left ventricle, thereby triggering myocyte hyperplasia to accommodate the diastolic load and reduce wall stress.[19] We did not measure hemoglobin content for any of our rats. However, biventricular hypertrophy is associated with anemia-induced hypertrophy in rats.[11,18] There was no indication of biventricular hypertrophy in our study rats.

Diet affects morbidity and mortality in laboratory rats.[9,10,16] For example, moderate dietary restriction lowers the incidence, severity, and progression of cardiomyopathy and degenerative lesions.[9] Conversely, ad libitum feeding increases heart weight, left ventricular myocardial fibrosis, cardiac myopathy, and renal abnormalities such as glomerular sclerosis, tubular basophilia, and interstitial fibrosis.[9,10] In fact, regardless of diet type, rats fed ad libitum develop cardiomyopathy by 2 y of age.[10] Our local vivarium facility confirmed that they have always used the described commercial rodent chow ad libitum for our rats. Although diet may be a factor, we did not find differences in Sirius red staining that would indicate fibrosis, nor did we note any renal abnormalities. Perhaps the LVH we observed in rats younger than 3 mo would have progressed to fibrosis at an older age. And given that Sprague–Dawley rats weighed more than Lewis rats, perhaps Sprague–Dawley rats consume more chow when fed ad libitum. Based on our findings, an experiment designed to examine effects of diet and aging on the prevalence and progression of LVH in separate strains of laboratory rats may be warranted.

The lifespan of all commercially available rat strains and stocks has been declining, possibly due to interaction between genomic and environmental factors.[9,16] Diet and feeding schedules may be the basis for this trend. Our data prompt speculation that LVH in young rats may shorten lifespan. Regardless of whether our speculation is true, investigators using Sprague–Dawley rats should be aware of this cardiac phenotype because study results may be affected. Perhaps cardiovascular quality control standards should be implemented by vendors to ensure that rodents meet healthy standards. In addition, further exploration of the Sprague–Dawley rat with LVH may improve our understanding of various congenital heart diseases.

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