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Mechanical Modulation of Vertebral Body Growth

Implications for Scoliosis Progression

Ian A. F. Stokes, PhD, Holly Spence, BS, PT, David D. Aronsson, MD, and Nicholas Kilmer, MD

Study Design. The authors developed a rat-tail model to investigate the hypothesis that vertebral wedging during growth in progressive spinal deformities results from asymmetric loading in a "vicious cycle."

Objectives. To document growth curves with axial compression or distraction applied to tail vertebrae to determine whether compression load slows growth and distraction accelerates it.

Summary of Background Data. Progression of skeletal deformity during growth is believed to be governed by the Hueter-Volkmann law, but there is conflicting evidence to support this idea.

Methods. Twenty-eight 6-week-old Sprague-Dawley rats were assigned to one of three groups: compression loading, distraction loading, or sham (apparatus applied without loading). Under general anesthesia, two 0.7-mm diameter stainless steel percutaneous pins were used to transfix each of two vertebrae. The pins were glued to 25-mm diameter external ring fixators. Springs (load rate, 35 g/mm) were installed on three stainless steel threaded rods that were passed through holes in each ring and compressed with nuts to apply compression or distraction forces between 25–75% of bodyweight. Vertebral growth rates in *μm/day* were measured by digitizing the length of the vertebrae images in radiographs taken 0, 1, 3, 5, 7, and 9 weeks later.

Results. The loaded vertebrae grew at 68% of control rate for compressed vertebrae and at 114% for distracted vertebrae. (Differences statistically significant, $P < 0.01$ by analysis of variance.) For the compressed vertebrae, the pinned vertebrae, which were loaded at one of their two growth cartilages, grew at a reduced rate (85%), although this effect was not apparent for the distraction animals.

Conclusions. The findings confirm that vertebral growth is modulated by loading, according to the Hueter-Volkmann principle. The quantification of this relationship will permit more rational design of conservative treatment of spinal deformity during the adolescent growth spurt. [Key words: animal model, caudal vertebrae, progressive deformity, scoliosis] **Spine 1996; 21:1162–1167**

From the Department of Orthopaedics and Rehabilitation, University of Vermont, Burlington, Vermont.
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Scoliosis deformities, independent of etiology, progress more during skeletal growth, although curves more than 40° Cobb continue to progress after skeletal maturity.[2,26] Progression of skeletal deformity during growth is believed to be governed by the "Hueter-Volkmann Law,"[10,25] which states that growth depends on the amount of compression of the growth plate—it is retarded by increased compression and accelerated by reduced compression.[1,6,9,12,15,19] If this is true, then scoliosis would produce asymmetric loading, which would cause asymmetric vertebral growth resulting in a "vicious cycle"[15,16] (Figure 1). This process may occur in the discs also. Xiong et al[29] showed that even small scoliotic curves have wedging asymmetry of the vertebrae and the discs. The concave side of a curve is presumed to experience greater compression load, decelerating growth of the vertebral bodies compared with the convex side, according to the principles of the Hueter-Volkmann law. Lonstein and Carlson[11] reviewed and statistically analyzed records of progression of idiopathic scoliosis deformities and found that the main risk factors are curve magnitude and skeletal immaturity. This is consistent with the hypothesis that mechanical factors (asymmetry of vertebral loading) produce an asymmetric growth rate, producing a final curve magnitude dependent on the magnitude of the current curve and with the amount of residual growth.

To quantify the supposed mechanism of scoliosis progression in which load asymmetry in vertebrae and discs results in progressive wedging, it is necessary to quantify the load asymmetry (as a function of curve magnitude) and the growth response to load. The current study is concerned with the effects of load on vertebral growth. Although it has been well accepted as a guiding principle for the management of childhood skel-

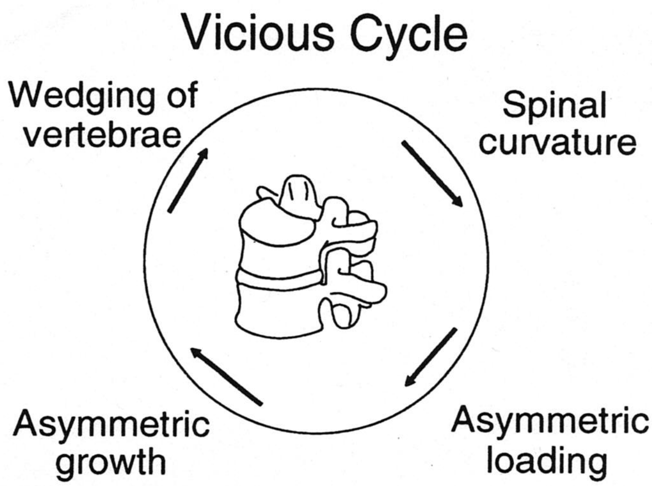

Figure 1. The concept of a "vicious cycle," whereby spinal curvature increases during growth because it leads to asymmetric loading of vertebrae, which in turn causes asymmetric growth and additional wedging of the vertebrae.

etal deformities, there is conflicting evidence to support the Hueter-Volkmann Law, and much of the evidence is qualitative.[22]

A rat-tail model was developed to quantify the vertebral growth response to mechanical loading by using springs to apply a constant load to the caudal vertebrae. Rat-tail vertebrae were chosen because they are accessible to experimental intervention, and they grow linearly by about 25% during the 9-week duration of the experiment. During this time, the animals more than double their bodyweight. The human thorax also grows linearly by about 25% during adolescence.[13,24,27]

In the present study, it was hypothesized that mechanical forces applied chronically to growing vertebrae would modulate their growth in accordance with the Hueter-Volkmann "law." The purpose of this study was to quantify the applied load and the growth response with uniform axial compression or distraction applied to rat caudal vertebrae.

■ Methods

An external fixator, similar to an Ilizarov device with percutaneously inserted pins transecting tail vertebrae, was used to apply measured forces to the tails of the rats (Figure 2). Twenty-eight 6-week-old Sprague-Dawley rats were assigned to one of three groups: compression-loading (10 animals), distraction-loading (10 animals), or sham (eight animals). In the sham group, the apparatus was applied without the springs that were used to apply the load. The rats were anesthetized with an intraperitoneal injection of xylazine (5–10 mg/kg) and ketamine (40–80 mg/kg) along with local circumferential block with 1% lidocaine at the proximal end of the tail. The individual vertebrae of the rat tail were palpated, and selected intervertebral disc spaces were identified and marked with a 27-gauge needle placed into the disc space. A line midway between the two needles was drawn on the skin to indicate the intended insertion point of the pins. Two 0.7-mm diameter stainless steel percutaneous pins were used to transfix each of two vertebrae. For the distraction-loading and sham experiments, the eighth and eleventh caudal vertebrae were instrumented; for compression-loading experiments, the eighth and tenth were used. Thus, there were two pinned and two loaded vertebrae for distraction and sham experiments; for compression experiments, only one loaded intermediate vertebra was used for stability. All procedures with live animals were reviewed and approved by the University of Vermont Institutional Animal Care and Use Committee.

A variable speed electric drill was used to drill the two pins into the selected vertebrae. The entry point was on the dorsal–lateral aspect of the tail—one on the left and one on the right. Care was taken to place the pins within the transverse plane. The pins were glued to 25-mm diameter external ring fixators made from 1-mm thick aluminum washers using cyanoacrylic glue (Loctite type 447) and "Locquic" accelerator (both from Loctite Corp., Newington, CT). The washers were pretreated by sand blasting and surface preparation with "Primer-T" (Loctite Corp.) surface conditioner to improve the glue adhesion.

Three stainless steel threaded rods (2.1-mm diameter × 51-mm long) were passed through holes radially distributed around each ring. They were attached to the proximal ring with nuts and locked with cyanoacrylic glue. Sleeves were placed on the rods to allow the distal washer to slide with minimal friction. Loads were then applied to the distal washer by placing three 17.45-mm long springs (load rate, 35g/mm) in conjunction with lock nuts to apply forces to the rings (Figure 2). After surgery, the animals were given buprenorphine, 0.3 ml, (0.05 mg/kg) subcutaneously after 8 hours for analgesic purposes.

The spring lengths were measured with a digital caliper and adjusted weekly to control the length of the springs (and hence the force applied by the springs) while maintaining the tail straight. The magnitude of load applied was between 25% and 75% of bodyweight (Figure 3). The spring forces were measured weekly and adjusted to maintain the force as a constant proportion of each animal's bodyweight.

Vertebral longitudinal growth rates were measured by digitizing the length of the vertebrae images in radiographs (Figure 4). Radiographs were made 0, 1, 3, 5, 7, and 9 weeks after application of the apparatus. The distances between the tube, tail, and the high resolution film were controlled to standardize the magnification. The lengths of each loaded vertebra, each pinned vertebra, and two proximal and two distal control

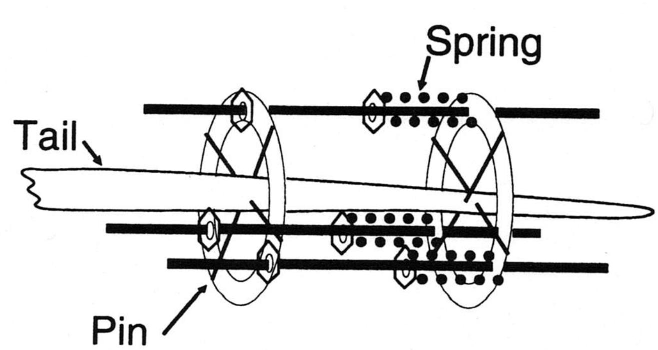

Figure 2. Diagram of distraction apparatus on rat tail.

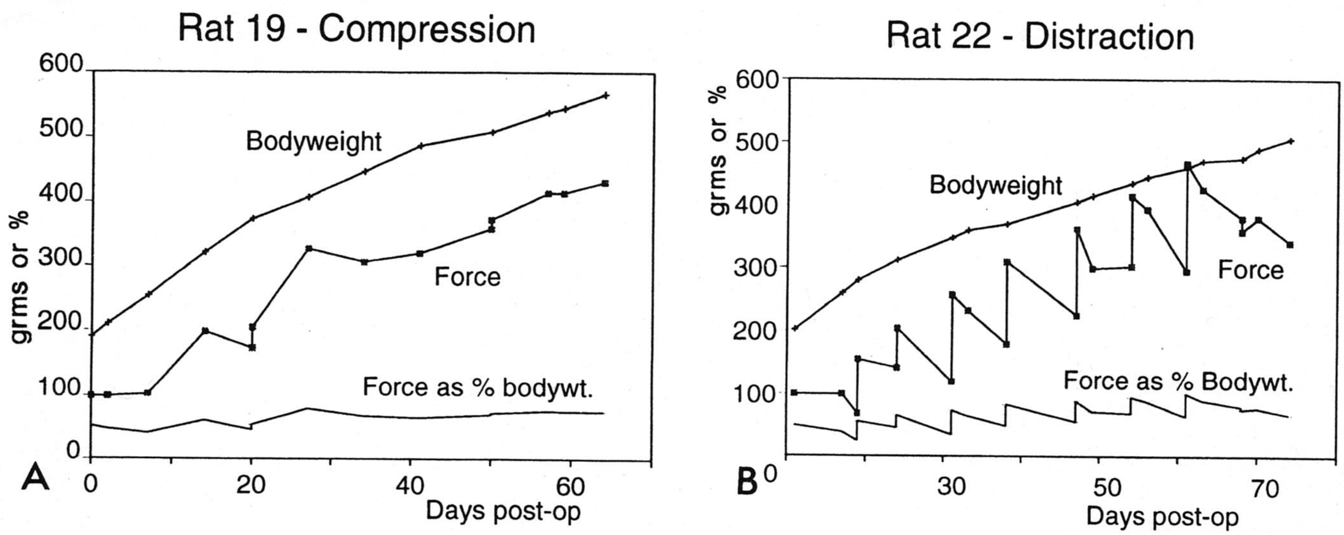

Figure 3. Examples of loading curves for two animals. **(A)** Rat 19 with compression forces applied to the tail. **(B)** Rat 22 with distraction forces applied to the tail. The weekly adjustments to the load magnitude are evident.

vertebrae were measured in each radiograph (Figure 5). The vertebral disc margin at each end of each vertebra was digitized using a back illuminated digitizing tablet (GTCO Corp, Rockville, MD) interfaced to a personal computer. Histologic comparisons verified that the digitized points represented the disc–epiphysis margin. The distance between the digitized points was calculated in millimeters and corrected for x-ray magnification. A linear regression line was fitted to the digitized lengths as a function of the number of days after installation of the apparatus (Figure 6). The slope of the regression line gave the growth rate in μm/day.

Results

The vertebrae in each tail were divided into three groups—1) unloaded (control) vertebrae (two distal and

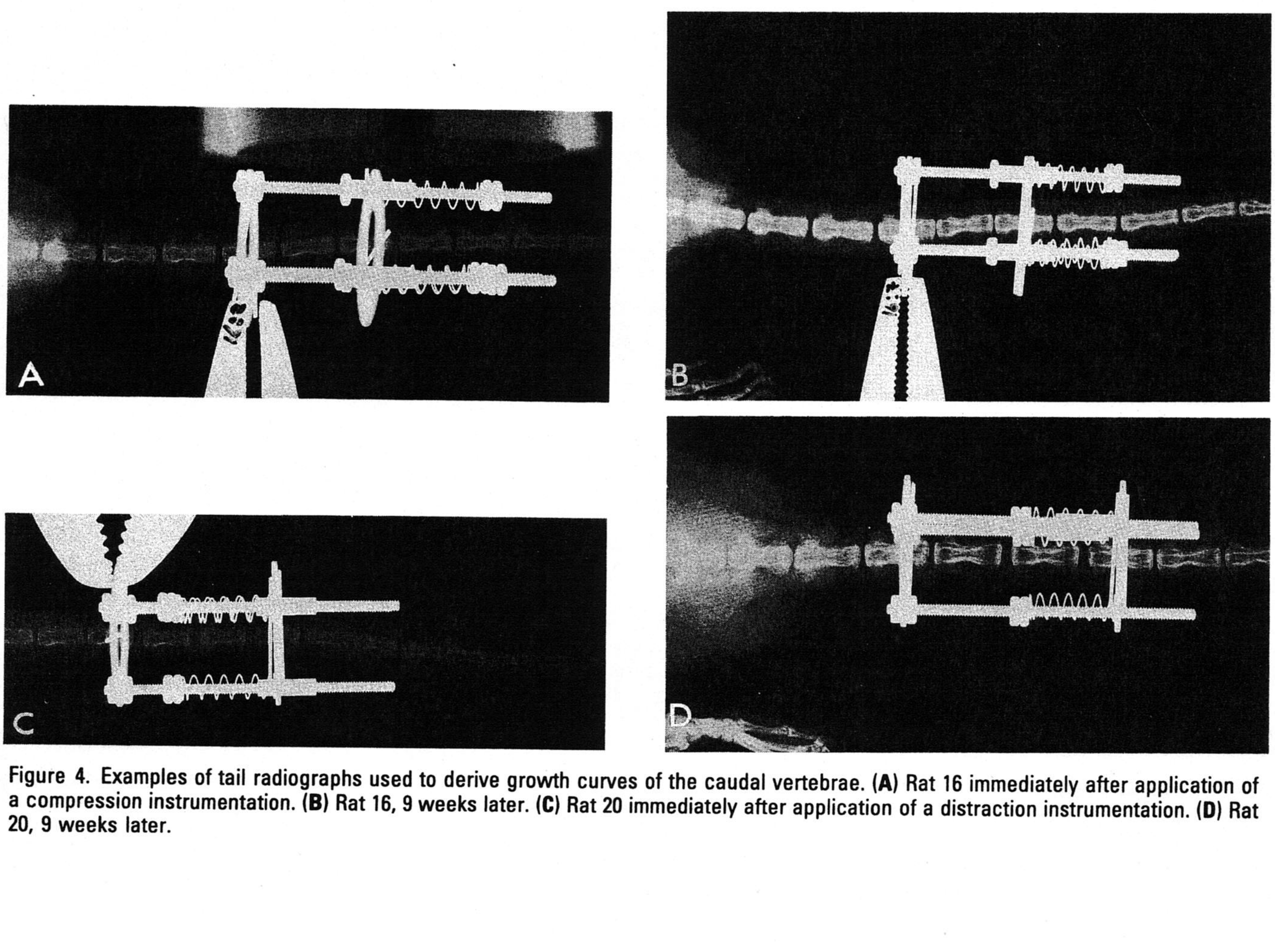

Figure 4. Examples of tail radiographs used to derive growth curves of the caudal vertebrae. **(A)** Rat 16 immediately after application of a compression instrumentation. **(B)** Rat 16, 9 weeks later. **(C)** Rat 20 immediately after application of a distraction instrumentation. **(D)** Rat 20, 9 weeks later.

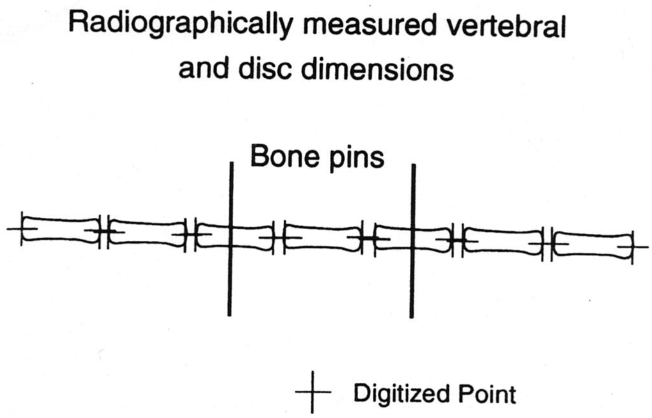

Figure 5. Diagram indicating the points digitized and used to calculate vertebral lengths. Two control vertebrae proximal to the apparatus and two control vertebrae distal to it were digitized, along with pinned vertebrae and the intermediate (loaded) vertebrae. For compression experiments, there was one intermediate (loaded) vertebrae; for distraction and sham animals, there were two.

two proximal to the instrumentation); 2) pinned vertebrae (which were loaded at one growth plate by the springs); and 3) loaded vertebrae (Figure 5). Vertebral growth rates averaged 33 μm/day for sham animals, 35 μm/day for compression animals, and 45 μm/day for distraction animals. Because of these differences in the overall growth rates of the animals, each measured growth rate was expressed as a percentage of the growth rates averaged from the four unloaded vertebrae in that animal.

Tables 1 and 2 show that the compressed vertebrae and pinned vertebrae grew at a slower rate than the unloaded control levels, whereas distracted vertebrae

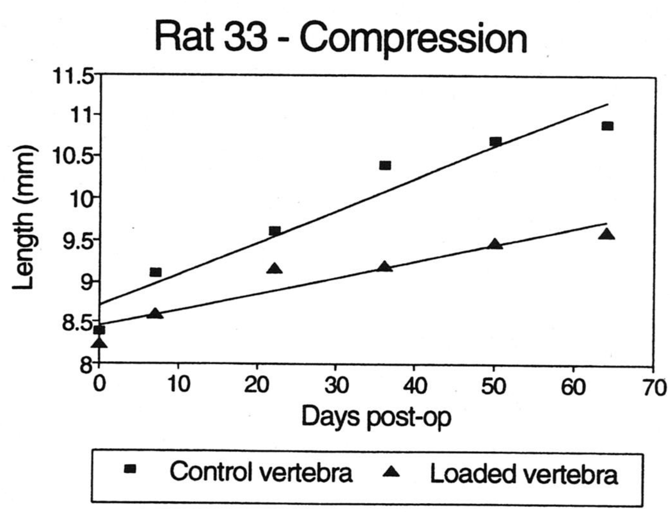

Figure 6. Examples of growth curves for two caudal vertebrae of rat 33. Plotted points correspond to the lengths of vertebrae (mm) measured from each of the six radiographs. The slope of the linear regression lines fitted through the measured points gave growth velocities in μm/day. In this example, the control vertebra grew at 42.3 μm/day; the compression-loaded vertebra grew at 21.5 μm/day.

Table 1. Mean Vertebral Growth Rates (μm/day) by Level and Group

	1 C	2 C	3 P	4 L	5 L	6 P	7 C	8 C
Compression animals	39.2	40.7	32.1	25.6		32.1	37.8	34.6
Distraction animals	45.2	47.4	46.6	49.4	48.6	42.3	40.7	41.4
Sham animals	34.8	33.8	30.3	35.3	34.3	32.7	32.0	29.6

C = control level. P = pinned level. L = loaded level.

grew faster. The loaded vertebrae grew at 68% of control rate for compressed vertebrae and at 114% for distracted vertebrae. These differences were statistically significant ($P < 0.01$ by analysis of variance). Under compression, the pinned vertebrae (which were loaded at one of their two growth cartilages) grew at a reduced rate (85% of that of unloaded control subjects), although this effect was not apparent for the distraction animals.

Although all animals were classified by group (sham, compression, or distraction), the magnitude of the forces varied between animals in the loaded groups in the range of 25–100% of bodyweight. There was a significant correlation ($R^2 = 0.44$) between the magnitude of the load and the growth rate of the loaded vertebrae (Figure 7).

■ Discussion

Results of the present study confirm that vertebral growth can be modulated by mechanical loading in these experimental animals, according to the Hueter-Volkmann principle and provide quantification of the magnitude of this effect. It remains to be determined whether the magnitude of the asymmetry of vertebral loading in the growing human spine with scoliosis and the magnitude of the growth response would be sufficient to explain the observed rates of progression. In humans, longitudinal growth of the vertebral body occurs in the cartilage of the physeal plate,[3] although most other species, including the rat, have an epiphysis with a secondary ossification center between the growth cartilage and the intervertebral disc. Radiographic measurements[13,24,27] show that there is about 25% of longitudinal growth in the thorax during adolescent growth,

Table 2. Average Growth Rates, Expressed as a Percentage of Those for Unloaded Vertebrae

Group	Control (unloaded) Vertebrae (SD)	Pinned Vertebrae (SD)	Loaded Vertebrae (SD)
Compression	100 (12)	85 (14)	68 (17)
Distraction	100 (11)	103 (14)	114 (16)
Sham	100 (13)	97 (15)	108 (13)

SD = standard deviation.